A Diversity-Oriented Approach to the Palladium-Catalyzed Modular Assembly of Conjugated Compounds and Heterocycles:

High-Value Compounds from Trichloroethylene

by

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Abstract

Trichloroethylene, a simple and very inexpensive material, has been identified as a tri- and tetrafunctionalizable building block. A combination of selective palladium-catalyzed cross-coupling reactions with standard lithiation and electrophilic quenching yields a wide variety of unsaturated linear or cyclic compounds in excellent yields in few synthetic steps.

Dichlorovinyl ethers, obtained from a nucleophilic displacement reaction with trichloroethylene, are the basic starting materials. Two sets of conditions have been developed to achieve the reaction of either electron-rich or –deficient phenols with trichloroethylene to give the resultant dichlorovinyl ethers in high yields. Site selective palladium-catalyzed cross-coupling for the specific functionalization of a single C-Cl bond was developed, and could install alkyl, alkenyl, alkynyl and (hetero)aryl moieties. The resulting electrophiles could be reacted with a second organometallic nucleophile forming trisubstituted, electron-rich alkenes, dienes, trienes or enynes in only two or three steps. Alternatively, the product from the first cross-coupling reaction could be isolated, deprotonated and quenched with an electrophile, then cross-coupled with a second organometallic nucleophile to give tetrasubstituted, electron-rich alkenes and dienes.

In the course of studying the site selective cross-coupling, it was found that prolonged exposure of the C^1-functionalized materials to palladium promoted an intramolecular C-H activation, forming 2-substituted benzofurans. This reaction proved to be very general, and a wide variety of benzofurans were synthesized, containing both electron-withdrawing and electron-donating group groups in the donor arenes, as well as alkyl, alkenyl, alkynyl and aryl functionalities at the 2-position. This method was also extended to the synthesis of 2-substituted indoles from anilines, trichloroethylene and boronic acids.

ACKNOWLEDGEMENTS

This journey was only possible (and enjoyable) because of the presence and aid of many individuals. Most importantly, I would like to thank my supervisor and mentor, Dr. Phil Hultin. The guidance, advice and support that Phil provided throughout my studies is greatly appreciated. Phil encouraged creativity and the exploration my own ideas, even as a new grad student, while providing focus and direction and stressing practicality. I would not be the scientist I am today without his encouragement. I would also like to thank my advisory committee that became my examining committee: Dr. Peter Budzelaar, Dr. John Sorensen and Dr. Brian Hasinoff. Thank you for your comments, advice and support over the years, and for the comments regarding my thesis. I want to specifically thank Peter for his organometallics course, my first on the subject. Without this experience and Peter's enthusiasm for the subject, this project would never have turned out this way. I am also grateful for Peter's open door, and his willingness to discuss all aspects of my chemistry. I would also like to thank Dr. Mark Lautens for his careful reading of my thesis, and for his thoughtful comments. I am also thankful for the Department of Chemistry's faculty and staff for their support.

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To Beer Fridays: thank you for always being there. To all of my family and friends: thank you for all of your support and encouragement over the years. I am grateful.

A year passed: winter changed into spring, spring changed into summer, summer changed back into winter, and winter gave spring and summer a miss and went straight on into autumn... until one day...

Narrator, Monty Python and the Holy Grail (1975)

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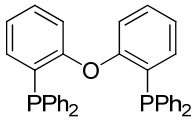
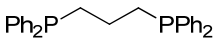
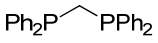
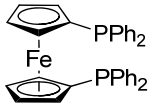
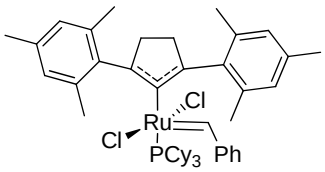
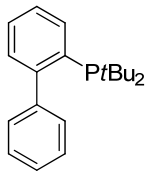
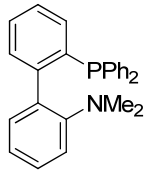
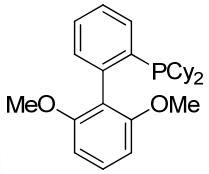
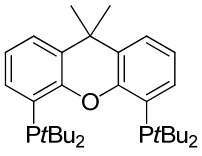
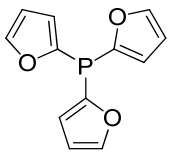
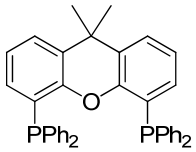
Ac	Acetyl
Aq	Aqueous
Ar	Aryl
9-BBN	9-Borabicyclo[3.3.1]nonane
B_{cat}	Catechol borane
B_{pin}	Pinacol borane
Boc	*tert*-Butoxycarbonyl
bipy	2,2'-dipyridine
br	broad
Bu	*n*Butyl
Cat.	Catalytic amount or catalyst
CMD	Concerted metalation-deprotonation
Conv.	Conversion
COSY	Correlated spectroscopy
Cy	Cyclohexyl
d	Doublet
DBA	Dibenzylideneacetone
dd	Doublet of doublets
DCM	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyanobenzoquinone
DIPEA	Diisopropylethylamine

DMA	Dimethylacetamide
DMPA	4-(Dimethylamino)pyridine
DMF	Dimethylformamide
DPEphos	Bis(2-diphenylphosphinophenyl)ether 
DPPB	1,4-Bis(diphenylphosphino)butane 
DPPE	1,2-Bis(diphenylphosphino)ethane 
DPPF	1,1'-Bis(diphenylphosphino)ferrocene 
δ	Chemical shift in ppm
Δ	Reflux
EAS	Electrophilic aromatic substitution
EI	Electron impact
Equiv	equivalents
ESI	Electrospray ionization
Et	Ethyl
J	Coupling constant (in NMR)
g	gram
Grubbs' 2nd	Grubbs' 2nd generation catalyst, 
h	hour

HMBC	Heteronuclear multiple bond correlation
HMPA	Hexamethylphosphoramide
HRMS	High resolution mass spectrometry
HSQC	Heteronuclear single quantum coherence
Hz	Hertz
JohnPhos	2-(Di-*t*-butylphosphino)biphenyl 
KIE	Kinetic isotope effect
m	Multiplet
mCPBA	*m*-Chloroperbenzoic acid
mmol	Millimole
Me	Methyl
mw	Microwave
NBS	*N*-Bromosuccinimide
NMI	*N*-Methyl imidazole
NMR	Nuclear magnetic resonance
Nu	Nucleophile
[O]	Oxidation
OA	Oxidative addition
o/n	Overnight
Ph	Phenyl

PhDavePhos	2-(Diphenylphosphino)-2'-(N,N-dimethylamino)biphenyl 
pK_a	Acid dissociation constant
PMP	*p*-Methoxyphenyl
ppm	Parts per million
Pr	Propyl
RE	Reductive elimination
s	Singlet
Sia	Siamyl (3-methylbutan-2-yl)
S-Phos	2-Dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl 
t	Triplet
t	*Tert*
TBDPS	*t*Butyldiphenylsilane
*t*Bu-Xantphos	9,9-Dimethyl-4,5-bis(di-*t*-butylphosphino)xanthene 
TCE	Trichloroethylene
TEA	Triethylamine
TFA	Trifluoroacetic acid
TFAT	Trifluoroacetyl triflate

TFP	Tri-(2-furyl)phosphine 
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Trimethylsilane
Ts	*p*-Toluenesulfonyl (tosyl)
Xantphos	9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene 

CHAPTER 1 : INTRODUCTION AND BACKGROUND

1.1 Introduction

In 1975, Hendrickson described the ideal synthesis as one that "creates a complex skeleton from simpler starting materials and so must link several such synthon molecules via construction reactions. Ideally, the synthesis would start from available small molecules so functionalized as to allow constructions linking them together directly, in a sequence only of successive construction reactions involving no intermediary refunctionalizations, and leading directly to the structure of the target, not only its skeleton but also its correctly placed functionality."[1] Or, more succinctly, the only truly necessary steps in any synthesis are those that form the skeleton. The terms 'atom economy',[2] 'step ecomony'[3] and 'redox economy'[4] are often used, and are meant to emphasize the fact that all synthetic manipulations should be performed in such a way that all atoms in all reagents should be incorporated into the immediate product, and indeed the final product, and that formation of non-skeletal bonds (including protecting groups and corrective redox reactions) are unproductive and should be avoided.[5*] This is, of course, a lofty goal.

There are two predominant types of synthetic goals in organic synthesis: target-driven total synthesis, and diversity-oriented synthesis[6] (DOS; function-oriented synthesis[3] may be considered a variant of DOS) where the goal is no longer a single product but rather a family of products, either driven by the development of a new synthetic method or by need as in drug discovery. Small organic molecules are needed not only as new drugs and pharmaceuticals, but also as probes of biological systems in

[*] It should be noted that a perspective review discussing an ideal synthesis and the current state of the art was published at the same time this thesis was being written, with similar sentiments. See also Gaich and Baran, *J. Org. Chem.* **2010,** *75*, 4657-4673.

chemical biology.[7] An effective diversity-oriented synthesis begins with a single (ideally simple and inexpensive) substrate that may be easily transformed into a large collection of compounds. The collection or family of compounds must be both structurally complex and diverse, as it is often unknown what structure will be the most successful in the target application. Structural diversity is often more difficult to achieve,[8,9] but may done by using alternative building blocks or by developing branching reaction pathways.[8]

The development of any new synthetic method is inherently diversity-driven. A method that is successful with dozens of similar reagents (any compound with a specific reactive centre, regardless of the composition of the rest of the reagent) with little to no modification of the basic synthetic method is clearly superior to a method that works for only one or two different types of reagents. This, of course, is not true for target-oriented synthesis, as a single method is required for a single synthetic step, and these are modified as needed to maximize the success of each step. While the 'economic' philosophies above are generally discussed within the context of target-driven synthesis ("total synthesis"), the goal of a truly efficient, or ideal, synthesis is universally relevant.

It follows that if the only indispensible steps in a synthetic sequence are those that form the backbone of the target, then it is clear that development of carbon-carbon bond forming reactions is the cornerstone of organic synthesis. While there are many traditional methods for C-C bond formation (vide infra), it was the advent of palladium- and other transition metal-catalyzed cross-couplings that revolutionized organic synthesis and the types of structures easily accessible. Transition-metal catalyzed reactions have been described as ideal for creating the consummate synthesis. While this was in reference to metal-catalyzed cycloadditions, cross-coupling may apply as well, as these are "concise, efficient, cost- and resource-effective, environmentally benign, quick and simple to conduct. A special emphasis is placed on new transition metal-catalyzed reactions that, in the absence of catalyst, would be forbidden or difficult to achieve."[10] As palladium-catalyzed carbon-carbon bond forming reactions are at the crux of both modern organic synthesis and this thesis, an introduction to palladium-catalyzed carbon-

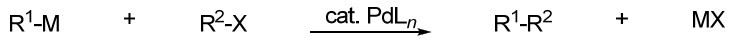
carbon bond formation as a general topic will be presented, both in general terms and in relation to different organometallic nucleophiles. An overview of the established syntheses of alkenes then benzofurans will follow. The specific methods of synthesizing alkenes and benzofurans will also be discussed in terms of atom economy mentioned at the beginning of the introduction: how close are modern synthetic methods to being able to incorporate all atoms from reactants into products? The objectives of the thesis research will be presented, followed by the results and discussion. The conclusion will not only summarize the research performed in this thesis, but will also discuss the methods developed within the context of atom economy.

1.2 Palladium Chemistry

1.2.1 Cross-Coupling

Cross-coupling is defined as the coupling of an organometallic species, R^1-M, and an organohalide R^2-X, to give a new organic species, R^1-R^2 and MX as a stoichiometric byproduct. These reactions are catalyzed by a transition metal, most often palladium (Scheme 1), though other transition metals may be used.[11] Cross-coupling requires that both components be pre-activated prior to carbon-carbon bond construction – one as the halide or pseudohalide, and the other as the organometallic. In general, these reactions are thermodynamically favorable, and it is usually the formation of the MX byproduct that allows these reactions to proceed in the forward direction.

Scheme 1. Generic palladium-catalyzed cross-coupling.



The following sections will describe palladium-catalyzed chemistry. First a basic discussion on the mechanism of palladium-catalyzed cross-coupling reactions will be presented, followed by discussions of the different flavours of carbon-carbon bond forming cross-coupling reactions as based on different organometallic nucleophiles. These will include Heck, Sonogashira, Stille, Kumada-Corriu, Negishi, Hiyama, and finally Suzuki-Miyaura cross-coupling reactions; their strengths and weaknesses will be highlighted.

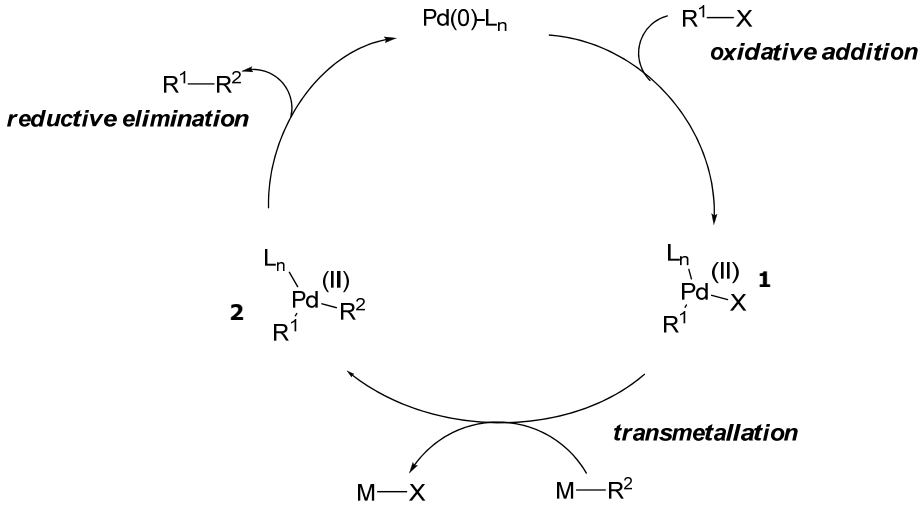
1.2.1.1 Mechanism

Most palladium-catalyzed reactions, particularly cross-coupling reactions, proceed through a Pd(0)-Pd(II) cycle (Scheme 2); catalytic cycles involving Pd(IV) are usually

only invoked in direct functionalization reactions (see sections 1.2.2 and 1.2.3). There are three elementary steps in a standard palladium-catalyzed cross-coupling (Scheme 2): oxidative addition of an organohalide or pseudohalide to Pd(0) to give Pd(II) complex **1**, transmetallation of an organometallic reagent to Pd(II) giving intermediate **2**, and finally reductive elimination that both yields the cross-coupled product and regenerates Pd(0). Details about the mechanism of palladium-catalyzed cross-couplings are best known for Stille reactions with organostannanes ($R\text{-}SnR'_3$, section 1.2.1.4), but are believed to be applicable to most palladium-catalyzed pathways.[12] In general, Pd(0) compounds are nucleophilic and Pd(II) compounds are electrophilic. It should be explicitly noted that the mechanistic outline as presented in Scheme 2 highlights only the major elementary steps; there are many other more subtle steps involved, such as σ- and π-coordination of reagents, ligand association, dissociation, etc., which will not be discussed in any detail in this thesis as these are highly variable and dependent on the specific reaction conditions. While neutral palladium species are implied in this scheme, anionic[13] or cationic[14] palladium intermediates may be present under some conditions. Charged transition metals have markedly different reactivities than their neutral analogues.

Palladium is generally added to a reaction as a pre-catalyst, either as Pd(II) or as Pd(0). If palladium is added as a Pd(II) salt, it must be reduced to Pd(0) prior to entering the catalytic cycle (see schemes below). A ligand is usually added as well to form the active catalytic species, though this is not necessary in all cases. Common Pd(II) species include $Pd(OAc)_2$, $PdCl_2$, $PdCl_2(CH_3CN)_2$, and $[PdCl(allyl)]_2$. The most common Pd(0) species is Pd_ndba_m (with or without a chloroform molecule) where *n* and *m* may be of varying stoichiometry.

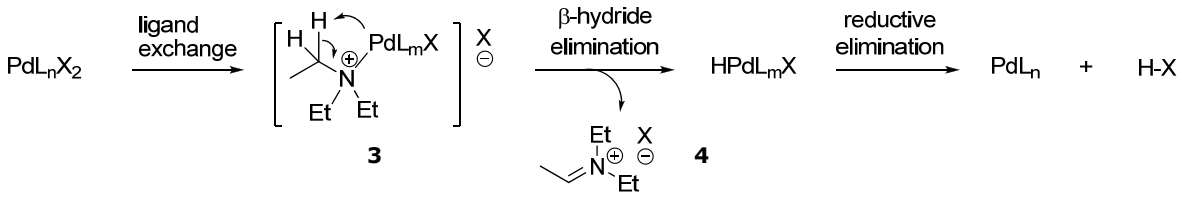
Scheme 2. Generalized mechanistic scheme for a Pd-catalyzed cross-coupling.



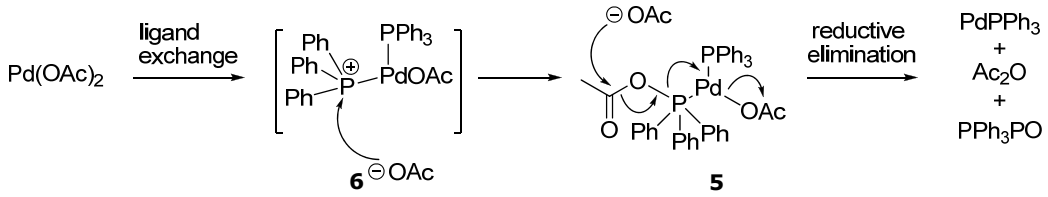
In the generalized mechanistic scheme, formation of the active palladium catalyst is the first step. If the palladium source is Pd(II), a reduction to Pd(0) must occur. This can be done via addition of a reducing agent such as DIBAL-H or a trialkylaluminum (these are no longer common methods). Reduction is more conveniently carried out with trialkylamines (Scheme 3), phosphines (Scheme 4), alkenes (Scheme 5) or an organometallic reagent such as butyl lithium (Scheme 6). The mechanisms of the reductions are not always well-understood, but generalized mechanisms are postulated below. In an amine reduction of PdX_2, triethylamine (TEA) nucleophilically displaces an anion from PdX_2 giving intermediate **3** which eliminates a hydride from the β-position of TEA yielding an iminium ion **4** and a Pd(II) HX salt. After reductive elimination, Pd(0) is formed with an equivalent of HX (Scheme 3). Phosphine reductions proceed in a related fashion; for example, triphenyl phosphine displaces an acetate anion from PdX_2 to give **6** which is oxidized by acetate (giving **5**). A second equivalent of acetate attacks intermediate **5**, and following reductive elimination, Pd(0) is formed with acetic anhydride and triphenylphosphine oxide (Scheme 4). In the presence of both an amine and a phosphine, reduction of palladium(II) acetate by phosphine is much faster than reduction by the amine.[15] When Pd(II) is treated with an alkene, the alkene first coordinates to

Pd(II) (**7**) then the alkene inserts into a Pd-X bond to give **8**. As in the case of reduction by triethylamine, this yields Pd(II)·HX, which gives Pd(0) and HX after reductive elimination (Scheme 5). In the final mode of reduction, two equivalents of an organometallic will nucleophilically attack PdX_2 giving Pd(II) intermediate **2** which will reductively eliminate R-R and yield Pd(0) (Scheme 6). Fluoride ions may also reduce Pd(II) to Pd(0).[16]

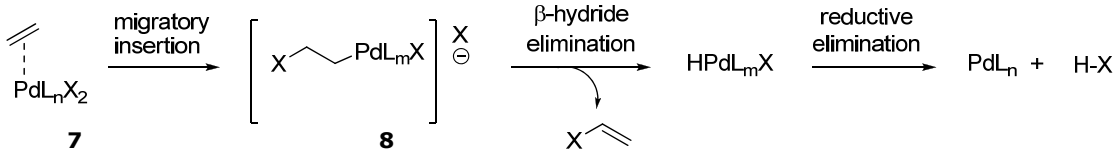
Scheme 3. Reduction of PdX_2 by triethylamine.



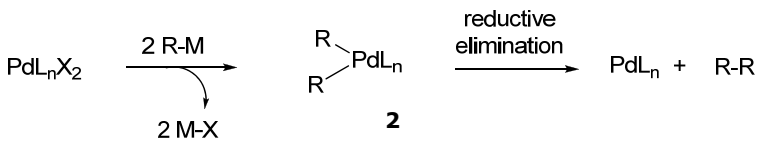
Scheme 4. Reduction of $Pd(OAc)_2$ by triphenylphosphine.



Scheme 5. Reduction of PdX_2 by an alkene.



Scheme 6. Reduction of PdX_2 by an organometallic reagent.



As stated above, the most common Pd(0) source is Pd_ndba_m. The dissociation of DBA and association of a second (added) ligand to palladium is a dynamic process and is often not complete in mild conditions.[12] The different palladium complexes are in equilibrium with each other[17,18] and can have vastly different catalytic properties.[19] DBA is not usually involved in the active steps of the catalytic cycle, but even so, it can have a profound effect on the rate of reaction,[20,21] particularly on the rate of oxidative addition.[20] The mode of deactivation is normally by sequestering palladium into a catalytically inactive (resting state) $L_nPd(dba)_m$ complex.[19]

The ligand plays perhaps the most significant role in palladium-catalyzed chemistry in terms of both steric and electronic effects. Most common ligands are phosphine-based and can be monodentate (like triphenylphosphine **11**) or bidentate (such as DPEphos **12**) but nitrogen-based ligands such as **10** and *N*-heterocyclic carbenes like **9** may also be used (Figure 1). The ligand in Scheme 2 is represented as L_n, indicating ambiguous coordination number as the number of ligand molecules coordinated to palladium will vary between the steps and the denticity (binding mode) of the ligand. The steric size of the ligand also impacts coordination to the metal centre.[22]

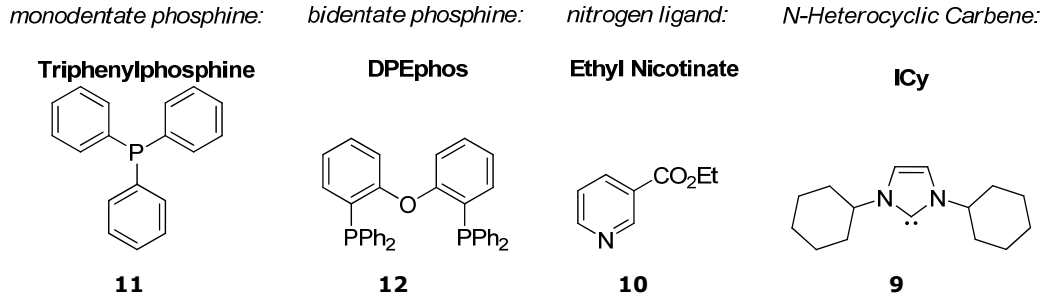


Figure 1. Representative ligand classes for Pd-catalyzed chemistry.

To generalize, ligands have both electronic and steric influence, and these will be discussed in context of phosphine ligands. Tolman described the measurement of electron donor-acceptor abilities of phosphines based on carbonyl stretching frequencies of $Ni(CO)_3L$ complexes.[23] A better PR_3 donor will have a lower frequency of vibration (of CO) due to back-donation into CO π^* orbitals.[24] All phosphine ligands are π acceptors.[25] Triarylphosphines substituted with electron-withdrawing groups are much less basic[26] and are poorer σ-donors[27] than phosphines substituted with electron-donating groups. Trialkyl phosphines are better σ-donors than triaryl phosphines, and therefore create a more electron-rich palladium centre.[28] The application of trialkyl phosphine ligands has been critical, for example, in the development of cross-coupling reactions of relatively unreactive aryl chlorides.[29-31] The increased electron-density at palladium facilitates oxidative addition, as this increases the nucleophilicity of palladium and aids in the stabilization of higher oxidation states.[32]

In addition to the electronic component of the phosphine, the steric component of a ligand has an enormous effect on the reactivity of the corresponding catalytic complex it forms with palladium. In general, bulky ligands facilitate reductive elimination, but if they are too big, can retard oxidative addition. They are several different terms to describe or quantify the steric contribution of the ligand, depending on the type of ligand evaluated. Tolman coined the term 'cone angle' (Θ, Figure 2*a*) to describe the volume of monodentate phosphines.[33,34] This is the most commonly used descriptor of ligand bulk, though there are others.[35]

The greater conformational flexibility of bidentate ligands as compared to monodentate ligands have made the compilation of descriptors for bidentate ligands more difficult.[36] The term 'bite angle' (β_n, Figure 2*b*)[37] is used to describe bidentate ligands, and it is the chelation angle P-M-P. Bidentate ligands can play unique roles in cross-coupling reactions,[38] and even change the selectivity of a reaction.[39,40] The observed angle is a compromise between the ligand's natural bite angle (influenced by backbone constraints and repulsion between the phosphorus substituents) and the angle preferred

by the metal atom (mainly electronic in nature).[41] Most bidentate ligands naturally assume a *cis* geometry around a metal centre; however, ligands with a very large bite angle will assume a *trans* geometry. Large bite angle ligands, unsurprisingly, promote reductive elimination by forcing the organic groups around palladium (as in intermediate **2**) closer together. While bite angle is a useful parameter, it neglects the steric environment around phosphorus.

Recently, two new terms have been coined in attempts to develop an analogous cone angle definition as related to bidentate ligands. Solid-cone angles, Ω_S, then converted to generalized cone angle Θ_b, have been calculated for several bidentate ligands.[42,43] A length parameter (A_L, Figure 2*c*) and the percent buried volume of a metal centre by a ligand has also been proposed to describe ligand bulk.[44]

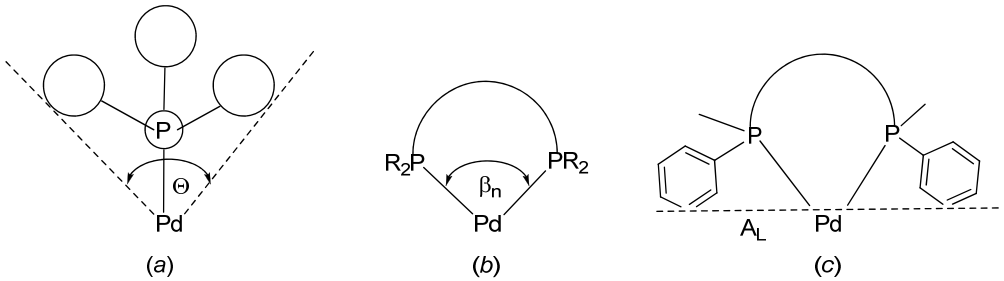


Figure 2. Ligand descriptors: cone angle (*a*), bite angle (*b*) and length parameter (*c*).

Oxidative addition is the first step in the catalytic cycle after generation of the active catalyst (Scheme 2), and may occur via a number of mechanisms.[45] For example, in the concerted oxidative addition, this is an associative bimolecular attack of the nucleophilic Pd(0) complex on the organohalide electrophile.[12] The geometry of the d^{10} Pd(0) is tetrahedral and changes to a square planar arrangement as a d^8 Pd(II). The general reactivity order of different electrophiles toward palladium is outlined in Figure 3.[46] While acyl halides are reactive toward palladium, aldehydes, ketones, esters,

amides, nitro groups and nitriles are generally inert. The low reactivity of aldehydes, other carbonyl groups, and alkyl halides is attributed to the relatively high electronegativity of palladium, which results in a proportionately low polarity C-Pd bond. The relative non-polarity of the C-Pd bond leads to excellent chemoselectivity and functional group tolerance. Note that the trend presented in Figure 3 is only valid for a single X species.

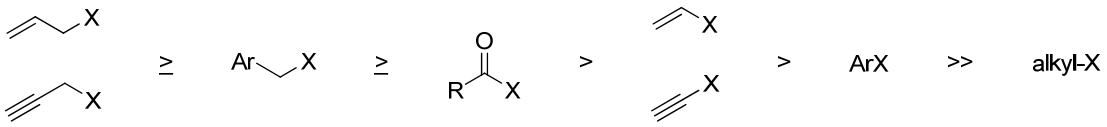


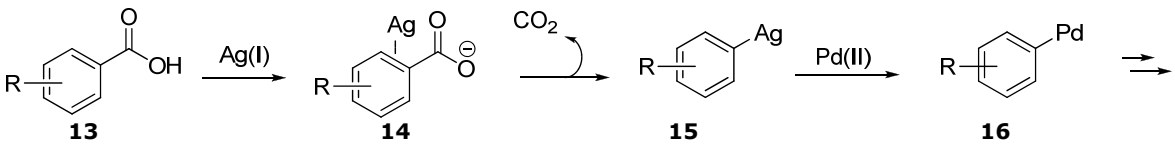
Figure 3. Generalized functional group reactivity toward palladium(0).[46]

Halide ions can also act as anionic ligands to palladium, and can therefore play a significant role in cross-coupling reactions beyond influencing the rate of oxidative addition. Chloride ions in particular play myriad roles in cross-couplings and their influence has been fairly extensively studied.[47] Although the steric effects, electronic properties (σ- and π-bonding), polarizability, nucleophilicity and the *trans*-effect of halides[48] can be significant, these roles will not be discussed in detail as they are highly variable and condition-dependent.[49]

In terms of the reactivity of the (pseudo)halides, iodides are usually the most reactive, followed by triflates and bromides, and chlorides generally have the lowest reactivity. This trend is related to the C-X bond strength where the C-I bond energy is on average 210 kJ/mol, C-Br is 280 kJ/mol and C-Cl is 330 kJ/mol.[50] Oxidative insertion into C-F bonds is much less well-known, and only recently have practical applications of this been published.[51,52] Triflates are the most common pseudohalide and are excellent leaving groups, although phosphonates and many others can be used.[53] For example, carboxylic acids 13 can in some cases act as leaving groups; metal-mediated

decarboxylation from 14 to 15 leads to oxidative-addition-like products 16 (conceptually similar to **1**) via transmetallation (Scheme 7).[54] In contrast to standard cross-coupling however, this requires starting from a Pd(II) species, so a stoichiometric oxidant is required to oxidize Pd(0) at the end of the cycle to Pd(II); in this case, silver is acting as both the promoter of decarboxylation and oxidant of palladium. In all cases, (pseudo)halides substituted with an electron-withdrawing group undergo faster oxidative addition than those substituted with electron-donating groups.

Scheme 7. Silver-mediated decarboxylation to generate an organopalladium species.



13 **14** **15** **16**

As alluded to above, there are many factors to consider when optimizing a palladium-catalyzed reaction (Figure 4). The palladium source needs to be evaluated in terms of oxidation state, as well as coordinating ligands. The ligand needs to be chosen and it can be phosphine, arsine, nitrogen or carbene based, and mono- or bidentate (or more); additionally, the ratio of phosphine to palladium can have a significant effect of the rate of the reaction.[29,55,56] Most palladium-catalyzed reactions require a base, either to activate the organometallic (as in Suzuki couplings, section 1.2.1.8) or to neutralize the stoichiometric amount of acid produced (as in the Heck reaction, section 1.2.1.2). The base may be a soluble organic base, such as triethylamine, or an inorganic base like carbonate or bicarbonate (as Na, K, Cs or Ag salts). In some cases, additives (e.g. silver acetate or lithium chloride) are very useful and/or essential. The solvent also plays a significant role and can even change the entire course of a reaction. Less important influences include concentration and the reaction temperature, but these can have dramatic effects, particularly in chemoselective reactions.

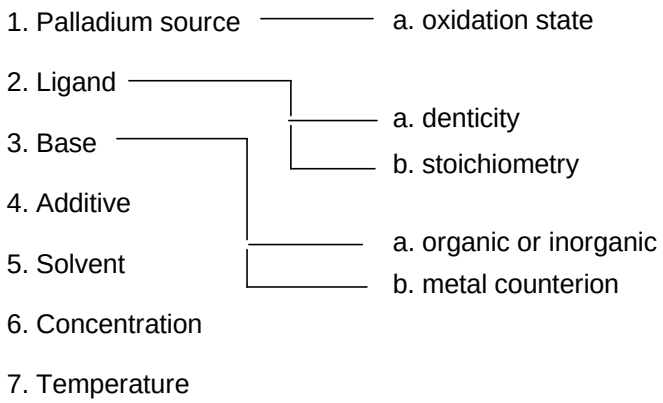


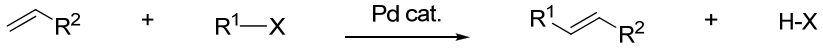
Figure 4. Optimizable or adjustable parameters in palladium-catalyzed cross-couplings.

Despite all the degrees of freedom and the seemingly limitless possible combinations, palladium-catalyzed cross-coupling is highly successful and has become indispensible for carbon-carbon bond formation[57] over the last few decades. A summary of the classifications of palladium-catalyzed cross-coupling reactions organized according to electrophile and nucleophile types can be found in a book recently published.[11]

1.2.1.2 Heck Reaction

The alkenylation of halides and related processes were first demonstrated by Heck in 1968.[58-63] Although it is not technically a cross-coupling, the Heck reaction (Scheme 8) is often grouped with cross-coupling reactions due to mechanistic similarities.

Scheme 8. The general Heck reaction.

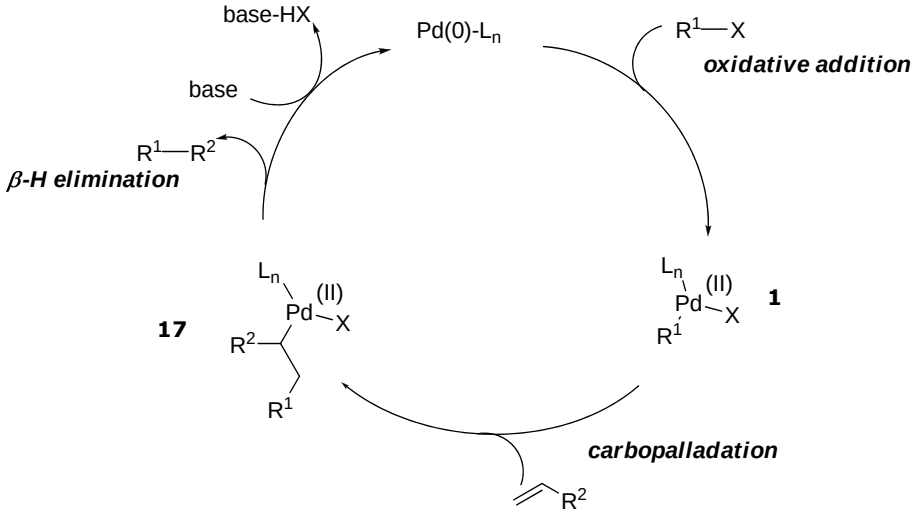


Both cross-coupling and Heck reactions start via the oxidative addition of a halide to the active palladium(0) catalyst, which is generally a coordinatively unsaturated 14-electron complex. While in cross-coupling transmetallation occurs next (Scheme 2), in the Heck reaction the organopalladium intermediate **1** carbopalladates[64] an alkene giving

a σ-alkyl palladium(II) species **17**, which, after β-hydride elimination, gives the new alkene and a palladium(II)-HX complex (Scheme 9). The palladium salt, when in the presence of a base, is deprotonated regenerating Pd(0).[65] The regioselectivity of carbopalladation is influenced by both steric and electronic factors. Alkene coordination to Pd(0) prior to oxidative addition may stall the catalytic cycle.[66]

The reaction was historically between aryl halides and alkenes, although vinyl, benzyl or allyl electrophiles are becoming much more commonplace. Alkyl halides may be used provided there are no β-hydrogens. The reaction works best when the alkene is monosubstituted or 1,1'-disubstituted as they are more reactive than 1,2-disubstiuted alkenes due to decreased steric effects.[67] Trisubstituted alkenes are not typically good substrates for this reaction, and only a few examples are known. An excellent summary of the types of alkenes and the regioselectivity of the Heck reaction thereon has been published.[68] The conditions are very mild and tolerant of a wide variety of appendant functional groups.

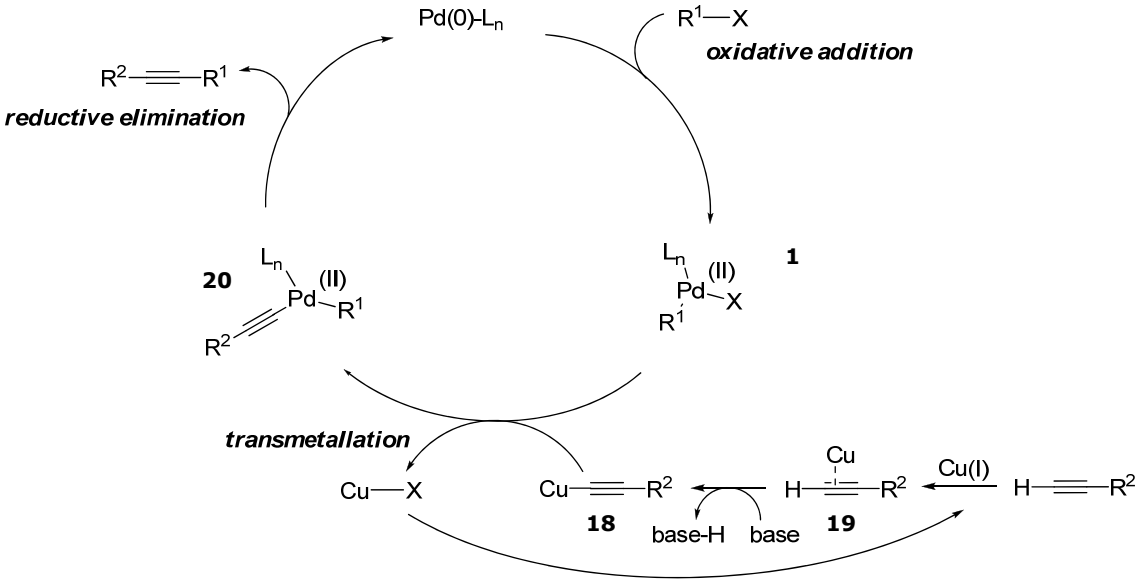
Scheme 9. Generalized Mechanism of the Heck Reaction.



1.2.1.3 Sonogashira Cross-Coupling

The Sonogashira reaction is by far the most preferred method to alkynylate an organohalide. The reaction was first published in 1975,[69] and the reaction conditions have not changed much since then. The reaction usually requires both palladium and copper, typically in a 1:2 molar ratio. The basic reaction mechanism[70] is shown in Scheme 10, as it differs from the standard cross-coupling mechanism in Scheme 2. The copper(I) salt (most often CuI) coordinates to the alkyne (**19**), increasing the acidity of the alkyne proton so it may be deprotonated to give the copper acetylide **18**. The organocopper species may then transfer the alkyne to oxidative addition product **1** forming intermediate **20**, which reductively eliminates the disubstituted alkyne and regenerates Pd(0).

Scheme 10. General mechanism of the Sonogashira reaction.



The conditions are very mild and the reaction is often successful at room temperature. The Sonogashira reaction is generally performed in an amine solvent (triethylamine and diisopropylamine are the most common), although this is not required.

If the reactants are base-sensitive, THF is the most common alternate solvent for the reaction. The homocoupling of the alkyne via Glazer coupling is the most common side product, but is minimized by excluding oxygen. The reactivity order of electrophiles follows that outlined in Figure 3. A very useful review discussing different catalytic systems as well as applications of the Sonogashira reaction in organic synthesis was recently published.[71] Terminal metal acetylenes such as alkynylzinc, alkynylboron and alkynyltin reagents can also be used; however, the alkynyl metal has to be pre-synthesized and the metal is used in stoichiometric amounts, making these reactions less efficient than Sonogashira reactions in which the metal acetylide is generated in situ and the reaction is thus catalytic in copper.[72]

1.2.1.4 Stille Cross-Coupling

This reaction between an organohalide and an organostannane was first reported in 1979 by Stille[73] and it is perhaps the best understood cross-coupling in terms of mechanism.[74] Similar to the Heck reaction, the active catalyst in this case is an unsaturated 14-electron palladium(0) complex, which forms a 16-electron palladium(II) species after oxidative addition.[75] Alkynylstannanes can be formed from, for example, the corresponding alkynyl silicon species, and vinyl stannanes can be synthesized via hydrostannylation of alkynes. Organostannanes are not very nucleophilic, which has two major implications; while a higher temperature is needed to facilitate transmetallation, the reaction shows a wide functional group tolerance. When unsymmetrical tetraorganostannanes are used, tin will transfer sp^2 and sp hybridized ligands in preference to sp^3 (alkyl) ligands. For example, the palladium-catalyzed reaction between Ph-$SnBu_3$ and PhI will yield biphenyl and not phenylbutane. Even though no acid is produced as a byproduct from this reaction, a fluoride source is sometimes added to activate the organostannane for transmetallation. While traditional Stille cross couplings utilize tetraorganostannanes, monoorganic tin compounds can be used, and as a result, the reaction can proceed under milder reaction conditions.[76] Despite its broad scope and mild reaction conditions,[77] the Stille reaction

suffers from the high toxicity of the tin compounds and difficulty of removing side products. It is therefore usually avoided.

1.2.1.5 Kumada-Corriu Cross-Coupling

Sometimes simply referred to as Kumada cross-coupling, the transition metal-catalyzed reaction between Grignard reagents and organohalides was first published in 1972.[78,79] Grignard reagents are both quite basic and nucleophilic; the substrate scope of the Kumada-Corriu reaction is therefore more limited than the Stille reaction, related to the limited functional group tolerance, although this is beginning to improve.[80,81] The conditions for cross-coupling are otherwise very mild, and Kumada reactions can proceed at very low temperatures; a recent publication reported cross-coupling at -65 ^{o}C,[82] the lowest temperature reported for any cross-coupling. This is due to the high nucleophilicity of organomagnesium reagents which can undergo rapid transmetallation. Palladium can be used as the transition metal (and Pd-catalyzed Kumada couplings follow the general catalytic cycle as shown in Scheme 2), but, as in the original publications, nickel-catalyzed reactions are more common

1.2.1.6 Negishi Cross-Coupling

Negishi coupling generally refers to cross-coupling reactions using organozinc reagents, but the term may also include reactions with organoaluminum and organozirconium reagents, among others. Negishi first published the results with organozinc reagents in 1977.[83] These nucleophiles may be prepared via reductive metallation of organohalides, or via transmetallation from organolithiums and –magnesiums,[84] as well as boranes, alanes and organozirconium species, which themselves may be accessed from hydrometallation of carbon-carbon multiple bonds. Direct carbozincation is also possible in some cases.[85] Interestingly, organozinc reagents are typically more reactive than either organolithiums or organomagnesiums under palladium-catalyzed conditions,[86-88] opposite to the reactivity order observed in standard electrophilic reactions. Therefore,

organozinc species offer a highly useful combination of high reactivity in the presence of palladium with low basicity/nucleophilicity, leading to high chemoselectivity.[89] The transmetallation reaction between palladium (or nickel[90]) and an organozinc has recently been studied in detail.[91] In addition to palladium-catalyzed cross-coupling with organozinc reagents, copper, nickel, cobalt(II) and (III), iron(II) and manganese(II) can also effect cross-coupling.[84] As no acid is formed as a byproduct in the reaction, there is no need to add a base.

The Negishi cross-coupling is most efficient for aryl-aryl, aryl-alkenyl, alkenyl-aryl and alkenyl-alkenyl cross-couplings (sp^2-sp^2), and is also useful for alkynyl and allyl cross-couplings.[85] Cross-coupling with alkylzincs is most efficient with Me_2Zn and other primary alkyl derivatives; other alkylzinc species are prone to isomerization in the presence of a transition metal.[85] Organozinc reagents must be handled with some care as they are sensitive to both air and moisture, but the Negishi cross-coupling (along with the Suzuki coupling, see section 1.2.1.8) remains one of the most widely used cross-coupling variants.[92]

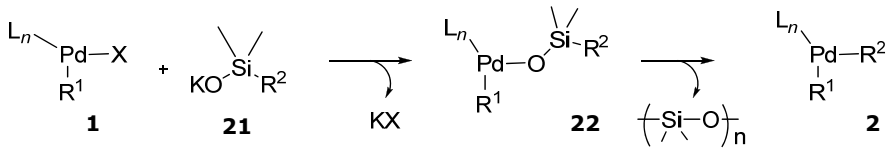
1.2.1.7 Hiyama and Hiyama-Denmark Cross-Coupling

Organosilanes, the nucleophilic component in Hiyama cross-coupling, are generally quite unreactive, despite their apparent similarity to organostannanes. While tetracoordinate organostannanes are capable of directly transferring an organic moiety to palladium, the analogous organosilanes cannot. It was generally believed that fluoride ions added to silanes to produce a pentacoordinate species for transmetallation,[93] though recent computational experiments suggest that these complexes are not formed at all.[94] Rather, the transmetallation more likely involves a palladium fluoride complex or proceeds by fluoride attack on a palladium-coordinated organosilane.[94] Even with activation by fluoride, organosilanes are not particularly reactive; one of the earliest reports of organosilane-based cross-couplings was between iodobenzene and the dipotassium salt of pentafluorostyrylsilicate and not only were the conditions quite harsh despite simple

substrates, but the desired adduct was isolated in poor yield.[95] There are only a few examples of cross-coupling using functionalized trimethylsilanes, and this low reactivity poses a significant limitation on the use of organosilanes as nucleophiles in cross-coupling.

More recently, organosilanols have been utilized instead of silanes and this modification (the Hiyama-Denmark cross-coupling reaction) has been met with much more success.[96,97] The reactions between (pseudo)halides and vinyl-, alkynyl-, aryl-, and heteroarylsilanols (as their alkali metal salt, **21**) are fairly general and robust.[96] Additionally, with the Denmark modification additional activation (i.e. by fluoride) is no longer required, and transmetallation does not occur through a pentacoordinate organosilane but rather from the covalent intermediate **22**, resulting from nucleophilic displacement of the halide on the palladium(II) species **1** from oxidative insertion into the C-X bond of the electrophile by **21** (Scheme 11). After transmetallation from **22** to give **2**, reductive elimination of R^1-R^2 occurs, and the catalytic cycle restarts (as shown in Scheme 2).

Scheme 11. Transmetallation in Hiyama-Denmark cross-coupling.



Organosilanols can be prepared using a few different methods, including quenching an organolithium with hexamethylcyclotrisiloxane ($(Me_2SiO)_3$) or chlorodiisopropylsilane (iPr$_2$SiClH) followed by chlorination and hydrolysis, or direct hydrosilation of a carbon-carbon triple bond.[93] The conditions used in standard Hiyama-Denmark cross-couplings are very mild and will tolerate a wide variety of functionalities, but currently cannot cross-couple alkyl groups as either the nucleophilic or electrophilic component.

1.2.1.8 Suzuki-Miyaura Cross-Coupling

The Suzuki-Miyaura (or sometimes simply Suzuki) cross-coupling employs boronic acids or other organoboron reagents as nucleophiles, and is one of the most widely used cross-coupling variant, along with the Negishi coupling described in section 1.2.1.7. Not only are many organoboron reagents commercially available, they are relatively easy to prepare if needed, the conditions for cross-coupling are generally mild and tolerant of water and a variety of other functional groups, as organoboronic acids are not very nucleophilic. Additionally, good regio- and stereoselectivity may be achieved where applicable; the reaction is not particularly sensitive to steric influences. Finally, organoboron reagents are non-toxic, and the boron-based byproducts are usually easy to separate from the desired product.[98]

A general representation of the different kinds of organoboron reagents that have been used in cross-coupling reactions is shown in Figure 5. Boronic acids (R-B(OH)$_2$) and esters (R-B(OR')$_2$)[99] are the most commonly employed boron reagents in Suzuki coupling. They are widely applicable, but suffer from some drawbacks. The propensity to dehydrate yielding cyclic anhydrides can be particularly problematic. This dehydration is often only partial and results in uncertain stoichiometry of the boronic acid component, which is critical in many applications.

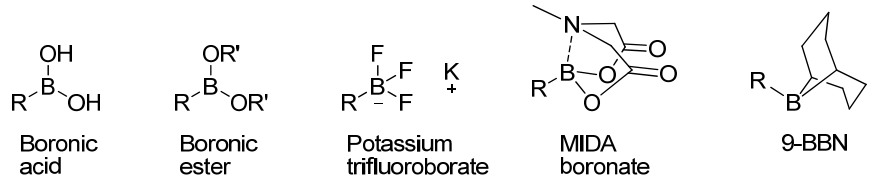


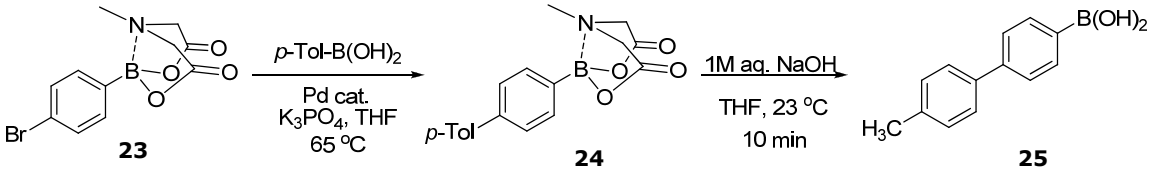
Figure 5. Organoboron reagents used in cross-coupling reactions.

Two alternate types of organoboron reagents have recently been developed in attempts to increase the efficiency of Suzuki coupling, and these are potassium organotrifluoroborates and MIDA boronates. The potassium organotrifluoroborates were

developed by Molander and coworkers.[100,101] They have shown that aryl-,[102] heteroaryl-,[103] alkenyl-,[104,105] alkynyl-[106] and alkyl-[107] trifluoroborates undergo cross-coupling under very mild conditions. These compounds are easily synthesized from the corresponding boronic acid by reaction with KHF_2 in aqueous conditions.[100,101] The major advantage of potassium trifluoroborates over boronic acids is their long-term air and moisture stability.[101]

Similarly, MIDA boronates are very stable organoboron reagents, and also easily prepared from boronic acids.[108] Like potassium trifluoroborates, MIDA boronates substituted with aryl, heteroaryl, alkenyl and alkyl groups have all been shown to be reactive in cross-coupling reactions.[108] The greatest utility of MIDA boronates, however, is their *unreactivity* under standard, anhydrous palladium-catalyzed cross-coupling conditions. While this initially sounds like a disadvantage, this permits a highly useful and selective functionalization of a bifunctional molecule containing the MIDA boronate motif and some other reactive handle. For example, MIDA boronate-functionalized aryl bromide **23** was cross-coupled with an aryl boronic acid to give **24**, leaving the MIDA boronate untouched by the anhydrous conditions (Scheme 12).[109] The MIDA boronate can be hydrolyzed to give boronic acid **25**. This can be done in two discrete steps,[109] or the MIDA boronate may be reacted under conditions such that the boronic acid is slowly released and cross-coupled in situ,[110] particularly useful for cross-coupling unstable boronic acids, such as 2-pyridyl boronic acid.

Scheme 12. Selective cross-coupling reaction with a MIDA boronate-containing electrophile.[109]



23 **24** **25**

While alkyl boronic acids are often not useful in cross-coupling, trialkylboranes, most notably 9-alkyl-9-BBN and alkyl(disiamyl)borane, may readily cross-couple with a variety of organic electrophiles.[111] The requisite starting materials are obtained via a simple hydroboration of a terminal alkene with either 9-BBN-H or $HB(Sia)_2$ to give the primary organoborane. These compounds are highly sensitive to air and moisture, and are usually synthesized and cross-coupled in one pot. The regioselectivity of the initial hydroboration of a terminal alkene can be reversed to give secondary organoboron reagents, if performed in the presence of a rhodium catalyst.[112]

The catalytic cycle generally follows that described in Scheme 2. The cross-coupling itself is tolerant of and can even benefit from water.[113] However, if water-sensitive functional groups are present in either the electrophile or nucleophile, water must obviously be avoided. Transmetallation is often the rate-determining step due to the low nucleophilicity of organoboron reagents, though, as stated above, this imparts large functional group tolerance to this overall process. A base is required for this reaction; organoboron compounds do not normally react with palladium(II) species, but ate-complexes (anionic, four-coordinate boron species) formed from reaction of boronic acids and bases react readily via a variety of mechanisms.[114] Cesium bases such as Cs_2CO_3 and CsOH often impart an acceleration of rate as compared to sodium or potassium bases.[114] Fluoride salts (CsF, Bu_4NF, etc.) are useful alternates, especially when base-sensitive nucleophiles or electrophiles are in use.[115] A summary of less conventional substrates and catalytic conditions used in the Suzuki-Miyaura cross-coupling reaction has recently been published.[116]

1.2.1.9 Summary

A summary of nucleophiles that can be used in palladium-catalyzed cross-coupling reactions are shown in Table 1, and are grouped according to the metal countercation.[92]

Table 1. Summary of organometallic nucleophiles used in cross-coupling reactions.

metal	scope	use	general comment[92]
Zn	broad	broad	most reactive
B	broad	broad	most chemoselective
Sn	broad	broad	toxic
Cu	limited	broad	alkynylation only
Mg	limited	moderate	try before Zn[a]
Al	limited	moderate	try before Zn[a]
Zr	limited	moderate	try before Zn[a]
Si[b]	limited	limited	low reactivity

[a]As mentioned in 1.2.1.6, organozinc reagents are often prepared from these organometallics, and it is therefore more efficient to first attempt cross-coupling prior to transmetalating to zinc. [b]Reactions using silanols as the organosilicons reagent is increasing scope of the Hiyama reaction.

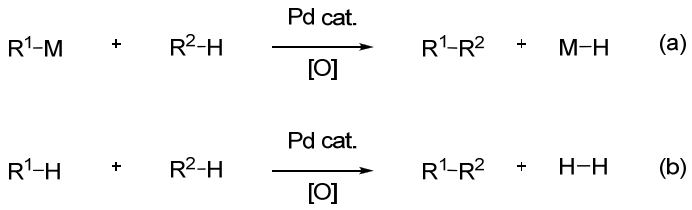
While cross-coupling reactions are well established and, in general, highly successful for a wide variety of substrates, both partners require pre-activation prior to the carbon-carbon bond forming event. Eliminating one or both pre-activation events increases the efficiency and shortens the overall process. These 'direct' functionalizations (usually arylations, and will be discussed within this context) can be divided into two classes: 1) oxidative direct arylations between an unactivated arene and an

organometallic reagent or two unactivated arenes (section 1.2.2) and 2) non-oxidative direct arylations between an unactivated arene and a (pseudo)halide (section 1.2.3).

1.2.2 Oxidative Direct C-H Functionalization

A generalized oxidative direct C-H functionalized reaction is shown in Scheme 13. In addition to the transition metal catalyst, this reaction requires a stoichiometric amount of an oxidant.

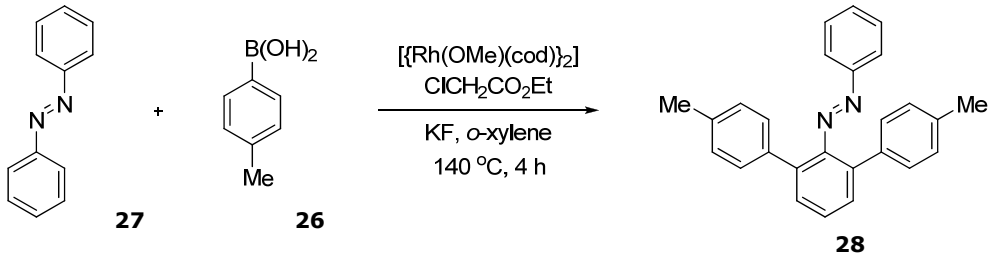
Scheme 13. Generic palladium-catalyzed oxidative direct arylations, where R^1-H, R^2-H or both are unactivated arenes.



The direct arylation in Scheme 13, equation a, in which one partner is an organometallic reagent, suffers from a few limitations. First, the organometallic reagent must be synthesized. This is usually done by lithiation of a halide followed by quenching with an appropriate metal precursor, for example, with trimethylborate to form a boronic acid. In other cases, it is possible to directly functionalize the arene via transition metal catalysis; boronic acids can be formed via direct iridium-catalyzed borylation. In either case, this sequence adds an additional step to the overall sequence. Additionally, this type of oxidative direct C-H functionalization reactions generate stoichiometric amounts of undesired materials.[117] The combination of these makes this coupling less desirable, and although some success has been recently found in this area,[117] it will not be discussed in much detail in this thesis outside of the description of the mechanism (section 1.2.2.1).

The direct oxidative coupling between two unactivated arenes (Scheme 13, equation b) is obviously much more efficient, as it eliminates both problems discussed above and starts from the simplest possible materials. Due to the abundance of C-H bonds in organic compounds, often several C-H bonds in a single compound have similar bond dissociation energies, and regioselectivity becomes a major issue. Nitrogen-based directing groups such as amides or nitro groups can overcome this problem in some cases but presents a severe structural limitation. Scheme 14 illustrates a rhodium-catalyzed oxidative double direct arylation between azobenzene **27** and an aryl boronic acid (**26**) to give **28**,[118] and Scheme 15 shows a palladium-catalyzed cross-coupling between two unactivated arenes (**29** and **30**) to form **32**, taking advantage of the directing ability of nitrogen in **29**.[119] The mechanism of that transformation has since been elucidated, and through a variety of kinetic and isotopic labeling experiments, it was determined that a Pd(II)/Pd(0) catalytic cycle was operative, where benzoquinone **31** was used as the oxidant.[120] A detailed analysis of different directing groups in the direct acetoxylation of arenes was recently published.[121]

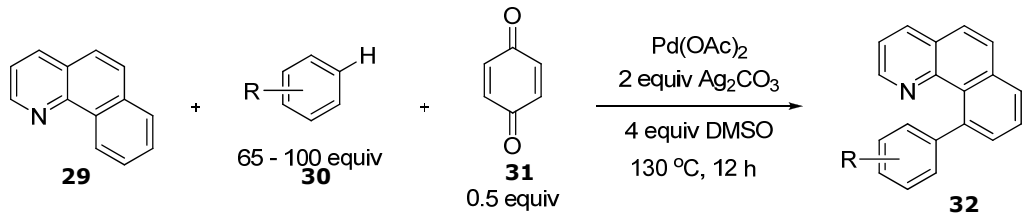
Scheme 14. Rhodium-catalyzed double direct arylation of azobenzene.[118]



27 **26** **28**

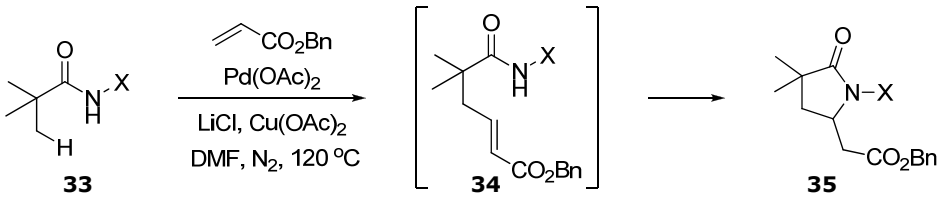
39%

Scheme 15. Palladium-catalyzed functionalization of benzo[h]quinoline using unactivated arenes.[119]



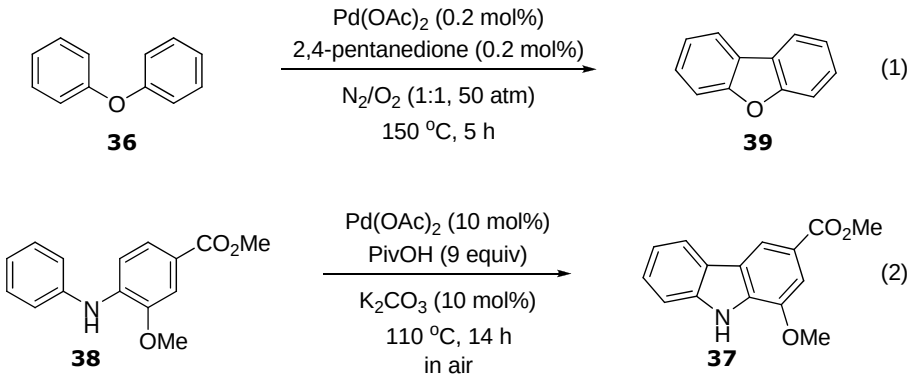
The oxidative direct arylation is most commonly applied to arene C-H bonds, but successful functionalization of sp^3 C-H bonds is now a tangible possibility. A recent example[122,123] is shown in Scheme 16, in which amide **33** is treated with palladium in the presence of an alkene to give **34** via an oxidative Heck reaction. Subsequent intramolecular hydroamination yielded amide **35**.

Scheme 16. Palladium-catalyzed direct olefination of an sp^3 C-H bond.[122,123]



Oxidative direct arylation has also been successfully used in the construction of dibenzofurans **39** (Scheme 17, equation 1)[124] and carbazoles **37** (Scheme 17, equation 2) from diaryl ethers **36** and amines **38**, respectively.[125]

Scheme 17. Synthesis of dibenzofurans and carbazoles via direct arylation.[124,125]



While direct dehydrogenative C-H functionalization is limited to only a small number of cases, this process is still in its infancy, and it is expected that great things will come.

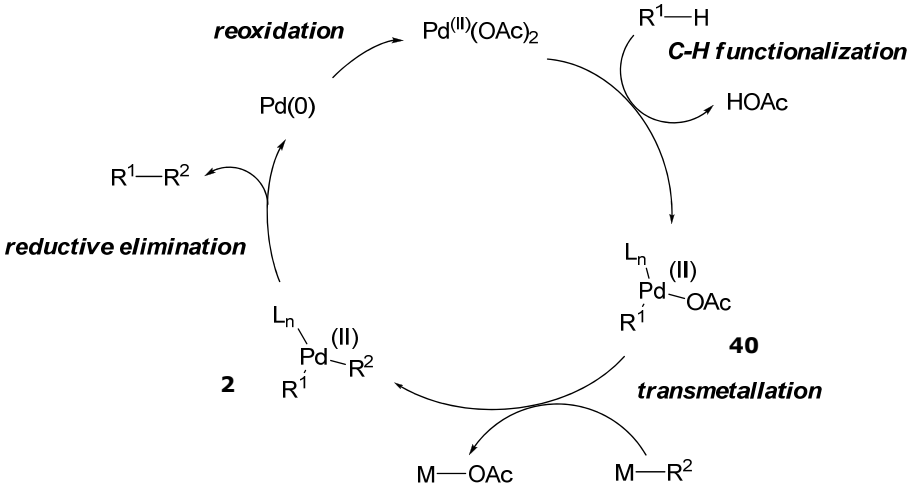
1.2.2.1 Mechanisms

There are a few different mechanistic pathways that this general reaction may proceed through. Two types of mechanisms dominate oxidative direct arylation: Pd(II)/Pd(0) catalysis or Pd(II)/Pd(IV) catalysis, and both will be briefly described.

Pd(II)/Pd(0) Catalysis

A typical Pd(II)/Pd(0) catalytic cycle is given in Scheme 18.[126] The similarity between this and the Pd(0)/Pd(II) mechanism shown in Scheme 2 is obvious. The catalytic cycle begins via a C-H activation of the starting unactivated arene to give palladium(II) intermediate **40**. At this point, the catalytic cycle that follows is similar to that seen in cross-coupling reactions. A transmetallation step yields the diaryl Pd(II) complex **2** and subsequent reductive elimination then gives desired product R^1-R^2 and Pd(0). The Pd(0) must be reoxidized to Pd(II) to restart the catalytic cycle.

Scheme 18. A typical Pd(II)/Pd(0) catalytic cycle between an unactivated arene and an organometallic reagent.

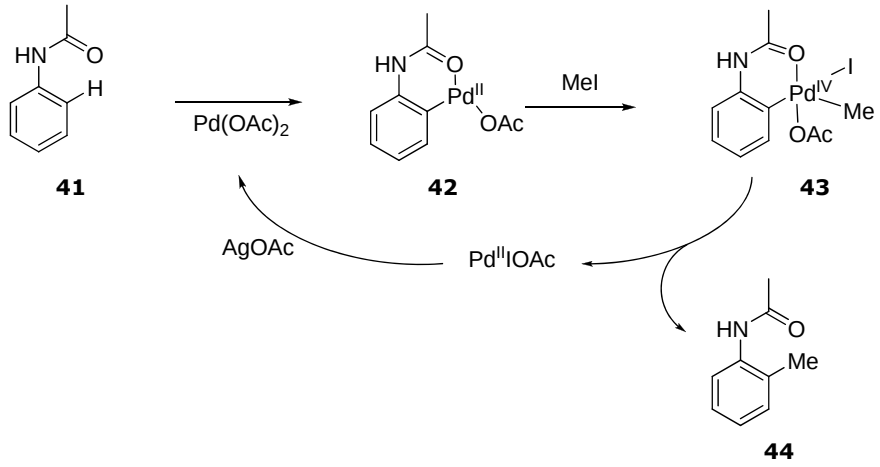


This reaction proved challenging to achieve at first; palladium(II) in general reacts more readily with organometallics than with unactivated arenes. Initial attempts at this process produced only homocoupled organometallic species, and the arene was isolated unchanged.[126] These issues were eventually resolved, and the oxidative coupling of arenes and organometallics became more useful.[126]

Pd(II)/Pd(IV) Catalytic Cycle

One of the earliest reports of a Pd(II)/Pd(IV) catalytic cycle was an *ortho*-alkylation reaction of acetanilide (Scheme 19).[127] The reaction began via directed activation of the *o*-C-H bond of acetanilide (**41**) to give Pd(II) species **42**. Following oxidative addition of iodomethane to give Pd(IV) complex **43**, the methylated acetanilide **44** was produced after reductive elimination, regenerating a Pd(II) iodide complex. The oxidative addition of iodomethane to Pd(II) to produce Pd(IV) has been confirmed separately by both Canty[128,129] and Sanford.[130-132] The Pd(II)/Pd(IV) cycle most commonly occurs in the presence of obvious oxidants, such as hypervalent iodine species like $[Ph_2I][BF_4]$[133] and $[Ph_2I][PF_6]$,[134] and many others.[135]

Scheme 19. Pd(II)/Pd(IV) catalysis for the *o*-methylamine of acetanilide.[127]

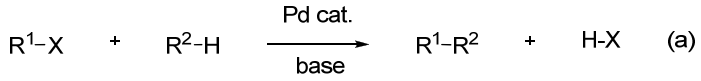


Despite the success of the reactions presented here, and included in the cited reviews, oxidative direct arylation is not nearly as efficient as standard cross-coupling reactions, particularly in regards to regioselectivity and/or the necessity for a directing group.[126] However, this field is still in its infancy and it is likely that this general process will become much broader in scope and more widely used.

1.2.3 Non-Oxidative Direct C-H Functionalization

Until regioselective oxidative direct arylations reactions become practical, the best compromise between accessibility and reactivity is found with direct C-H activation between a halide and an unactivated (usually) arene (Scheme 20). This reaction has probably had the greatest impact on bi(hetero)aryl synthesis to date.[117] A number of transition metals have been shown to be effective in promoting these reactions,[136] but this discussion will focus on the chemistry of palladium in these processes. A general overview of the topic may be found elsewhere.[137]

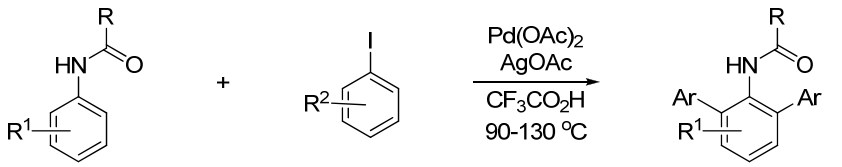
Scheme 20. Palladium-catalyzed direct C-H functionalization.



Organohalides are generally easily accessible and can be quite inexpensive; if they are not commercially available, the selective halogenation of arenes can often be achieved. Chlorides are by far the most economical, and great effort has gone into increasing the reactivity of these reagents because of that.[30] A number of reviews of direct arylation for the synthesis of (hetero)aryl-substituted (hetero)arenes have been published over the last three years.[117,138-142]

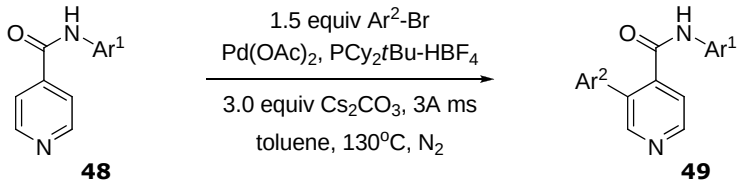
A very mild synthesis of arylated compounds **47** by intermolecular coupling of anilides **45** and iodoarenes **46** was reported recently (Scheme 21).[134] While it was possible the mechanism was proceeding via a Pd(II)/Pd(IV) catalytic cycle,[126] the authors could not rule out a Pd(0)/Pd(II) σ-bond metathesis (see section 1.2.3.1) mode of C-H activation. Yu has recently published a similar report on the amide-directed palladium-catalyzed arylation of isonicotinic acids **48** to give arylated compounds **49** from aryl bromides (Scheme 22).[143]

Scheme 21. Direct arylation of anilides with iodoarenes.[134]



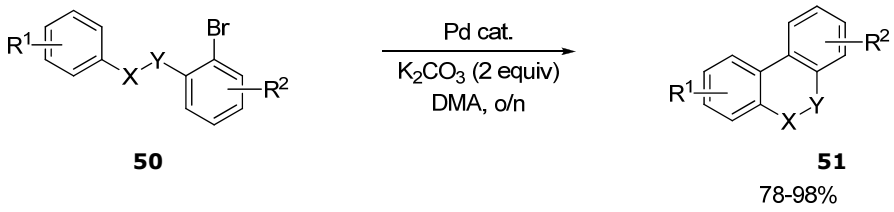
45 **46** **47**

Scheme 22. Regioselective, amide-directed palladium-catalyzed direct arylation of isonicotinic acids.[143]



Very useful intramolecular and intermolecular direct arylations have been published by Fagnou and coworkers. One of the earliest examples from this group reported the synthesis of oxygen and nitrogen heterocycles **51** as well as carbocycles from brominated diaryl ethers, amides and ethanes **50** (Scheme 23).[144] This general process has also been demonstrated to include the use of aryl chlorides,[145] extended to intermolecular processes,[146] and it has been used within the context of natural product synthesis.[147-149] The Fagnou group has also developed one-pot, double or triple palladium-catalyzed functionalizations that include a direct arylation.[150]

Scheme 23. Fagnou's preparation of heterocycles via direct arylation.[144]



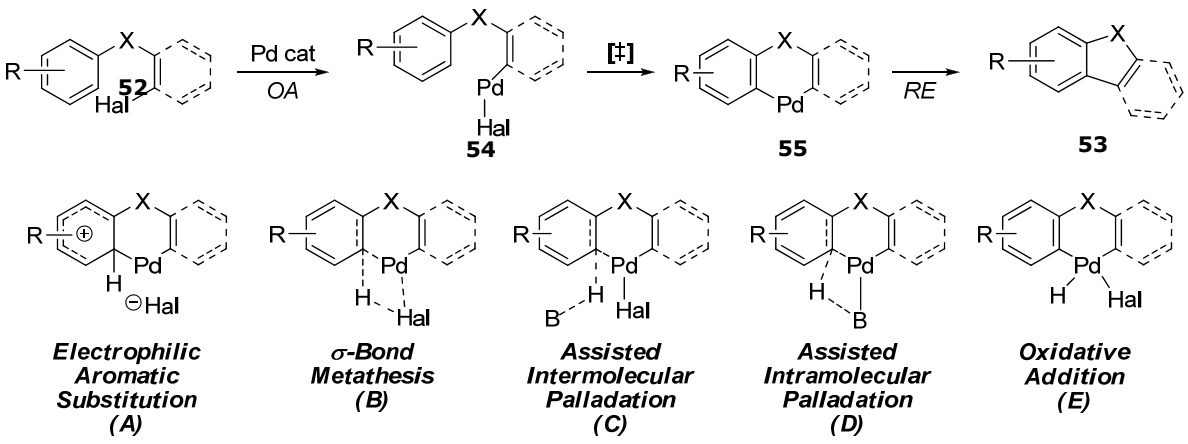
These are just the tip of the iceberg on the types of substrates accessible via direct arylation. For more examples, readers are encouraged to consult the reviews listed above. The rest of the section will focus on the mechanisms of these reactions.

1.2.3.1 Mechanisms

A few different mechanisms for C-H activation have been proposed and are summarized in Scheme 24.[138,151] For simplicity, the mechanism will be discussed in relation to intramolecular processes, though direct arylation itself is not limited in such a manner.

As in cross-coupling mechanisms, direct arylation begins via oxidative insertion of palladium into the carbon-halogen bond of the starting substrate **52**. The palladium(II) intermediate **54** undergoes intramolecular C-H activation to give palladacycle **55**, which, after reductive elimination yields the hetero- or carbocycle **53**. The discussion in this section will focus on the different mechanisms of C-H activation, or transition state(s) between **54** and **55**.

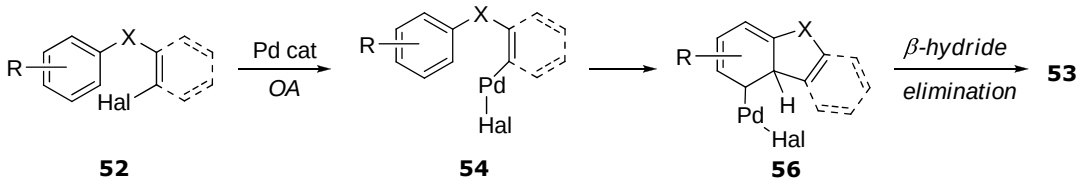
Scheme 24. Possible transition states for the intramolecular C-H functionalization.[138,151] Ligands are omitted for clarity.



There are five major postulated modes of C-H activation (Scheme 24),[138,151] namely electrophilic aromatic substitution (EAS, ***A***), σ-bond metathesis and the related assisted inter- and intramolecular palladation (***B***, ***C*** and ***D***, also referred to as concerted metalation-deprotonation, CMD) and oxidative addition (***E***). C-H activation processes

that occur via transition states ***A*** – ***D*** invoke a Pd(0)/Pd(II) catalytic cycle, whereas C-H activation via oxidative addition ***E*** requires a Pd(0)/Pd(II)/Pd(IV) cycle. In that case, intermediate **55** would have two additional anionic ligands not shown, and would thus be Pd(IV). Some groups have suggested a Heck-type mode of C-H activation proceeding through intermediate **56** (Scheme 25),[152-156] though this is no longer seriously considered as this is not a geometrically or electronically reasonable process.[157] The rest of this section will discuss EAS, σ-bond metathesis (where the assisted palladations ***C*** and ***D*** are included to keep the discussion clear) and oxidative addition in more detail.

Scheme 25. Heck-type C-H functionalization.



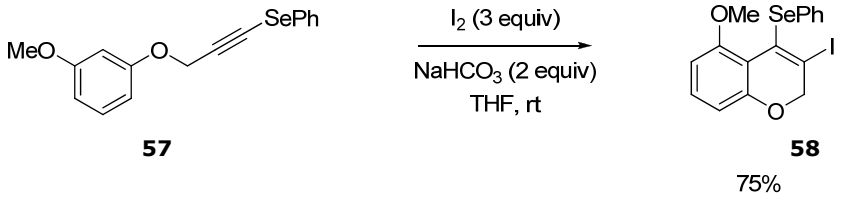
Electrophilic Aromatic Substitution

Electrophilic aromatic substitution is well understood outside of organopalladium chemistry, and the mechanistic rules that control such reactions are commonly known. A similar set of rules applies in palladium-catalyzed chemistry as well. To generalize, π-electron donating groups are *ortho*- and *para*- directors, and accelerate the rate of reaction of arenes with electrophiles. Such activators include, but are not limited to, alkyl groups, alkoxyl and hydroxyl groups, and amines. In contrast, electron-withdrawing groups, typified by the nitro group, cyano groups and esters, are *meta*-directors and may significantly retard the rate of EAS. Halogens behave differently; they are *ortho*- and *para*- directors like standard electron-donating groups, but slow the reaction similar to electron-withdrawing groups. Palladium-catalyzed EAS is subject to the same electronic effects.

As examples of regioselectivity in a non-palladium-catalyzed cyclization known to proceed via EAS, the unsymmetrically substituted **57** yielded a single isomer **58**, where

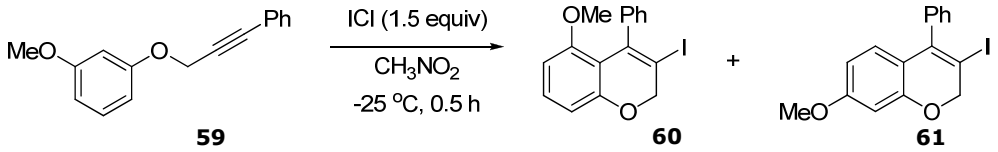
direct arylation occurred at C^2 (Scheme 26).[158] A similar electrophilic cyclization studied by Larock and coworkers gave a slightly different result. When the aryl propargylic ether **59** was treated with ICl in nitromethane, two regioisomeric benzopyrans were observed, with **60** predominating over **61** in a 3:2 ratio (Scheme 27).[159]

Scheme 26. Electrophilic cyclization of an aryl propargylic ether.[158]



57 **58** 75%

Scheme 27. Larock's synthesis of 2*H*-benzopyrans.[159]

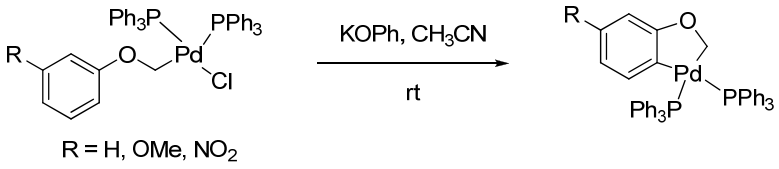


59 **60** 49% **61** 33%

Within the context of palladium-catalyzed direct arylation, Echavarren and coworkers have studied the formation of carbazoles and dibenzofurans from diarylamines and diarylethers extensively.[160-163] In a mechanistic study, they reported direct intramolecular arylation of palladated *m*-substituted phenols **62** (R=H, OMe, NO_2, Scheme 28).[160] While in all cases the 6-palladium complexes **63** were formed, the nitro-substituted phenol reacted the slowest, and the methoxy-substituted phenol reacted the fastest. Both additional triphenylphosphine ligand and a variety of bidentate ligands slowed the palladation. These observations, in combination with the absence of any detectable kinetic isotope effect, led to the conclusion that the intramolecular direct palladation was proceeding via EAS. In general , the combination of small KIEs with an increased observed rate in the presence of electron-donating substituents are good

support for an EAS mechanism.[164] Low KIEs alone are not sufficient evidence; for example, the C-H activation of dimethylbenzylamine with palladium acetate showed a small KIE and the original hypothesis was that an EAS mechanism was active.[165] However, a computational examination of the possible transition states demonstrated that a σ-bond metathesis-like pathway was much more likely.[166]

Scheme 28. Electrophilic aromatic substitution reactions to produce palladacycles.[160]



R = H, OMe, NO_2

62 **63**

σ-Bond Metathesis and Related Mechanisms

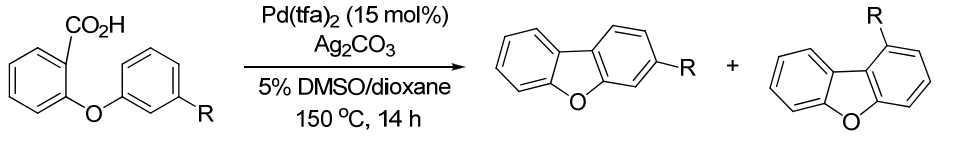
Fagnou and coworkers have published a series of papers on both the scope and mechanism of some intramolecular direct arylation reactions for the synthesis of heterocycles (as shown in Scheme 23).[144,146,150,167,168] In an initial examination of the cyclization of aryl benzyl ethers to heterocycles, both electron-rich and deficient arenes cyclized well, and when unsymmetrically substituted **66** cyclized (R=OMe), heterocycles **65** and **64** were formed in a 21:1 ratio (Scheme 29).[144] Later, a more detailed study was performed, in which compounds **66** with R = Me, *i*Pr, *t*Bu, CF_3, NO_2, CO_2Me, Cl and F were cyclized to the corresponding heterocycle under Pd/PCy_3 catalysis;[146] in all cases but one, isomer **65** was the major product, in ratios of 3.2:1.0 to >30:1. The only exception was the cyclization of a fluoro-substituted analogue (**66**, R = F). In this case, regioisomer **64** predominated in a ratio of 4.3:1.0. An intramolecular KIE of 4.25 was found in this reaction, and the authors concluded that these data were most consistent with a metathesis-like C-H activation, via one of transition states **B** – **D** (Scheme 24).

Scheme 29. Fagnou's synthesis of oxygenated heterocycles.[144]

66 **65** **64**

Glorius has reported an interesting decarboxylation-direct arylation process for the synthesis of dibenzofurans.[54] Part of the mechanism of this reaction was outlined in Scheme 7. Two examples of regioselective direct arylation were presented; when *m*-methyl substituted diarylether **67** was treated with palladium and silver, a 1.8:1.0 mixture of 3-methyl **68** and 1-methyl **69** was isolated (Scheme 30). When the *t*butyl analogue **70** was reacted under the same conditions, only 3-*t*butyl dibenzofuran **71** was isolated, indicating that steric effects can have a strong influence on the outcome of the reaction. Intermolecular competition experiments showed that a methoxy substituent could increase the rate of C-H functionalization, whereas a fluoro substituent retarded the rate. The KIE in this reaction was determined to be approximately equal to 4. An assisted intermolecular palladation (transition state **C**, Scheme 24) was proposed for the mechanism of C-H activation.

Scheme 30. Glorius's synthesis of dibenzofurans.[54]



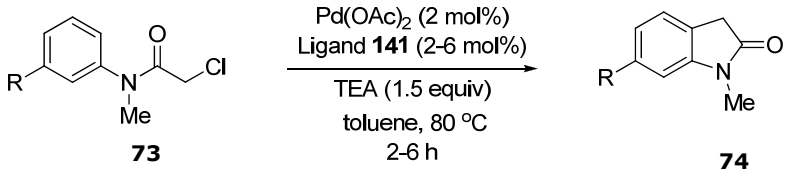
R=Me **67** 1.8 **68**: 1 **69**

R=*t*Bu **70** 100 **71**: 0 **72**

Hennessy and Buchwald have reported a synthesis of oxindoles **74** from *N*-acyl anilides **73** (Scheme 31).[153] In this reaction, both electron-poor and electron-rich anilides could easily react. In the unsymmetrical examples where R=Me, OTBS or CF_3,

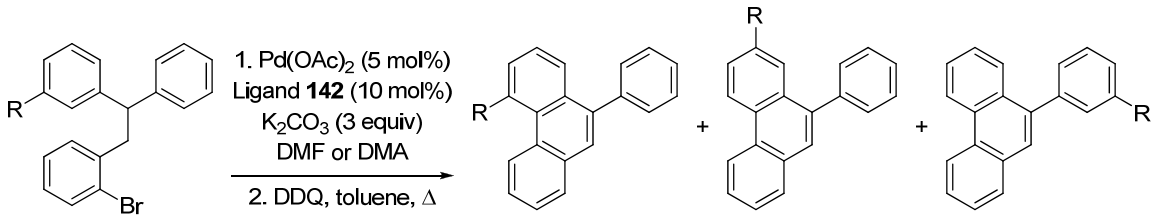
oxindole **74** was always formed in regioselectivities >14:1 over the other possible isomer (not shown). Interestingly, the intramolecular KIE was determined to be ~4 but no KIE was observed in the intermolecular case. It was concluded that σ-bond metathesis (transition state **B**, Scheme 24) was the likely mode of C-H activation, though other mechanisms could not be definitively ruled out.[153]

Scheme 31. Buchwald's synthesis of oxindoles.[153]



In studies on the syntheses of phenanthrenes **76** - **78** from triaryl ethanes **75** (Scheme 32), Echavarren and coworkers performed a series of intramolecular competition experiments.[161,162] When R=OMe (**75a**), the ratio of **76a**:**77a**:**78a** was observed to be 1.1:0.3:1.0; this means that the methoxy-substituted arene reacted faster than the unsubstituted arene, and in the methoxy-substituted arene, the more sterically encumbered position (*ortho* to OMe) reacted faster than the C-H *para* to the OMe group. When R=Cl in **75b**, the ratio of **76b**:**77b**:**78b** was 0.8:1.1:1.0. In this case, the substituted arene again reacted faster than the unsubstituted arene, but the less sterically hindered C-H bond on the Cl-substituted arene reacted in preference to the *ortho* C-H bond. The fact that both the OMe and Cl substituted arenes reacted faster than the unsubstituted arene is not surprising, as OMe and Cl are both σ-electron-withdrawing groups and π-electron-donating groups. The reason for the switch in regioselectivity is not obvious. The authors later examined the same reaction using Xantphos as a ligand for palladium[163] and found similar electronic effects. After performing a significant number of calculations to explore the C-H functionalization in detail,[161-163] they proposed an assisted proton abstraction mechanism (transition states **C** or **D**, Scheme 24).

Scheme 32. Echavarren's synthesis of phenanthrenes via intramolecular C-H activation.[161,162]



76a, R=OMe **77 a, R=OMe** **78a, R=OMe** **75 a, R=OMe**

76b, R=Cl **b, R=Cl** **b, R=Cl** **b, R=Cl**

Oxidative Addition (Pd(0)/Pd(II)/Pd(IV))

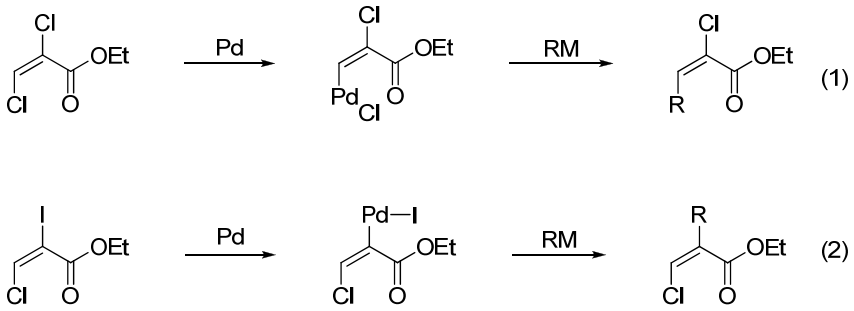
As stated above, when oxidative addition is the mode of C-H activation, this must proceed via a Pd(IV) intermediate. In some cases, this mode is simply not considered[151]. However, even in cases where a Pd(IV) pathway is a possibility, σ-bond metathesis cannot be definitively ruled out.[134,169] This pathway is much more likely in C-heteroatom bond formations, as discussed in section 1.2.2.1.

1.2.4 Site Selectivity

The synthesis of polysubstituted arenes, particularly heteroarenes, is very important. Heterocycles are ubiquitous in drug-like compounds and they show broad and varied biological activities.[170] Palladium-catalyzed functionalization of polyhalogenated heterocycles constitutes one of the most effective and common methods of preparing these compounds. As discussed above (section 1.2.1.1), the reactivity of carbon-halogen bonds toward palladium is usually in the order C-I > C-Br > C-Cl. As these bonds are chemically different, the selective functionalization of one over the other is referred to as chemoselective, and exploitation of the reactivity differences of the different halogens is a useful way to selectively functionalize heterocycles (or arenes) substituted with different halogens. The selectivity is generally attributed to the difference in rates of oxidative addition, and can be used to 'override' intrinsic reactivities. For example, in α,β-dihalo

unsaturated esters, the β-X bond is more reactive when the α and β positions are substituted with the same halogen (Scheme 33, equation 1). However, Ogilvie has demonstrated that a β-chloro-α-iodo unsaturated ester first reacts at the α-position as C-I is more reactive than C-Cl (Scheme 33, equation 2).[171-174] This chemistry is discussed in more detail in section 1.3.3 (Scheme 54).

Scheme 33. Generalized cross-coupling reactions of α,β-dichloro unsaturated ester and β-chloro-α-iodo unsaturated ester to give alternate products.



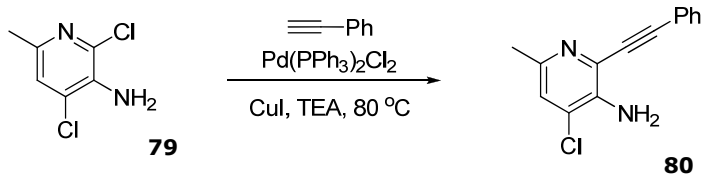
The selective functionalization of a carbon-halogen bond in the presence of another is referred to as site selective, though regioselective is sometimes used. Two reviews discussing such chemistry in heterocycle functionalization have been published.[175,176]

Heteroatoms are quite effective at directing reactivity in multiply halogenated compounds. In general, the most electron-poor site will react first, based on the faster oxidative insertion into such bonds. For example, alkynylation proceeded selectively at the 2-position when 2,4-dichloropyridine **79** was treated with phenylacetylene in the presence of palladium and copper (Scheme 34).[177] Compound **80** was the only product detected, and was isolated in excellent yield.

Some theoretical predictions of selectivity in polyhalogenated heterocycles have been done by Merlic, Houk and coworkers in order to better understand the mechanisms governing site selectivity.[178,179] Simple bond dissociation energies (BDEs) are insufficient,

as the BDEs of C^2-H and C^3-H of furan are identical, yet 2,3-dibromofuran is known to react solely at C^2 in the presence of palladium. The LUMO (π^*) of the heterocycle (related to frontier molecular orbital interactions) and the HOMO of Pd(0) also play a role in achieving selectivity. This clearly shows that additional substituents on the heterocycle can heavily influence selectivity, as well as the ligands on palladium, so far as they influence the HOMO of Pd, and that this is, in fact, a very complex process.

Scheme 34. Site selective, palladium-catalyzed alkynylation of a dichloropyridine.[177]



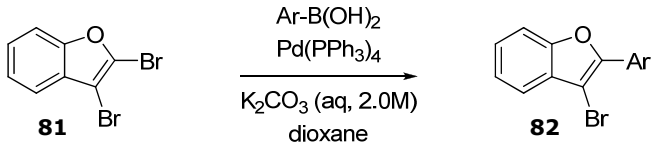
79 **80**

90%

A simple and very practical method for predicting selectivity has been rationalized via analysis of the ^{1}H chemical shifts of the corresponding hydrogenated starting materials.[180] In order to predict the site of first cross-coupling on a polyhalogenated heterocycle, the ^{1}H chemical shifts of the unhalogenated starting materials are measured. For example, in 2,3,5-tribromobenzofuran, it has been determined that the reactivity order towards palladium oxidative insertion is C^2-Br > C^5-Br > C^3-Br, or that C^2-Br will react first (Figure 6). This order of reactivity directly parallels the ^{1}H NMR chemical shifts of the parent benzofuran; H^2 is the most downfield, followed by H^5 and then H^3, in a sense quantifying the electron-deficiency of those C-H bonds. For example, when 2,3-dibromobenzofuran **81** is reacted with aryl boronic acids in the presence of palladium, 2-aryl benzofurans **82** are produced selectively (Scheme 35).[176,181-183]

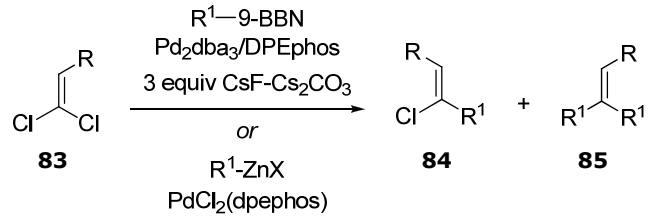
Figure 6. ^{1}H chemical shifts to predict reactivity order of polybrominated benzofuran.[180]

Scheme 35. Site selective cross-coupling of 2,3-dibromobenzofuran.[176,181-183]



The site selective functionalization of polyhalogenated alkenes has also been fairly extensively examined.[184] The selective monofunctionalization of 1,1-dichloroalkenes (accessible from aldehydes and $CHCl_3$[185] or CCl_4[186]) has been looked at by Minato and Tamao,[187] and more recently by both Negishi[188] and Roulland[189] (Scheme 36). When dichloroalkene **83** were treated with an organozinc, mixtures of (*Z*)-alkene **84** and doubly functionalized alkene **85** were observed using a Pd/DPEphos catalytic system.[188] Ratios ranged from 1:1 to 30:1 in favour of **84**, depending on the substrates. In contrast, using an alkyl-9-BBN derivative, the Pd/DPEphos system gave nearly exclusively (*Z*)-monofunctionalized alkene **84**.[189] It should be noted that Roulland found that using Xantphos in place of DPEphos (**12**) gave similar selectivities but higher isolated yields.

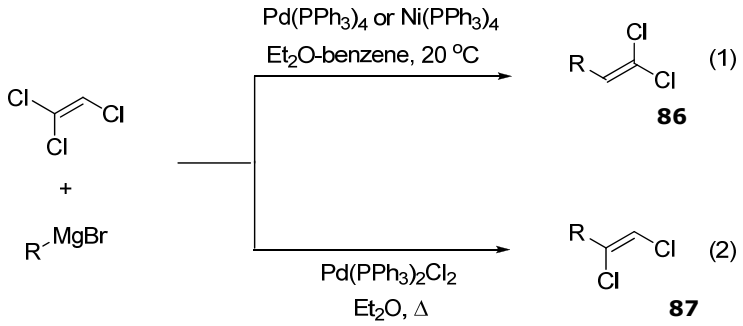
Scheme 36. DPEphos in the selective monofunctionalization of 1,1-dichloroalkenes.



The regioselective functionalization of 1,2-dihaloalkenes has been less explored,[184] likely because they are more difficult to prepare. Most examples of regioselective monofunctionalization of 1,2-dihaloalkenes via cross-coupling occur on α,β-unsaturated esters,[184,190-195] with a few exceptions.[196-199] These reactions often proceed through elimination.[196,200-202]

Palladium-catalyzed cross-coupling with trihalogenated alkenes is typified by reactions involving TCE. Interestingly, different results have been reported by two different groups when the cross-coupling between TCE and Grignard reagents were performed under very similar conditions (Scheme 37). Normant[203] reported the selective synthesis of 1,1-dichloroalkenes **86** from TCE and Grignard reagents (Scheme 37, equation 1) whereas Minato[187] reported 1,2-alkenes **87** as the major products (Scheme 37, equation 2). Attempts in our laboratory to develop a selective monofunctionalization of TCE using boronic acid nucleophiles have been unsuccessful so far.[204]

Scheme 37. Palladium-catalyzed cross-coupling between TCE and Grignard reagents.



1.2.5 Summary

Palladium-catalyzed functionalization of (poly)halogenated substrates has revolutionalized organic synthesis over the last 30 years. As has been discussed, this process is very general in terms of organometallic nucleophiles that may be used, as well as organic electrophiles. While cross-coupling reactions (1.2.1) have historically dominated this

field, direct functionalizations (sections 1.2.2 and 1.2.3) are now practical in many cases, greatly simplifying and reducing the cost of small organic molecule synthesis.

1.3 Synthesis of Alkenes

1.3.1 Introduction

Tri- and tetrasubstituted alkenes are ubiquitous in organic chemistry, and are found in many biologically active compounds, such as ratjadone (**88**)[205,206] and (*Z*)-tamoxifen (**89**) (Figure 7).[207] Tamoxifen is one of the most important drugs in clinical use for treating breast cancer.

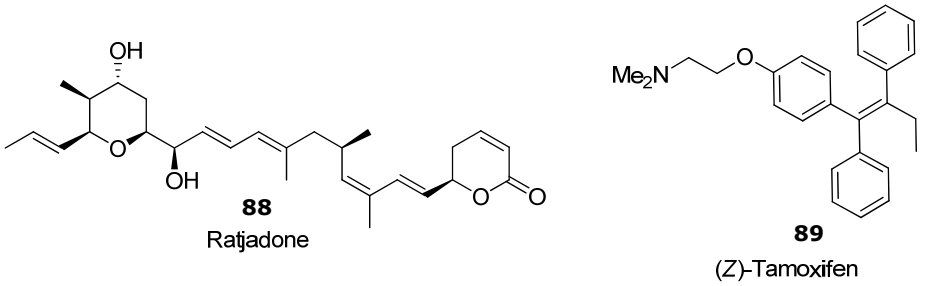


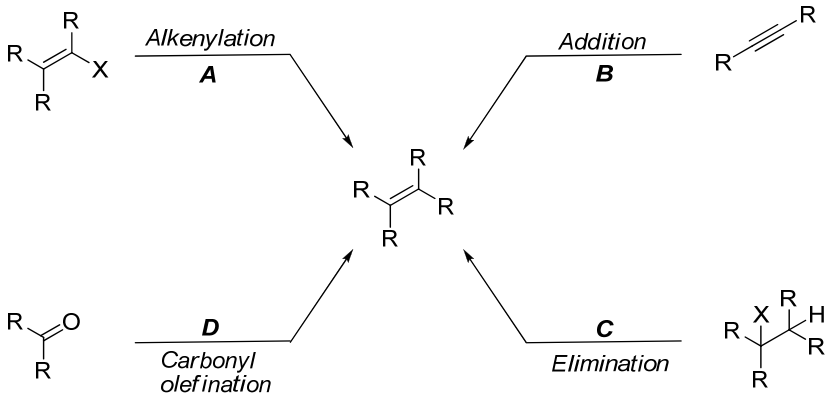
Figure 7. The structures of Ratjadone and (Z)-Tamoxifen.

A significant amount of research has gone into developing syntheses of tri- and tetrasubstituted alkenes,[208-212] but it still remains a challenge to synthesize these compounds isomerically pure with four different substituents, and, as is important in drug discovery, with diverse functionality; most synthetic methods have some intrinsic structural limitation.

A summary of the routes to synthesize alkenes is shown in Scheme 38. Alkenylation and addition (***A*** and ***B***) are typically mediated by transition metals, whereas carbonyl olefination and elimination (***C*** and ***D***) typify the more traditional syntheses. There are different methods for the synthesis of trisubstituted alkenes[188,213-237] versus tetrasubstituted alkenes,[238-243] but there are fewer synthetic methods capable of

generating both tri- and tetrasubstituted alkenes.[244-249] Unsurprisingly, the synthesis of tetrasubstituted alkenes is typified by the synthesis of tamoxifen, **89**.[196,249-255] A description of some of these syntheses will be presented in the following sections.

Scheme 38. General synthetic routes to alkenes. Adapted from reference 212.



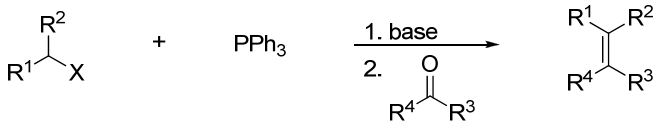
1.3.2 Traditional Methods

This section will describe the more 'traditional' methods of alkene synthesis, via non-metal catalyzed preparation (see 1.3.3 for a discussion of those methods). While many of these reactions have been known for some time, more recent applications or developments will be highlighted where possible with a discussion on the advantages/disadvantages associated with them. This section will be brief, as the main focus of this thesis is development of metal-catalyzed methods.

Perhaps the best-known method for the synthesis of alkenes is the Wittig reaction, and variations of it (a variant of equation ***D*** in Scheme 38). Generalized in Scheme 39, the net reaction is between an alkyl halide and a ketone, as mediated by triphenylphosphine. Though the Wittig reaction historically was one of the most common method for synthesizing alkenes (and continues to be widely used today), the reaction suffers from several drawbacks. In simple cases, where R^1 and R^2 are alkyl groups, the major product will be the *Z*-alkene. If one of R^1 or R^2 is an electron-withdrawing group

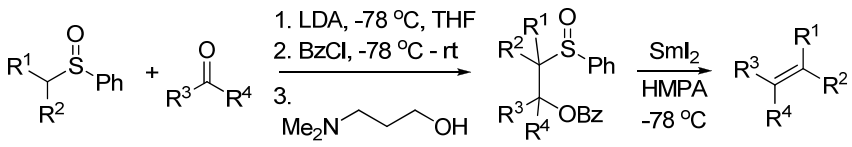
(the Wittig-Horner or Horner-Wadsworth-Emmons modification), the *E*-isomer will predominate. While a ketone has been drawn as the carbonyl component, this reaction is most successful with aldehydes, and gives mediocre results at best with ketones. Esters cannot be used in this capacity. Because of these, the Wittig is really only practical for disubstituted alkenes, and in some cases, trisubstituted alkenes.

Scheme 39. The Wittig reaction, and the synthesis of *E*- and *Z*-alkenes.



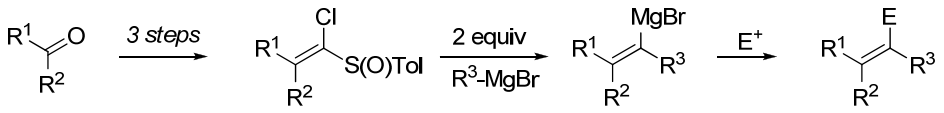
Markó and coworkers have demonstrated the use of sulfoxides in a Julia-Lythgoe olefination (Scheme 40).[215] Disubstituted alkenes were isolated in ~70% yields, and the *E*/*Z* selectivities were generally >94:6. Trisubstituted alkenes could also be synthesized, though isolated yields of the products were somewhat lower and selectivities were much lower (2:1 – 3:1, with one example of 10:1). The reactions to produce tetrasubstituted alkenes were low yielding, though the *E*/*Z* selectivities were good. This is a nice method in that all of di-, tri- and tetrasubstituted alkenes could be synthesized via a trivial modification of the starting materials though this was not always straightforward. More importantly, the reaction is not stereospecific; though in many cases sufficient selectivity was observed, the reaction is not mechanistically constrained to produce a single stereoisomer. In addition to the variable stereoselectivity, the yields were highly substrate dependent.

Scheme 40. Multisubstituted alkenes via a Julia-Lythgoe olefination from sulfoxides and carbonyls.[215]



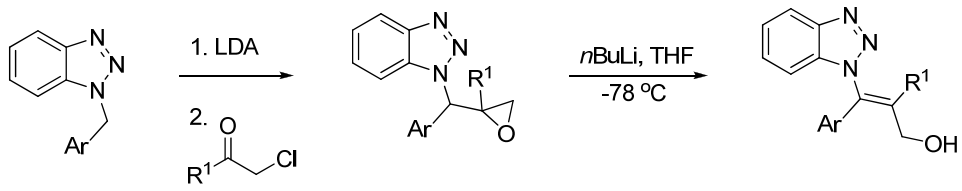
Satoh et al. published a route to tri- and tetrasubstituted alkenes, also derived from carbonyl compounds (Scheme 41).[219] The yields of the alkenes from the final step were generally good, 58-80%, but in cases where $R^1 \neq R^2$, *E*/*Z* ratios were low. Additionally, the sulfoxide required three steps from the carbonyl, greatly detracting from the efficiency of the process.

Scheme 41. Tri- and tetrasubstituted alkenes from carbonyl compounds and Grignard reagents.[219]



Kim and Park have published a route to benzotriazole-substituted allylic alcohols (Scheme 42).[238,256] A variety of aryl groups on the benzotriazole could be tolerated, though the R^1 of the donor carbonyl compound could only be a *tert*-alkyl or an aryl moiety. The resulting tetrasubstituted alkenes were isolated in modest yields (40-80%), with *E*/*Z* selectivities ranging from 1:1 to nearly sole formation of the *Z*-isomer. The benzotriazole derivative is easily accessed in one step from benzotriazole, and the α-chloroketone requires synthesis.

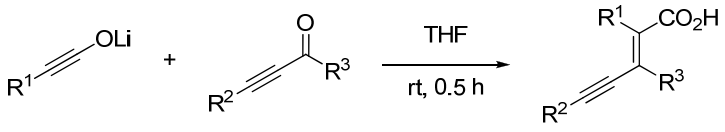
Scheme 42. Benzotriazole-substituted allylic alcohols.[238,256]



Shindo and coworkers have reported a very nice synthesis of enyne carboxylic acids (Scheme 43).[239] In this example, the tetrasubstituted alkenes were isolated in generally good yields, and with excellent *Z*/*E* ratios (except where R^3 = Ph, where the

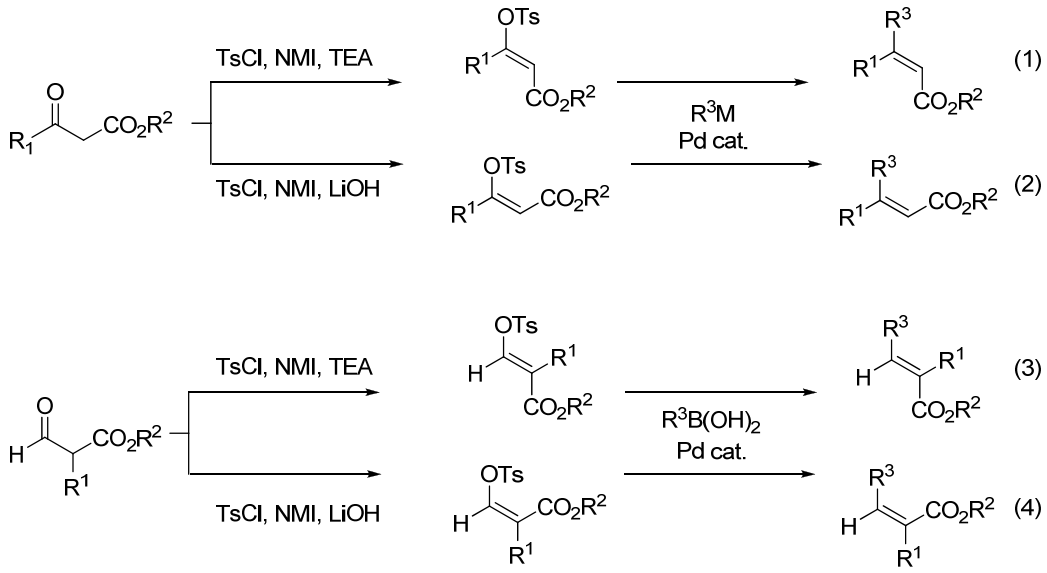
ratio was 1:1 or 3:1), though the examination of the scope of the reaction was not thorough. This is a useful method for the synthesis of these compounds, save for the need of synthesis of the starting materials. Ynolates may be prepared via treatment of 2,2-dibromoethyl ester with *t*BuLi; alkynyl ketones were prepared here in a two step procedure from a terminal alkyne and an aldehyde. Shindo et al. have also published several variations of this reaction.[257-262]

Scheme 43. Tetrasubstituted alkenes via addition of ynolates to alkynyl ketones.[239]



Tanabe and coworkers published papers on the selective synthesis of α,β-unsaturated esters from β-carbonyl esters (Scheme 44).[245,246] This general process is very modular; starting from a ketone derivative gives β,β-disubstituted-α,β-unsaturated esters (Scheme 44, equations 1 and 2), whereas starting from an aldehyde yields α,β-disubstituted-α,β-unsaturated esters (Scheme 44, equations 3 and 4). Moreover, the stereoselectivity in each route is controlled via the choice of base. The vinyl tosylates were generally formed in good yields and excellent stereoselectivity. The final substituent is installed via palladium-catalyzed cross-coupling of the resulting vinyl tosylate, which generally proceeded smoothly. The major drawback to this method is the required synthesis of the starting carbonyl compounds, though this was straightforward and usually high yielding.

Scheme 44. Selective syntheses of substituted α,β-unsaturated esters from β-carbonyl esters.[245,246]



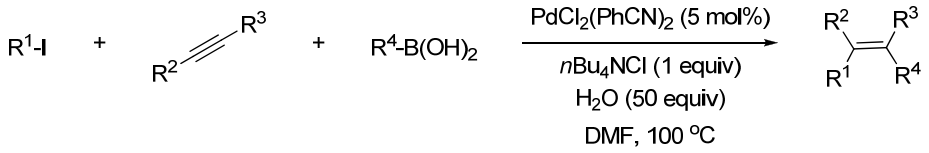
1.3.3 Metal Catalyzed Methods

This section will focus on the use of metal-mediated reactions in the synthesis of multisubstituted alkenes, particularly those that feature a palladium-catalyzed reaction. This is usually via functionalization of pre-existing alkenes, which distinguishes this type of process from the more traditional routes discussed above that generally construct the alkene.

Additions of organometallic nucleophiles across alkynes (Scheme 38, equation ***B***) have been studied by many different groups under many different conditions. Larock published a useful synthesis of alkenes, dienes and trienes via palladium-catalyzed addition of iodides and boronic acids across alkynes (Scheme 45).[252,263,264] The iodide and the boronic acid could be either aryl- or alkenyl-derived, and thus the product could be selected to be an alkene, diene or triene via simple choice of starting materials. Alkynes with sterically or electronically different R^2 and R^3 groups or symmetrical alkynes were used in this transformation to either favour regioselective addition of across the

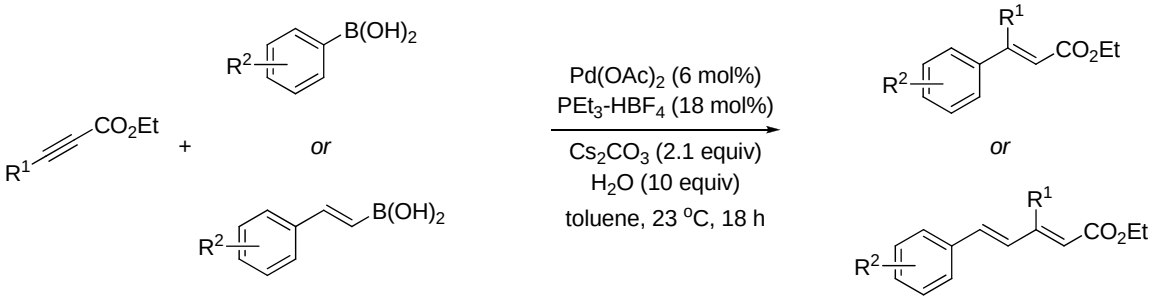
alkyne, or to avoid regioselectivity issues altogether. Good yields and selectivities were observed in the product alkenes.

Scheme 45. Tetrasubstituted alkenes from iodides, alkynes and boronic acids.[252,263,264]



Ogilvie has published a palladium-catalyzed conjugate addition of boronic acids to alkynyl esters to give trisubstituted alkenes (Scheme 46).[222] In optimization reactions, it was found that if PEt_3 was replaced with other ligands such as P*t*Bu_3, significant amounts of the α-aryl isomer formed in competition with the observed β-aryl ester. The yields of the unsaturated esters were moderate, and ranged from 50-85%. A terminal alkynyl ester was not a good substrate for this reaction, and the corresponding product was isolated in only 10% yield. Boronic esters were unreactive nucleophiles. Acetylenic sulfones have also been shown to undergo a similar reaction with organozinc reagents as catalyzed by copper.[248]

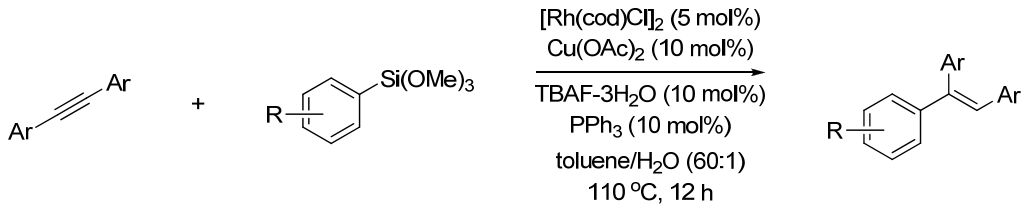
Scheme 46. Palladium-catalyzed conjugate addition of boronic acid to alkynyl esters.[222]



Cheng has studied the rhodium-catalyzed addition of aryl trimethoxysilanes to symmetrical alkynes (Scheme 47).[228] The trisubstituted alkenes were isolated in 50-90%

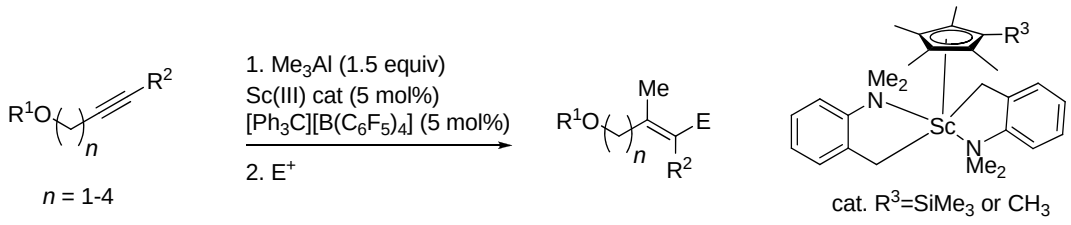
yields, though hindered silanes could not be used as nucleophiles in this reaction. The role of copper in this reaction was unclear but copper was definitely required as very little trisubstituted alkene could be obtained in its absence.

Scheme 47. Rhodium-catalyzed addition of trimethoxysilanes to symmetrical alkynes.[228]



In another example of this basic reaction pathway, Hou and coworkers examined a scandium(III)-catalyzed methylalumination of alkynes (Scheme 48).[240] A variety of oxygen-tethered alkynes could be used in this process, though the scope of the electrophile was limited to formaldehyde, allyl bromide, or iodide. Additionally, the intermediate organoaluminate (not shown) could be reacted with iodobenzene in the presence of $ZnCl_2$ and $Pd(PPh_3)_4$ in a Negishi reaction. This is indeed a useful reaction, and high regioselectivities were observed with unsymmetrical alkynes, but at the cost of requiring a directing group. The alkenes were isolated in excellent yields, from 70% to greater than 90%.

Scheme 48. Oxygen-directed, scandium-catalyzed methylalumination of alkynes.[240]

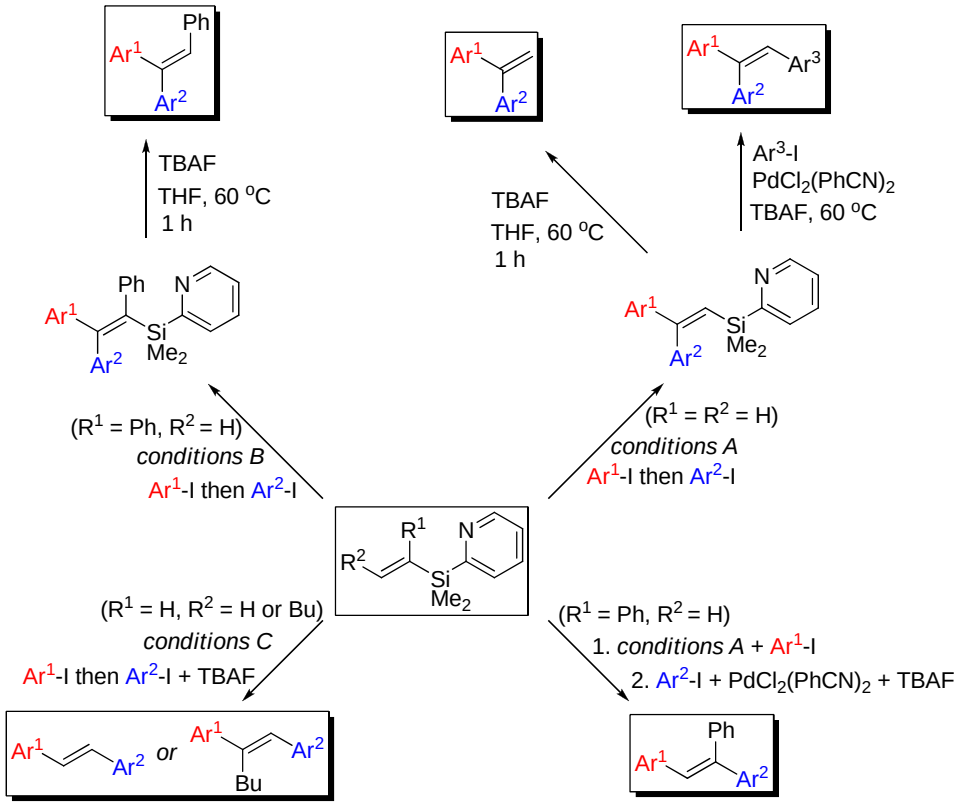


Yoshida and coworkers reported an efficient and modular route to multisubstituted alkenes using a pyridine-substituted vinyl silane as a template (Scheme 49).[265] Variations of Heck coupling, Hiyama coupling and protodesilylations produced a multitude

of diaryl ethylenes and triaryl ethylenes. The pyridine was able to direct the Heck couplings, and the silane was able to act either as a nucleophile in cross-couplings in the presence of a fluoride ion or as a traceless directing group, as it could be replaced with a hydrogen atom following the palladium-catalyzed couplings.

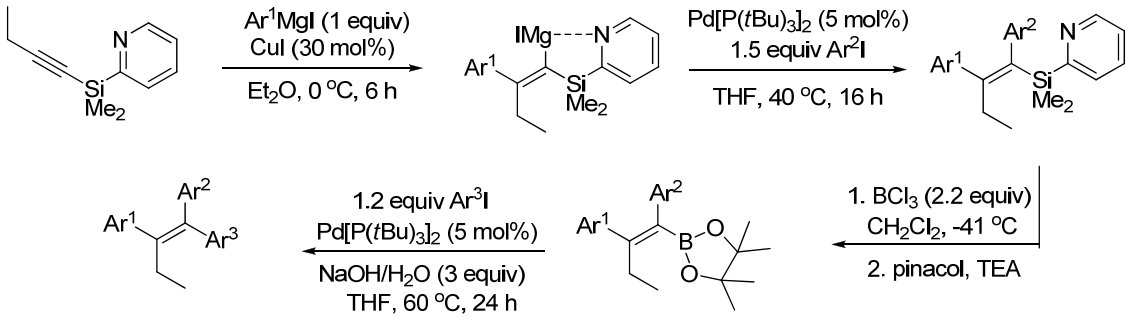
The basic idea was applied to a modular assembly of tamoxifen (**89**) and analogues thereof (Scheme 50).[251] The optimized route as described below worked well for a variety of aryl groups in all of the 1, 2 and 3 positions. The starting material required two synthetic steps from commercially available materials, and thus this route required a total of six steps, though it should be noted that the first two steps in Scheme 50 can be done in one pot. The major drawback was the unfortunate inability of the tetrasubstituted silane to participate efficiently in cross-couplings to complete the synthesis, thus a transmetallation to the vinyl boronic ester was required. As in Scheme 49, the regio- and stereochemistry of the alkene was established via chelate-controlled copper-catalyzed organomagnesium addition across the alkynyl silane as the first step.

Scheme 49. Di- and trisubstituted alkenes from vinyl silanes.[265]



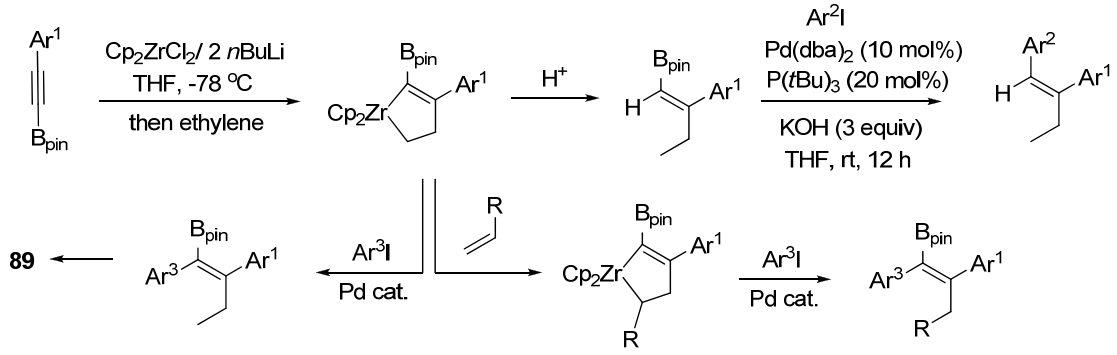
conditions A: Pd_2dba_3 (2.5 mol%), TFP (5 mol%), TEA, MS 4A, THF. 60 °C
conditions B: Pd_2dba_3 (2.5 mol%), $P(OPh)_3$ (10 mol%), DIPEA, MS 4A, THF. 60 °C
conditions C: $Pd(OAc)_2$ (10 mol%), TFP (10 mol%), TEA, THF. 60 °C

Scheme 50. Synthesis of Tamoxifen (**89**) and analogues.[251]



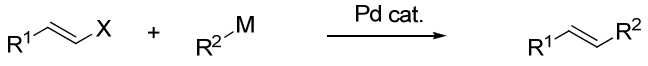
Nishihara and coworkers recently published a similar route to tri- and tetrasubstituted alkenes from alkynyl pinacolato boronates via zirconation and sequential cross-coupling reactions (Scheme 51).[253] A wide array of alkenes are easily accessible via only simple modifications of the general method.

Scheme 51. Tamoxifen and analogues synthesized from 1-alkynylboronates.[253]



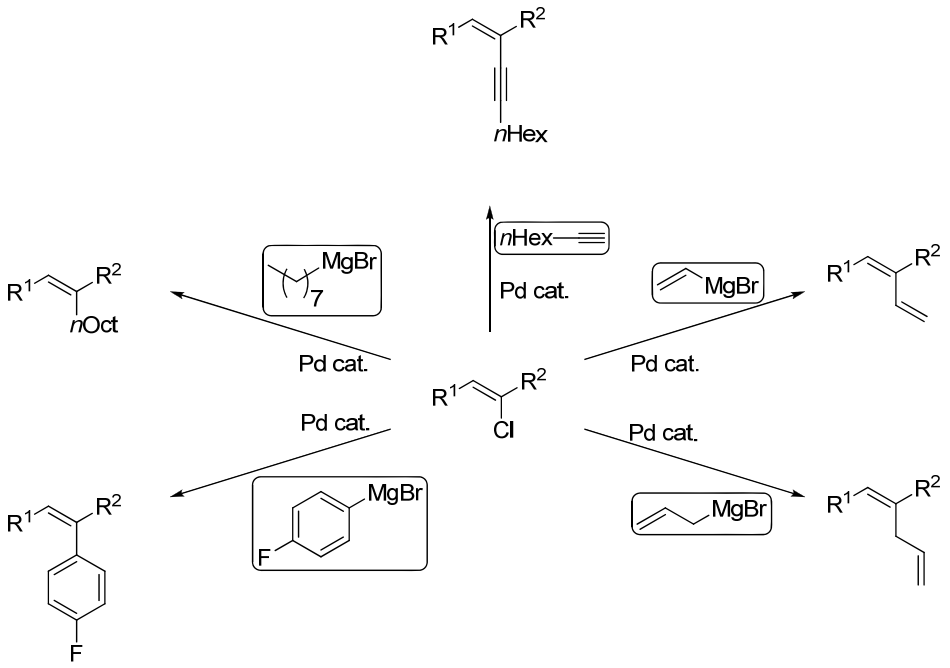
The most widely used synthesis of alkenes by far is the palladium-catalyzed functionalization of haloalkenes (Scheme 52).[243,248,266-270] Any of the methods discussed in section 1.2.1 can be used for this basic transformation. The only requirements are a suitable organic electrophile, some organometallic nucleophile and an efficient catalyst; while this sounds trivial, finding an 'efficient catalyst' can be challenging. Most reactions utilizing vinyl halides as electrophiles are favorable processes,[11] so this will not be discussed in detail here due to the enormous number of examples in the literature. Some discussion on the selective functionalization of polyhalogenated alkenes has been presented in section 1.2.4.

Scheme 52. Generalized palladium-catalyzed functionalization of haloalkenes.



For example, Negishi has reported the functionalization of chloroalkenenes.[188] This paper reported the successful cross-coupling reactions of chloroalkenes with a variety of organomagnesium and organozinc reagents, as well as terminal alkynes. Though several different palladium catalysts were required, alkyl, alkenyl, aryl and alkynyl groups could be incorporated to give a variety of functionalized alkenes, dienes, enynes and styrenes (Scheme 53).

Scheme 53. Negishi's palladium-catalyzed functionalization of chloroalkenes.[188]

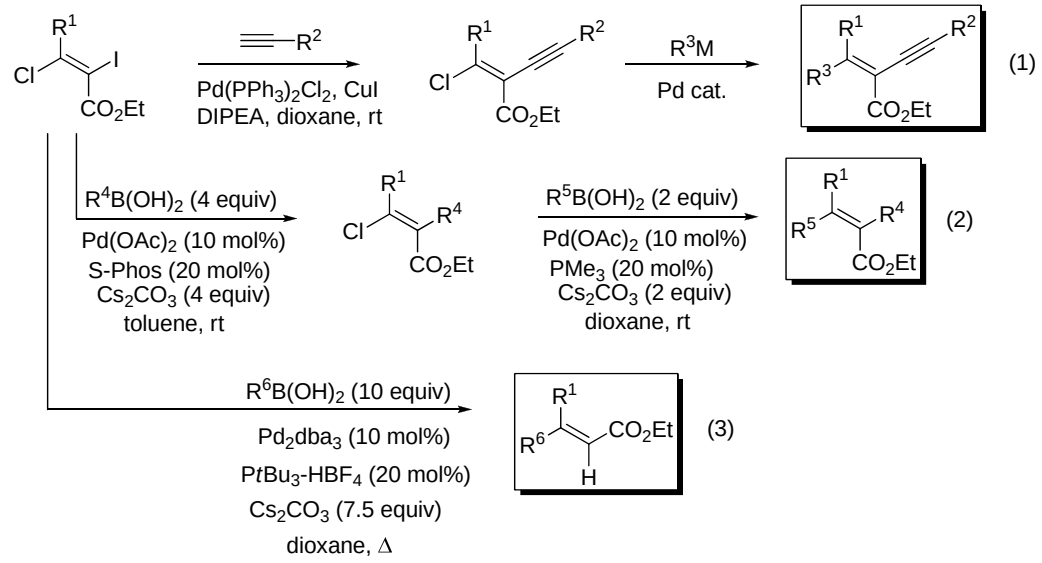


A very useful example of the selective synthesis of multisubstituted alkenes was published in a series of papers from Ogilvie and coworkers, where they have been developing stepwise functionalizations of α,β-dihalo-α,β-unsaturated esters to synthesize either tri- or tetrasubstituted alkenes (Scheme 54).[171,173,174] For example, Sonogashira coupling followed by a second cross-coupling synthesized enynes in good yields (Scheme 54, equation 1). Two sequential Suzuki couplings yielded tetrasubstituted alkenes (Scheme 54, equation 2). Interestingly, the product of the first Suzuki coupling depended on the conditions employed. When the β-chloro-α-iodo-α,β-unsaturated ester

was treated with a different set of cross-coupling conditions in the presence of a boronic acid yielded an interesting isomerized trisubstituted alkene (Scheme 54, equation 3).

The starting β-chloro-α-iodo-α,β-unsaturated esters are easily accessible in one step from alkynyl esters. Different reaction conditions were required for each palladium-catalyzed step, making the overall synthesis not amenable to one-pot routes.

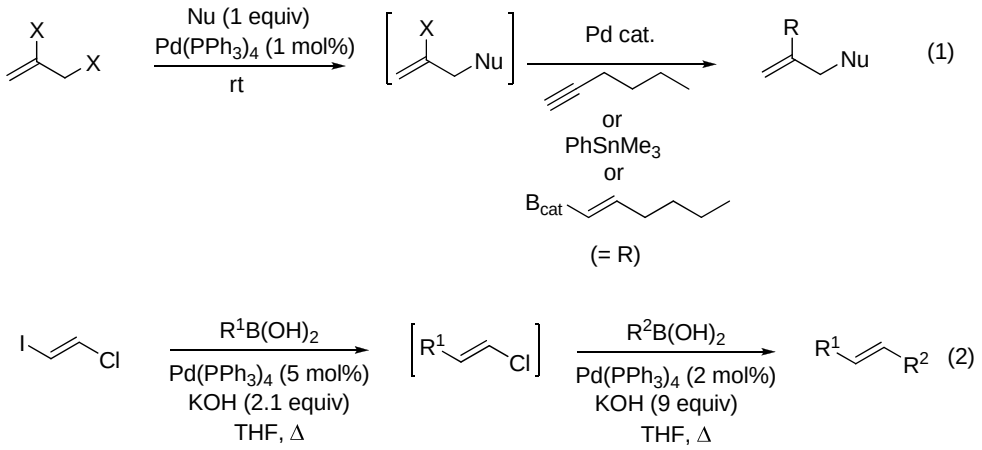
Scheme 54. Tri- and tetrasubstituted alkenes from β-chloro-α-iodo-α,β-unsaturated esters.[171,173,174]



The stepwise functionalization of simple starting materials to complex targets in a minimal number of discrete synthetic manipulations and/or purifications is a general goal. For example, while it is useful to selectively functionalize one carbon-halogen bond in a dihaloalkene, it would obviously be more efficient to selectively functionalize *each* C-X bond in one pot, provided, of course, that the vinyl halide is not the target. To this end, Organ and coworkers have been developing one-pot, stepwise functionalizations of doubly activated substrates. In an early paper, the stepwise functionalization of 2,3-dibromo- or 2,3-dichloropropene, and (*E*)-2-chloro-1-iodoethene via palladium-catalyzed chemistry was reported (Scheme 55).[271] The intermediates could be isolated if desired.

The uses of these 'olefin templates', as well as others, were explored in other related chemistries.[272-277] The isolated yields of the products were generally very good, and certainly point in the direct of an 'ideal' synthesis of complex molecules from simple and inexpensive building blocks.

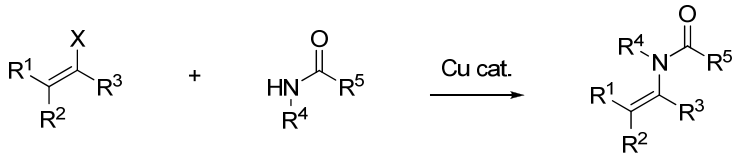
Scheme 55. Organ's stepwise palladium-catalyzed functionalizations of doubly activated substrates.[271]



Electron-Rich Alkenes (vinyl amines and amides, and enol ethers)

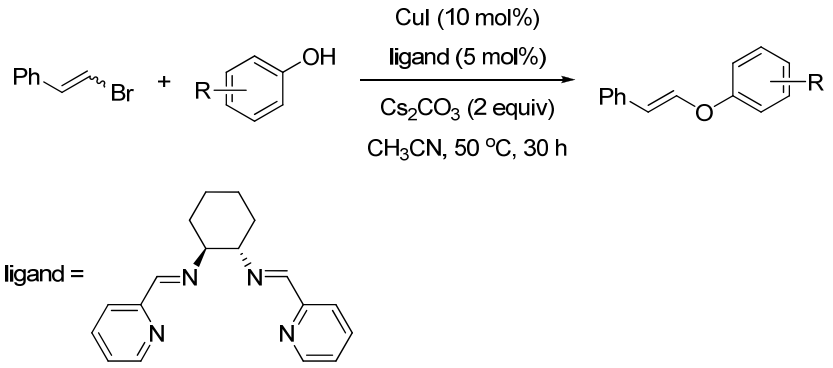
There has been far less work on the metal-catalyzed synthesis of heteroatom-substituted alkenes (electron-rich alkenes) as compared to the fully carbon-functionalized alkenes above.[208] The syntheses of vinyl amides have been reported more frequently than vinyl ethers, and these compounds are generally prepared via copper-catalyzed cross-coupling of amides with vinyl halides (Scheme 56.)[278-285] or potassium alkenyltrifluoroborate salts.[286]

Scheme 56. General route to the synthesis of vinyl amides.



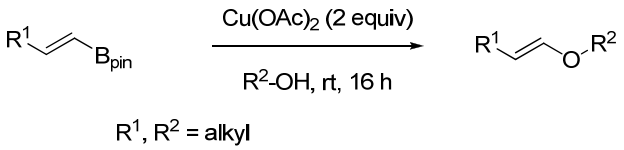
Analogous syntheses of vinyl ethers have been reported. For example, Taillefer reported the coupling of β-bromostyrene with phenols to give aryl vinyl ethers in 74-90% yields (Scheme 57).[287] Bao and Lv developed the same reaction with a β-keto ester as a ligand, and the aryl vinyl ethers were isolated in 79-95% yields.[288] While this reaction was highly successful with *trans*-β-bromostyrene, *cis*-β-bromostyrene could not be used as a substrate.

Scheme 57. Coupling of phenols with vinyl bromides to give vinyl ethers.[287]



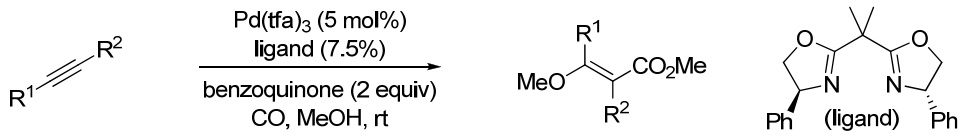
Recently, Merlic has reported an alternate route to vinyl ethers (Scheme 58).[289] Other than the need to prepare the vinyl boronate, this method is highly modular, efficient and provides rapid access to simple dialkyl vinyl ethers as well as allyl vinyl ethers, most often used as substrates in Cope rearrangements and very difficult to access otherwise. However, this basic process relies on hydroboration for the synthesis of the vinyl boronate, the overall synthesis of vinyl ethers using this reaction suffers from the same limitations that hydroboration does.

Scheme 58. Copper-mediated coupling of vinyl boronates and aliphatic alcohols to give vinyl ethers.[289]



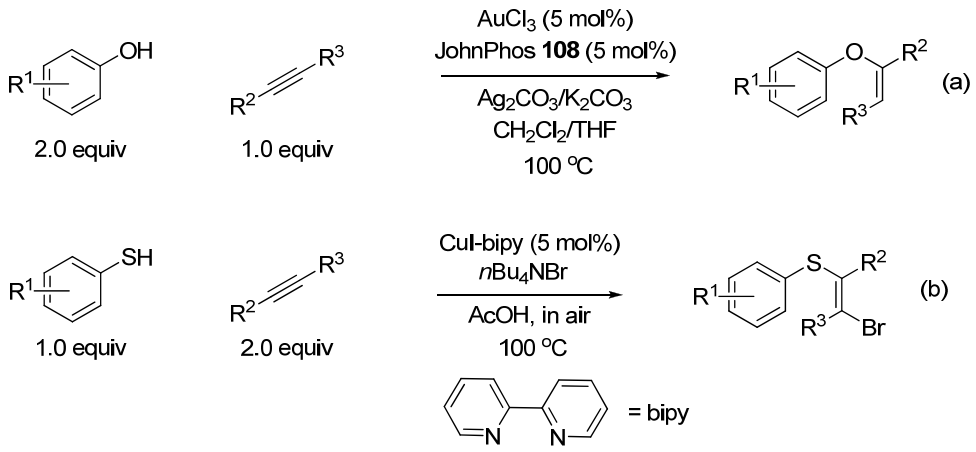
An interesting and useful route to tri- and tetrasubstituted, push-pull alkenes was published recently by Kato, Akita and coworkers (Scheme 59).[290] The process was quite general for terminal alkynes (R^2 = H), though good regioselectivity with internal alkynes could only be achieved when R^2 = CO_2Et. This basic β-methoxy-α,β-unsaturated ester substructure is found in numerous natural products, and this method is an excellent way to prepare them.

Scheme 59. Tri- and tetrasubstituted alkenes from alkynes, carbon monoxide and methanol.[290]



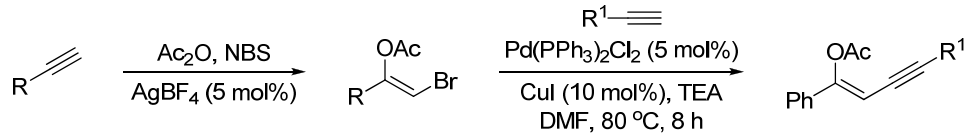
1,2-Disubstituted aryl vinyl ethers[291] and sulfides[292] are very useful compounds and have been synthesized via gold-catalyzed addition of phenol (Scheme 60, equation a) or copper-catalyzed addition of thiophenol (Scheme 60, equation b) across an internal alkyne. These reactions are generally high yielding and are only a single step from commercially available materials. However, regioselectivities were poor and highly substrate-dependent in examples using unsymmetrical alkynes, and therefore this general reaction has limited synthetic practicality. The methods described here collectively complement the published procedures for the synthesis of trisubstituted unsaturated esters.[245,246]

Scheme 60. Examples of phenol and thiophenol additions across triple bonds.



A similar approach to the synthesis of enol esters has been recently reported by Jiang et al.[293] The synthesis of the β-halo enol esters was generally performed from aryl acetylenes and NBS (Scheme 61), but aliphatic alkynes could also be used. NIS or NCS could replace NBS to synthesize the corresponding iodo- and chloroenol esters. The authors emphasized the importance and usefulness of these compound types, and performed two examples of cross-coupling reactions on the resulting vinyl bromide to give electron-rich enynes in good yields.

Scheme 61. The synthesis of β-bromo enol esters and their use in a Sonogashira reaction.[293]



1.3.4 Summary

Alkenes, electron-rich alkenes[224,294-300] and dienes[301-309] (vinyl ethers in particular) have many uses as substrates in organic synthesis, and thus their preparation is critical.

They are often made from enolizable aldehydes or ketones, and are thus non-trivial to prepare with a wide variety of functionality and/or stereoselectively, which presents a limitation on those routes for their synthesis.

1.4 Synthesis of Benzofurans

1.4.1 Introduction

Heterocycles form the core of many biologically active materials. Because of this, many different heterocycles are referred to as 'privileged', where a privileged structure is a structural type that binds to many unrelated protein receptors with high affinity.[310] At first the term was used to describe benzodiazepines and benzazepines, but has now expanded to include indoles[311] and the benzofuran nucleus is now considered to be privileged (Figure 8).[312]

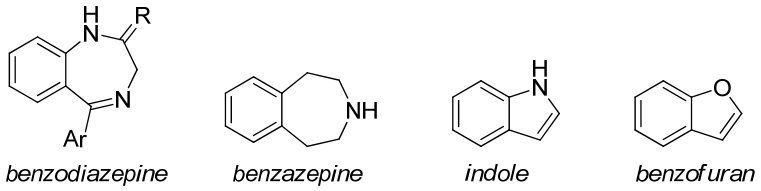


Figure 8. Examples of privileged heterocyclic core units.

Benzofurans are important pharmacophores.[313-318] The structures of a few benzofurans either once investigated as potential drugs or currently used as drugs are shown in Figure 9. The 2-alkyl-5-aryl benzofuran ABT-239 is an H_3-receptor antagonist developed by Abbott, and has been investigated as a potential treatment for ADHD, Alzheimer's disease, and schizophrenia.[317,319] Amiodarone is an antiarrhythmic agent, sold under the trade names Pacerone and Aratac. A related compound called dronedarone[320] (Figure 9), was approved in February 2009 by the FDA. Recent research suggests that dronedarone could also be used in stroke prevention.[321] Benzbromarone is a uricosuric agent used in the treatment of gout.[322] Brofaromine is a reversible inhibitor of monoamine oxidase A (RIMA) that inhibits the oxidative deamination (breakdown) of

epinephrine, norepinephrine, serotonin, and dopamine. This drug is used primarily in the treatment of anxiety and depression.[323,324] Egonol is a benzofuran isolated from *Styrax japonicum*, and showed activity as a pyrethrum synergist.[325] Other benzofurans isolated from the genus *Syrax* show a range of biological activities including insecticidal, fungicidal, antimicrobial, antiproliferative, cytotoxic and antioxidant properties.[325] Corsifuran C is a 2-aryl benzofuran related to compounds with reported antifungal, antibacterial, insect feeding deterrent, free radical scavenging, antioxidant, cyclooxygenase and estrogenic activities.[326] 2-Arylbenzofurans in general have reported antioxidant, antiplasmodial, anti-HIV, and estrogenic activities, as well as anticancer activities.[327]

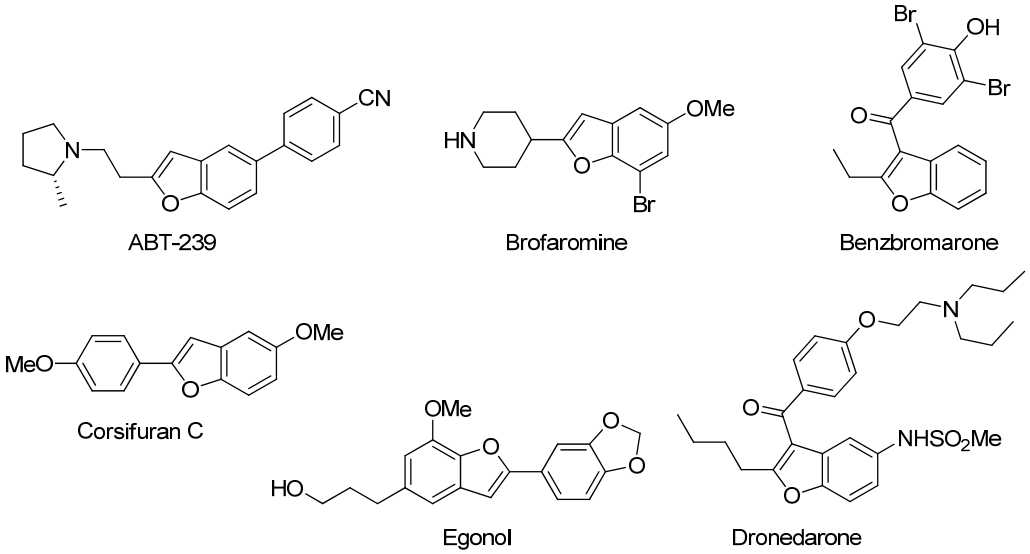


Figure 9. Examples of biologically important benzofurans.

As these basic structures have such varied biological activities, it is probably obvious that much research has gone into developing syntheses, both efficient and amenable to the synthesis of analogues. The possible retrosynthetic disconnections of the benzofuran nucleus to commercially available materials are shown in Figure 10, and

will be discussed in the following sections. The construction of benzofurans has been discussed in detail in several review articles. [312,328-331]

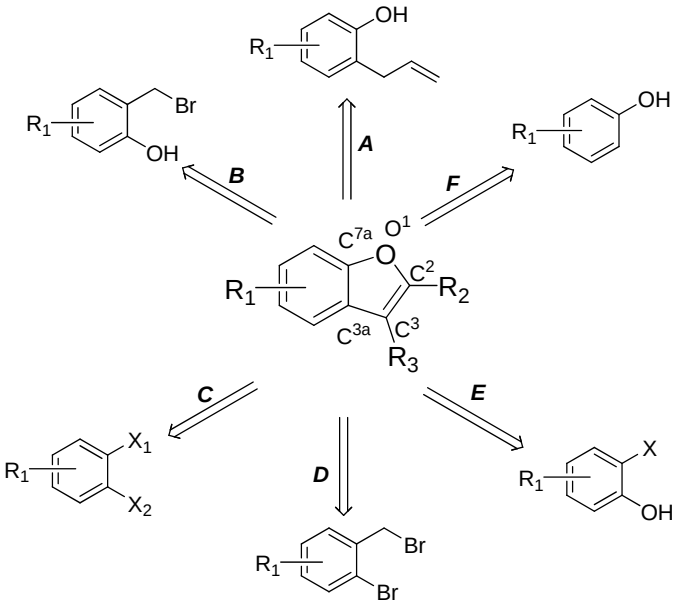


Figure 10. Disconnections of benzofurans to commercially available scaffolds.

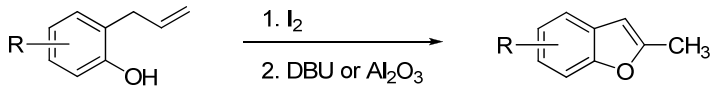
The following sections will give examples of syntheses via each of these routes, and are organized according to the basic starting material of the process. As was the case in the discussion on alkene synthesis, the advantages and disadvantages of each process specifically (related to the individual synthesis) and generally (related to the basic synthetic plan) will be discussed. While several different synthetic strategies from each general disconnection will be discussed, this is not meant to be comprehensive, as the examples chosen are meant to highlight routes that not only build the benzofuran nucleus, but also functionalize it.

1.4.2 Disconnection A (C^2-C^3): Benzofurans from *O*-Allyl Phenols

The first route to be discussed is the synthesis of benzofurans from 2-allylphenols, which can be cyclized with iodine (Scheme 62)[332-334] or NBS[335] or *O*-functionalized and cyclized via ring-closing metathesis (Scheme 63).[336-338] The iodocyclization-elimination route

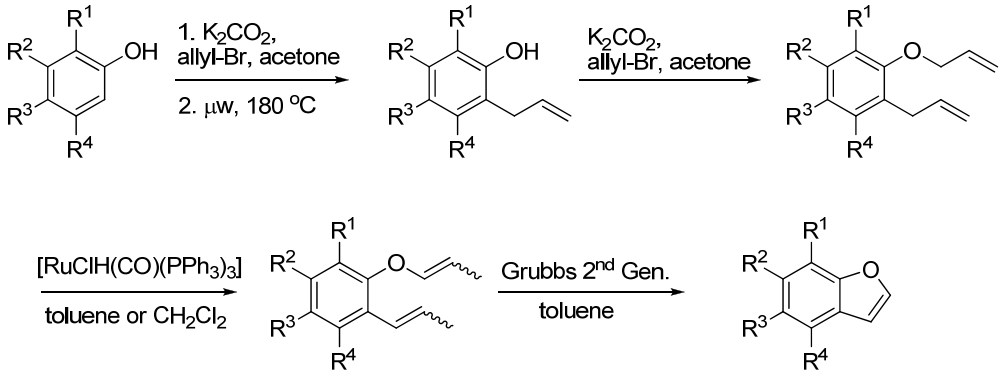
depicted in Scheme 62 required two steps from the 2-allylphenol, and the 2-methyl benzofurans were isolated in moderate yields. This route is, of course, dependent on the ability to access the requisite 2-allylphenol, which may not be simple in all cases (vide infra). A Wacker-type cyclization may also be used to cyclize allyl phenols via treatment with $PdCl_2$ in the presence of an oxidant.[339-341]

Scheme 62. Benzofurans from 2-allylphenols.[332-334]



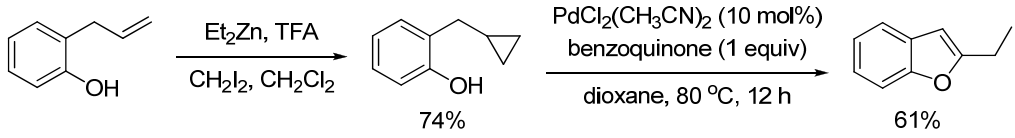
The synthesis of benzofurans from functionalized 2-allylphenols via RCM is also possible (Scheme 63),[336-338] but has some drawbacks. For example, while the starting phenol could be converted to the corresponding 2-allylphenol in two steps, one *ortho* position had to be blocked by a functional group; alternatively, the 2-allyl phenol was synthesized from a symmetrically substituted phenol to avoid regioselectivity issues. Unfortunately, while both the isomerization and RCM used ruthenium catalysts, two different catalysts had to be used, necessitating an intermediate purification step. Finally, only 2,3-unsubstituted benzofurans could be accessed using this method, as 1) the starting functionalized diallyl compound required for the synthesis of substituted benzofurans would be difficult to synthesize using this method and 2) the RCM would not likely work on what would be highly substituted alkenes. The yields in each step were also highly variable and substrate-dependent.

Scheme 63. Benzofurans from functionalized 2-allylphenols via RCM.[336-338]



An alternate cyclization strategy of 2-allyl phenol to 2-ethylbenzofuran was published by He and Yudin.[342] Allyl phenol was first cyclopropanated then treated with palladium and an oxidant to give the 2-ethylbenzofuran (Scheme 64). It should be noted that this strategy was also applicable to cyclopropanation of 2-vinyl benzoic acids and benzamides to give 6-membered benzofused heterocycles.

Scheme 64. Cyclopropanation and cyclization of 2-allyl phenol to 2-ethylbenzofuran.[342]

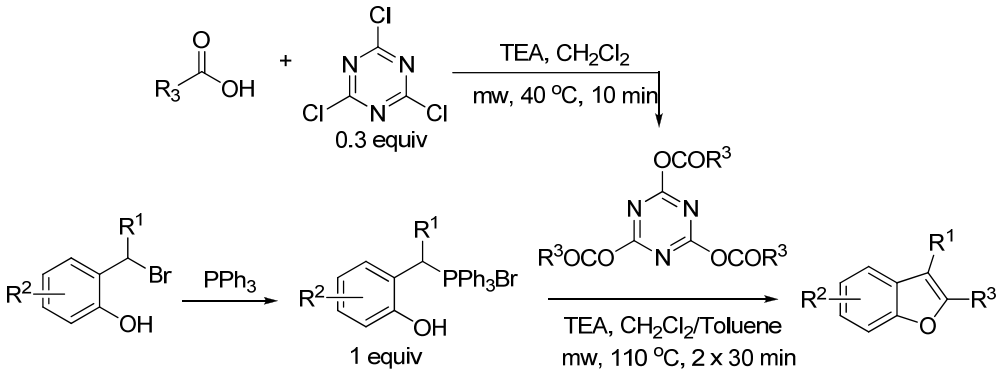


1.4.3 Disconnection B (O^1-C^3): Benzofurans from α-Bromocresols

Giacomelli and coworkers described a synthesis of 2-substitued benzofurans from α-bromocresols and carboxylic acids (Scheme 65).[343,344] The major drawback in this example is the required, highly functionalized starting material, which may not be easy to access in all cases, and the use of stoichiometric amounts of activating reagents (triphenylphosphine and the trichlorotriazine) is less than ideal. However, benzoic acids, carbamic acids, and alkenyl carboxylic acids were all compatible starting materials in the

reaction. Amino acids could also be employed in this reaction to give chiral 2-substituted benzofurans, and little epimerization at the α-centre of the amino acid was detected.

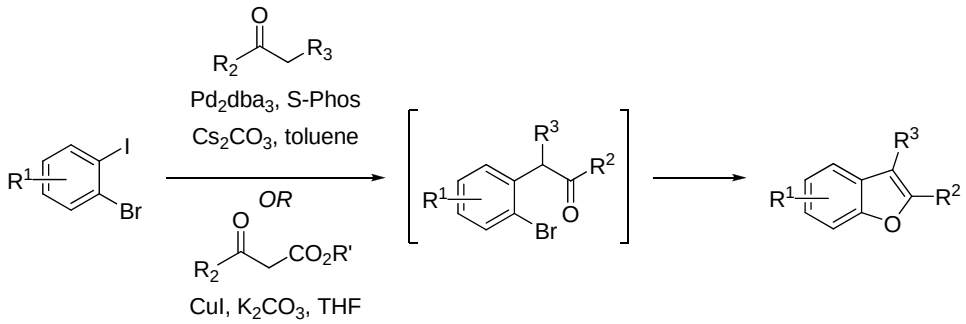
Scheme 65. Benzofurans from α-bromocresols and carboxylic acids.[343,344]



1.4.4 Disconnection C (C^{7a}-C^{3a}): Benzofurans from 1,2-Dihaloarenes

The standard method for transforming 1,2-dihaloarenes to benzofurans is via sequential *C*-(α)-arylation of a ketone followed by intramolecular *O*-arylation. For example, benzofurans have been synthesized from ketones and aryl halides via a two-step, sequential palladium-catalyzed α-arylation of a carbonyl compound, copper-catalyzed *O*-arylation,[345] and a one-pot palladium-catalyzed α- then *o*-arylation from symmetrically substituted 1,2-dibromoarenes.[346,347] As the latter protocol starts from a symmetrical arene, only one regioisomeric benzofuran may be obtained using that method. Regioselectivity issues may also be avoided by starting with an arene with two different halogens, as they will react with transition metals at different rates. For example, 2-bromo-1-iodoarenes will first undergo α-arylation at the C-I bond, followed by intramolecular *O*-arylation at the C-Br bond, and may be catalyzed in one pot by either palladium[348,349] or copper[350] (Scheme 66).

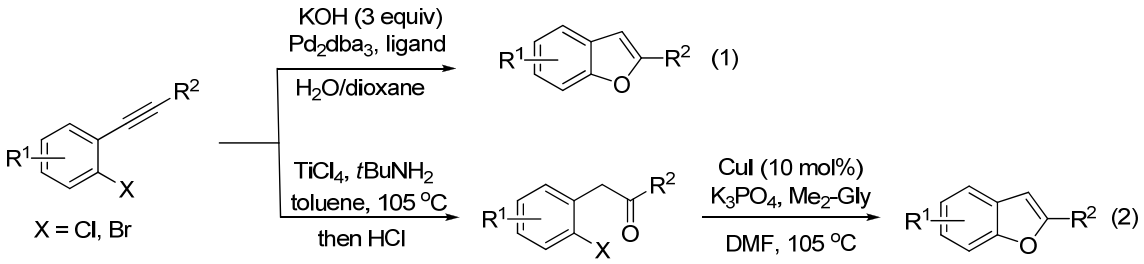
Scheme 66. One-pot synthesis of 2,3-disubstituted benzofurans from 1,2-dihaloarenes and ketones.



Alternatively, 2-halo-alkynyl arenes (synthesized from 1,2-dihaloarenes using Sonogashira chemistry) may be transformed directly to a 2-substituted benzofuran (Scheme 67, equation 1)[351] or indirectly via a ketone intermediate (Scheme 67, equation 2).[352]

These are useful preparations of 2,3-disubstituted benzofurans. The one-pot C-O, C-C bond forming processes are clearly more useful than the two-pot procedures, but all suffer from requiring either restrictive symmetrical substrates or expensive dihalogenated arenes to avoid regioselectivity issues.

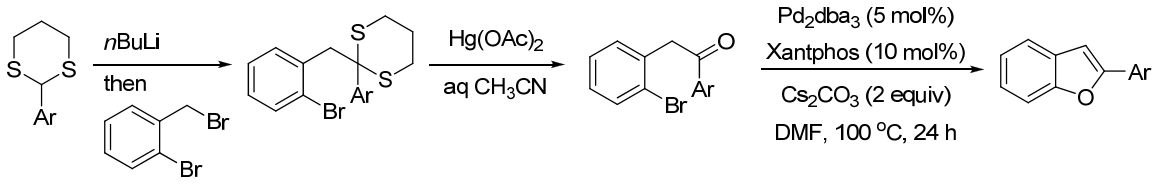
Scheme 67. Benzofurans synthesized from 2-halo-alkynyl arenes.



1.4.5 Disconnection D (C^{7a}-O^1): Benzofurans from *o*-Bromo Benzyl Bromide

One report of the transformation of *o*-bromo benzyl bromide to benzofurans is shown in Scheme 68.[353] While the intramolecular palladium-catalyzed aryl ether formation in the last step is a useful transformation, the cumbersome synthesis of the requisite ketone detracts from the overall utility of the reaction. This process is really just a variation of that presented in Scheme 66.

Scheme 68. Benzofurans from *o*-bromo benzyl bromides.[353]

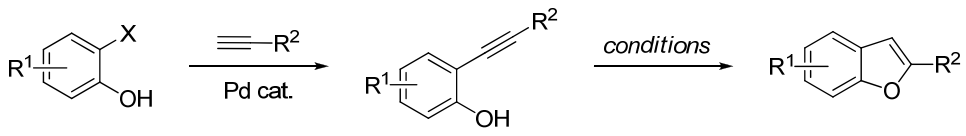


1.4.6 Disconnection E (O^1-C^3): Benzofurans from 2-Substituted Phenols

Several different 2-substituted phenols (other than bromocresols, see section 1.4.3) have been transformed over several steps to the corresponding benzofurans, including salicylaldehydes[354-356] 2-hydroxybenzophenones,[357,358] and 2-hydroxyacetophenones.[359,360] However, the most common starting material is a 2-halophenol, usually, but not exclusively 2-iodophenol. A wide variety of methods for the synthesis of 2-functionalized benzofurans from 2-halophenols have been published. This is often accomplished via a Sonogashira cross-coupling reaction to give a 2-alkynylphenol, which is then cyclized to give the benzofuran (Scheme 69).[361] This may be done from both *O*-functionalized alkynyl phenols (with or without transition metals)[362-369] and unprotected alkynyl phenols directly.[370-379] The transition metal-catalyzed cyclization has also been used in tandem with a second transition metal-catalyzed reaction.[202,380-385] While highly useful and often

quite general, this requires an *o*-halogenated phenol as the primary material, which not only can be quite expensive, but may also be difficult or require a couple of steps to synthesize, if not commercially available.

Scheme 69. The general synthesis of benzofurans from 2-halo phenols.

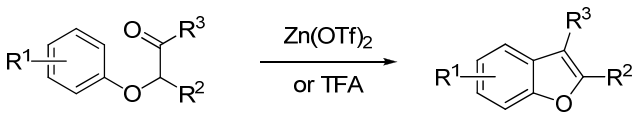


1.4.7 Disconnection F (C^2-C^{3a}): Benzofurans from Phenols

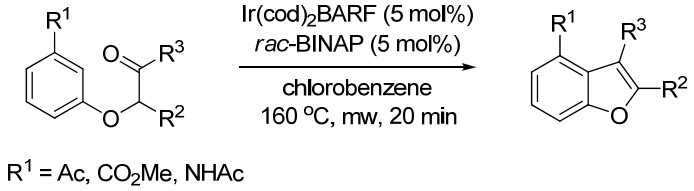
Direct routes from simple phenols would both minimize direct costs of the starting materials[386] and reduce the number of manipulations prior to the key assembly of the heterocycle nucleus.

A cyclodehydrative approach to benzofurans from phenols is a straightforward method. α-Aryloxy ketones or esters, prepared either via nucleophilic displacement of an α-chloroketone[387] or reaction of a propargylic alcohol[388] with the corresponding phenol, undergo dehydration when treated with either $Zn(OTf)_2$[388] or trifluoroacetic acid[387] (Scheme 70). Alternatively, a *meta* ketone, ester or amide functionality can direct iridium insertion into the *ortho* C-H bond of an analogous α-aryloxy substituted ketone which then undergoes a cyclodehydration to give the 2,3-disubstituted benzofuran after addition to the tethered ketone (Scheme 71).

Scheme 70. Cyclodehydrative cyclization of α-aryloxy ketones or esters to 2,3-disubstituted benzofurans.



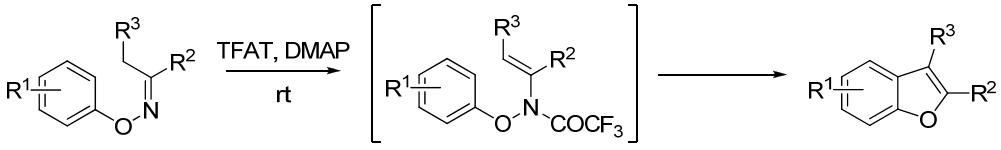
Scheme 71. Directed iridium-catalyzed cyclodehydrative synthesis of benzofurans from α-aryloxy ketones.



R^1 = Ac, CO_2Me, NHAc

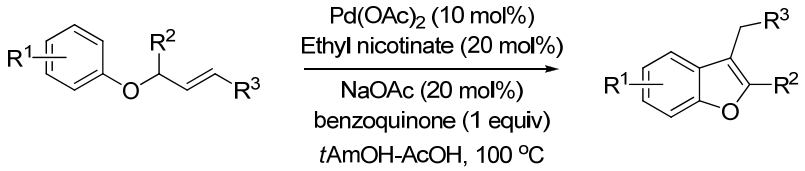
Naito and coworkers reported the net transformation of *O*-aryl oxime ethers to 2,3-disubstituted benzofurans (Scheme 72).[389] The first step of the process is the *N*-trifluoroacetylation of the oxime ether using a combination of trifluoroacetyl triflate (TFAT) and 4-dimethylaminopyridine (DMAP). This is followed by a sigmatropic rearrangement to a 2-amido-2,3-dihydrobenzofuran (not shown) which then undergoes elimination to yield the 2,3-disubstituted benzofuran. Yields of the benzofurans were generally good, however, the regioselectivities observed in reactions from 3-substituted phenols were poor.

Scheme 72. Rearrangement and cyclization of *O*-aryl oxime ethers to benzofurans.[389]



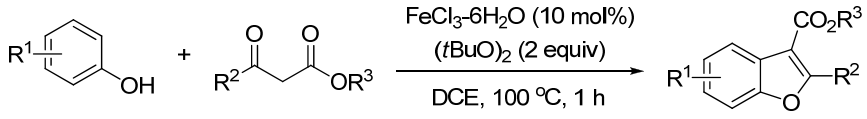
Stoltz has reported palladium(II)-catalyzed oxidative cyclizations of allylphenols (Scheme 73).[390,391] The benzofurans were isolated in good yields, and the unsymmetrical phenols examined cyclized to a single benzofuran regioisomer. The major limitation here is the requirement of electron-rich phenols. Youn later reported a similar approach.[392] A related, directed cyclization of aromatic imines to unsaturated benzofused heterocycles has been reported by Bergman and Ellman.[393-395]

Scheme 73. Oxidatve cyclizations of allylphenols to benzofurans.[390,391]



Finally, Li et al. have reported an iron-catalyzed synthesis of benzofurans from phenols and β-ketoesters (Scheme 74).[396] The yields of the benzofurans were moderate to good, and excellent regioselectivity was generally observed when the starting phenol was unsymmetrical. Notably, the reaction also tolerated halogen substituents, leaving a useful handle on the resulting benzofuran for future transformations.

Scheme 74. Iron-catalyzed synthesis of benzofurans from phenols and β-ketoesters.[396]



1.4.8 Summary

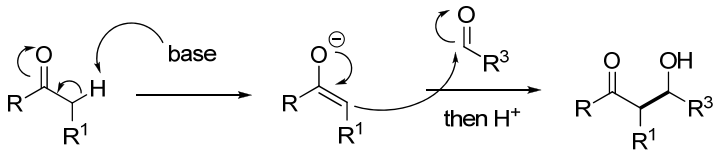
While these results certainly point in the direction of a broad and general route to benzofurans from simple starting materials, all suffer from restrictive functional group requirements, limited scope, multistep synthesis or some combination thereof.

1.5 Thesis Objectives

The general goal of this thesis work was to develop conditions for multiple α-functionalizations of enolate or enolate equivalents in a single synthetic operation. While research started with explorations of enolate chemistry, it gradually developed into explorations of the chemistry of chlorinated enol ethers. This section briefly chronicles this substantial change by first describing the early work with enolates followed by the transition into work with enol ethers. It is concluded with a general description of the findings that comprises this thesis.

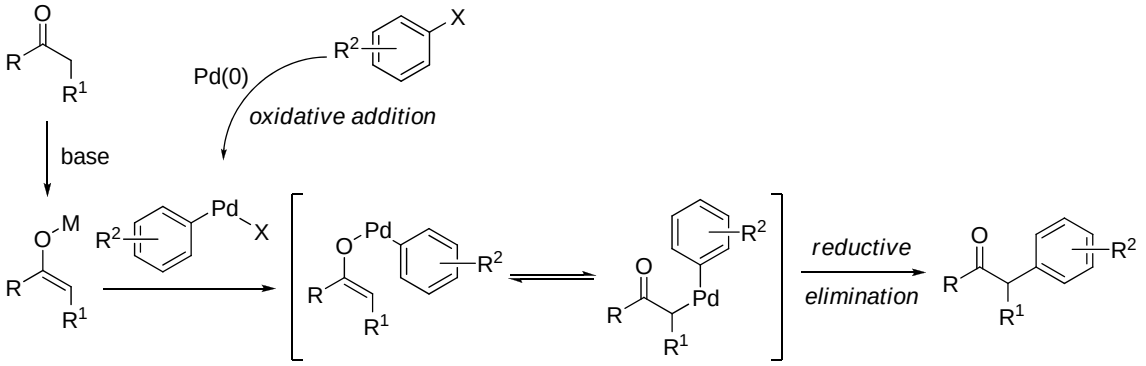
Enolate chemistry is very diverse as enolates are excellent nucleophiles in both the aldol addition (for example) and palladium-catalyzed chemistry. The basic reaction mechanism for an aldol reaction (or related Mannich reaction) is shown below (Scheme 75).[397] The metal enolate generated via deprotonation of a carbonyl derivative adds to a second carbonyl, usually an aldehyde (or an imine in the Mannich reaction, not shown), forming a new carbon-carbon bond to give the aldol adduct.

Scheme 75. The basic mechanism of an aldol reaction.



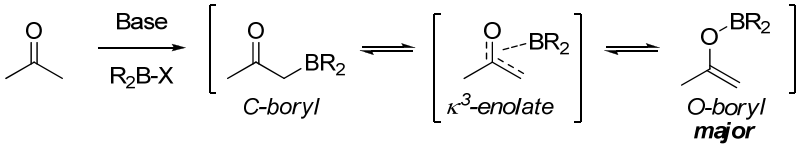
The reaction mechanism of palladium-catalyzed α-arylation of a carbonyl compound is similar to that of the aldol addition and is shown below (Scheme 76).[398] Like the aldol addition, the reaction starts from a carbonyl compound and is deprotonated to give a metal enolate, which undergoes a ligand substitution reaction with a Pd(II) complex (derived from oxidative insertion of palladium into a carbon-halogen bond of an electrophile), which, after reductive elimination, gives the arylated adduct.

Scheme 76. Generalized steps in α-arylation.



Organoboron compounds are excellent nucleophiles for a variety of palladium-catalyzed cross-coupling reactions (Suzuki-Miyaura coupling, section 1.2.1.8). Boronic acids or esters are the most common partners, but 9-BBN derivatives (alkyl) are becoming more and more useful. While boron enolates are easily made under mild conditions, they have never been examined as nucleophiles in palladium-catalyzed chemistry. This could be because boron enolates exist mainly in the *O*-boryl form while a *C*-boryl enolate would be ideal for cross-coupling Scheme 77), or because trivalent boron reagents are not nucleophilic enough to transmetalate to palladium. Boron enolates are also very labile and undergo rapid hydrolysis, even in the presence of small amounts of water.

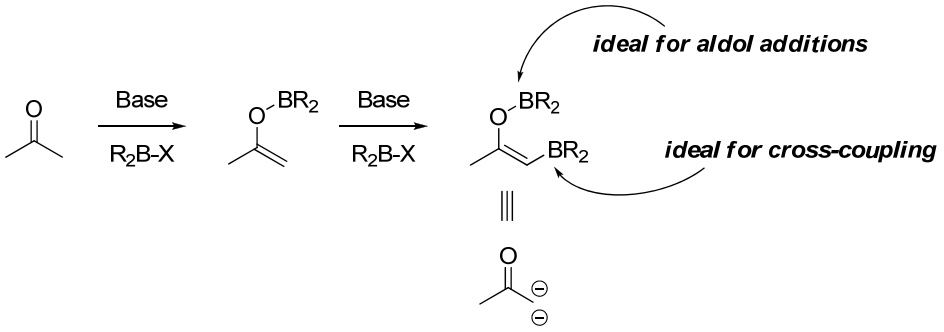
Scheme 77. Tautomeric forms of a generic boron enolate



In 1999, a report of a doubly borylated enolate was released.[399] Acetone, or an acetic acid derivative, when treated with excess base and boron reagent first forms the expected *O*-boryl enolate, but also undergoes a second enolization after the initial mono

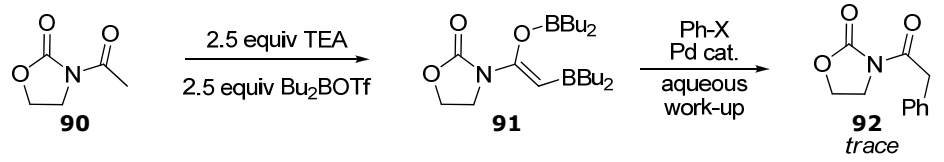
boron enolate is formed, giving a doubly borylated enolate (DBE, Scheme 78). This species reportedly behaved as a normal boron enolate and could add to two equivalents of an aldehyde giving a double aldol adduct. More importantly, two *different* aldehydes could be added in a stepwise manner, producing double aldol adducts with different substituents.[399] This result suggested the possibility of sequential α-arylation via palladium-catalyzed chemistry from the α-C-B bond and traditional aldol chemistry from the O-B bond in one pot.

Scheme 78. The doubly borylated enolate.[399]



In exploring the palladium-catalyzed α-arylation of DBEs, we decided to work with *N*-acetyl oxazolidinone **90** as a simple precursor. The DBE **91** was easily and rapidly formed; however, after considerable experimentation, the desired adduct **92** could only be detected in trace amounts.

Scheme 79. Attempted palladium-catalyzed arylation of a DBE.



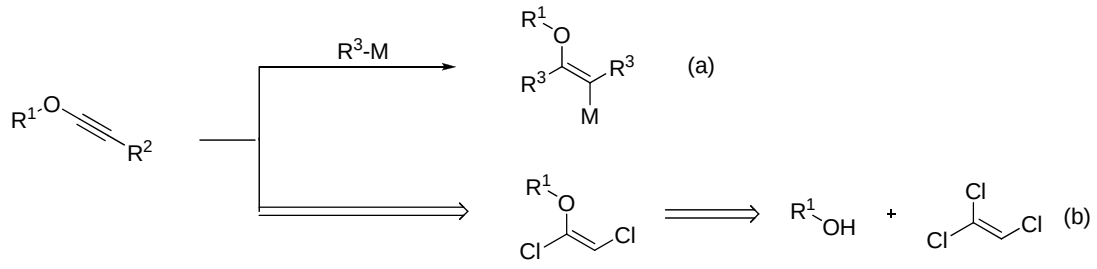
90 **91** **92** *trace*

The alternative to enolizing an existing carbonyl group is to reductively functionalize an acetylenic ether (Scheme 80, equation a). The initial plan was to hydro-

or carbometalate a silyl acetylenic ether (where $R^1 = R'_3Si$) to give a *differentially* double metalated enolate (similar to the reaction in Scheme 88 in section 2.1). The most general and simple route to an acetylenic ether is via the elimination of HCl from 1,2-dichlorovinyl ethers (Scheme 80, equation b).

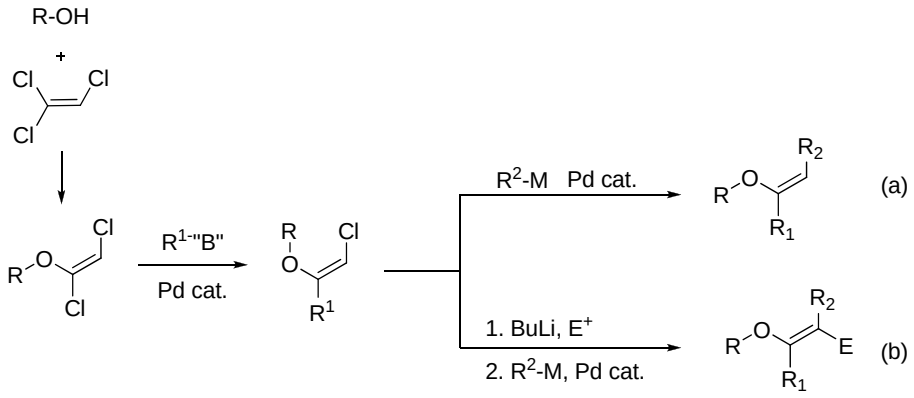
In considering this possibility, it became obvious that the dichlorovinyl ether (formally the enol ether of an α-chloro acyl chloride) was potentially a highly useful template itself. The thesis goals thus changed from exploring enolates as diverse nucleophiles to the chemistry of enol ethers as diverse electrophiles and the demonstration that 1,2-dichlorovinyl ethers are simple, polyfunctionalizable two-carbon templates.

Scheme 80. Alternate routes to enolates and enol ethers.



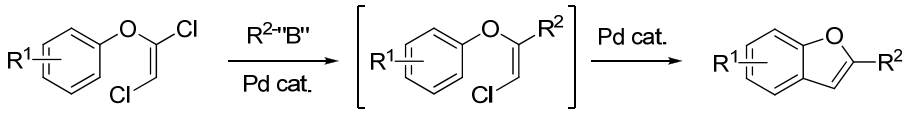
This thesis begins with the synthesis of dichlorovinyl ethers and amides (section 2.2), followed by the development of site selective, palladium-catalyzed functionalization of those electrophiles (section 2.3). Those chemistries set the stage for the subsequent and selective functionalization of trichloroethylene into a diverse array of electron-rich (oxygen substituted) alkenes (Scheme 81, equation a; section 2.4). The monofunctionalized intermediate may also be deprotonated and quenched with an electrophile and then resubjected to cross-coupling conditions with a second organometallic. In this way, a diverse array of tetrasubstituted alkenes may be accessed in a modular fashion (Scheme 81, equation b; section 2.4).[400]

Scheme 81. Tri- and tetrasubstituted electron-rich alkenes from alcohols, trichloroethylene, two organometallics and an optional electrophile.



During the course of that study, it was discovered that prolonged exposure of the monofunctionalized intermediate to palladium led to intramolecular direct C-H activation. The cross-coupling/direct arylation could, in fact, be done in one pot, generating 2-functionalized benzofurans in only two steps from inexpensive commercial materials (Scheme 82).[401] The scope of this reaction, as well as some mechanistic investigations will also be discussed (section 2.5).[402]

Scheme 82. 2-Benzofurans from 1,2-dichlorovinyl ethers and organoboron reagents.



CHAPTER 2 : RESULTS AND DISCUSSION

2.1 Introduction

Dichlorovinyl ethers were identified as the key starting materials for all studies in this work. They are easily generated by the reaction of an alcohol with trichloroethylene (Scheme 80, equation b). Before the discussion of the synthesis and application of the dichlorovinyl ethers used in this work, a brief introduction to the history of the synthesis of these compounds, as well as selected modern applications in synthesis, will be presented. For older examples of the use of trichloroethylene in organic synthesis, details can be found in a general review on the subject.[403]

The study of the reactions between nucleophiles and TCE began as early as 1937[404] when the reaction of sodium benzenethiolate (PhSNa) with TCE was studied. While a single product was reported to be produced in that reaction, the structure and geometry of the adduct was unknown, and was not established until 1957.[405] One of the first reports of the reaction of phenol with TCE was published in 1963 (Scheme 83).[406] More than a decade later, a modified procedure employing DMSO as a solvent was reported.[407] While these procedures were generally high yielding, reports of explosions suspected to be due to generation of dichloroacetylene[407] detracted from the appeal of using these methods.

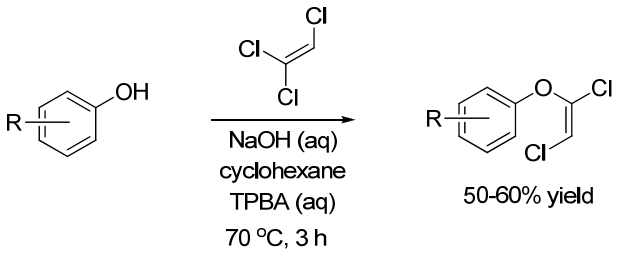
Scheme 83. The first reported reaction between phenol and trichloroethylene.[406]

93

An alternative set of conditions for the synthesis of dichlorovinyl aromatic ethers was published in 1988 by Pielichowski. In this method, a phenol and trichloroethylene

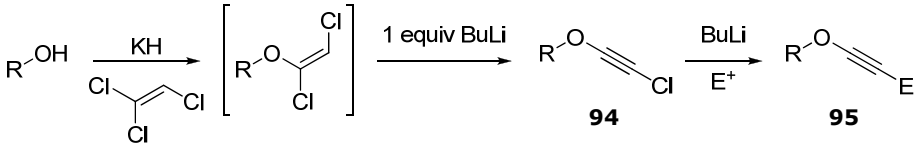
were combined in a water-cyclohexane mixture in the presence of sodium hydroxide and a quaternary ammonium chloride to give the corresponding dichlorovinyl ethers (Scheme 84).[408] This procedure was reported to be successful for both electron-rich (e.g. *p*-cresol) and electron-poor (e.g. *p*-nitrophenol) phenols in modest yields.

Scheme 84. Synthesis of dichlorovinyl aromatic ethers under phase-transfer catalysis.[408]



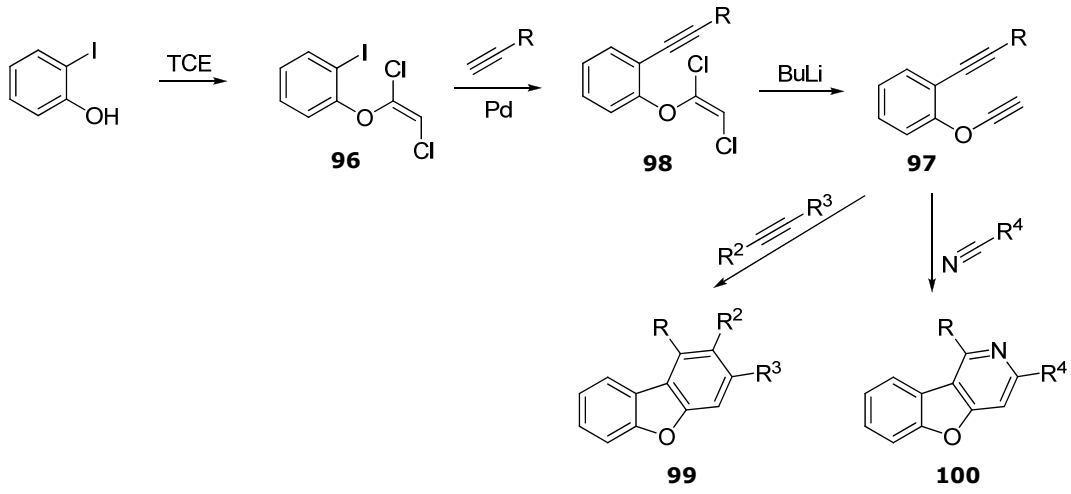
In 1987, Greene and coworkers reported a very practical synthesis of dichlorovinyl ethers derived from either aliphatic or aromatic alcohols and trichloroethylene.[409,410] Most often, however, these ethers were not isolated, but rather were treated with excess butyllithium which caused elimination of HCl to form an acetylenic ether in situ (Scheme 85).[411-418] If one equivalent of butyllithium is employed, the terminal chloro acetylenic ether **94** may be isolated; use of excess butyllithium followed by quenching with an electrophile can generate terminally functionalized acetylenic ethers **95**.

Scheme 85. Formation of acetylenic ethers from dichlorovinyl ethers.[409,410]



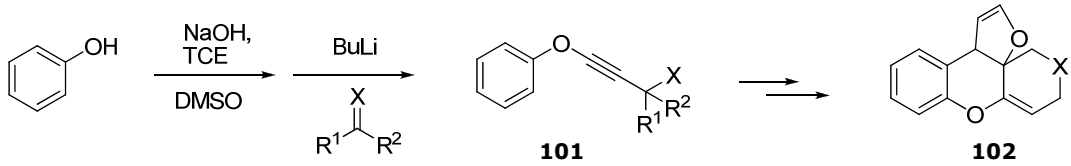
In fact, the most common use of trichloroethylene is for the synthesis of acetylenic ethers. For example, Komine and Tanaka have reported the synthesis of dibenzofurans from *o*-iodophenol (Scheme 86).[417,419] In this case, standard addition of the phenol to TCE gave the dichlorovinyl ether **96**; Sonogashira coupling of that compound with a terminal alkyne gave **98**. Standard treatment of the dichlorovinyl ether with excess butyllithium induced elimination. The resulting diyne **97**, when reacted with either an internal alkyne or a nitrile gave dibenzofuran **99** or azo derivative **100**, respectively.

Scheme 86. Dibenzofuran synthesis from a diyne derived from *o*-iodophenol.[417,419]



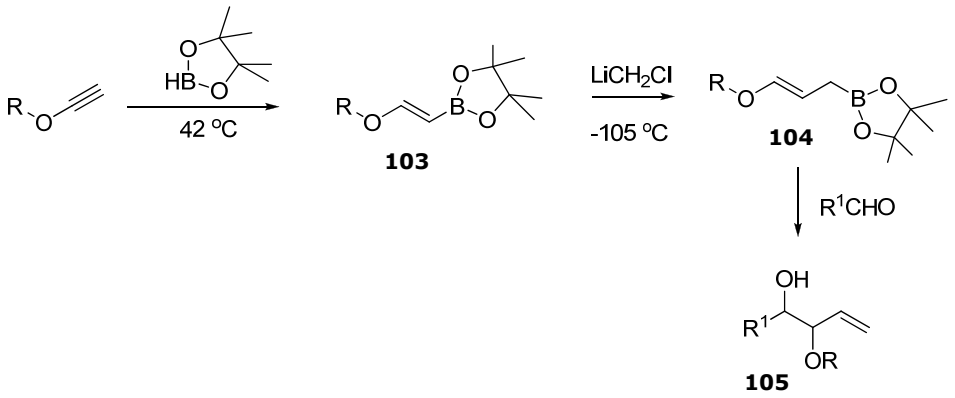
Similarly, Hashmi has generated ynols from phenols and TCE; following the reaction between phenol and TCE, the dichlorovinyl ether was treated with excess butyllithium and quenched with a carbonyl compound to give propargyl alcohols and amines **101**; a few additional synthetic manipulations (not shown) yielded the heterocycles **102** (Scheme 87).[418]

Scheme 87. Hashmi's synthesis of heterocycles from 1,2-dichlorophenol ethers.[418]



In many cases, the ynol ethers generated from dichlorovinyl ethers are simply reduced or otherwise functionalized back up to a vinyl ether.[304,420-434] An interesting use of acetylenic ethers in this way was reported by Hoffmann. The ynol ethers obtained from the corresponding dichlorovinyl ethers were hydroborated to give **103** and then homologated to yield allyl boronates **104** (Scheme 88).[427,429] The allyl boronates **104** then reacted with aldehydes intra- or intermolecularly to give 1,2-diols **105**.

Scheme 88. Synthesis of 1,2-diols from acetylenic ethers.[427,429]

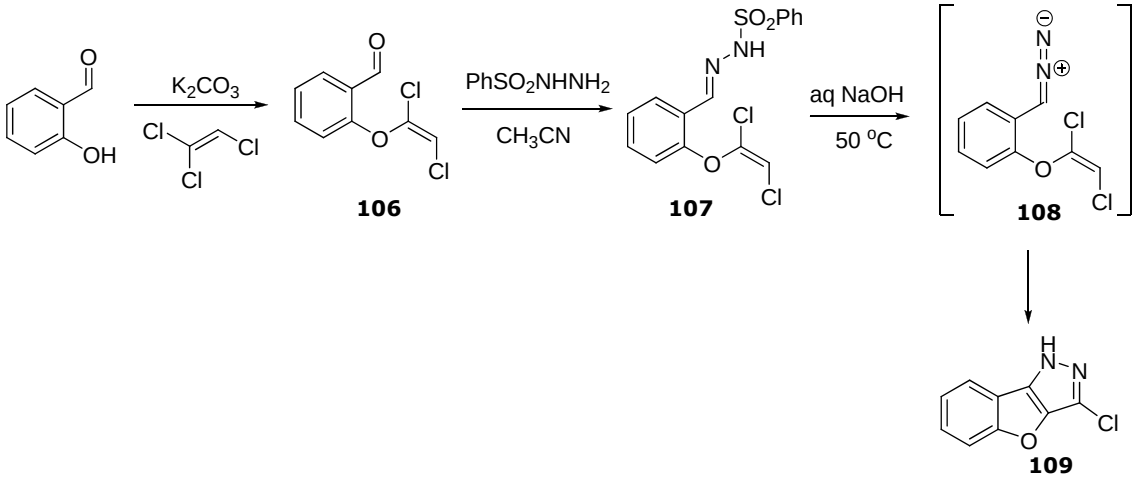


There are few examples of direct uses 1,2-dichlorovinyl ethers that do not involve the manipulation of the oxidation state. One such example is the report from Sales and Mani which describes the transformation of derivatized aryl vinyl ethers into benzofuropyrazole **109** (Scheme 89).[435] Salicylaldehyde was first converted to the corresponding dichlorovinyl ether **106** via reaction with TCE; the resulting adduct was then condensed with benzenesulfonyl hydrazine to give **107**. Treatment of **107** with NaOH induced hydrolysis to **108** and dipolar cycloaddition in one pot to give benzofuropyrazole **109**.

These methods, while both general and very useful for preparing heterocycles and enol ethers, in a sense 'waste' the stereochemical purity and identity inherent in the (*E*)-1,2-dichlorovinyl ethers. In contrast, the work in this thesis represents one of the few other examples of the direct use of these highly useful compounds. The results of these

experiments have been divided into four main parts: the synthesis of the 1,2-dichlorovinyl starting materials (section 2.2), the synthesis of multisubstituted alkenes (sections 2.3 to 2.5), and the synthesis of benzofurans (section 2.6) and other heterocycles (section 2.7). While each section will be discussed separately, they are interrelated and areas of crossover will be specifically highlighted with references to the appropriate sections.

Scheme 89. Sales and Mani's synthesis of benzofuropyrazoles.[435]



2.2 Synthesis of 1,2-Dichlorovinyl Ethers and Amides

2.2.1 Introduction

This thesis focuses on the functionalization of dichlorovinyl ethers, and to a much lesser extent amides and sulfides. While examples of the synthesis of most these substrate types had been reported prior to this work (section 2.1 and appropriately referenced in subsequent text), the adaptation of literature protocols was not always straightforward, therefore a description of the syntheses of the starting materials precedes the discussion of the utilization of these compounds.

2.2.2 Phenol Donors

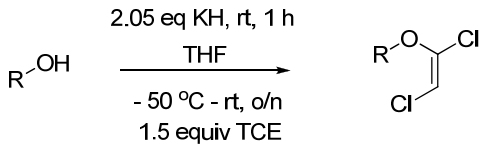
As stated in section 2.1, the first practical synthesis of dichlorovinyl ethers came from Greene in 1987.[409,410] While only two of the dichlorovinyl ethers synthesized were isolated in the initial reports it seemed reasonable that all could be isolated and Greene's method was selected as the basis for the syntheses of all dichlorovinyl ethers.

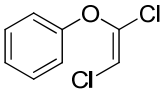
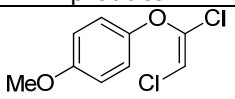
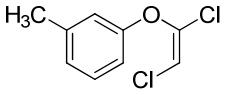
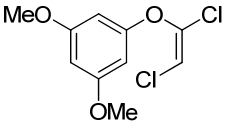
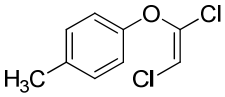
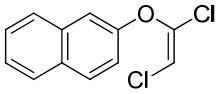
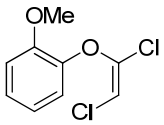
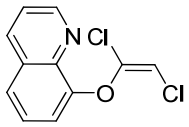
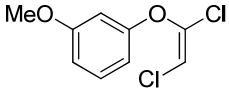
As the initial goal of this research was not the synthesis of a particular compound, but rather invention of a broadly applicable method, the first task was to select an appropriate oxygen nucleophile. Phenols were chosen for four reasons: 1) Greene and others had fairly extensively demonstrated the success of the reactions with aliphatic alcohols; 2) the scope of the reactions between phenols and trichloroethylene had not been extensively studied in the literature; 3) the resulting dichlorophenol ethers are much less volatile than their aliphatic analogues (at least from simple and inexpensive commercially available alcohols) and were anticipated to be easier to handle; and 4) we also anticipated that using an alcohol tethered to an arene ring might eventually permit further elaboration to heterocyclic compounds.

2.2.2.1 Electron-Rich Phenols

Phenols containing electron-donating groups (e.g. methyl and methoxy) were synthesized first, and it was found that direct application of Greene's procedure[409] was both straightforward and quite general (Table 2). With simple derivatized phenols, the yields were generally quite high; the phenol, 3- and 4-methyl phenol adducts **93**, **111** and **113**, respectively, were isolated in high yields (entries 1 – 3). However, it was found that while 3- and 4-methoxyphenol and 3,5-dimethoxyphenol easily reacted with TCE under these conditions to give adducts **117**, **110** and **112** (entries 5 – 7), the 2-methoxy derivative **115** was isolated in extremely poor yield (entry 4). This was partially attributed to solubility issues upon purification, but only half of the expected product mass was recovered from the crude reaction mixture. The source of the difference in reactivity is not clear. Unsurprisingly, 2-naphthol also reacted easily with TCE to give **114** in good yield (entry 8), but 8-hydroxyquinoline adduct **116** appeared to suffer from solubility issues during purification and could only be isolated in modest yield (entry 9).

Table 2. Synthesis of dichlorovinyl ethers from electron-rich phenols.



entry	product	yield[a]	entry	product	yield[a]
1	 **93**	92%	6	 **110**	97%
2	 **111**	97%	7	 **112**	58%
3	 **113**	97%	8	 **114**	74%
4	 **115**	7%	9	 **116**	28%[b]
5	 **117**	98%			

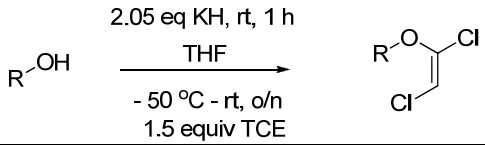
[a]Isolated yields. [b]Poor solubility effected isolation.

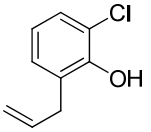
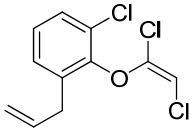
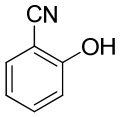
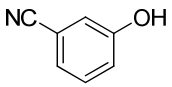
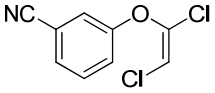
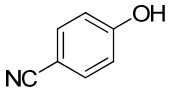
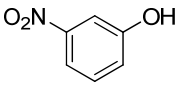
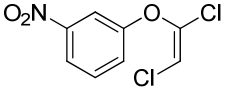
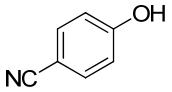
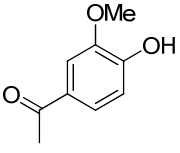
2.2.2.2 Electron-Poor Phenols

The application of Greene's protocol to phenols substituted with electron-withdrawing groups was much less straightforward, and the success of the reaction was highly dependent on the position of the electron-withdrawing group. 6-Allyl-2-chlorophenol **118**, 3-nitrophenol **121** and 3-cyanophenol **124** all reacted smoothly under these conditions and adducts **119**, **122** and **125** were isolated in excellent yields (Table 3, entries 1, 3 and 5). However, 2-cyanophenol (**120**), 4-cyanophenol (**123**), 4-

nitrophenol (**126**) and 4'-hydroxy-3'-methoxyacetophenone (acetovanillone, **127**) all failed to react at all under these conditions (Table 3, entries 2, 4, 6 and 7).

Table 3. Reaction of potassium salts of phenols substituted with an electron-withdrawing group with trichloroethylene.



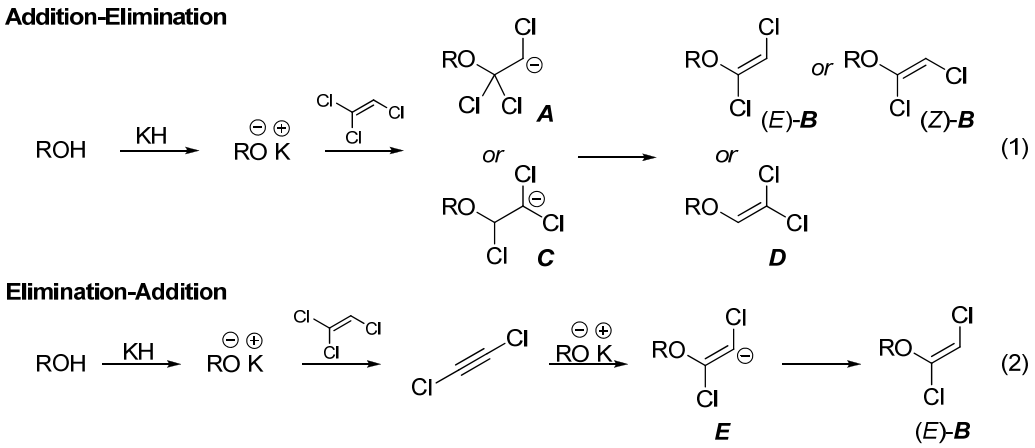
entry	phenol	product	yield[a]
1	 **118**	 **119**	63%
2	 **120**	-	N.R.[b]
3	 **121**	 **122**	90%
4	 **123**	-	N.R.[b]
5	 **124**	 **125**	97%
6	 **126**	-	N.R.[b]
7	 **127**	-	N.R.[b]

[a]Isolated yields. [b]N.R. indicates no reaction.

Before a discussion on difference in reactivity can take place, a discussion on the mechanism of formation is necessary. The reaction may be occurring through one of two different mechanisms: addition-elimination or elimination-addition (Scheme 90). In the addition-elimination mechanism (Scheme 90, equation 1), the potassium alcoholate adds directly to trichloroethylene to give an intermediate anion. Collapse of the anion to eliminate chloride yields a dichlorovinyl ether. However, isomeric anions and thus isomeric dichlorovinyl ethers are possible. Formation of anion ***A*** by addition of the alcoholate to C^1 of trichloroethylene leads to observed 1,2-dichlorovinyl ethers ***B***, though, both (*E*) and (*Z*) isomers are possible. If the alcoholate adds to C^2 of trichloroethylene, anion ***C*** results, which forms 1,1-dichlorovinyl ether ***D***, inconsistent with observed products.

In the elimination-addition mechanism of dichlorovinyl ether formation (Scheme 90, equation 2), the potassium alcoholate generated from deprotonation of the alcohol by KH deprotonates trichloroethylene to eventually yield dichloroacetylene. The potassium phenolate is regenerated from the second equivalent of KH, and nucleophilically adds across the dichloroacetylene to give the dichlorovinyl anion ***E*** and eventually the dichlorovinyl ether (*E*)-***B*** when quenched with a proton source.

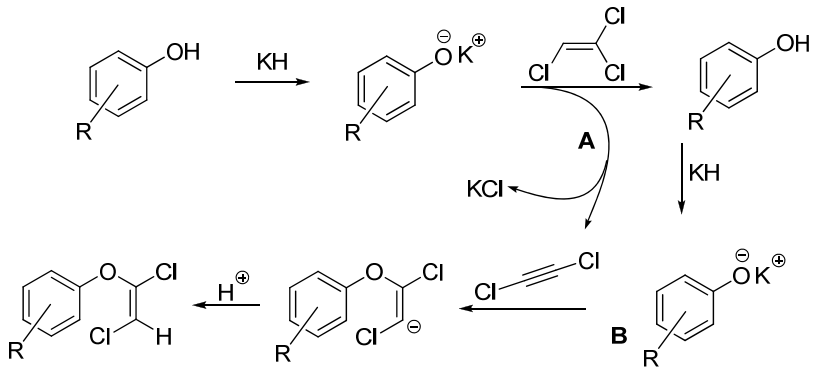
Scheme 90. Addition-elimination and elimination-addition mechanism of formation of dichlorovinyl ethers from an alcohol and trichloroethylene.



The absence of a mixture of products argues against the addition-elimination pathway. Additionally, the product of reaction between an alcoholate and trichloroethylene would be anion ***C*** not ***A***, and 1,1-dichlorovinyl ethers would be the expected product.[436] Greene has shown that alcoholates and amides react with separately and unambiguously formed dichloroacetylene.[410] The observation that potassium alcoholates do react with dichloroacetylene is not conclusive evidence alone that the overall reaction *has* to proceed via formation of dichloroacetylene. However, that knowledge in combination with the absence of isomeric dichlorovinyl ethers strongly supports an elimination-addition mechanism (Scheme 90, equation 2).

The results in Tables 2 and 3 may now be rationalized by considering both the pK_as of the phenols and the elimination-addition mechanism of the reaction of potassium alcoholates with trichloroethylene (shown in more detail in Scheme 91). The potassium phenolate generated from deprotonation of the phenol by KH first deprotonates trichloroethylene, yielding dichloroacetylene (step **A**). The potassium phenolate is regenerated from the second equivalent of KH, and nucleophilically adds across the dichloroacetylene (step **B**), giving the dichlorovinyl anion and eventually the dichlorovinyl ether when quenched with a proton source.

Scheme 91. Mechanism of reaction between phenol and trichloroethylene to give dichlorovinyl ethers.

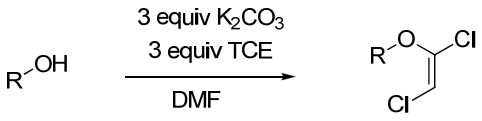


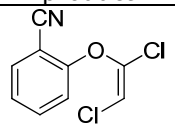
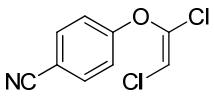
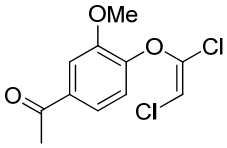
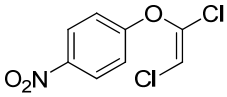
These conditions were developed and optimized for reactions with aliphatic alcohols whose pK_as are around 30 in DMSO.[437,438] Phenol has a pK_a of 18.0 in DMSO, while phenols substituted with electron donating groups have somewhat higher pK_as (*p*-cresol and *p*-anisole have pK_as of approximately 19);[439] however, these potassium phenolates are still both basic enough to deprotonate trichloroethylene and nucleophilic enough to add across dichloroacetylene. While all phenols with electron-withdrawing groups have lower pK_as, the pK_as of those with the electron-withdrawing group in the 3-position are not quite as attenuated as those with an electron-withdrawing group in the 2- or 4-positions. The potassium salts of those phenols are either not basic enough to deprotonate trichloroethylene or not nucleophilic enough to add to dichloroacetylene. Pielichowski's report that the synthesis of the dichlorovinyl ether from *p*-nitrophenol required a strongly basic, biphasic mixture (Scheme 84)[408] suggests that potassium *p*-nitrophenolate itself is not basic enough to deprotonate trichloroethylene (Table 4). Attempts at reproducing reactions based on Pielichowski's conditions were unsuccessful.

The report from Sales and Mani on the synthesis of dichlorovinyl ethers from salicylaldehydes (Scheme 89)[435] was encouraging. Reasoning that their method could apply to electron-poor compounds in general, this method was applied to the synthesis of cyano- and nitro-substituted dichlorovinyl ethers.

Indeed, adducts **128**, **129** and **130** were isolated in excellent yields (Table 4, entries 1 – 3). However, the adduct derived from *p*-nitrophenol could not detected at all. This observation is in agreement with Sales and Mani's observation that 2-formyl-4-nitrophenol could not react with trichloroethylene under these conditions. Greene and coworkers had previously reported that catalytic amounts of methanol were necessary to generate dichloroacetylene both in the absence of a stoichiometric nucleophile[410] and to promote the reaction of more acidic thiophenols with trichloroethylene.[440]

Table 4. Synthesis of dichlorovinyl ethers from electron-poor phenols.



entry	product	yield[a]
1	 **128**	68%
2	 **129**	94%
3	 **130**	80%
4	 **131**	88%[b]

[a]Isolated yields. [b]Required a catalytic amount of methanol in addition to above reagents.

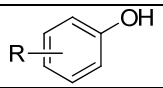
When a catalytic amount of methanol was added to the mixture of *p*-nitrophenol, TCE and K_2CO_3 in DMF at 70°C, the reaction proceeded smoothly and adduct **131** was isolated in an excellent yield (Table 4, entry 4). This result confirms the suspicion that while potassium *p*-nitrophenolate is nucleophilic enough to add across dichloroacetylene,[441] it is not basic enough to deprotonate trichloroethylene.

It is not obvious why the K_2CO_3/DMF conditions are more successful in promoting the reaction between electron-poor phenols than KH/THF conditions are. It is not a solely a temperature factor. Attempts at performing the reaction between *p*-nitrophenol and

TCE under Greene's KH/THF conditions with or without catalytic amounts of methanol failed, even at refluxing temperatures (65 ^{o}C). As it is known that methanol promotes the formation of dichloroacetylene in the absence of a potassium phenolate basic enough to do so, dichloroacetylene is presumably being generated in both THF and DMF. Therefore, either *p*-nitrophenolate cannot add to dichloroacetylene in THF, or it does so but undergoes the reverse reaction and no net reaction ever occurs. In general, ionic compounds are stabilized by highly polar solvents. One common measure of solvent polarity is the dielectric constant. Solvents with a high dielectric constant are of high polarity. DMF has a dielectric constant of 37 whereas THF has a dielectric constant of 7.6, and DMF is much more polar than THF.[442] The successful reaction between *p*-nitrophenolate and dichloroacetylene in DMF could be due to the ability of DMF to stabilize the vinyl anion intermediate (Scheme 91), preventing a reverse elimination of the phenolate.

Table 5 is a compilation of the different phenols used in this study, their respective pK_as (in DMSO), and the conditions required for efficient synthesis of the corresponding dichlorovinyl phenyl ether. It appears that Greene's KH/THF conditions[409] are sufficient for inducing reaction between phenols with pK_as of approximately 14 or higher. More acidic phenols require Sales and Mani's conditions,[435] and a small amount of methanol aids in the formation of dichloroacetylene in the most extreme cases.

Table 5. The pK_a of phenols in DMSO, and conditions required to induce addition across trichloroethylene to give dichlorovinyl aromatic ethers.

	**pK_a**[439]	**conditions**
H	18	
2-OMe	17.8	
3-OMe	17.8	
4-OMe	19.1	
(2-Naphthol)	17.2	KH/THF, $^{-}$50 °C – rt[a]
3-Me	18.9	
4-Me	18.9	
3-CN	14.8	
3-NO_2	14.4	
2-CN	12.1	K_2CO_3/DMF/70 °C[b]
4-CN	13.2	
4-NO_2	**10.8**	K_2CO_3/DMF/70 °C[b] **+ MeOH**

[a]Table 2. [b]Table 4.

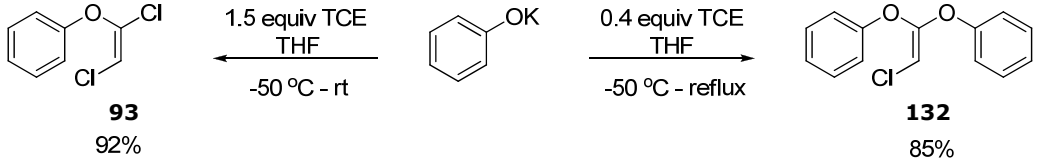
The results from the combination of Table 2 and Table 4 cover the electronic spectrum of substituted phenols and demonstrate that any phenol can likely be induced to react with trichloroethylene under one of these sets of conditions.

2.2.2.3 Exploration of Alternate Conditions

One of the alternate methods that were explored was switching the limiting reagent in the reaction of phenol with trichloroethylene. As reported in Table 2, when phenol is used as the limiting reagent, in the presence of 1.5 equivalents of TCE, **93** is isolated in excellent yield. However, when 2.5 equivalents of phenol are treated with

trichloroethylene, the ketene acetal **132** is isolated in good yields (Scheme 92). It should be noted that while the first substitution took place at or below room temperature, the substitution reaction of potassium phenolate with **93** required refluxing temperature.

Scheme 92. Mono- and di- reaction of phenol with TCE.



93
92%

132
85%

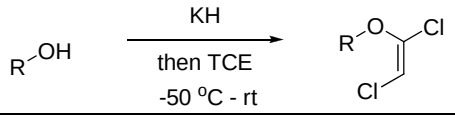
In an attempt to explore the effect of the base, the reaction was performed using NaH in place of KH; however, the reaction was very slow at room temperature, and increasing the temperature to 65 °C led to the formation of a 6.3:1.0 mixture of products **93**:**132**.

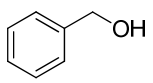
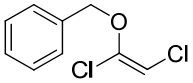
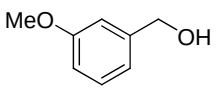
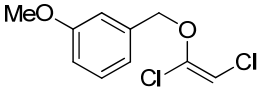
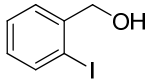
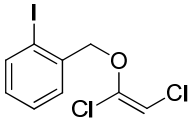
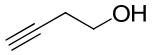
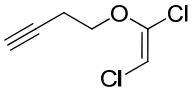
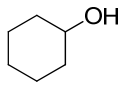
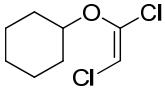
As briefly discussed above, phase-transfer protocols based on the work of Pielichowski[408,443] were also unsuccessful in our hands. Conversions were generally low, and in the reaction of phenol with TCE, a 1.5:1.0 mixture of **93**:**132** was observed by ^{1}H NMR analysis of the crude reaction mixture.

2.2.3 Aliphatic Alcohol Donors

Aliphatic alcohols had already been well established as excellent nucleophiles in this reaction (see section 2.1), so little exploration was done in this area. Our results are reported in Table 6. Reactions between benzyl alcohols **133**, **135** or **137** and trichloroethylene were facile, and dichlorovinyl ethers **134**, **136** and **138** were isolated in good yields (entries 1 – 3). Reaction between alkynol **139** and trichloroethylene also proceeded easily; however, the resulting dichlorovinyl ether **140** is very volatile, and purification via column chromatography resulted in a significant mass loss (entry 4). Not surprisingly, cyclohexanol **141** was also a good nucleophile, and **142** was isolated in excellent yield (entry 5).

Table 6. Aliphatic alcohols as nucleophiles in the reaction with TCE.



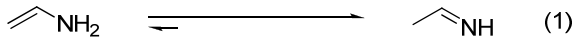
entry	R-OH	product	yield[a]
1	 **133**	 **134**	64%
2	 **135**	 **136**	87%
3	 **137**	 **138**	68%
4	 **139**	 **140**	20%
5	 **141**	 **142**	90%

[a]Isolated yield.

Use of triphenylsilanol as a nucleophile was attempted under a few conditions; however, in no case was any adduct detected. It would be expected that silanols would be good nucleophiles, so it is likely here that competing disiloxane formation was the problem. Commercial potassium salts of *tert*butanol and trimethylsilanol also failed to give isolable product; this is not surprising as Greene has reported that tertiary alcohols often gave unstable products[420] although the successful reaction between *tert*butanol and trichloroethylene using a different procedure (*t*BuOH, KH, TCE in THF with catalytic amounts of iodine) was recently reported.[444]

2.2.4 Aniline and *N*-Heterocyclic Donors

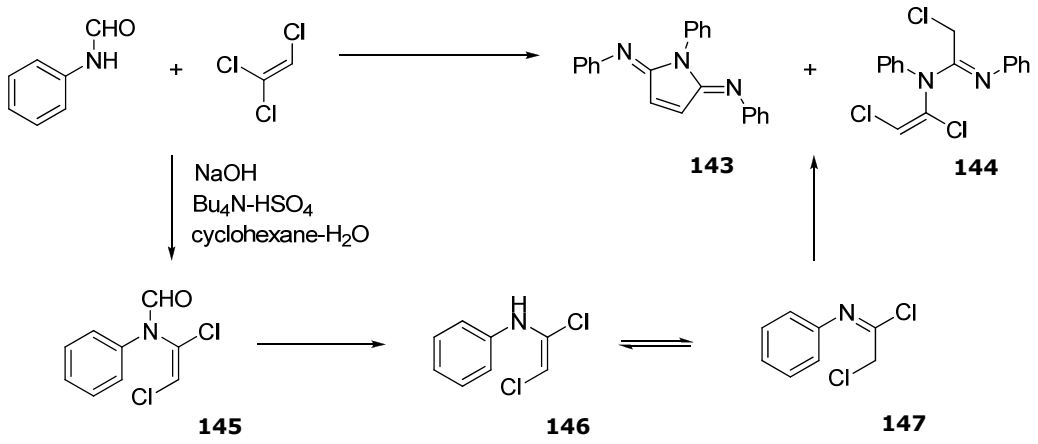
After successful synthesis of dichlorovinyl ethers from phenols, we wished to evaluate the functionalization of anilines to dichlorovinyl amides. Enamines are in tautomeric equilibrium with imines; in simple cases, that equilibrium lies heavily to the right (equation 1).[445]



(1)

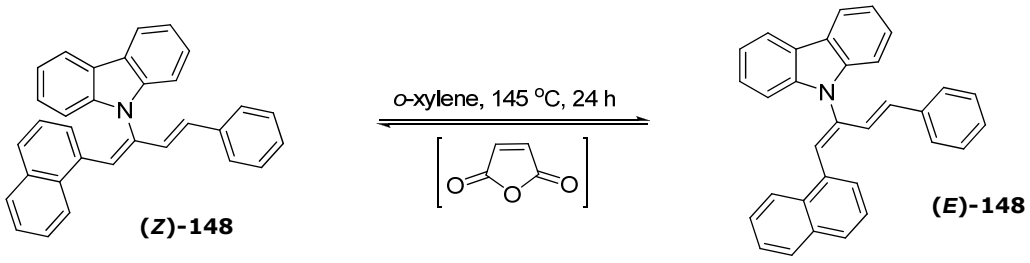
There are not many examples of the reactions of anilines with trichloroethylene, successful or otherwise. In fact, the reactions of aniline, *N*-methylaniline or diphenylamine with either trichloroethylene or tetrachloroethylene at 120 ^{o}C were all reported to give mixtures of products, none of which was a vinyl amine.[446] In the example of *N*-formyl aniline adding to TCE, the dichlorovinyl amide **145** was formed, but lost the formyl group to give the dichlorovinyl amine **146** (Scheme 93).[447] This intermediate isomerized to imine **147**, and further reacted to give products **143** and **144**. The authors also noted that they were unable to use aniline, *N*-methylaniline or diphenylamine, and hypothesized that aniline was simply not basic enough to generate the required dichloroacetylene from trichloroethylene under these conditions.[447] Dichlorovinylaniline **146** was reported by others to be unstable, rapidly isomerizing to **147**, even when synthesized under different conditions.[448]

Scheme 93. Reaction of *N*-formyl aniline with TCE.[446]



Isomerization of carbazole-based enamines has been observed in attempted Diels-Alder reactions (Scheme 94).[449] While the full details were not disclosed, the interchange between (*Z*)-**148** and (*E*)-**148** was attributed to either acid-catalyzed or thermal rearrangements or both. A similar isomerization was also observed in $CDCl_3$ and 1,2,4-trichlorobenzene.

Scheme 94. Isomerization of carbazole enamines.[449]



Taking these observations into consideration, it seemed likely that an appropriate *N*-protecting group on aniline would still allow it to participate in nucleophilic substitution reactions with trichloroethylene and would also prevent subsequent isomerization to the corresponding imine, either through loss of the protecting group as in Scheme 93, or via an iminium ion intermediate. For these reasons, carbonyl- and sulfonyl-based protecting

groups (other than formyl) were chosen to 'tie-up' the nitrogen lone-pairs and retain geometric stability of the dichloroenamine.

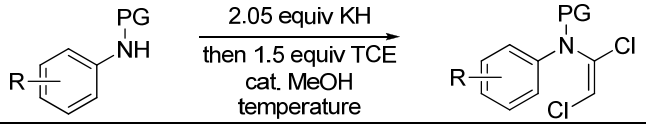
N-Acetyl aniline was first examined; while adduct **149** was isolated in modest yield (Table 7, entry 1), the ^{1}H NMR signals were broadened, suggesting hindered rotation about the amide bond. In contrast, the *N*-Boc and *N*-tosyl anilines only reacted cleanly with TCE in the presence of catalytic amounts of methanol, yielding adducts **150** to **155** (entries 2 – 7). In the case of *N*-Boc anilines, addition of methanol minimized the elimination of HCl from the resulting dichlorovinyl amides to form terminal chloro ynamides (Scheme 95). For example, when *N*-Boc aniline was reacted with trichloroethylene in the absence of methanol, a 1.65:1.00 mixture of dichlorovinyl amide **150** and ynamide **157** was isolated, as judged by analysis of the ^{1}H NMR spectrum of the unpurified crude reaction material, but when catalytic amounts of methanol were added (approximately 5 mol%), amide **150** was the sole product (Scheme 95). *N*-Boc-*m*-nitroaniline always underwent this elimination even in the presence of methanol, but the small amount of chloro ynamide could be easily separated from the desired dichlorovinyl amide **152** via column chromatography. The mild reaction could potentially be optimized to solely produce the ynamides, as these are useful compounds in their own right.[450,451] An attempt to react *N*-Boc-*p*-nitroaniline with TCE gave an intractable mixture of products.

In contrast to the reactions with the Boc-protected anilines, methanol was essential for reactions using *N*-tosyl anilines, and no reaction occurred in its absence. Even in the presence of methanol reaction with TCE was very slow in all cases (entries 5 – 7). With the simple *N*-tosyl aniline, only 61% of the dichlorovinyl amide **153** could be isolated after 3 days at reflux (Table 7, entry 5). However, the application of Sales and Mani's conditions[435] (as in Table 4) resulted in a much faster reaction and **153** was isolated in 68% yield after only 12 h (entry 6). *N*-Tosyl-*p*-methoxyaniline reacted faster than *N*-tosyl aniline, and **154** was isolated in good yield (entry 7). Not surprisingly, *m*-nitro tosyl aniline reacted much slower, and **155** could only be isolated in low yield after

3 days at reflux (entry 8). *N*-Tosyl-*m*-nitroaniline failed to react with trichloroethylene at all, even after days at reflux.

In addition to protected anilines, *N*-cyclohexyl-4-methylbenzamide could also react with TCE, giving adduct **156** in good yield (entry 9).

Table 7. Synthesis of dichlorovinyl amides.



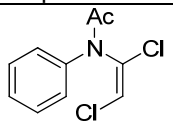
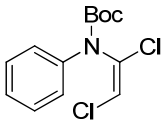
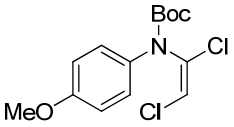
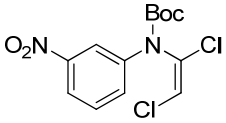
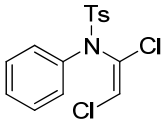
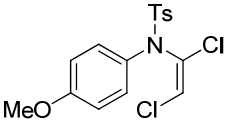
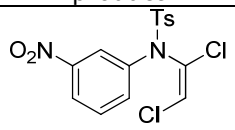
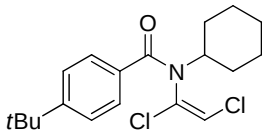
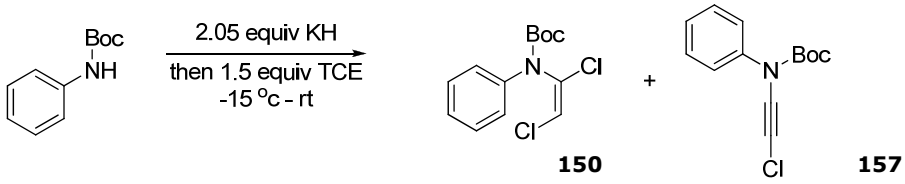
entry	temperature	t (h)	product	yield[a]
1	-15 °C - rt	12	 **149**	43%
2	-15 °C - rt	12	 **150**	84%
3	-15 °C - rt	12	 **151**	64%
4	-15 °C - rt	12	 **152**	83%
5	-15 °C – reflux	72	 **153**	61%
6[b]	70 °C	12		68%
7	-15 °C – reflux	72	 **154**	83%

Table 7 *con't*

entry	temperature	t (h)	product	yield[a]
8	-15 °C – reflux	72	 **155**	27%
9	-15 °C - rt	12	 **156**	66%

[a]Isolated yields. [b]1 equiv aniline, 3 equiv K_2CO_3, 3 equiv TCE, DMF, 70 °C, overnight.

Scheme 95. Effect of methanol on the elimination side reaction.

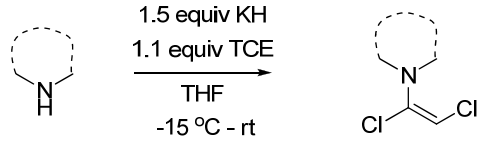


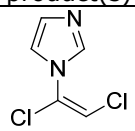
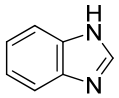
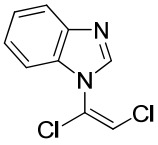
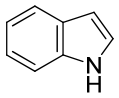
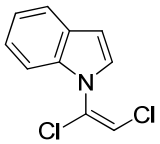
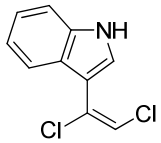
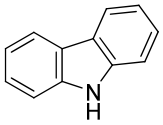
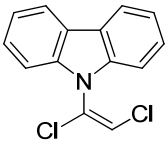
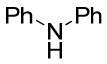
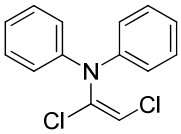
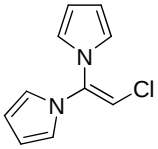
150 **157**

no methanol:	1.65	:	1.00
5 mol% MeOH:	1.00	:	0.00

The reactions of nitrogen heterocycles with TCE under phase-transfer conditions was studied fairly extensively by Pielichowski in the 1980s and 90s.[452-460] As was observed with phenolic nucleophiles (section 2.2.2.3), the application of the phase-transfer conditions with nitrogen nucleophiles was not very successful in our hands; the addition of carbazole to TCE was observed to be quite slow and use of Greene's conditions[409] proved more useful (Table 8). Imidazole and benzimidazole derivatives **159** and **161**, respectively, were isolated in good yields (entries 1 and 2).

Table 8. Synthesis of dichlorovinyl amines from nitrogen heterocycles.



entry	starting material	product(s)	yield[a]
1[b]	 **158**	 **159**	85%
2[b]	 **160**	 **161**	64%
3[c]	 **162**	 **163** 3  **164** 1	60%[d]
4[c]	 **165**	 **166**	34%
5	 **167**	 **168**	56%
6	 **169**	 **170**	6%[e]

[a]Isolated yields. [b]23 hour reaction time. [c]1.5 hour reaction time. [d]Combined yield of both isomers. [e]Degradation suspected.

Reaction between trichloroethylene and indole (**162**) gave a mixture of *N*- and *C*-functionalized dichloroethylenes **163** and **164** in a 3:1 ratio with a combined yield of 60% (entry 3). A similar 3:1 ratio of *N*:*C* alkylation was observed by Nilsson et al. in the nucleophilic substitution reaction between the sodium salt of indole and 1-phenyl-1-bromoethane.[461] In nucleophilic substitution reactions (S_N), if the electrophile is easily ionized, *N*(1)-alkylation is increased relative to *C*(3) alkylation and the reaction will proceed primarily through S_N1. Put in other terms, the 'harder' the electrophile, the more *N*(1) (S_N1) alkylation will be favoured.[462] Carbazole reacted a bit more sluggishly and gave adduct **166** in modest yield (entry 4). The analogous untethered diphenylamine **167** also reacted with TCE to give **168** in 56% yield. Interestingly, when the reaction was attempted with pyrrole (**169**), the expected monoadduct was not detected; rather the bis addition adduct **170** was isolated in low yield, and degradation during purification was observed. The pyrrole derivative has been prepared before from the potassium salt of pyrrole and TCE (under reflux) but was purified via distillation.[463]

2.2.5 Summary

A wide variety of oxygen- and nitrogen-based compounds were shown to be effective nucleophiles to functionalize trichloroethylene using one of two sets of conditions, with only minor modifications necessary. In cases in which the nucleophilicity of the potassium salt was predictably decreased, the addition of methanol proved to be necessary for reaction (Table 4, entry 4 and Table 7, entries 5, 7 and 8). This electronically and structurally diverse set of compounds was next evaluated in metal-catalyzed cross-coupling.

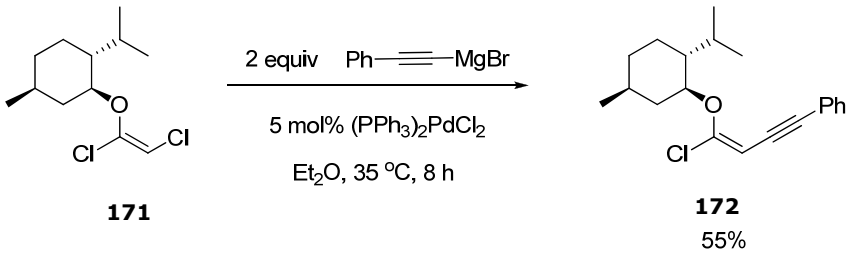
2.3 Site Selective Cross-Coupling

With the dichlorovinyl ethers and amides in hand, the focus of research turned to developing a palladium-catalyzed transformation of a single C-Cl bond. The development and optimization of such a method was necessary for the rest of the project, as this constituted the first step in the synthesis of both tri- and tetrasubstituted alkenes (section 2.4), as well the first step in the synthesis of benzofurans (section 2.5).

2.3.1 Introduction

There was only a single literature example of dichlorovinyl ethers participating as electrophiles in a palladium-catalyzed cross-coupling reaction prior to the start of the work in this thesis.[464] Schmidt and coworkers described the palladium-catalyzed cross-coupling of a magnesium acetylide and menthol-derived dichlorovinyl ether **171**. The resulting enyne **172** was reported to be isolated as a single isomer functionalized at C^2 (Scheme 96), though no characterization data were offered. The authors also mentioned that all other conditions attempted to alkynylate **171** (such as Stephens-Castro, Corey-House, or Sonogashira reactions) provided only trace amounts of **172** and in failed reactions, careful work-up procedures had to be followed to avoid hydrolysis of the starting material.

Scheme 96. Literature example of palladium-catalyzed functionalization of a 1,2-dichlorovinyl ether.[464]

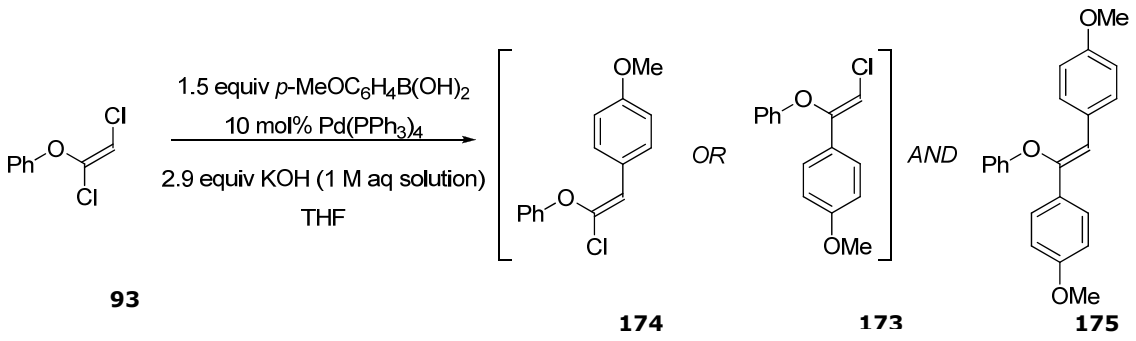


171 **172**
55%

As it appeared that dichlorovinyl ethers may be somewhat fragile in conditions used in highly basic palladium-catalyzed cross-couplings, we chose to first work with organoboronic acids as nucleophiles as they are air-stable, tolerant to a wide variety of functionality and conditions needed for efficient cross-coupling of organoboronic acids are generally very mild (section 1.2.1.8).[114,465]

As discussed in section 1.3.3, Organ and coworkers reported a one-pot, sequential cross-coupling of (*E*)-1-chloro-2-iodoethylene with two different boronic acids using the simple palladium catalyst, $Pd(PPh_3)_4$ (Scheme 55)[271] With our eye on the eventual goal of functionalizing both C-Cl bonds of our dichlorovinyl ethers, Organ's conditions for Suzuki coupling seemed promising and were applied to cross-coupling **93** with a boronic acid. Indeed, when dichlorovinyl ether **93** and 1.5 equivalents of *p*-methoxyphenyl boronic acid were combined in the presence of $Pd(PPh_3)_4$ and aqueous KOH in refluxing THF, Suzuki coupling ensued, and an approximately 1:1 ratio of a single monoarylated chlorovinyl ether (either **174** or **173**) to diarylated vinyl ether **175** was isolated (Scheme 97).

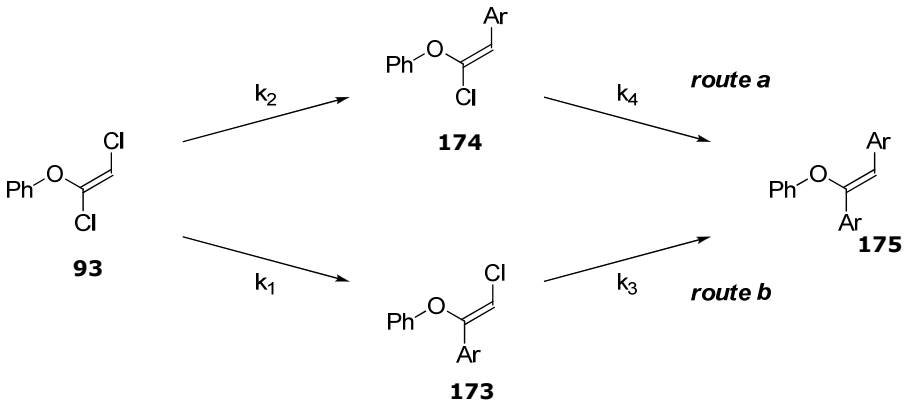
Scheme 97. Cross-coupling between dichlorovinyl ether **93** and 1.5 equiv boronic acid.



A simplified representation of the possible orders of reactions occurring in Scheme 97 and their corresponding rate constants are outlined in Scheme 98. The rate constant relating to formation of C^1-arylated compound **173** from **93** is designated k_1, and the

rate constant for formation of C^2-arylated compound **174** from **93** is k_2; k_3 and k_4 are the rate constants relating to formation of **175** from **173** and **174**, respectively. If k_1 and k_2 are comparable, then both **174** and **173** would be detected at the end of the reaction, so long as k_3 and k_4 are not significantly larger than k_1 and k_2. If all reactions are occurring at similar rates (i.e. $k_1 \approx k_2 \approx k_3 \approx k_4$), then the reaction is occurring via routes a and b (Scheme 98) at the same time, and all of **174**, **173** and **175** would be observed. If the rate of the second arylation from either **174** or **173** to **175** is faster than the rate of formation of **174** or **173** from **93** (i.e. k_3 or $k_4 >> k_1$ or k_2), then when all the boronic acid is consumed, there would be mostly **175** with unreacted **93**, as **174** or **173** would be consumed as soon as they formed. The equal ratio of mono- (**174** or **173**) to diarylated (**175**) adducts suggested that the first equivalent of boronic acid was installed at a single position, or that k_1 (or k_2) is sufficiently larger than k_3 (or k_4) that once the first cross-coupling was complete, cross-coupling occurred at the second position.

Scheme 98. Outline of the possible routes to formation of both mono- and diarylated adducts in the Suzuki coupling using 1.5 equivalents of $ArB(OH)_2$ with **93**.



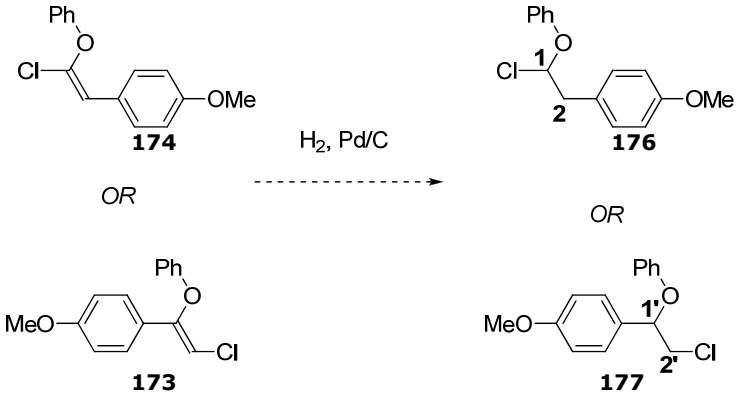
It was also possible that both **173** and **174** were being produced in the reaction between **93** and 1.5 equivalents of boronic acid; if the rate of the second arylation was sufficiently greater than the first arylation (i.e. $k_3 >> k_1$ or $k_4 >> k_2$), then only one of **173** or **174** would be observed in the overall reaction. However, when the reaction was repeated using only a single equivalent of *p*-methoxyphenyl boronic acid with respect to

93, a single product was formed in high yield, although it was not certain at this point whether this product was C^2 functionalized **174** or C^1 functionalized **173**.

We suspected that the monoarylated product was C^1 functionalized **173**. Electronically, 1,2-dichlorovinyl ether **93** is similar to 2,3-dibromobenzofuran **81**, which has been demonstrated to undergo site selective cross-coupling to give 2-aryl-3-bromobenzofuran **82** (Scheme 35).[466] As discussed in section 1.2.4, oxidative addition is known to occur at the most electron-poor centre, and C^1 is more electron-poor than C^2 in 1,2-dichlorovinyl ether **93** due to the polarization of the double bond by oxygen. However, given Schmidt's results in Scheme 96, we needed to unambiguously assign the structure of monoarylated compound reported in Scheme 97 to either **174** or **173**.

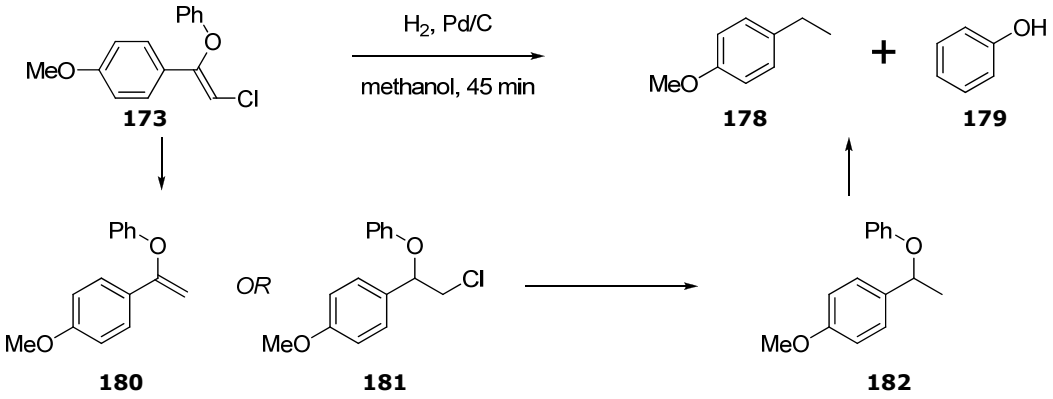
Hydrogenation of **174** or **173** to **176** or **177** (Scheme 99) was selected as the method for assigning the structure of the monoarylated adduct. Compound **176** is a chloromethyl ether at C^1 (1H, ^{1}H NMR chemical shift ~ δ 5.5 ppm) and has a benzylic carbon at C^2 (2H, δ ^{1}H NMR chemical shift ~ δ 2.3 ppm) whereas **177** is a benzyl ether at $C^{1'}$ (1H, ^{1}H NMR chemical shift ~ δ 4.5 ppm) and an alkyl chloride at $C^{2'}$ (2H, ^{1}H NMR chemical shift ~ δ 3.5 ppm); as these would have distinctly different ^{1}H NMR spectra, hydrogenation followed by simple ^{1}H NMR analysis of the product would unambiguously assign the cross-coupling product to either **174** or **173**.

Scheme 99. Expected products from hydrogenation of **174** and **173**.



When the monoarylated adduct (**174** or **173**) was hydrogenated, an equimolar mixture of 4-methoxyethylbenzene (**178**) and phenol (**179**) was isolated (Scheme 100), clearly demonstrating that the cross-coupling occurred at C^1-Cl and not C^2-Cl and that the monoaryl adduct could be assigned structure **173**. These products formed from three sequential reductions of **173**. The first reduction would reduce either the C-Cl bond or the alkene, giving products **180** or **181**, respectively. The second reduction would then reduce either the alkene or C-Cl bond, depending on the product of the first reduction, yielding **182**. Compound **180** could also be formed via elimination of HCl from **181**. Benzyl ether **182** is easily reduced under these conditions, giving the tell-tale products **178** and **179**. Overreduction of **176** from **174** would have yielded 1-phenoxy-2-(4-methylphenyl)ethane as the sole product, and would not further break down to the observed products **178** and **179** under these conditions.

Scheme 100. Hydrogenation of mono arylated adduct to assign site selectivity.



This also makes sense in light of the discussion in section 1.2.4; the ^{1}H NMR shift of C^1-H is δ 6.46 ppm, as compared to δ 4.17 ppm of C^2-H; H^1 is more downfield and therefore more electron-poor. The analogous chlorinated compounds should undergo site selective reactions with palladium at C^1-Cl.[180]

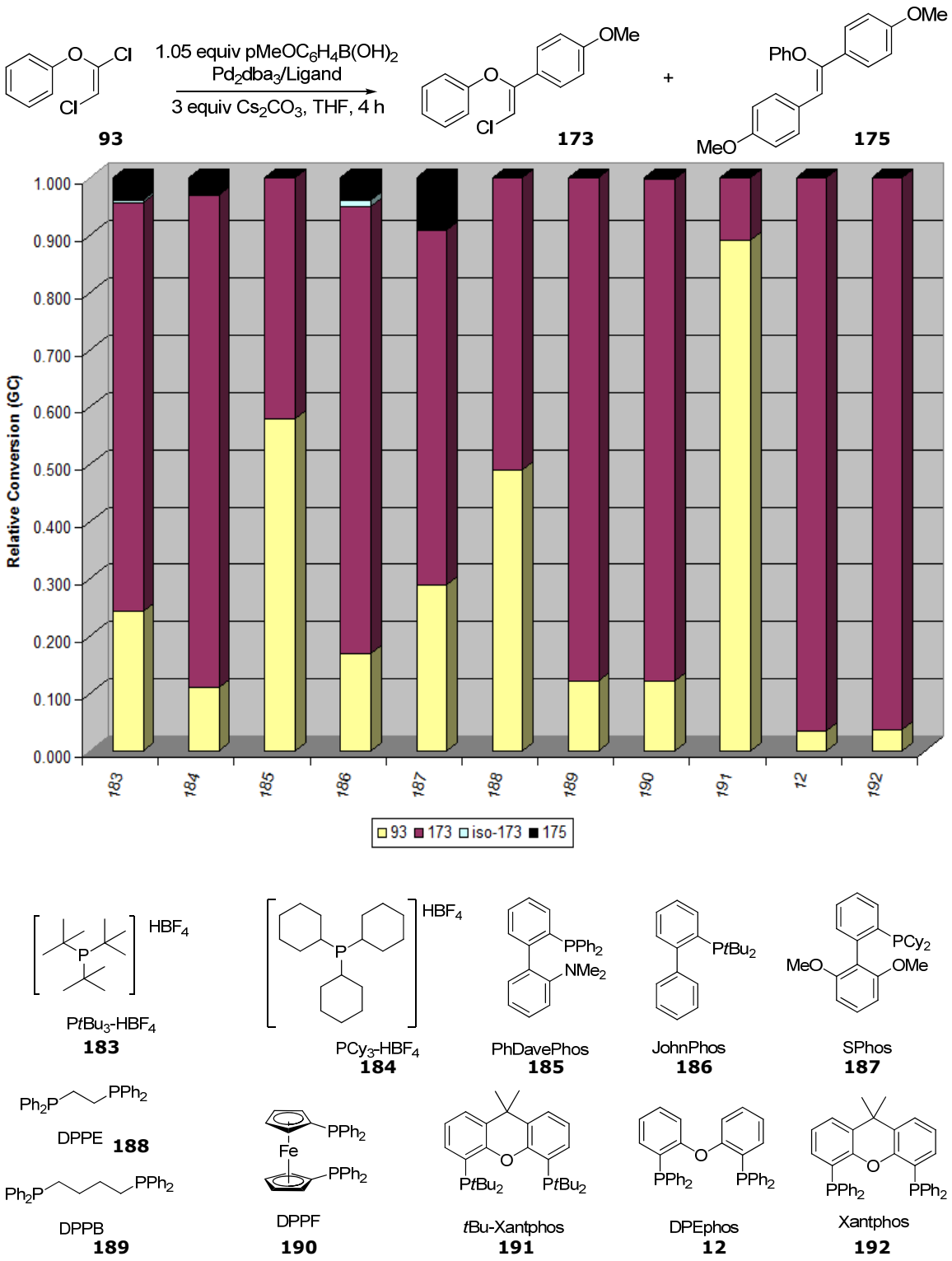
Figure 11. Order of reactivity of a dichlorovinyl ether and ^{1}H chemical shifts of the analogous ethyl vinyl ether.

We have demonstrated that analogous cross-coupling reactions can be performed with alkyl organoborane and organozinc reagents, as well as terminal alkynes; all reactions occur with excellent site selectivity and give a single product (see section 2.3.3). While we only performed the hydrogenation of a monofunctionalized adduct to determine site selectivity for structure determination of the adduct from the reaction above, all types of cross-coupling adducts (i.e. C^1-alkyl, -alkenyl, and –alkynyl) were shown to be able to undergo a direct arylation to give 2-substituted benzofurans (section 2.5). This second reaction proves that the first cross-coupling reaction does occur at C^1-Cl selectively and not at C^2-Cl. Our results are in clear contrast with Schmidt's report that cross-coupling between their alkyl derived dichlorovinyl ether and a magnesium acetylide occurred at C^2-Cl (Scheme 96).[464] Given that we have shown that a wide variety of organometallic nucleophiles react with dichlorovinyl ethers in the presence of palladium with the same (complete) site selectivity, it is likely that the structure of the cross-coupling adduct isolated by Schmidt et al. was misassigned.

2.3.2 Optimization of Suzuki Coupling

With the first cross-coupling determined to occur selectively at C^1, we then moved on to optimize the chemistry and explore the scope of the reaction. While explorations of the scope of Suzuki cross-couplings using the aqueous $Pd(PPh_3)_4$ conditions developed by Organ[271] were in progress (vide infra), we were also exploring the combination of Pd_2dba_3 with a variety of ligands as catalysts in the cross-coupling between **93** and *p*-

methoxyphenyl boronic acid in the presence of Cs_2CO_3 in refluxing THF (Figure 12). In all cases, the reaction were halted after 4 hours and the crude reaction mixture was analyzed by GC/MS for consumption of starting material **93** and formation of product(s) **173** and/or **175**. Palladium catalysts derived from electron-rich phosphines P*t*Bu$_3$·HBF$_4$ (**183**) and PCy$_3$·HBF$_4$ (**184**), as well as biarylphosphines JohnPhos (**186**) and S-Phos (**187**) were unselective; while a single isomer of monoarylated material **173** could be detected, the second cross-coupling to give diarylated **175** proceeded before complete consumption of **93**. Additionally, palladium ligated with either P*t*Bu$_3$·HBF$_4$ (**180**)[467] or JohnPhos (**186**) produced compound **174**, an isomer of compound **173**. We are not completely sure of its structure. Given that these ligands promoted double arylation, it is possible that it is the C^2-arylated isomer, and we have tentatively assigned the structure of this product to **174**. It could also be the geometrical isomer of **173** ((*E*)- **173**); this material was never isolated for characterization. Palladium-*t*butyl-Xantphos (**191**) was the least effective catalyst, leading to only 11% conversion of **93** to **173**, and the catalyst from palladium and PhDavePhos (**185**) was only slightly more reactive and showed roughly 42% conversion after 4 h. Of the remaining bidentate ligands, palladium ligated with DPPE (**188**) was the slowest (~51% conversion), followed by DPPB (**189**) and DPPF (**190**) (both ~87% conversion) and the palladium complex derived from either Xantphos (**192**) or DPEphos (**12**) gave about 96% conversion to monoarylated intermediate **173** after 4 h.



Conditions: 2.5 mol% Pd_2dba_3, 7.5 mol% **183** - **185** or 5 mol% **12**, **186** – **192**. The data are normalized to 1.

Figure 12. Ligand screen for site selective cross-coupling on dichlorovinyl ether.

There is a correlation between the bite angle of the bidentate ligands and the relative converions from **93** to **173** (Figure 13). DPPE, the ligand with the smallest bite angle studied, formed a catalyst with palladium that converted only 51% of **93** to **173**. Increasing the bite angle of the ligand to 99° created a more active catalyst; employing either DPPB or DPPF as the ligand led to over 80% conversion to **173** after 4 hours. Increasing the bite angle further (DPEphos has a bite angle of 104° and Xantphos has a bite angle of 110°) led to an even more active catalyst, and **93** was nearly completely converted to **173** when either ligand was employed. However, the catalyst derived from Pd and *t*BuXantphos, which has a bite angle of 140°, was a poor catalyst, and only 11% conversion of **93** to **173** was detected after 4 hours. These data suggest that catalysts with ligands having bite angles around 100° are optimal; catalysts having smaller bite angle ligands likely undergo slower reductive elimination, whereas catalysts with large bite angle ligands are likely to be slower in oxidative additions. It should be noted that *t*BuXantphos is more electron-rich than any of the other bidentate phosphines studied, and this may also influence the relative rate.

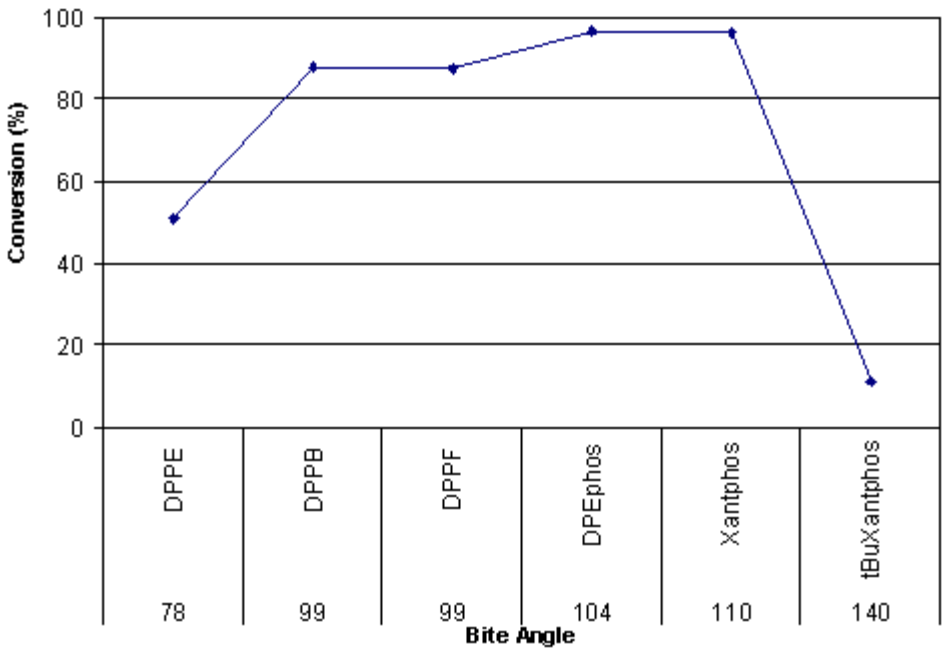
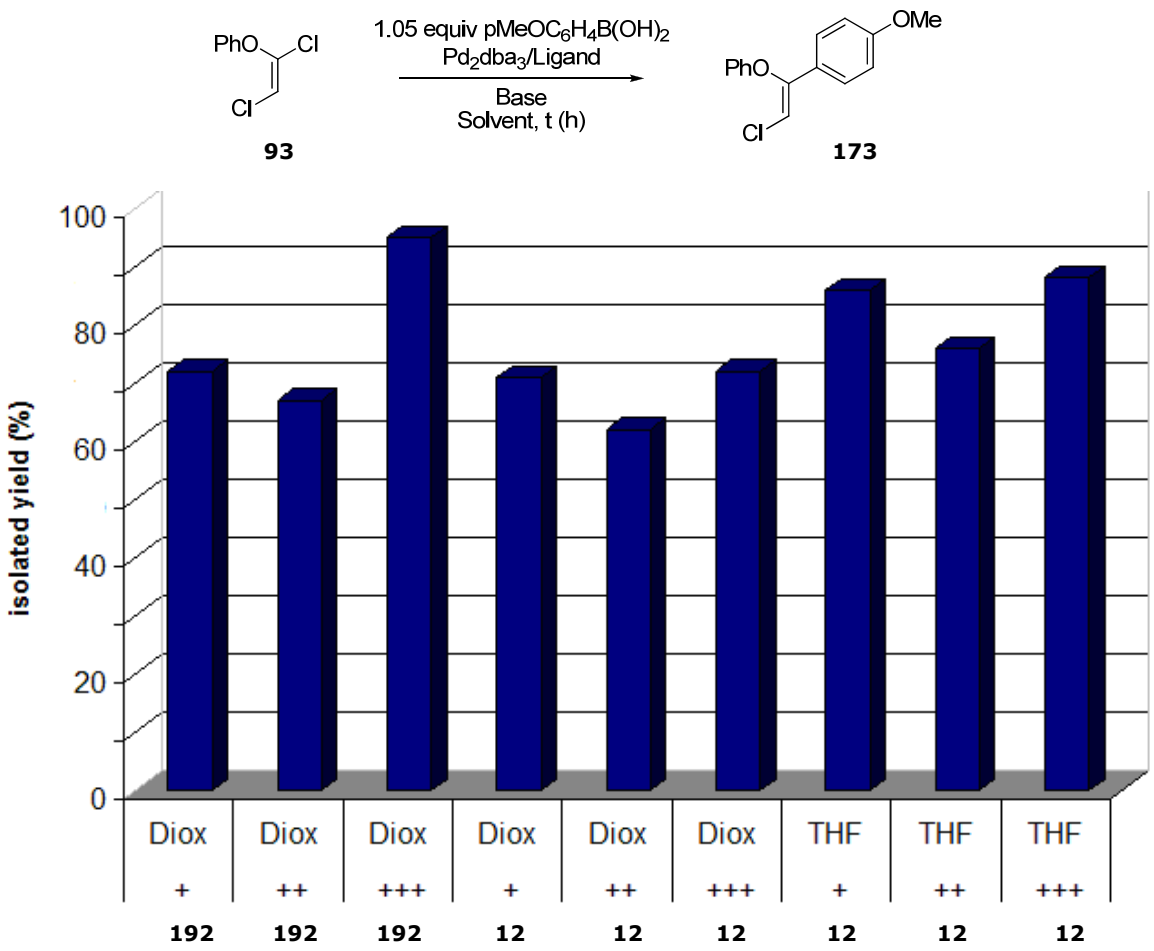


Figure 13. Bite angle of the phosphine ligand and the relationship to conversion of **93** to **173**.

Correlation between conversion and cone angle of the corresponding monodentate phosphines is not obvious as the catalysts containing these ligands tended to be less selective than those containing bidentate ligands (Figure 12).

After determining that catalysts with either DPEphos (**12**) or Xantphos (**192**) as ligands showed the highest reactivity under these conditions, we sought to evaluate the effect of the base and the temperature on the transformation (Figure 14). While reactions in THF (65 ^{o}C) generally took about 5 h to go to completion, reactions in dioxane were complete in about 1 hour. When Xantphos **192** was used as the ligand, it didn't matter much if the base was CsF or Cs_2CO_3, but the isolated yield of **173** was greatly improved by using the CsF-Cs_2CO_3 couple (Figure 14). With DPEphos **12** as the ligand however, the rate of reaction was about the same with CsF or CsF-Cs_2CO_3 but the yield was somewhat lower when Cs_2CO_3 was used alone. This was the trend observed in

both THF at 65 °C and in dioxane at 100 °C in, though isolated yields of **173** were higher when THF was used as the solvent.

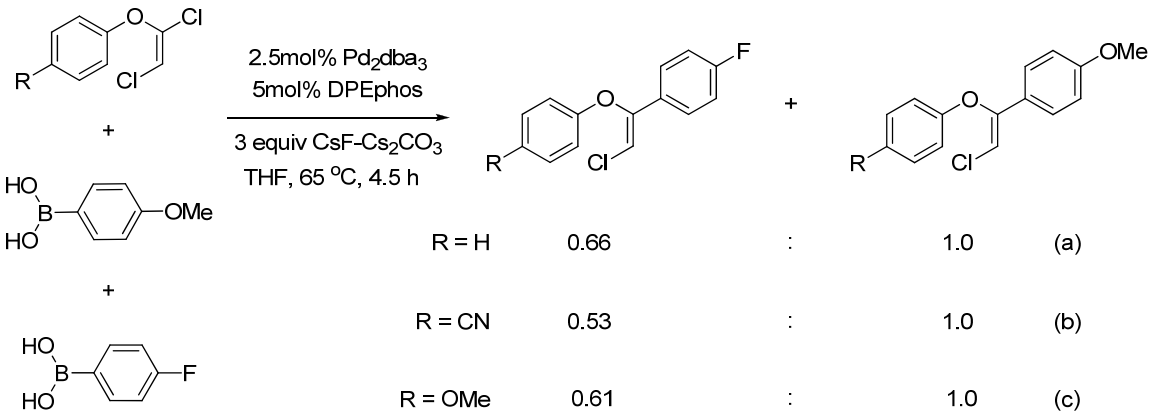


Legend: Diox = dioxane (all reactions ran for 1 hour), THF (all reactions ran for 6 h). + = CsF only (3 equiv), ++ = Cs_2CO_3 only (3 equiv), +++ = CsF-Cs_2CO_3 (3 equiv each). All yields reported are those of isolated pure material.

Figure 14. The effect of base and solvent with Xantphos **192** and DPEphos **12** as ligands on Suzuki cross-coupling**.**

We also briefly examined the mechanism of Suzuki coupling at C^1-Cl; though the basics of the mechanism are well-known (section 1.2.1.1), we wanted to ensure that we understood this part of the overall process. In the first of these experiments, an equimolar mixture of dichlorovinyl ether (one of **93**, **110** or **126**), *p*-fluorophenylboronic acid and *p*-methoxyphenylboronic acid were heated in the presence of palladium for 4.5 h. If oxidative palladium insertion into the C-Cl is rate determining, there would be approximately equal amounts of both the C^1 *p*-fluorophenyl and C^1 *p*-methoxyphenyl derivatives formed. This would only be true if all other competing pathways (e.g. degradation, homocoupling of the boronic acids) were occurring at the same rate for both the methoxy- and fluoro-functionalized compounds. If the transmetallation is rate determining, the methoxyphenyl derivative should be produced faster, as more electron-rich boronic acids undergo faster transmetallation. In all cases, the *p*-methoxyphenyl derivative was produced faster than the *p*-fluorophenyl derivative (Scheme 101), consistent with a rate-determining transmetallation step.

Scheme 101. C^1 arylation competition experiments varying the boronic acid.



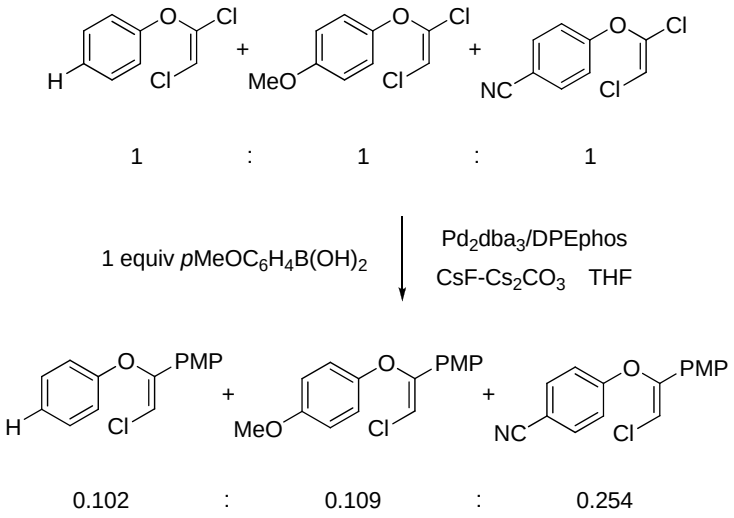
When we combined an equimolar mixture of **93**, **110** and **126** with *p*-methoxyphenylboronic acid in the presence of palladium, the *p*-cyanophenol derivative **126** was both consumed and converted to the monoarylated derivative fastest,

consistent with faster oxidative addition of electron-poor electrophiles (Scheme 102). The results of these experiments are not surprising, and are consistent with the standard palladium-catalyzed cross-coupling mechanism.[468]

It should be pointed out that the conditions found to be optimal for the cross-coupling of **93** with *p*-methoxyphenyl boronic acid are nearly identical to those reported by Roulland to be successful for monofunctionalizing 1,1-dichloroethylenes with alkyl-9-BBN compounds (Scheme 36).[189] In fact, our transformation was based on the conditions in that report.

With two sets of catalytic conditions in hand, both aqueous and anhydrous, the scope of the reaction was next to be explored. Ideally, all major types of organometallics would prove to be able to be incorporated under either one of these conditions: alkyl, alkenyl, aryl, heteroaryl, and alkynyl.

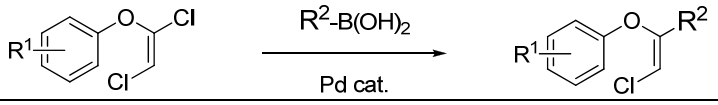
Scheme 102. C^1 arylation experiment varying the dichlorovinyl ether.



2.3.3 Scope of Cross-Couplings

Following the brief screenings of ligands and bases (section 2.3.2), we set out to synthesize a number of C^1-functionalized vinyl ethers. We found that C^1-aryl vinyl ethers **173** and **193** - **195** were easily synthesized from **93** using Roulland's Pd/DPEphos system with cesium bases in under 6 h (Table 9, entries 2, 3, 5 and 6). The relative ease of synthesis of both **194** and **173** is notable, as electron-poor boronic acids are generally less reactive than electron-rich boronic acids, and are more prone to homocoupling.[469] We also found that $Pd(PPh_3)_4$ in THF with aqueous KOH[271] resulted in a faster cross-coupling; reactions leading to **173** and **194** were complete in about 1 hour (entries 1 and 4). The reaction was also useful for C^1-arylating functionalized phenol derivatives, and adducts **196** – **199** were isolated in good yields (entries 7 – 11). The C^1-vinylated compound **200** could also be synthesized using either $Pd(PPh_3)_4$ (entry 12) or Pd/DPEphos (entry 13) as the catalyst in good yield from **93** and styryl boronic acid.

Table 9. Synthesis of (*Z*)-1-(hetero)aryl-2-chlorovinyl ethers



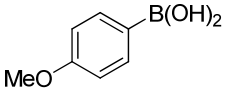
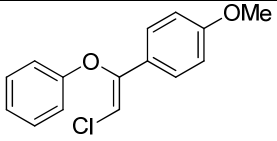
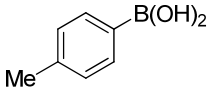
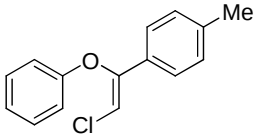
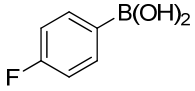
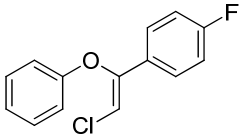
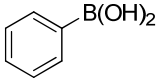
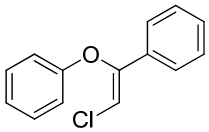
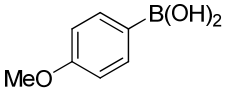
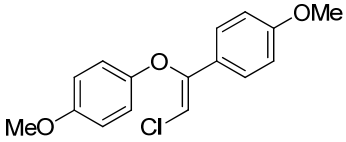
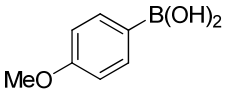
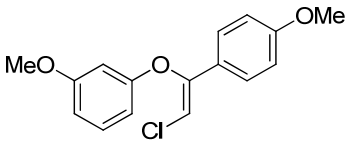
entry	boronic acid	conditions[a]	product	yield[b]
1		**A**	 **173**	85%
2		**B**		92%
3		**B**	 **193**	95%
4		**A**	 **194**	81%
5		**B**		87%
6		**B**	 **195**	60%
7		**A**	 **196**	57%
8		**B**		75%
9		**B**	 **197**	63%

Table 9 *con't*

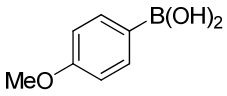
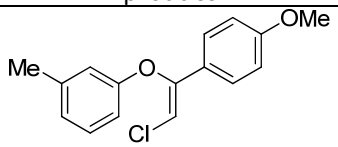
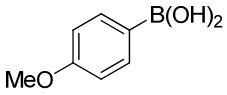
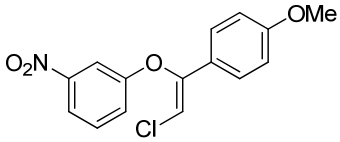
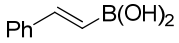
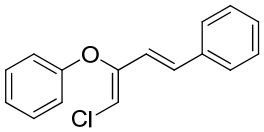
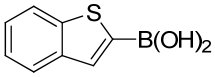
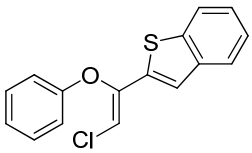
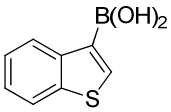
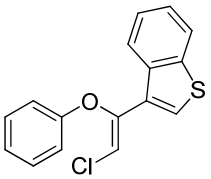
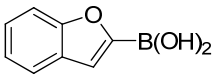
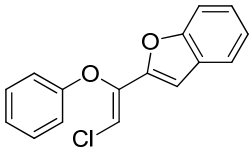
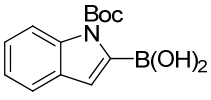
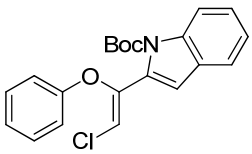
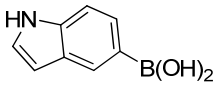
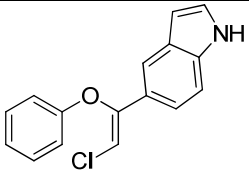
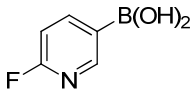
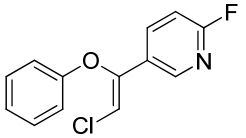
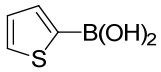
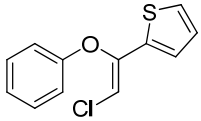
entry	reactants	conditions[a]	product	yield[b]
10		**B**	 **198**	64%
11		**B**	 **199**	80%
12		**A**	 **200**	63%
13		**B**		60%
14		**A**	 **201**	30%
15		**B**		N.R.
16		**A**	 **202**	68%
17		**B**		N.R.
18		**A**	 **203**	40%
19		**B**		N.R.
20		**A**	 **204**	52%
21		**B**		N.R.

Table 9 *con't*

entry	reactants	conditions[a]	product	yield[b]
22		**A**	 **205**	47%
23		**B**		13%
24		**A**	 **206**	67%
25		**B**		54%
26		**A**	 **207**	73%
27		**B**		18%

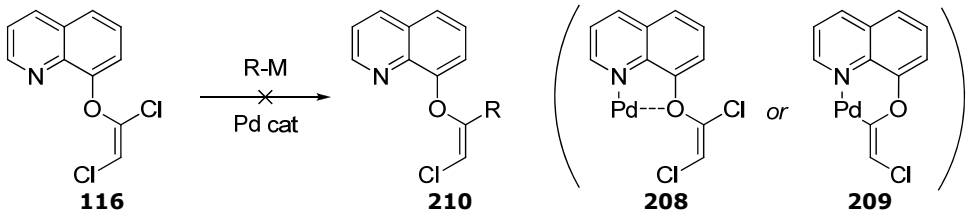
[a]Conditions **A**: 5 mol% $Pd(PPh_3)_4$, 1.05 equiv $RB(OH)_2$, 2.5 equiv KOH (1.0M in H_2O), THF, 65 °C. Conditions **B**: 2.5 mol% Pd_2dba_3, 5 mol% DPEphos, 3 equiv CsF, 3 equiv Cs_2CO_3, THF, 65 °C. [b]Isolated yields.

We found most heteroarylboronic acids to be generally unreactive in the presence of the Pd/DPEphos catalytic system (Table 9, entries 15, 17, 19 and 21), although some product could be isolated from cross-coupling between **93** and 5-indole boronic acid (entry 23), 4-fluoro-3-pyridylboronic acid (entry 25) or 2-thiophenyl boronic acid (entry 27). However, the $Pd(PPh_3)_4$/aqueous KOH system was much more general and provided the vinyl heteroaromatic species **201** – **207** in modest to good yields (entries 14, 16, 18, 20, 22, 24 and 26). 2-Metalloheteroaryls are not particularly stable and are difficult to cross-couple, accounting for the low yields in these cases.[470,471]

Quinoline derivative **116** did not participate in any cross-coupling reactions attempted (Scheme 103). This is possibly due to vinyloxy quinoline **116** itself coordinating to the palladium metal in a bidentate fashion and sequestering it via **209**. This could render it catalytically useless. Alternatively, if palladium can insert into the C^1-

Cl bond of **116**, transmetallation and/or reductive elimination from complex **209** would be difficult due to chelation of the nitrogen atom and **210** would not form.

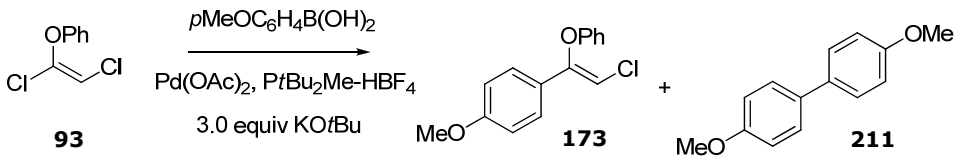
Scheme 103. Attempted cross-coupling of quinoline derivative **116** and postulated palladium complexes.



116 **210** **208** **209**

We also briefly evaluated the C^1-Cl Suzuki coupling at room temperature. Using 5 mol% $Pd(OAc)_2$ with 10 mol% P*t*$Bu_2Me{\cdot}HBF_4$, 3 equiv KO*t*Bu and 1.05 equiv pMeO-C_6H_4-$B(OH)_2$,[472] the conversion to monoaryl **173** was 17% in dioxane and 87% in *tert*butanol after 12 h at room temperature (Table 10); however, in both cases, small amounts of other (unknown) products could be detected by ^{1}H NMR of the crude material, as well as significant amounts of 4,4'-dimethoxybiphenyl **211**. Interestingly, using P*t*$Bu_2Me{\cdot}HBF_4$ as the ligand under the conditions listed in Figure 12 led to complete conversion of **93** to **173**, in contrast to the lower selectivities observed using similar ligands P*t*$Bu_3{\cdot}HBF_4$ **183** and $PCy_3{\cdot}HBF_4$. **184** (Figure 12).

Table 10. Attempted Suzuki couplings at room temperature.



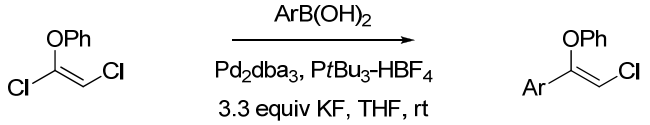
			ratios[b]		
entry	solvent	conversion[a]	**93**	**173**	**211**
1	*t*BuOH	40%	1.0	0.67	1.2
2	dioxane	13%	1.0	0.15	0.12

[a]From **93**. [b]Ratios were estimated by analysis of the ^{1}H NMR spectrum of the crude reaction mixture.

Encouraged by those results, the conditions were modified slightly according to a literature procedure for the Suzuki coupling of aryl chlorides with boronic acids (Table 11).[29] Reactions between dichlorovinyl ether and both *p*-methoxyphenyl (entry 1) and phenyl boronic acid (entry 2) proceeded smoothly, and there was high conversion to the desired aryl vinyl chlorides **173** and **195**. In contrast, reaction between vinyl ether **93** and *p*-fluorophenyl boronic acid was quite slow at room temperature, giving only 21% and 33% conversion to **194** after 16 and 68 h, respectively (entry 3). These results may be consistent with palladium oxidative insertion into the C^1-Cl bond as the fastest step, and a rate-determining slow step of transmetallation (Scheme 2). Similarly, cross-coupling between **93** and heteroaromatic boronic acids were generally quite slow, but modest amounts of the desired adducts **205**, **206** and **207** could be detected by ^{1}H NMR analysis of the crude material isolated from the corresponding reactions after 68 h of reaction time (entries 4 – 6). Cross-coupling using *trans*-phenylethenyl (styryl) boronic acid gave corresponding diene **200** in good conversion only after 68 h (entry 7). The non-linear relationship between reaction time and relative conversion to product (entries

3, 5 and 7) is curious; this could indicate catalyst decomposition and/or some induction period prior to formation of the active catalyst in the presence of those boronic acids. If this is the case, then the results are not supportive of a rate-determining transmetallation. Further experiments would need to be performed to gain better understanding of the system, and to optimize the room temperature cross-coupling reaction.

Table 11. Room temperature Suzuki cross-couplings using Pd/P*t*Bu$_3$ catalytic system.

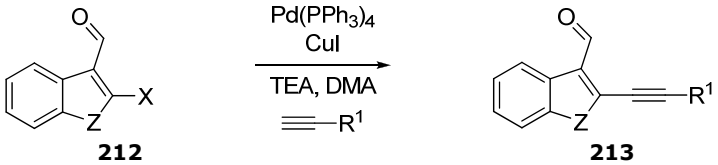


entry	Ar	product	conversion[a]
1	*p*-MeO-C_6H_4-	**173**	78%[b]
2	C_6H_5-	**195**	99%[b]
3	*p*-F-C_6H_4-	**194**	21%[b] (33%[c])
4	4-F-3-pyridinyl	**206**	28%[b]
5	2-thiophenyl	**207**	5%[b] (52%[c])
6	5-indolyl	**205**	30%[b]
7	(*trans*)-C_6H_5-CH=CH-	**200**	5%[b] (76%[c])

[a]Conversion is the ratio of product to starting material as estimated by ^{1}H NMR analysis of the crude reaction mixture. [b]After 16 h at room temperature. [c]After 68 h at room temperature.

After conditions were developed for the incorporation of aryl and heteroaryl groups into the dichlorovinyl ether, conditions were sought for the alkynylation of these compounds. Tiano and Belmont[473] had recently published conditions for Sonogashira coupling at C^2 of 2-halobenzofurans and indoles **212** to give alkynylated heterocycles **213** (Scheme 104). We reasoned that the dichlorovinyl ethers would have similar electronics, and that Tiano and Belmont's conditions should be applicable to our substrates.

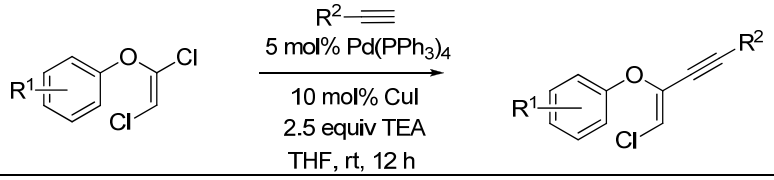
Scheme 104. Tiano and Belmont's alkynylation of heterocycles.[473]

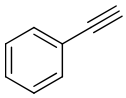
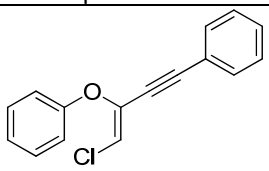
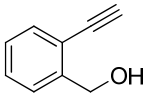
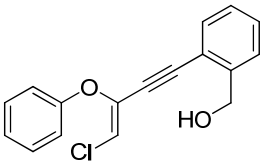
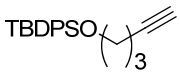
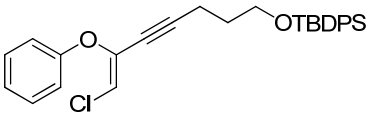
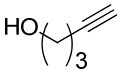
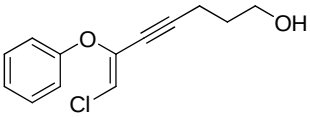
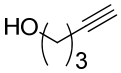
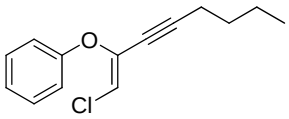
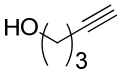
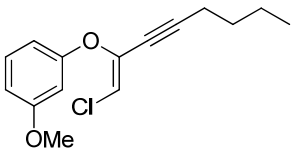
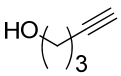
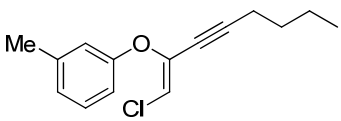


Z = O, NMe, NBn
X = Cl, Br

However, the cross-coupling between dichlorovinyl ether **93** and phenyl acetylene as performed according to the conditions presented in Scheme 104 gave the corresponding enyne in only 12% isolated yield. A simple change of solvent from DMA to THF led a great improvement in reactivity, and we found the alkynylation of dichlorovinyl ethers **93**, **111** and **117** to be facile, yielding a variety of chloro enynes in excellent isolated yields (**214** to **220**, Table 12). Dichlorovinyl ether **93** was successfully cross-coupled with a variety of terminal alkynes (entries 1 – 5), including both aromatic and aliphatic alkynes. These conditions were also found to be able to tolerate a free alcohol (entries 2 and 4), though products **215** and **217** slowly decomposed at room temperature. These conditions could also be used to cross-couple between methoxy- and methyl-derivatized compounds **111** and **117** with hexyne (entries 6 and 7).

Table 12. Sonogashira Cross-Couplings

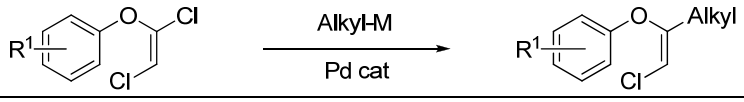


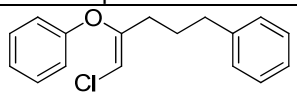
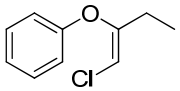
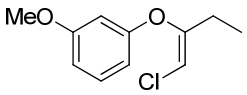
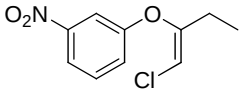
entry	reactants	product	yield[a]
1	**93** + 	 **214**	78%
2	**93** + 	 **215**	95%
3	**93** + 	 **216**	56%[b]
4	**93** + 	 **217**	90%
5	**93** + 	 **218**	77%
6	**117** + 	 **219**	64%
7	**111** + 	 **220**	65%

[a]Isolated yields. [b]There was only 66% conversion to adduct **216** as estimated by ^{1}H NMR of the crude reaction mixture.

With conditions to install aryl, heteroaryl, alkenyl and alkynyl groups at C^1 in hand, the incorporation of alkyl groups was the next task. Numerous catalytic systems were tested in the cross-coupling of **93** with *c*Hex-$B(OH)_2$ as the alkyl boronic acid, but all attempts failed; we were never able to isolate any corresponding alkylated vinyl ether. Only unreacted starting material and some degradation products could be recovered from these reactions. This was not entirely surprising as secondary alkyl boronic acids are challenging partners in cross-coupling reactions.[474] A direct application of Roulland's conditions for the cross-coupling of 1,1-dichloroethene with a 9-BBN-alkyl derivative (Scheme 36)[189] to our system was successful; the C^1-alkyl vinyl ether **221** was isolated in excellent yield (the organoboron reagent was synthesized in situ via hydroboration of allyl benzene with 9-BBN-H, Table 13, entry 1). Similarly, by adopting Negishi's method for cross-coupling dialkyl zinc reagents,[188] C^1 ethyl vinyl ethers **222** and **223** were isolated in excellent yields (entries 2 and 3). Not surprisingly, reaction between nitro functionalized dichlorovinyl ether **131** and diethyl zinc did not lead to clean conversion to **224**, and instead gave an intractable mixture of materials (entry 5).

Table 13. Synthesis of (Z)-1-alkyl-2-chlorovinylethers.



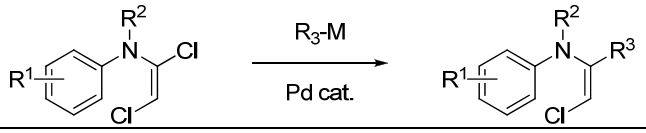
entry	reagents	conditions[a]	product	yield[b]
1	**93** + Allyl benzene 9-BBN-H	**A**[c]	 **221**	83%
2	**93** + Et_2Zn	**B**	 **222**	67%
3	**117** + Et_2Zn	**B**	 **223**	44%
4	**131** + Et_2Zn	**B**	 **224**	Intractable mixture

[a]Conditions **A**: 1.2 equiv 9-BBN-H, 1.2 equiv allyl benzene, rt, 1 h, then **93**, 2.5 mol% Pd_2dba_3, 5 mol% Xantphos, 3 equiv CsF-Cs_2CO_3, THF, 65 °C, 16 h. Conditions **B**: 1.1 equiv Et_2Zn, 2.5 mol% Pd_2dba_3, 5 mol% DPEphos, DMF or THF, rt, 12 h. [b]Isolated yields. [c]Allyl benzene was treated with 9-BBN-H for one hour prior to addition of the other reagents. See experimental section for details.

The 1,2-dichlorovinyl amides and amines were also examined in cross-coupling (Table 14). The *N*-acetyl aniline **149** and benzamide **156** degraded under all cross-coupling conditions tried. *N*-Tosyl aniline **153**, in contrast, reacted readily with *p*-methoxyphenyl boronic acid to give arylated compound **225**; using the standard DPEphos conditions, adduct **225** was isolated in 81% yield (entry 1) but the corresponding room temperature reaction was quite slow, and after 25 h, only 41% of **225** was isolated (entry 2). Using $Pd(PPh_3)_4$/aqueous KOH conditions gave an intractable mixture of products. The *N*-tosyl *p*-methoxy (**154**) and *m*-nitro (**155**) compounds also reacted with *p*-methoxyphenyl boronic acid under the room temperature conditions, giving adducts

226 and **227** in moderate isolated yield (entries 3 and 4). In contrast to the *N*-tosyl protected vinyl amides, the *N*-Boc-protected vinyl amides reacted cleanly with *p*-methoxyphenyl boronic acid under aqueous conditions and catalyzed by $Pd(PPh_3)_4$ (entries 5 – 7). The Pd/DPEphos catalytic system was also effective for the cross-coupling of *m*-nitro compound **152**, and **230** was isolated in good yield (entry 8). Finally, Sonogashira conditions could be applied to the functionalization of **153**, and alkynylated compound **231** was isolated in excellent yield (entry 9).

Table 14. Palladium-catalyzed functionalization of 1,2-dichlorovinyl amides.



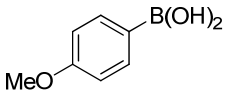
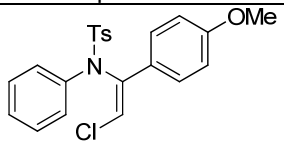
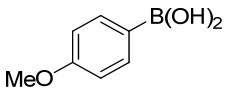
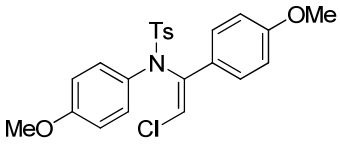
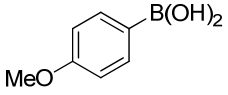
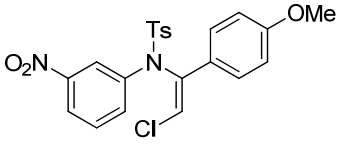
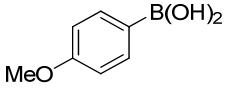
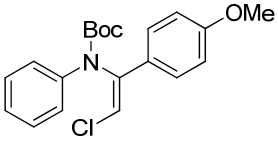
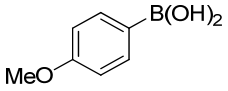
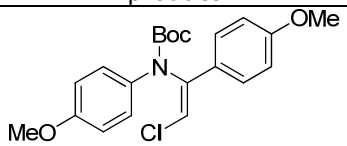
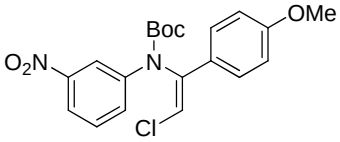
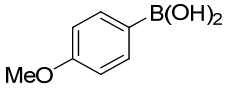
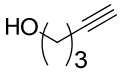
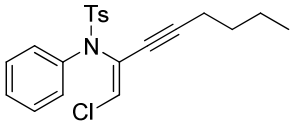
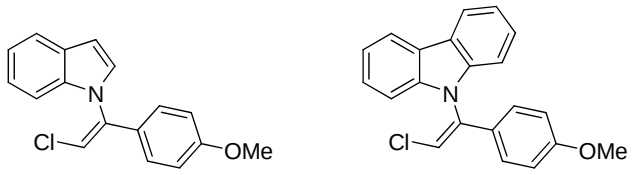
entry	reagents	conditions[a]	product	yield[b]
1	**153** + 	**A**	 **225**	81%
		B		41%
3	**154** + 	**B**	 **226**	61%
4	**155** + 	**B**	 **227**	79%
5	**150** + 	**C**	 **228**	52%

Table 14 *con't*

entry	reagents	conditions[a]	product	yield[b]
6	**151** + 	**C**	 **229**	54%
7	**152** +	**C**		
8		**A**	**230**	74%
9	**153** + 	**D**	 **231**	94%

[a]Conditions **A**: 1.05 equiv *p*-methoxyphenyl boronic acid, 2.5 mol% Pd_2dba_3, 5 mol% DPEphos, 3 equiv CsF-Cs_2CO_3, THF, 65 °C, overnight. Conditions **B**: 1.05 equiv *p*-methoxyphenyl boronic acid, 2.5 mol% Pd_2dba_3, 5 mol% P*t*Bu_3·HBF_4, 3.3 equiv KF, THF, rt, overnight. Conditions **C**: 1.05 equiv *p*-methoxyphenyl boronic acid, 5 mol% $Pd(PPh_3)_4$, 2.5 equiv KOH (1.0M in H_2O), THF, 65 °C, overnight. Conditions **D**: 1.1 equiv hexyne, 5 mol% $Pd(PPh_3)_4$, 10 mol% CuI, 2.5 equiv TEA, THF, rt, overnight. [b]Isolated yields.

Dichlorovinyl indole, carbazole, imidazole and benzimidazoles **159** to **166** were reacted with *p*-methoxyphenyl boronic acid under the aqueous $Pd(PPh_3)_4$ catalytic conditions. TLC and ^1H NMR analysis of all of the crude reaction mixtures showed clean but incomplete conversion to the corresponding arylated vinyl ethers after 16 h of reaction. However, these compounds proved not to be indefinitely stable, and by the time they were purified, only a small amount of the corresponding adduct could be isolated. The compounds synthesized from indole (**232**) and carbazole (**233**) are shown in Figure 15. If optimized, this method could be very useful, as functionalized enamines such as these are used in a wide variety of applications and are difficult to access by conventional enamine synthesis.[449]



232 **233**

Figure 15. Products from the cross-coupling reaction between indole **163** and carbazole **166** and *p*-methoxyphenyl boronic acid.

2.3.4 Summary

The development of palladium-catalyzed site selective cross-coupling between dichlorovinyl ethers, amides and amines and a variety of organometallics was generally a success. Using one of two simple catalytic systems, we could install aryl, heteroaryl, and alkenyl groups at C^1 of the dichlorovinyl compounds. Arylation can also be done at room temperature, though this process is not very general at this time. Enynes were easily synthesized via Sonogashira coupling with a terminal alkyne, and alkyl groups could be installed at C^1 using either organozinc or 9-alkyl-BBN derivatives as the organometallic.

With the basic palladium-catalyzed reactivity of dichlorovinyl ethers and amides at C^1 established, and a wide variety of functionalized chlorovinyl ethers in hand, the next step was to examine their reactivity at C^2 and develop the synthesis of electron-rich tri- and tetrasubstituted alkenes.

2.4 Functionalization of 1-Chlorovinyl Ethers

In developing the syntheses of both tri- and tetrasubstituted alkenes, optimization of conditions for both cross-coupling at C^2-Cl and for C^2-H functionalization were required. We first looked at C^2-Cl functionalization of the vinyl chlorides **134**, **173**, **193**, **200**, **214**, **218** and **221** synthesized in section 2.3.3 to generate trisubstituted alkenes (section 2.4.1), followed by the synthesis of tetrasubstituted alkenes (section 2.4.2).

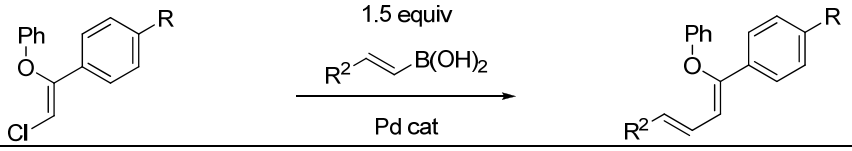
2.4.1 Trisubstituted Alkenes

When the cross-coupling of the vinyl chlorides **173** and **193** with boronic acids was first explored, the obvious first attempt was with the Pd/DPEphos conditions developed for the C^1 functionalization. While DPEphos was found to be a suitable ligand for C^1 site selective cross-coupling, it was hoped that it could still create an efficient catalyst in combination with a palladium source for cross-coupling at C^2; if the same catalytic system could be used for cross-coupling at both C-Cl bonds, the development of a one-pot sequential cross-coupling would require only minimal optimization. Unfortunately, attempts to cross-couple the *p*-methoxyphenyl derivative **173** with alkenyl boronic acids under these conditions were unsuccessful, and no reaction was observed, even after extended reaction times (Table 15, entries 1, 3 and 5).

When considering alternate cross-coupling conditions, we recalled that during the screening of conditions for C^1 arylation (Figure 12), using S-Phos **187** as the ligand led to the most diarylated product (though it was unselective between C^1 and C^2), suggesting that the catalyst containing this ligand could be highly active within the context of specific C^2-functionalization. In fact, conditions slightly modified from those used in a procedure for the functionalization of different vinyl chlorides[188] were effective for cross-coupling vinyl chloride **193** with alkenyl boronic acids to produce electron-rich dienes **234** and **235** in excellent yields (Table 15, entries 2 and 4).[475] Applying these conditions to cross-

coupling **193** with *p*-fluorostyryl boronic acid was less successful, and **236** was isolated in low yield along with 79% of the starting vinyl chloride (entry 6). This likely reflects a slower rate of transmetallation of electron-poor boronic acids. Only one isomer of the resulting 1-phenoxy-1,3-butadienes could be detected in both the ^{1}H NMR of the crude isolated material and the purified material in all cases.

Table 15. Synthesis of (*Z*,*E*)-1-phenoxy-1,3-butadienes from (*Z*)-2-chloro-1-arylvinyl ethers.



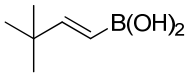
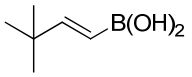
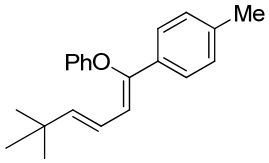
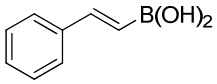
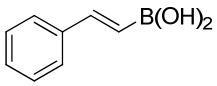
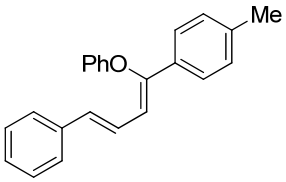
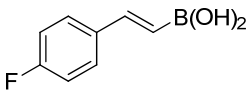
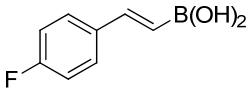
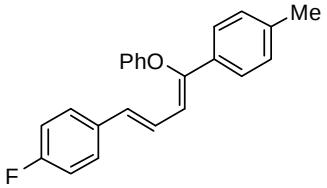
entry	reactants	conditions[a]	product	yield[b]
1	**173** + 	**A**	-	N.R.
2	**193** + 	**B**	 **234**	87%
3	**173** + 	**A**	-	N.R.
4	**193** + 	**B**	 **235**	65%
5	**173** + 	**A**	-	N.R.

Table 15 con't.

entry	reactants	conditions[a]	product	yield[b]
6	**193** + 	**B**	 **236**	15%[c]

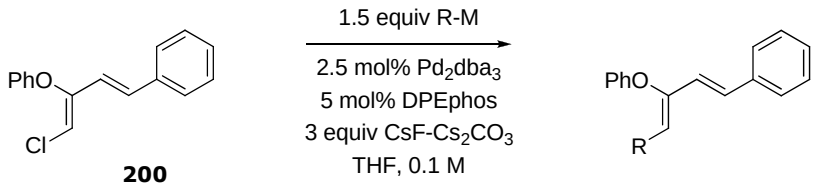
[a]Conditions **A**: 1 equiv vinyl chloride **173**, 1.5 equiv R-$B(OH)_2$, 2.5 mol% Pd_2dba_3, 5 mol% DPEphos, 3 equiv CsF, 3 equiv Cs_2CO_3, 0.4M in dioxane, heated at 100 °C overnight. Conditions **B**: 1 equiv vinyl chloride **193**, 1.5 equiv R-$B(OH)_2$, 5 mol% $Pd(OAc)_2$, 10 mol% S-Phos, 2.2 equiv Cs_2CO_3, 0.1M in toluene, heated at 110 °C overnight. [b]Isolated yields. [c]79% of the starting material was recovered.

The reactions in Table 15 generated 1-phenoxy-1,3-butadienes from C^1-aryl vinyl chlorides and alkenyl boronic acids; conversely, cross-coupling C^1-alkenyl vinyl chlorides with aryl boronic acids would synthesize isomeric 2-phenoxy-1,3-butadienes. In contrast to the functionalization of the arylated adducts above, Suzuki coupling between C^1 alkenyl derivative **200** and aryl boronic acids proceeded smoothly using the Pd/DPEphos catalytic system (Table 16), and good isolated yields were obtained for C^2 arylated dienes **237** and **238** (entries 1 and 2). We also obtained electron-rich trienes **239** and **240** by replacing the aryl boronic acid with a vinyl boronic acid, in good yields (entries 3 and 4). Notably, an aryl chloride was unreactive under these conditions (**240**, entry 4), leaving a useful handle for further palladium-catalyzed transformations.[30]

All attempts to effect Sonogashira coupling (section 1.2.1.3) between **200** and terminal alkynes failed, and unreacted starting material was recovered in all cases. However, C^2-alkynylation via cross-coupling between **200** and potassium phenylethynyl trifluoroborate was more successful, and dienyne **241** was isolated in modest yield (Table 16, entry 5). It should be noted that this reaction (and indeed, all reactions we attempted employing potassium trifluoroborate salts as nucleophiles) became black and

gummy, hampering stirring. This could have contributed to catalyst deactivation, as the bulk of the mass balance recovered from this reaction was unreacted starting material.

Table 16. Synthesis of 2-phenoxy-1,3-butadienes, hexatrienes and a dienyne from (*Z*)-1-chloro-2-aryloxy-1,3-butadiene.



200

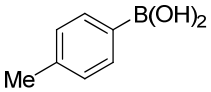
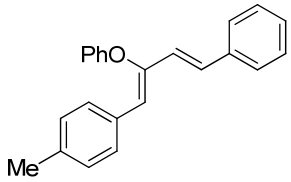
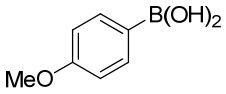
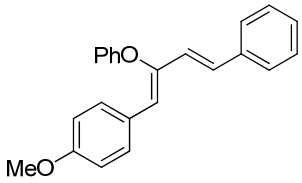
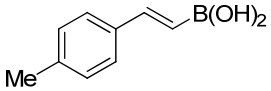
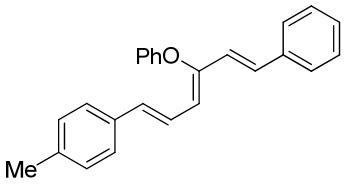
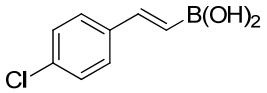
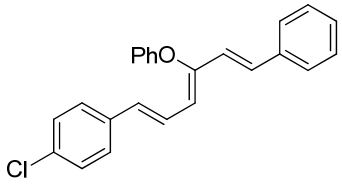
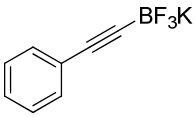
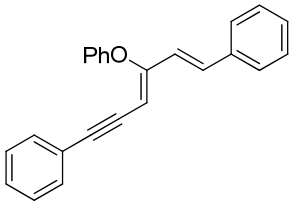
entry	R-M	product	yield[a]
1		 **237**	53%
2		 **238**	78%
3		 **239**	52%

Table 16 con't.

entry	R-M	product	yield[a]
4		 **240**	64%
5		 **241**	20%[b]

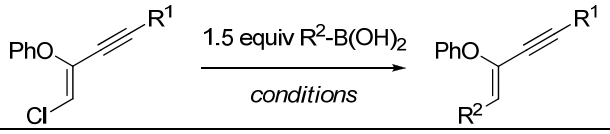
[a] Isolated yields. [b]65% Unreacted starting material recovered as well.

Though C^2 alkynylation was somewhat difficult, functionalizing electron-rich enynes with a variety of aryl-, heteroaryl- and alkenylboronic acids proved much more facile (Table 17). The Pd/DPEphos catalytic system was found to be active for cross-coupling reactions between chloroenynes and a variety of boronic acids (Table 17). For example, enyne **214** was successfully cross-coupled with both electron-rich and electron-poor aryl boronic acids and the adducts **242** and **243** were isolated in good yields (entries 1 and 2). An ortho-functionalized boronic acid could be installed on the phenyl substituted enyne **214**, giving **244** in good yield (entry 3). Similarly, enyne **218** cross-coupled with an aryl boronic acid to give adduct **245** in modest yield (entry 4).

Heteroarenes could also be installed at C^2; however, similar to attempts to cross-coupling heteroarenes at C^1 (Table 9), attempts to cross-couple 3-pyridinyl boronic acid with enyne **218** using the standard Pd/DPEphos conditions failed (Table 17, entry 5). Success was met in this case when the catalytic system was changed to $Pd(PPh_3)_4$ in aqueous THF, and enyne **246** was isolated in modest yield (entry 6). Similarly, application of the aqueous $Pd(PPh_3)_4$ conditions to the synthesis of **247** and **248** were moderately successful, but in both cases, the reaction did not go to completion and some

unreacted starting material was recovered (entries 7 and 8). Additionally, alkenyl boronic acids could be successfully cross-coupled via Pd/DPEphos catalysis, giving dieneynes **249** - **251** in good yields (entries 9 – 11). Again, an aryl chloride was tolerated under these conditions (**251**, entry 11). Attempts to cross-couple **214** and 3-chloropropenyl boronic acid were unproductive and led only to intractable mixtures of materials.

Table 17. Enynes and dienynes from 1-alkynyl vinyl ethers.



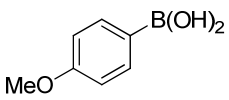
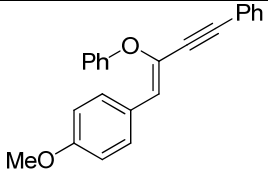
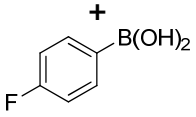
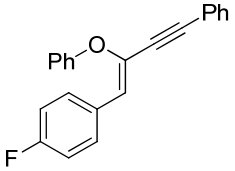
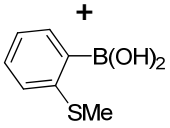
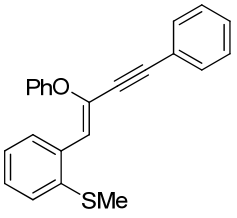
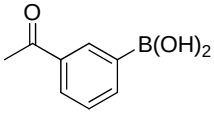
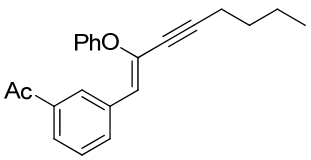
entry	reagents	conditions[a]	product	yield
1	**214** + 	**A**	 **242**	82%
2	**214** + 	**A**	 **243**	77%
3	**214** + 	**A**	 **244**	69%
4	**218** + 	**A**	 **245**	54%

Table 17 *con't*

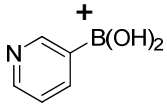
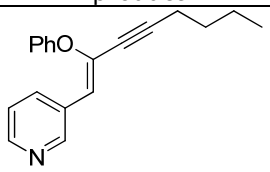
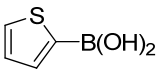
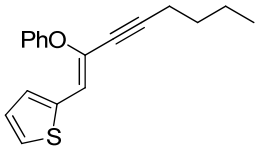
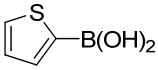
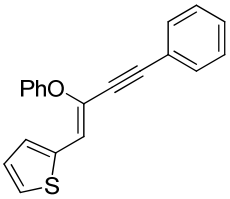
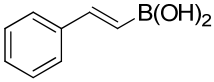
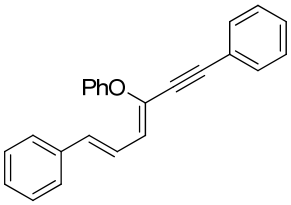
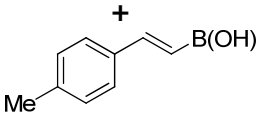
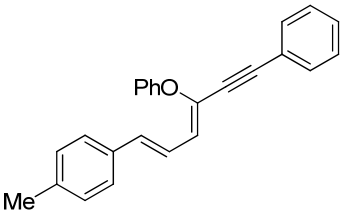
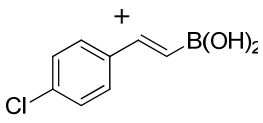
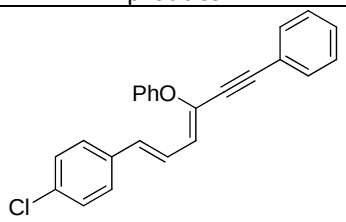
entry	reagents	conditions[a]	product	yield
5	**218** + 	**A**	 **246**	0%
6		**B**		60%[b]
7	**218** + 	**B**	 **247**	29%[c]
8	**214** + 	**B**	 **248**	28%[d]
9	**214** + 	**A**	 **249**	76%
10	**214** + 	**A**	 **250**	65%

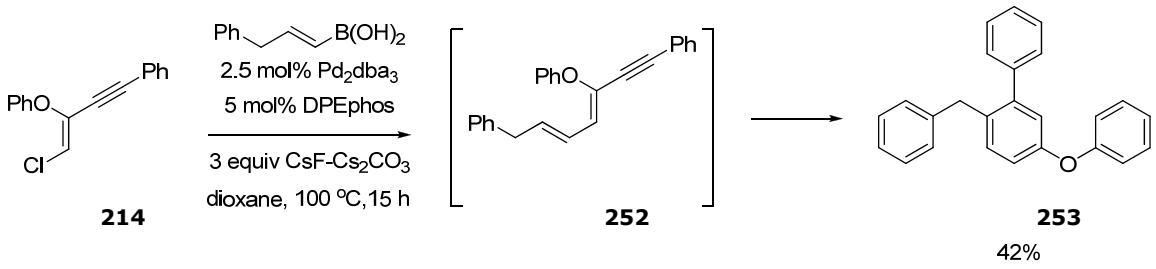
Table 17 con't.

entry	reagents	conditions[a]	product	yield
11	**214** + 	**A**	 **251**	46%

[a] Conditions **A**: 1 equiv vinyl chloride **214** or **218**, 1.5 equiv R-$B(OH)_2$, 2.5 mol% Pd_2dba_3, 5 mol% DPEphos, 3 equiv CsF, 3 equiv Cs_2CO_3, 0.4M in dioxane, heated at 100 ^oC overnight. Conditions **B**: 1 equiv vinyl chloride **214** or **218**, 1.5 equiv R-$B(OH)_2$, 5 mol% $Pd(PPh_3)_4$, 2.5 equiv KOH (aq), THF, 65 ^oC overnight. [b]15% recovered starting material. [c]40% recovered starting material. [d]Isolated 17% 2-(phenylethynyl)benzofuran as well.

Interestingly, when 3-phenylpropenylboronic acid was used as the nucleophile in a similar attempt to functionalize **214**, diaryl ether **253** was isolated as the sole identifiable product (Scheme 105). We assume the reaction proceeds through expected adduct **252**, though the mechanism of cyclization and aromatization to **253** is not obvious. We are currently exploring the scope of the reaction leading to this unexpected product, and believe this reaction may prove useful for a modular and simple synthesis of highly substituted biaryl ethers as an alternative to C-O bond formation via Buchwald-Hartwig coupling.[476]

Scheme 105. Synthesis of substituted biaryl ether as an overreaction product from the reaction between enynyl chloride **214** and 3-phenylpropenylboronic acid.

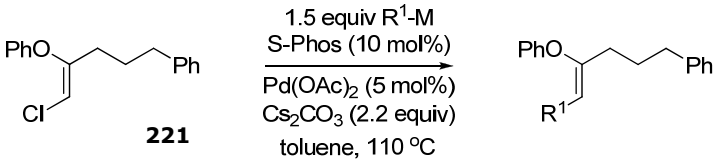


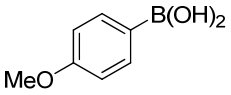
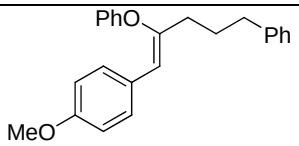
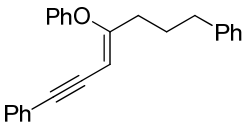
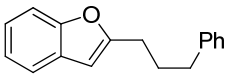
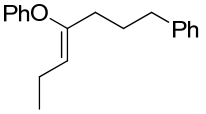
214 **252** **253**

42%

Next, we set out to functionalize the alkylated derivative **221**. All reactions attempted using the Pd/DPEphos (**12**) system failed, but the Pd/S-Phos (**188**) system generally worked well (Table 18). The electron-rich styrene **254** (entry 1) was isolated in excellent yield. However, when we attempted to create an electron-rich enyne from **221** and potassium phenylethynyl trifluoroborate, enyne **255** was isolated in only 24% yield (entry 3). In contrast to all other catalytic systems examined, Pd/S-Phos promoted direct arylation more readily than cross-coupling and the 2-alkyl benzofuran was the major product isolated (**256**, 46% yield. See section 2.5 for details on this process). This is likely due to the slow transmetallation of the potassium trifluoroborate that we have consistently observed in these anhydrous conditions[477] (for an example, see Table 16, entry 5). When Negishi coupling was performed on **221** with diethyl zinc under the same catalytic conditions, the dialkylvinyl ether **257** was isolated in 33% yield (entry 4); however, the conversion from the starting material was only 35% as estimated from the ^{1}H NMR spectrum of the crude material. No benzofuran was detected in this case, suggesting that perhaps under these conditions, either the reaction is simply very slow, or the palladium catalyst is somehow being deactivated. Unfortunately, the attempt to cross-couple **221** with 4-methylstyrylboronic acid led only to isolation of 1,4-bis(4-methylphenyl)-1,3-butadiene and 2-(3-phenylpropyl)benzofuran **256**.

Table 18. Functionalization of C^1 alkyl substituted **221**.



entry	R^1-M	product	yield (%)[a]
1		 **254**	85%
2		 **255**	24%[b]
		 **256**	46%
3	Et_2Zn	 **257**	33%[b]

[a]Isolated yields. [b]Only 35% conversion from starting material.

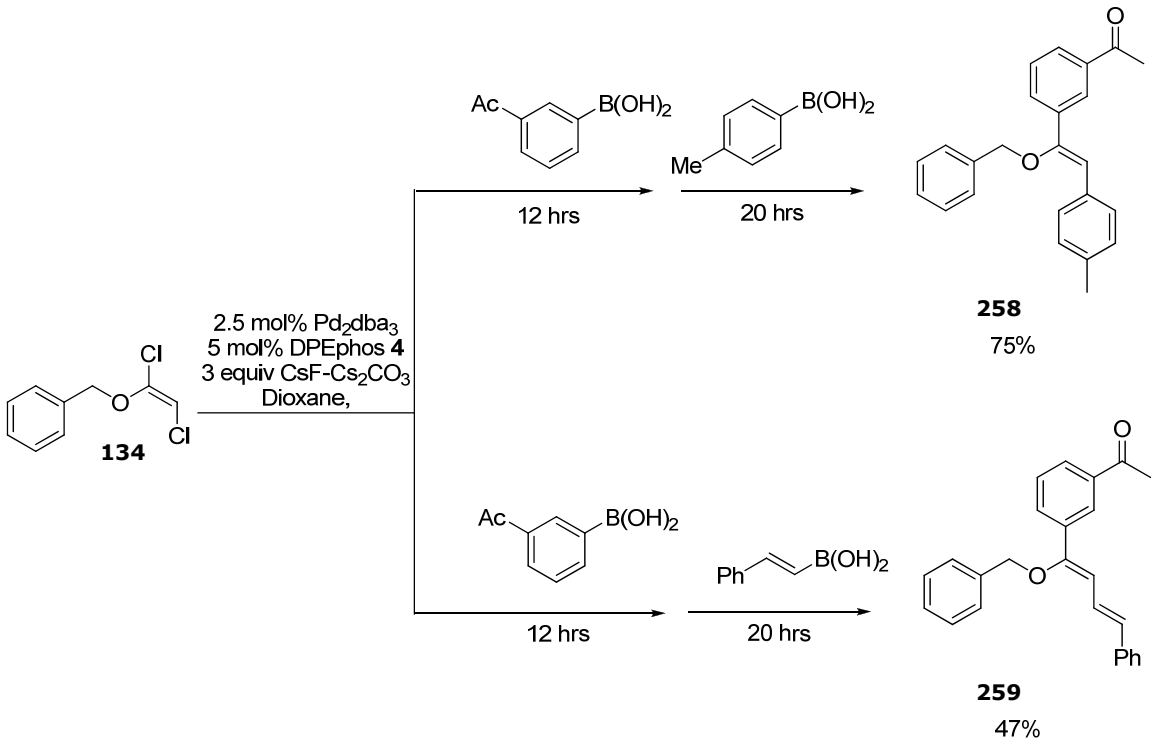
Finally, as the guiding principles inherent in developing these methods were to maximize efficiency and diversity in the synthesis of these families of compounds, we set out to develop a one pot, sequential cross-coupling of both C-Cl bonds of a dichlorovinyl ether. There were two major concerns that needed to be kept in mind: 1) the first cross-coupling needed to go to completion and leave no unreacted starting material upon consumption of the first boronic acid; and 2) direct arylation (section 2.5) was potentially

in competition with cross-coupling at C^2 (as observed in the formation of **256** in Table 18, entry 2).

In other studies, we observed that while cross-coupling was facile, direct arylation did not occur at all when the dichlorovinyl ether was derived from a benzyl alcohol rather than a phenol (see section 2.6.2). With that in mind, we attempted the one-pot reaction starting from the dichlorovinyl ether **134** derived from benzyl alcohol. We found that the one-pot double Suzuki coupling could be efficienty performed between benzyl vinyl ether **134** and two different boronic acids to give ether **258** and diene **259**, both in good isolated yields and each as single isomers (Scheme 106).

While this demonstrates a highly useful one pot approach to the two step synthesis of trisubstituted electron-rich alkenes from commercially available material, this reaction is highly dependent on the success of the first cross-coupling. As is pointed out by Organ,[271] the success of the first cross-coupling may not only prevent side reactions, but also greatly simplifies purification. In our experience, it is the number of molar equivalents of boronic acid or other organometallic nucleophile (with respect to the starting dichlorovinyl ether) that dictates success; if a particular product is desired, optimization of the first step should permit efficient one pot, bis Suzuki coupling.

Scheme 106. One-pot double Suzuki coupling with two different boronic acids to give trisubstituted vinyl ethers **258** and **259**.

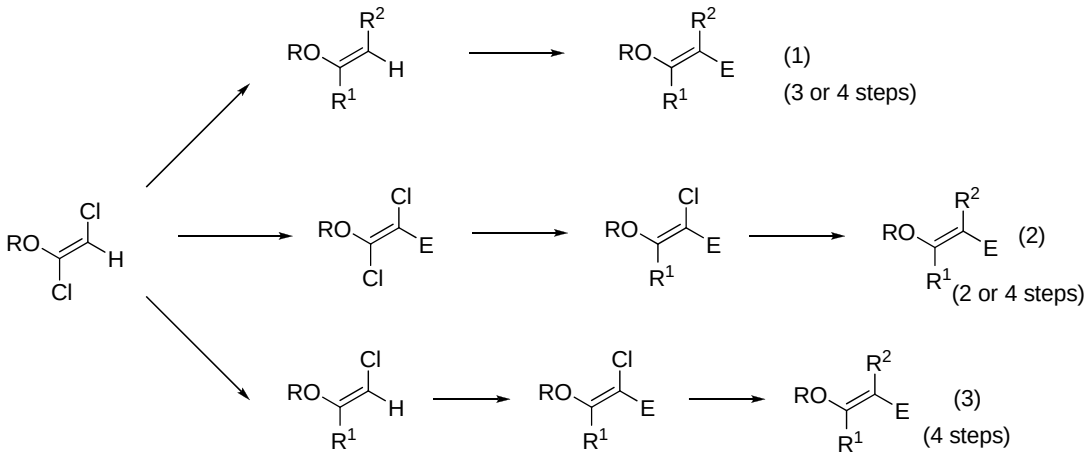


2.4.2 Tetrasubstituted Alkenes

When evaluating the possible methods of synthesizing tetrasubstituted alkenes from the basic dichlorovinyl ether template, three possible routes were hypothesized (Scheme 107). Lithiation of a trisubstituted alkene followed by electrophilic quench would give a tetrasubstituted alkene in three or four steps from commercially available materials (Scheme 107, equation 1), depending on whether the two cross-couplings were done in one or two pots. The second possible route consists of electrophilic substitution of the dichlorovinyl ether followed by two cross-coupling reactions (Scheme 107, equation 2) This route would take as many as four steps from commercial materials, but could be done in as few as two steps if the synthesis and electrophilic substitution of dichlorovinyl ethers and both cross-coupling reactions were each done in one pot. Finally,

tetrasubstituted alkenes could potentially be synthesized via sequential cross-coupling, deprotonation/electrophilic quench, and a second cross-coupling from a dichlorovinyl ether in four discreet steps (Scheme 107, equation 3). The efforts toward the synthesis of tetrasubstituted alkenes via each of these routes are discussed in the following sections.

Scheme 107. Possible routes to tetrasubstituted alkenes from 1,2-dichlorovinyl ethers.



2.4.2.1 Route One

Route 1 (Scheme 107, equation 1) is not practical; deprotonation of a C^2-alkyl compound (such as **257**) could result in deprotonation of the sp^3 proton rather than the sp^2 proton to form an allyl anion,[478] and polyenes would likely have selectivity issues as there would be more than one vinylic sp^2 C-H bond. While diarylvinyl ethers such as **175** would suffer no such selectivity issues, we have found that we are simply unable to successfully deprotonate these compounds.

2.4.2.2 Route Two

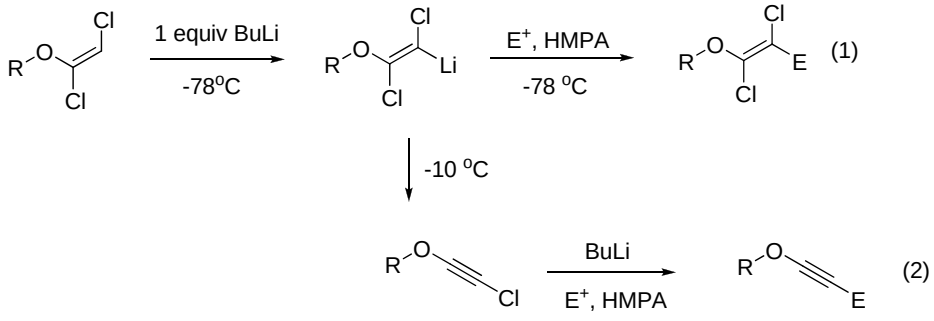
This route would be the most efficient way to synthesize electron-rich tetrasubstituted alkenes. To reiterate, we wanted first to optimize a one-pot nucleophilic substitution and deprotonation/electrophilic quench to yield the disubstituted dichlorovinyl ether in a

single synthetic step. Secondly, if both cross-coupling reactions could be done in one pot via sequential addition of two different boronic acids, the formation of tetrasubstituted alkenes would require only two pots and two purification steps. The following subsections outline the attempts to synthesize these compounds via this route.

2.4.2.2.1 C^2-H Functionalization

We first explored the basic chemistry of vinyllithiums derived from dichlorovinyl aromatic ethers via deprotonation with an alkyllithium reagent; the general transformation had already been reported by Greene in his exploration of the chemistry of aliphatic alcohol-based dichlorovinyl ethers.[420] As discussed in section 2.1, most of his group's work involved the in situ transformation of dichlorovinyl ethers to acetylenic ethers that may be further functionalized at the terminus of the alkyne by lithiation and quenching with an electrophile (Scheme 85). A more recent report from Greene's laboratory demonstrated that if the vinyllithium was quenched with an electrophile at low temperatures, a disubstituted dichlorovinyl ether was formed (Scheme 108, equation 1), as breakdown to the alkyne required higher temperatures (Scheme 108, equation 2).[479]

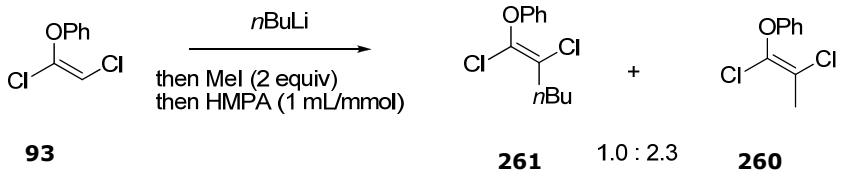
Scheme 108. Greene's synthesis of disubstituted dichlorovinyl ethers or acetylenic ethers from a β-alkoxyvinyllithium.



Both procedures reported using highly toxic hexamethylphosphoramide (HMPA) as a cosolvent during the addition of the electrophile, and we initially adopted this basic procedure. However, when the C^2-H of **93** was treated with butyllithium and quenched

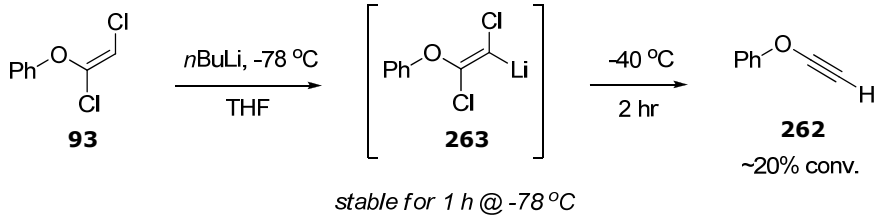
with iodomethane in the presence of HMPA, two products were observed: the expected C^2-methyl compound **260**, as well as some C^2-butylated compound **261**, presumably produced by addition of the vinyllithium to butyl iodide generated in situ (Scheme 109).

Scheme 109. Lithiation of dichlorovinyl ether followed by addition of methyl iodide in HMPA.



While **260** and **261** could be separated by column chromatography, a reaction that produces a mixture of products is obviously not ideal. Fortunately, the reaction was much more efficient in the absence of HMPA. The deprotonation of **93** took less than five min, and the intermediate vinyllithium **263** was found to be stable for at least one hour at -78 °C with no detectable elimination to the corresponding acetylenic ether (Scheme 110). The vinyllithium **263** was moderately stable at -40 °C, where there was only approximately 20% conversion to the acetylenic ether **262** after 2 h as estimated by analysis of the ^{1}H NMR of the unpurified reaction material (Scheme 110).

Scheme 110. Stability of vinyl lithium and partial elimination to ynol ether.

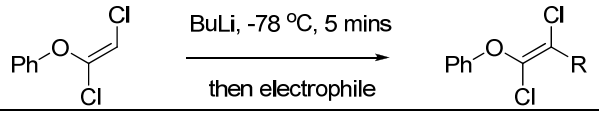


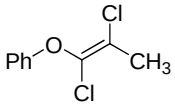
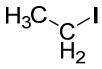
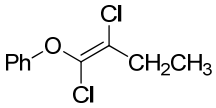
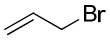
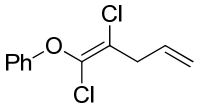
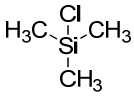
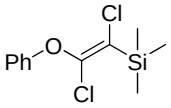
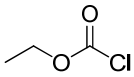
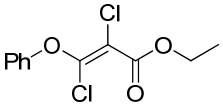
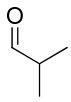
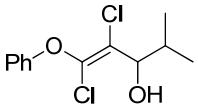
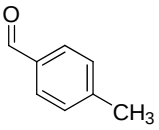
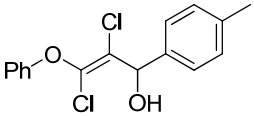
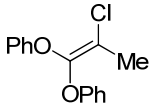
The lithiation of **93** followed by electrophilic quench proved to be quite general in the absence of HMPA, and many different electrophiles could be utilized (Table 19). Simple alkyl iodides such as methyl and ethyl iodide reacted smoothly with the

vinyllithium and adducts **261** and **264** were isolated in excellent yields (entries 1 and 2). Highly reactive electrophiles such as allyl bromide and chlorotrimethylsilane (TMSCl) were also tolerated in this reaction, and good yields of skipped diene **265** and vinyl silane **266** could be obtained (entries 2 and 4, respectively). The vinyl silane **266** synthesized in this manner is particularly interesting. Silanes on sp^2 carbons can act as nucleophiles in palladium-catalyzed chemistry (section 1.2.1.7), and vinyl silanes are very useful in a myriad of organic transformations.[480,481] Ethyl chloroformate was also a good electrophile, and α,β-dichloro-α,β-unsaturated ethyl ester **267** was isolated in moderate yield (entry 5). β-Phenoxy-α,β-unsaturated ethyl ester **267** is also referred to as a push-pull alkene[482] and is reactive to both electrophiles and nucleophiles.[483]

Aldehydes could also be used in this reaction, and allylic alcohols **268** and **269** were isolated in excellent yields (Table 19, entries 6 and 7); notable is the tolerance of an acidic α-proton in these highly basic reaction conditions (entry 6). The allylic alcohol moiety could also be viewed as another 'handle' for further synthetic transformation, as allylic alcohols are useful substrates in palladium-catalyzed Tsuji-Trost substitution reactions.[484,485] While some oxygen-substituted allylic alcohols similar to **268** and **269** are known, the literature syntheses of these compounds are not very general. Additionally, allylic alcohols are difficult to synthesize with increased vinyl substitution and/or in high stereochemical purity.[289,486-490] Di- and trisubstituted allylic alcohols can be particularly challenging to synthesize.[238,256] Finally, ketene acetal **132** (Scheme 92) was easily transformed into **270** via analogous deprotonation with butyllithium and quenching with iodomethane (entry 8).

Table 19. C^2-H Functionalization of dichlorovinyl ethers.

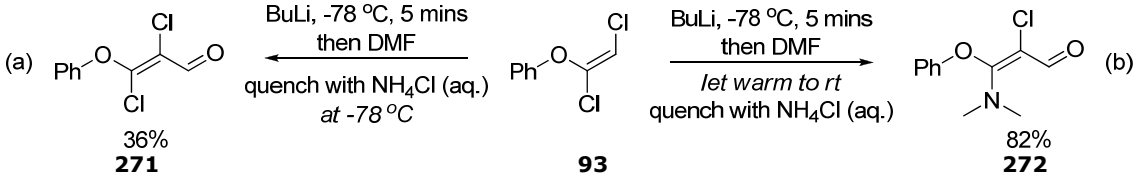


entry	electrophile	product	yield[a]
1		 **261**	76%
2		 **264**	85%
3		 **265**	66%
4		 **266**	89%
5		 **267**	56%
6		 **268**	92%
7		 **269**	94%
8[b]		 **270**	93%

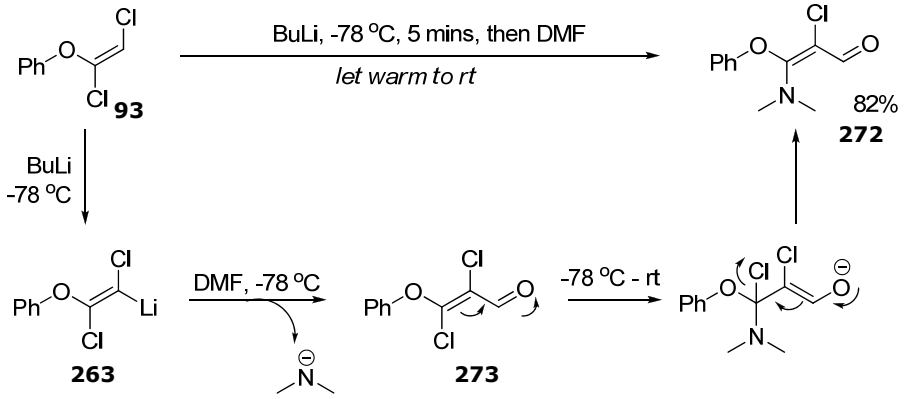
[a]Isolated yields unless otherwise noted. [b]From ketene acetal **132**.

We observed interesting results when attempting the reaction between vinyl lithium **263** and DMF. Analogously to the reactions reported in Table 19, the dichlorovinyl ether **93** was allowed to react with butyllithium at -78 °C for 5 minutes and was then quenched with an excess of DMF. After another 5 minutes, aqueous NH_4Cl was added at -78 °C, stirred for 15 minutes; the reaction was then removed from the cold bath and brought to room temperature. Purification of that material gave desired aldehyde **271** in 36% yield (**Scheme 111**, equation a). If, however, the reaction was allowed to warm to room temperature *prior* to quenching with aqueous NH_4Cl, dimethylamine-substituted aldehyde **272** was the major product (**Scheme 111**, equation b). A mechanism for the formation of **272** has been proposed and outlined below. The equivalent of dimethyl amide released as a byproduct from the reaction of vinyl lithium **263** with DMF reacted with **271** in situ via a conjugate addition with subsequent elimination of a chloride anion to give **272** in 82% yield (**Scheme 112**).

Scheme 111. Different products result from quenching the reaction that produces an acrolein from vinyl lithium **263** and DMF at different temperatures.

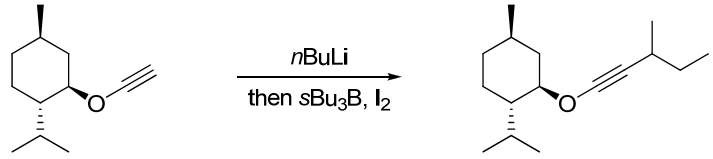


Scheme 112. Proposed mechanism for the formation of aldehyde **272**.



To date, we have been unable to utilize ketones, secondary alkyl halides, α-haloesters, or styrene oxide under these conditions, and quenching the vinyl lithium with γ-butyrolactone led to an intractable mixture of products. The problem of poor reactivity towards secondary alkyl halides could possibly be circumvented by using an analogous triorganoborane under similar conditions.[491,492] For example, Greene and coworkers synthesized substituted acetylene **275** from terminal acetylenic ether **274** (Scheme 113).[409] The lithium acetylide synthesized by deprotonation of **274** with *n*-butyllithium reacts with a triorganoborane to give a lithium acetylenic borate that yields **275** after treatment with molecular iodine.

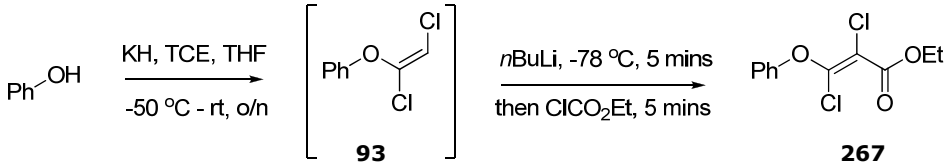
Scheme 113. Greene's synthesis of *sec*-alkyl acetylenic ethers.



274 **275**

Most importantly, and toward the goal of a two-pot synthesis of tetrasubstituted alkenes, we have also found that the reaction of phenol with TCE, followed by deprotonation with butyllithium and electrophilic quench with ethyl chloroformate can be done in one pot with no significant change in the isolated yield of α,β-unsaturated ester **267** (Scheme 114).

Scheme 114. One-pot synthesis of C^2-functionalized dichlorovinyl ethers.



93
not isolated

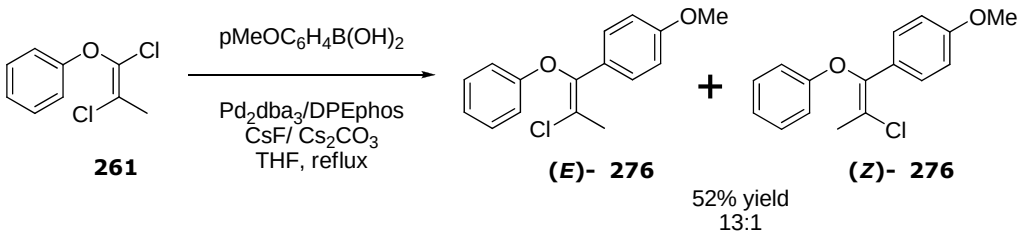
267
51%

2.4.2.2.2 Cross-Coupling on C^2-Functionalized Dichlorovinyl Ethers

Continuing on the route depicted in Scheme 107 equation 2, we performed a cross-coupling reaction on the alkylated material. Using what has become our standard Pd/DPEphos catalyzed cross-coupling conditions, we first tried the cross-coupling between methylated **261** and *p*-methoxyphenyl boronic acid (Scheme 115). The isolated yield was somewhat low at 52%, and gave a mixture of two products in an approximate 13:1 ratio. The isomers could be separated via flash chromatography. The major product was determined to be the expected (*Z*)-**276**. This was done by comparing the NMR spectra of this material to spectra of the product from the reaction between lithiated *p*-methoxyphenyl vinyl chloride **174** and iodomethane (see Table 20, entry 1). As the spectra of the materials from both routes were identical, we concluded that the major isomer resulting from cross-coupling **261** with *p*-methoxyphenyl boronic acid was (*Z*)-**276**.

The second compound was determined to be an isomer of **276** after analysis of the ^{1}H and ^{13}C NMR spectra. It is possible that this material could be either (*E*)-**276** or the compound that would result from cross-coupling at C^2 instead of C^1. However, many attempts to cross-couple isolated (*Z*)-**276** with other boronic acids failed under these conditions. Given that the catalyst derived from Pd_2dba_3/DPEphos is unable effect cross-coupling at C^2 of **276**, it is unlikely that this catalyst can effect reaction at C^2 of **261**. We therefore concluded that the second compound isolated from the reaction between **261** and *p*-methoxyphenyl boronic acid was (*E*)-**276**. When the same reaction was performed under the room temperature Suzuki conditions described in Table 11 (Pd_2dba_3/P*t*Bu_3·HBF_4), after 25 h the combined isolated yield of the two isomers was 45% with an improved ratio of 50:1 (*Z*)-**276**:(*E*)-**276**. An analogous cross-coupling between **261** and (*E*)-styrylboronic acid also gave a mixture of products with incomplete conversion, and we were unable to induce Sonogashira cross-coupling at all between the alkylated derivative **261** and terminal alkynes.

Scheme 115. Cross-coupling on C^2-methylated compound.

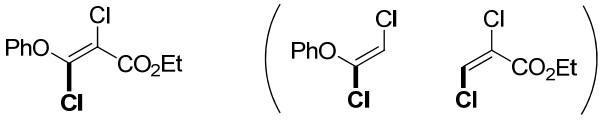


261 **(*E*)- 276** **(*Z*)- 276**

52% yield
13:1

Compound (*Z*)-**276** does not isomerizes under the conditions described in Scheme 115; subjecting the isolated material to these conditions results in no change (see Table 21). This suggests that under these conditions it is either **261** that is isomerizing in the presence of palladium, or the vinyl palladium species that would result from oxidative addition into the C^1-Cl bond of **261** is not configurationally stable.

Cross-coupling reactions between the dichlorovinylester **267** and aryl boronic acids were also explored. It is known that cross-coupling is selective for the β position in α,β-dihalounsaturated esters (Scheme 33),[171] and we have already confirmed the directing effect of the C^1-phenoxy substituent for selective C^1-Cl cross-coupling (section 2.3), therefore, we reasoned that C^1-Cl (C^β-Cl) should be activated by *both* substituents (Figure 16) and cross-coupling should be rapid and selective.



267

Figure 16. Hypothesized activation of β-Cl in a push-pull alkene; both the phenoxy and ester substituent in **267** should activate the same C-Cl bond toward oxidative addition by palladium (activated C-Cl bonds in bold).

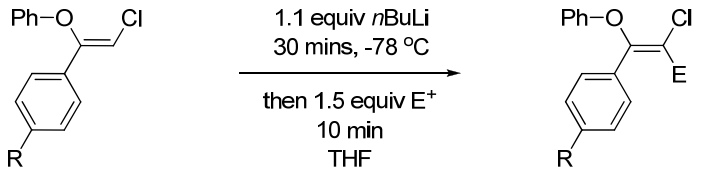
Unfortunately, when we attempted cross-coupling between the doubly functionalized dichloroethylene **267** and p-MeO-C_6H_4-$B(OH)_2$, we observed a mixture of products, similar to that observed with the 2-methyl substituted **261** (Scheme 115). This was disappointing, as the phenolic addition across TCE and the deprotonation/electrophilic quench may be done in a single synthetic operation (Scheme 114), these results ruled out the possibility of synthesizing tetrasubstituted alkenes via this route (Scheme 107, equation 2). We are currently trying to understand the source of this difficulty, and are exploring alternative catalytic systems.

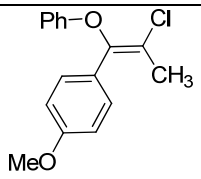
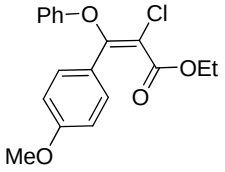
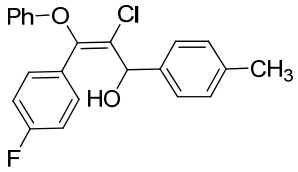
An alternative to cross-coupling at C^1 would be addition/elimination at that centre, as it is well-known that β-chloro-α,β-unsaturated esters are easily functionalized at that position to give a similar net reaction to cross-coupling at that carbon.[192,493] It is possible however that the phenol would eliminate in competition with the chloride and produce a mixture of products.

2.4.2.3 Route Three

As the previous results ruled out the route according to Scheme 107, equation 2, we turned to exploring the synthesis of tetrasubstituted alkenes via route 3 (Scheme 107, equation 3) and next explored C^2-H functionalization from C^1 arylated substrates. As we observed with the 1,2-dichlorovinyl ether **93**, deprotonations of vinyl ether **173** were rapid and the resulting vinyllithium compounds could be quenched with either iodomethane to give **276** or ethyl chloroformate to give **277**, both in excellent yields (Table 20, entries 1 and 2). Likewise, fluorinated derivative **194** was easily deprotonated and quenched with *p*-tolualdehyde and allyl alcohol **278** was isolated in modest yield (entry 3).

Table 20. Deprotonation and electrophilic quench using 1-aryl-2-chlorovinyl ethers.



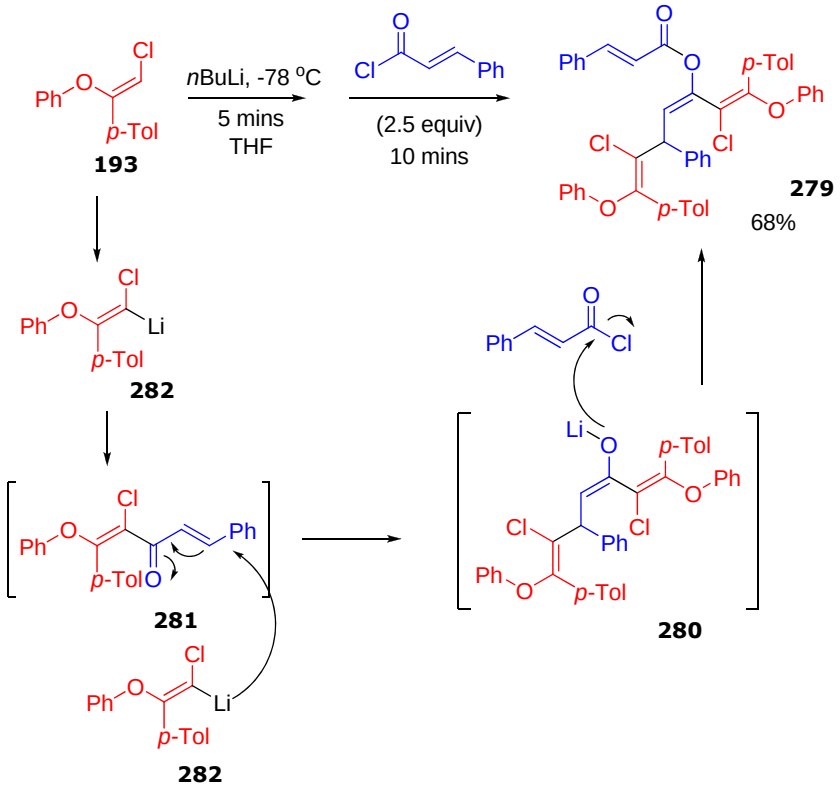
entry	starting material	electrophile	product	yield[a]
1	**173**	MeI	 **276**	95%
2	**173**	$ClCO_2Et$	 **277**	92%
3	**194**	*p*-C_6H_4-CHO	 **278**	50%

[a]All yields reported are those of isolated, analytically pure material.

When an analogous reaction between *p*-tolyl derivatized vinyl ether **193** and cinnamoyl chloride was performed, the expected divinyl ketone **281** was not the isolated product. Rather, the *O*-cinnamoyl heptatriene **279** was isolated in 68% yield (Scheme 116). A possible mechanism for the formation of **279** is also presented in Scheme 116. Presumably, vinyllithium species **282** is formed, which could react via the predicted addition to cinnamoyl chloride producing divinyl ketone **281**. At this point, it is thought that a second equivalent of vinyl lithium **282** adds to the divinyl ketone in a Michael fashion (1,4 conjugate addition) producing the lithium enolate **280**, which then reacts with a second equivalent of cinnamoyl chloride forming *O*-cinnamoyl heptatriene **279**

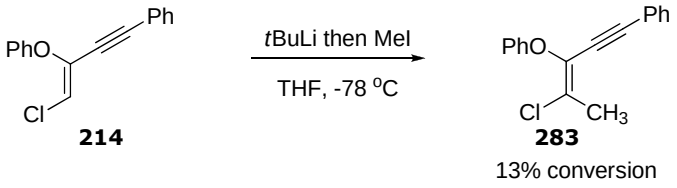
(Scheme 116). While this reaction was unexpected, it was reproducible, very fast, and could be performed on a moderate scale (see experimental section for details).

Scheme 116. Unexpected product **279** from reaction between vinyl ether **193** and cinnamoyl chloride, and the possible mechanism of its formation.



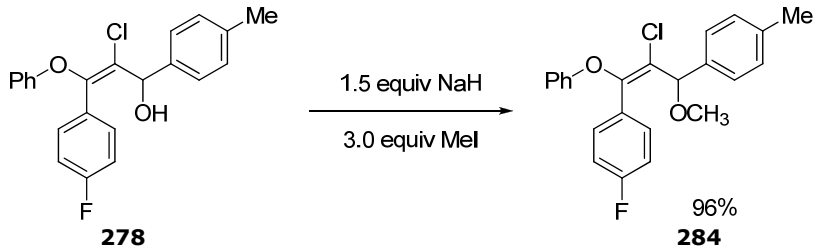
We have also tried to deprotonate C^1 alkynylated vinyl ether **214** by treatment with 1.1 equiv of *t*BuLi; however, the apparent solubility of the alkenyl lithium in THF was low and quenching with iodomethane resulted in only 13% conversion to the corresponding chlorinated trisubstituted enyne **283** (**Scheme 117**). Work to optimize this type of reaction is in progress.

Scheme 117. Alkylation of chloroenyne **214**.



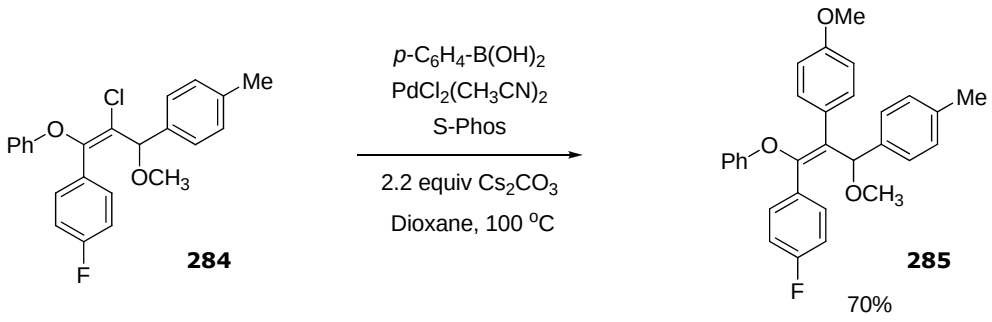
With the successful functionalization of trichloroethylene to give otherwise fully functionalized C^2-Cl vinyl ethers, the next step was to find suitable conditions for cross-coupling to generate tetrasubstituted alkenes. The alcoholic proton of vinyl ether **278** was protected as a methyl ether to give **284** (Scheme 118) to avoid potential incompatibilities or unforeseen difficulties involving the protic functionality while exploring cross-coupling conditions.

Scheme 118. Protection of alcohol functionality of **278** by methylation.



The first catalytic system we examined in the functionalization of **284** was the Pd/DPEphos system, which proved unable to effect the transformation. Several of catalytic systems that were reported in a recent publication by Negishi on the functionalization of vinyl chlorides[188] were also examined for their activity in the cross-coupling **284** and aryl boronic acids. Just as we observed in the C^2-functionalization in the synthesis of trisubstituted alkenes (e.g., Table 15), the catalyst that proved useful in this transformation was the catalyst derived from $PdCl_2(CH_3CN)_2$ and S-Phos **188**. This easily promoted the cross-coupling of **284** and *p*-methoxyphenyl boronic acid, and the resulting tetrasubstituted alkene **285** was isolated in excellent yield (Scheme 119).

Scheme 119. Cross-coupling on trisubstituted C^2-Cl vinyl ethers to give tetrasubstituted alkene **285**.



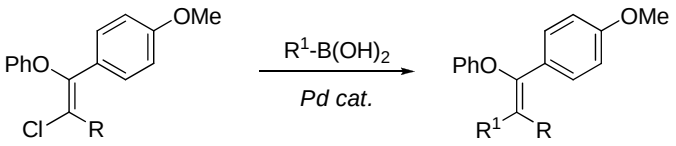
2.4.2.3.2 Scope

Using the conditions from the C^2-functionalization in the trisubstituted alkene synthesis (Table 15) rather than those given in Scheme 119, we set out to explore the scope of the reaction between methyl derivative **276** and unsaturated ester **277** and a variety of boronic acids. While the Pd/DPEphos catalyst system was unsatisfactory (Table 21, entries 1, 3, 5, 7, 9 and 11), excellent results were obtained in the C^2-functionalization promoted by Pd/S-Phos (entries 2, 4, 6 8, 10 and 12). Adducts **286** – **291** were isolated in good yields. Cross-coupling occurred readily with an electron-rich (entry 2), electron-poor (entry 4) and an *ortho*-substituted (entry 6) aryl boronic acid. Similarly, 1,2-substituted 1-phenoxy-1,3-butadienes **289** – **291** were easily assembled in high yields (entries 8, 10 and 12).

When analogous reactions were performed on α-chloro-α,β-unsaturated ester **277**, the Pd/DPEphos system gave the tetrasubstituted unsaturated esters **292** – **299** in good yields in many cases (Table 21, entries 13, 15, 17, 19, 21 and 23). However, it should be noted that in some cases, small amounts of 2-(4-methoxyphenyl)-3-carboxyethylbenzofuran (see **334** in Scheme 128, arising from intramolecular direct arylation rather than cross-coupling) could be detected by TLC and crude ^{1}H NMR. In general, the Pd/S-Phos system gave higher isolated yields of desired adducts **292** – **299**

than the Pd/DPEphos system did (entries 14, 16, 18, 22 and 24). Like reactions with the methyl derivative **276**, reaction between **277** and electron-poor (entry 14), electron-rich (entry 16) and *ortho*-substituted (entry 18) aryl boronic acids afforded tetrasubstituted esters **292** - **294** which were generally isolated in excellent yields. Additionally, vinyl boronic acids could be used, giving butadienes **295** – **299** in good isolated yields. As was seen in the synthesis of trisubstituted alkenes (Table 16 and Table 17), an aryl chloride did not participate in the cross-coupling reaction when reacted with a boronic acid in the presence of either Pd/DPEphos (entry 23) or Pd/S-Phos (entry 24) giving butadiene **297** in excellent yields. Finally, alkyl-substituted vinyl boronic acids could be utilized to give butadienes **298** and **299** in moderate to good yield (entries 25 and 26). In all cases, only one isomer could be detected in the ^{1}H NMR spectra of the crude material and the pure isolated product.

Table 21. Synthesis of Tetrasubstituted Alkenes.



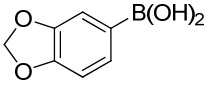
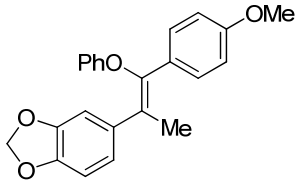
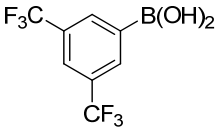
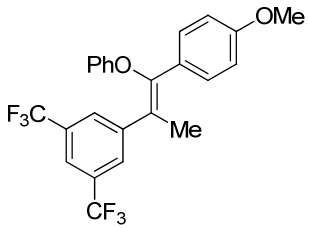
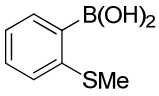
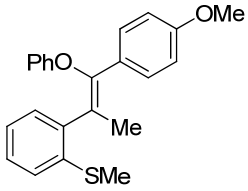
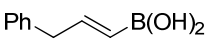
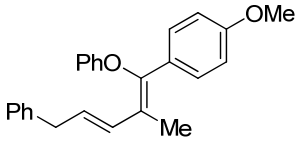
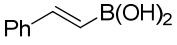
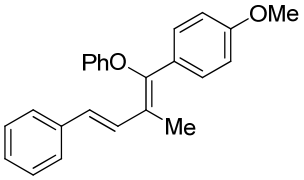
entry	reagents	Pd cat[a]	product	yield[b]
1	**276** + 	**A**	 **286**	N.R.[c]
2		**B**		76%
3	**276** + 	**A**	 **287**	N.R.
4		**B**		83%
5	**276** + 	**A**	 **288**	N.R.
6		**B**		55%
7	**276** + 	**A**	 **289**	N.R.
8		**B**		92%
9	**276** + 	**A**	 **290**	N.R.
10		**B**		74%

Table 21 *con't*

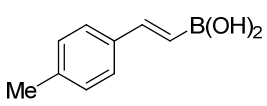
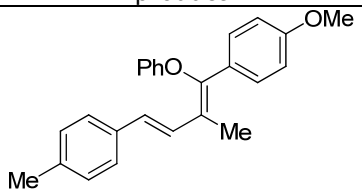
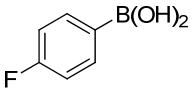
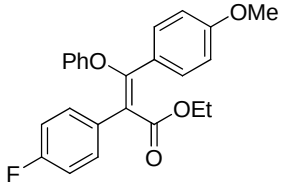
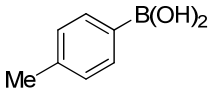
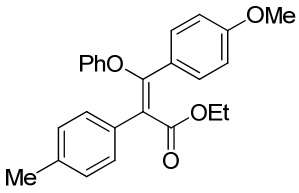
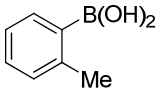
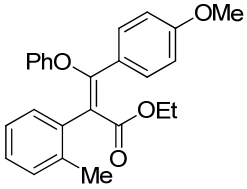
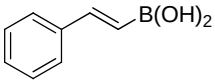
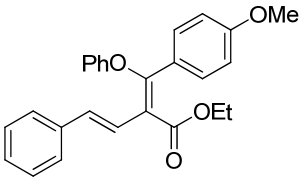
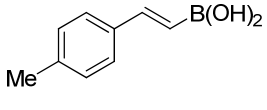
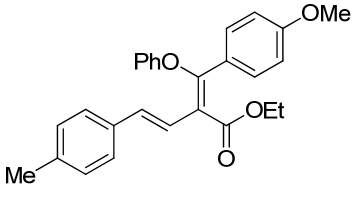
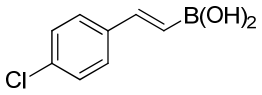
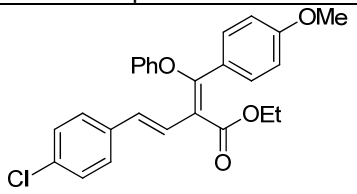
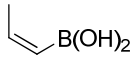
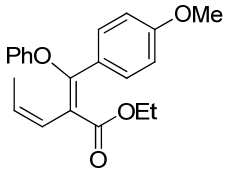
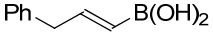
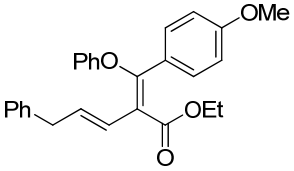
entry	reagents	Pd cat[a]	product	yield[b]
11	**276** + 	**A**	 **291**	N.R.
12		**B**		47%
13	**277** + 	**A**	 **292**	70%
14		**B**		72%
15	**277** + 	**A**	 **293**	75%
16		**B**		87%
17	**277** + 	**A**	 **294**	59%
18		**B**		89%
19	**277** + 	**A**	 **295**	82%
20		**B**		69%
21	**277** + 	**A**	 **296**	36%
22		**B**		91%

Table 21 *con't*

entry	reagents	Pd cat[a]	product	yield[b]
23	**277** + 	**A**	 **297**	62%
24		**B**		73%
25	**277** + 	**B**	 **298**	34%
26	**277** + 	**B**	 **299**	65%

[a] **A**: 1 equiv **276** or **277**, 1.5 equiv $RB(OH)_2$, 2.5 mol% Pd_2dba_3, 5 mol% DPEphos, 3 equiv CsF-Cs_2CO_3, dioxane, 100 °C, overnight; **B**: 1 equiv **276** or **277**, 1.5 equiv $RB(OH)_2$, 5 mol% $Pd(OAc)_2$, 10 mol% S-Phos, 2.2 equiv Cs_2CO_3, toluene, 110 °C, overnight. [b]Isolated yields. [c]No reaction.

2.4.3 Summary

To generalize our observations from sections 2.3 and 2.4, $Pd(PPh_3)_4$ is the most efficient catalyst for cross-coupling heteroaryl boronic acids, at either the C^1 of dichlorovinyl ethers or C^2 of vinyl chlorides. For C^1 functionalization, catalysts from any one of many different ligands in combination with palladium are capable of complete site selective cross-coupling, though catalysts based on either DPEphos or Xantphos are the most active. For C^2 functionalization, Pd/S-Phos is the most general in terms of electrophile and nucleophile scope and, in general, prevents intramolecular C-H activation side reactions. The major limitation of the Pd/S-Phos catalytic system was the inability to selectively C^2-functionalize a C^1-alkyl derivative without competing direct arylation (Table 18).

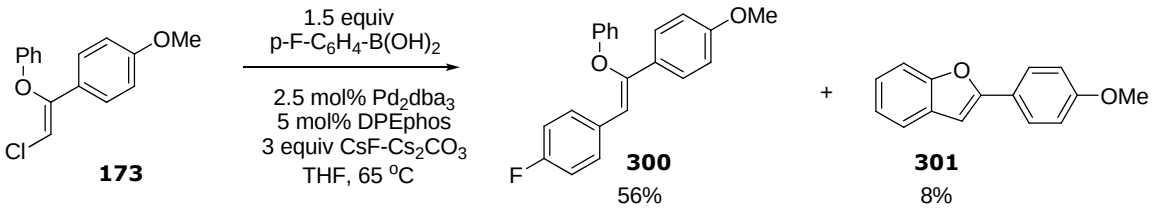
The synthesis of aryl vinyl ethers has been previously discussed in this thesis (Scheme 60). A method for the synthesis of substituted aryl vinyl ethers has been developed that can access essentially any desired substructure via a simple choice of order and flavour of organometallic reagent addition (e.g. aryl-aryl, alkenyl-aryl, aryl-alkenyl, etc.), making this method both modular and efficient, ideal in a diversity-oriented synthesis. This route is superior to previously-published approaches to aryl vinyl ethers (e.g. Sahoo et al.[291] Scheme 60) which suffered from limited substrate scope. Trichloroethylene is very inexpensive[494] and we demonstrated here that TCE is also a highly useful *tetra*functionalizable two-carbon linchpin for the direct and rapid synthesis of high–value end targets or platforms for nearly limitless[277,495] synthetic transformations.

2.5 Synthesis of Benzofurans

2.5.1 Introduction

In efforts to find appropriate conditions for C^2 arylation of C^1 arylated vinyl chlorides, in analogy to reactions reported in section 2.4.1, we first examined the applicability of the Pd/DPEphos catalytic system. These conditions were in fact useful for arylating compound **173** with 1.5 equivalents of *p*-fluorophenylboronic acid, and the desired diarylatedvinyl ether **300** was isolated in 56% yield (Scheme 120). However, a second product was identified when analysis of the ^{1}H NMR spectrum of the crude reaction material was performed. Isolation and characterization of this product showed it to be 2-(4-methoxyphenyl)benzofuran **301**, formed via apparent intramolecular C-H activation.

Scheme 120. C^2 cross-coupling experiment on **173** that produced diaryl vinyl ether **300** as well as benzofuran **301** as a byproduct.

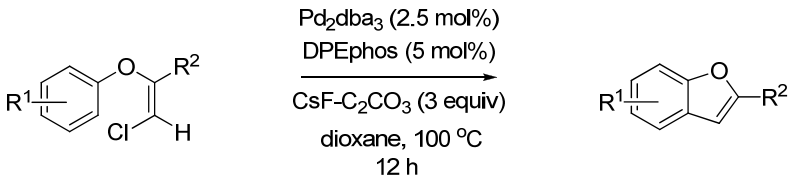


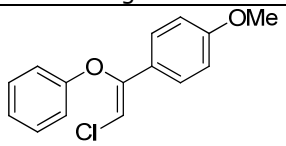
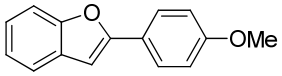
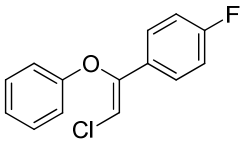
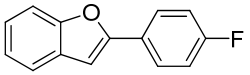
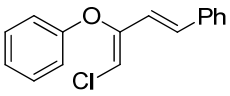
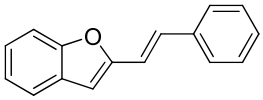
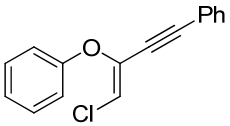
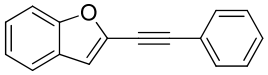
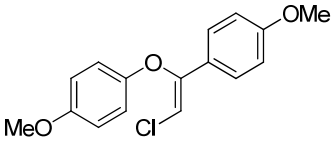
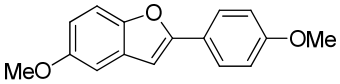
The apparently facile direct C-H functionalization of phenolic compounds led to a detailed exploration of this chemistry, and sections 2.5.2 and 2.5.3 describe the development, scope and some investigations into the mechanism of this process.

2.5.2 Optimization and scope of the one-pot Suzuki coupling/direct arylation

We were encouraged by the observation of a small amount of benzofuran formed during the course of the reaction described in Scheme 120. Repeating the reaction in the absence of boronic acid gave complete conversion to the benzofuran, and **301** was isolated in good yield (Table 22, entry 1). The reaction proved equally successful for the cyclization of *p*-fluorophenyl substituted **194**, and **302** was also isolated in good yields (entry 2). These conditions were also applicable to the cyclization of chloro-dienes and chloro-enynes, and 2-alkenyl benzofuran **303** and 2-alkynyl benzofuran **304** were easily synthesized from **200** and **214**, respectively (entries 3 and 4). A methoxy substituent on the phenol component was also well-tolerated under these conditions, and **305** was isolated in good yield (entry 5).

Table 22. Cyclization of (*Z*)-1-Substituted-1′-aryloxy-2-chloroethylenes.

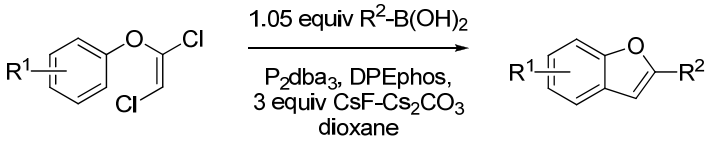


entry	starting material	product	yield[a]
1	 **173**	 **301**	86%
2	 **194**	 **302**	72%
3	 **200**	 **303**	32%[b]
4	 **214**	 **304**	80%
5	 **196**	 **305**	82%

[a]Isolated yield. [b]Low isolated yield attributed to solubility issues during isolation.

The direct application of the same cross-coupling conditions used to install the C^1 aryl moiety to the intramolecular C-H activation suggested the possibility of a sequential, one-pot Suzuki coupling/direct arylation, and this strategy is outlined in Scheme 121.

Scheme 121. Proposed one-pot synthesis and functionalization of benzofurans via sequential Suzuki coupling and direct arylation of 1,2-dichlorovinyl ethers.



During the exploration of C^1 functionalization, it was found that arylation using aqueous $Pd(PPh_3)_4$ was much faster than the corresponding reactions using Pd/DPEphos. The Pd/DPEphos reaction in THF at 65 °C took approximately 6 h, while the same reaction using $Pd(PPh_3)_4$ as the catalyst in aqueous THF was complete in as little as 1 hour (Table 9). To try to increase the rate of the Pd/DPEphos catalyzed reaction, the THF solvent was replaced by dioxane, and the temperature could therefore be increased to 100 °C. Not only was the arylation complete in about 1 hour (see results in Figure 14), but prolonged heating in the presence of palladium at that temperature induced C-H activation, and benzofuran formation was observed by TLC within a few hours. It was later found that THF could also be used as the solvent for one-pot Suzuki-coupling/direct arylation, but the concentration of the reaction mixture had to be increased (1.0 M in THF compared to as low as 0.14 M in dioxane) in order for the benzofuran to be formed at a reasonable rate. For convenience, most reactions were conducted in dioxane at 100 °C with a concentration of 0.4 M with, though this was not critical.

A brief survey of different ligands in sequential Suzuki coupling/direct arylation from both the parent dichlorovinyl ether **93** and *p*-cyano substituted dichlorovinyl ether **129** was performed. In the one-pot functionalization and cyclization of both **93** and **129**, DPEphos **12** as a ligand produced the most active catalyst in these reactions (Table 23, entries 1 and 6). Tricyclohexylphosphine **184** was almost as effective in the overall transformation of cyano compound **129** to **309**, although the overall conversion was

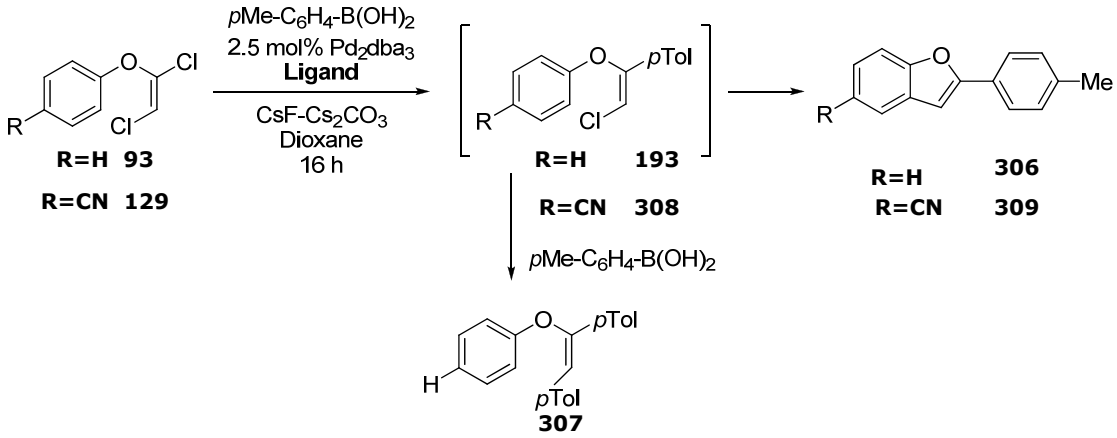
lower than that observed with DPEphos (roughly 67% conversion from **308** to **309**, entry 1, as compared to the 84% conversion achieved by DPEphos, entry 2).

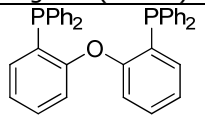
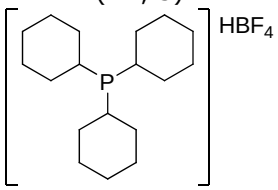
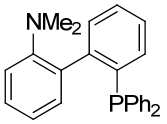
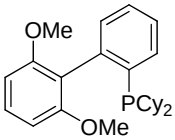
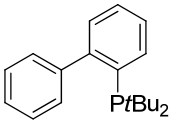
Examination of PhDavePhos (**185**), S-Phos (**187**) and JohnPhos (**186**) as ligands under these conditions with cyano-functionalized **129** as the substrate led to only incomplete conversion to the monoarylated compound **308** and no benzofuran could be detected in any of these reactions (Table 23, entries 3 – 5). When the ligand screen was repeated using toluene as a solvent, similar trends were observed. These data are interesting, and are in apparent contrast to Echavarren's observation that similar reactions involving an intramolecular C-H activation (see Scheme 28, section 2.5.3.6) were much slower with bidentate ligands (DPPF **190**, cyclooctadiene, phenanthroline) than with monodentate ones (such as PPh_3, $AsPh_3$).[160] It should be pointed out, however, that reactions in Table 23 show only the net results; these reactions do not indicate relative efficiency in the individual steps, and a faster direct arylation as mediated by Pd/DPEphos (**12**) versus PCy_3 (**184**) cannot be concluded from these results.

Somewhat different results were observed starting from unsubstituted dichlorovinyl ether **93**. As stated previously, DPEphos **12** was determined to be the best ligand in the one-pot Suzuki coupling/direct arylation (Table 23, entry 6). Unlike the observation that PCy_3 (**184**) could be an effective ligand in the sequential palladium-catalyzed reactions from cyano-substituted compound **129** (entry 2), the palladium complex derived from **184** was unable to induce complete Suzuki coupling of **93** and the corresponding benzofuran could not be detected. This is also in contrast to the observation that when **184** was examined as a ligand in the cross-coupling between **93** and *p*-methoxyphenyl boronic acid, some doubly arylated compound was observed (**175**, Figure 12) in THF at 65°C, but the doubly arylated **307** was not detected in the ^1H NMR spectrum here, in dioxane at 100 °C (Table 23, entry 7). Similar to the screening in Figure 12, ligands PhDavePhos (**185**), S-Phos (**186**) and JohnPhos (**187**) showed poor selectivity, and a mixture of starting material **93**, mono- (**193**) and diarylated (**307**)

vinyl ethers and benzofuran (**306**) could be identified in the ^{1}H NMR spectrum of the crude reaction mixtures (Table 23, entries 8 – 10).

Table 23. Ligand screen of the one-pot conversions of dichlorovinyl ethers **93** and **129** to 2-aryl benzofurans.



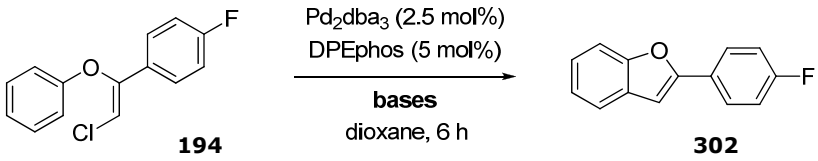
ligand (mol%)	entry	**129**: **308**: **309**[a]	entry	**93**: **193**: **306**: **307**
 (**12**, 5)	1	0: 1.0: 5.4	6	0: 0: 1.0: 0
 (**184**, 10)	2	0: 1.0: 2.0	7	1.0: 9.5: 0: 0
 (**185**, 10)	3	1.0: 4.6: 0	8	1.0: 8.8: 1.4: 1.73
 (**187**, 10)	4	1.0: 3.3: 0	9	1.0: 3.78: 0.25: 0.26
 (**186**, 10)	5	1.0: 1.4: 0	10	1.0: 2.78: 0.12: 0.52

[a]A similar trend was observed when the reaction was performed in toluene rather than dioxane.

With the confirmation that the Pd/DPEphos based catalytic system appeared to be ideal for the sequential Suzuki coupling/direct arylation, we examined the bases used in the direct arylation, similar to the study on the effect of the base on the C^1-Cl site selective cross-coupling. The role of the base in direct arylation was examined in relation to the conversion of aryl vinyl ether **194** to benzofuran **302** (Table 24). When no base was added to the reaction, approximately 8% conversion to benzofuran **302** was observed by NMR; this is approximately equal to the number of equivalents of palladium catalyst added to the reaction, and appears likely that a stoichiometric reaction occurred, but the production of acid from this process prevented catalytic turnover. Use of either CsF (entry 2) or Cs_2CO_3 (entry 3) alone showed low conversion of **194** to **302**; combining both bases in a single reaction resulted in nearly complete conversion to **302** (entry 4). However, replacing Cs_2CO_3 with K_2CO_3, still in combination with CsF lowered the conversion of **194** to **302** (entry 5). These data indicate that a combination of a fluoride and a carbonate base is ideal for this reaction, but the counterion does play a role. It should be noted, however, that the difference in conversion between entries 2 or 3 and 4 may also be related to the *total* equivalents of base, as in each case, three equivalents of each base were added to the reactions, so entries 2 and 3 had 3 equivalents of base, whereas entry 4 was conducted in the presence of 6 equivalents of base. This does not have any influence on the comparison of entry 4 to 5, as each of these experiment was conducted in the presence of 6 equivalents of base.

These results are different from what was observed in Suzuki coupling at C^1; in that case, CsF alone was able to promote cross-coupling as well as the CsF-Cs_2CO_3 base couple could, and Cs_2CO_3, while less efficient alone, could still promote the reaction moderately well (section 2.3.2, Figure 14). This suggests that if only cross-coupling at C^1 was desired without subsequent cyclization to the benzofuran, the Pd/DPEphos catalytic system would best be used with only CsF as the base. Similarly, the CsF-Cs_2CO_3 couple is optimal for the one-pot Suzuki coupling/direct arylation, and the combination of the two bases was employed in all subsequent work.

Table 24. Effect of the base on the efficiency of direct arylation.

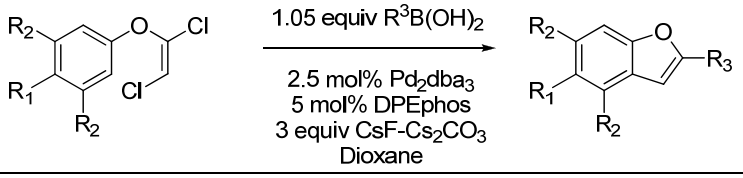


entry	base(s)[a]	conversion[b]
1	None	8%
2	CsF	18%
3	Cs_2CO_3	29%
4	CsF-Cs_2CO_3	98%
5	CsF-K_2CO_3	56%

[a]3 equiv of each base was added to the reaction. [b]Determined from integration of diagnostic signals in ^{1}H NMR of the crude material isolated from the reactions.

With the catalytic system optimized for C^1-Cl Suzuki coupling confirmed to be optimal for direct arylation as well, the scope of the one-pot preparation of benzofurans from dichlorovinyl ethers was examined (Table 25). This was first done with unsubstituted phenols (entries 1 – 7) and symmetrically substituted phenols (entries 8 – 20). The reaction was generally examined to produce 2-aryl benzofurans, but could also be applied to the synthesis of 2-alkenyl benzofurans (entries 6, 7 and 11). This method proved particularly successful for highly oxygenated benzofurans (entries 12 – 15), including the core structure of the Ebenfuran family of estrogen receptor modulators (entry 12, **317**)[315,327,496] and the natural product Corsifuran C (entry 13, **305**).[326]

Table 25. Benzofurans from symmetrical phenols.



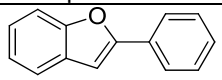
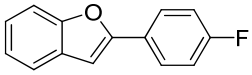
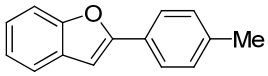
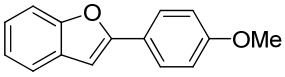
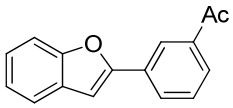
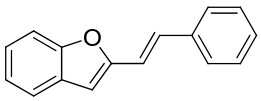
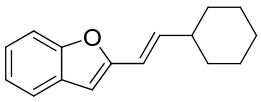
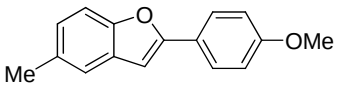
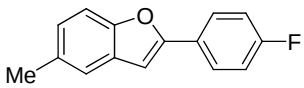
entry	reactants[a]	product	yield[b]
1	**93** + C_6H_5-B(OH)$_2$	 **310**	75%
2	**93** + 4-F-C_6H_4-B(OH)$_2$	 **302**	53%
3	**93** + 4-Me-C_6H_4-B(OH)$_2$	 **306**	51%
4	**93** + 4-OMe-C_6H_4-B(OH)$_2$	 **301**	74%
5	**93** + 3-Ac-C_6H_4-B(OH)$_2$	 **311**	50%
6	**93** + (*E*)-C_6H_5CH=CH-B(OH)$_2$	 **303**	71%
7	**93** + (*E*)-C_6H_{11}CH=CH-B(OH)$_2$	 **312**	59%
8	**113** + 4-OMe-C_6H_4-B(OH)$_2$	 **313**	87%
9	**113** + 4-F-C_6H_4-B(OH)$_2$	 **314**	76%

Table 25 *con't*

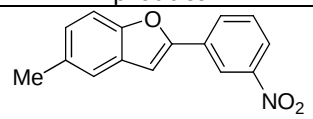
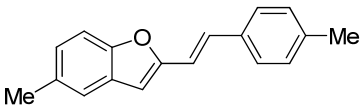
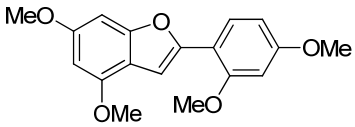
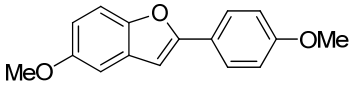
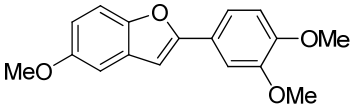
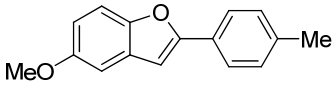
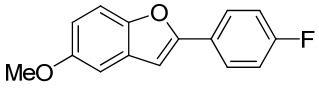
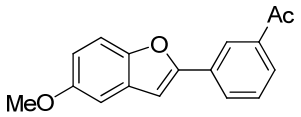
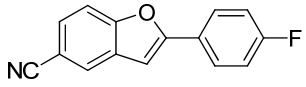
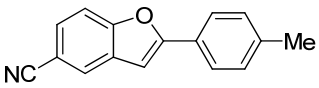
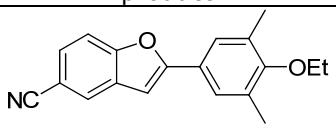
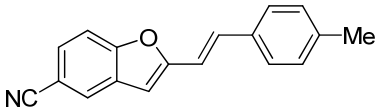
entry	reactants[a]	product	yield[b]
10	**113** + 3-NO_2-C_6H_4-B$(OH)_2$	 **315**	13%
11	**113** + (*E*)-4-Me-C_6H_4CH=CH-B$(OH)_2$	 **316**	71%
12	**112** + 2,4-$(MeO)_2$-C_6H_4-B$(OH)_2$	 **317**	80%
13	**110** + 4-MeO-C_6H_4-B$(OH)_2$	 **305**	82%
14	**110** + 3,4-$(MeO)_2$-C_6H_3-B$(OH)_2$	 **318**	90%
15	**110** + 4-Me-C_6H_4-B$(OH)_2$	 **319**	69%
16	**110** + 4-F-C_6H_4-B$(OH)_2$	 **320**	68%
17	**110** + 3-Ac-C_6H_4-B$(OH)_2$	 **321**	36%
18	**129** + 4-F-C_6H_4-B$(OH)_2$	 **322**	81%
19	**129** + 4-Me-C_6H_4-B$(OH)_2$	 **323**	85%

Table 25 *con't*

entry	reactants[a]	product	yield[b]
20	**129** + 3,5-Me_2-4-EtO-C_6H_2-B$(OH)_2$	 **324**	87%
21	**129** + (*E*)-4-Me-C_6H_4CH=CH-B$(OH)_2$	 **325**	60%

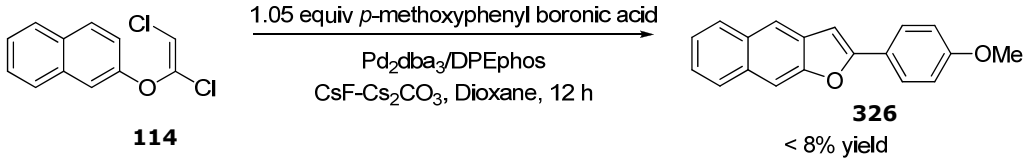
[a]Reactions could be run as 0.4M (with respect to dichlorovinyl ether, see experimental) solutions in dioxane at 100 °C or 1.0M solutions in THF at 65 °C with comparable results. [b]Isolated yields

While most benzofurans with reported biological activity are very electron-rich and often substituted with numerous oxygen-based groups, the ability to incorporate other groups would be very useful for three reasons. First and primarily, there are not many reported syntheses of benzofurans containing electron-withdrawing groups, due to the difficulty in incorporating starting materials containing these functionalities and/or developing chemistry compatible with these groups.[350,351,373,497,498] Developing a sequence of reactions that can build a key structural motif regardless of the substitution pattern and electronic properties of the building blocks is intrinsically and obviously more useful than a synthetic process useful for only a couple of different substrates. Finally, nitro groups, nitriles, and acetates are easily transformed into other functional groups and would thus act as simple and inexpensive handles for further synthetic treatments. It should also be noted that methoxy groups can also be further manipulated by other transition metals.[499-504]

Attempts to use heterocyclic boronic acids in this process failed entirely; when 3-pyridyl, 2-formyl-3-thiophenyl, or 3-furyl boronic acids were used, only starting material was recovered, consistent with observations that the aqueous $Pd(PPh_3)_4$ system is

required to cross-couple these boronic acids (Table 9). Additionally, any attempts to use *o*-thiomethylphenyl boronic acid halted at the monoarylated stage and no benzofuran containing this arene could be constructed. Curiously, attempts to use the dichlorovinyl ether derived from 2-hydroxynaphthalene (**114**) were not very successful and mass recovery from the crude reaction mixture was low in all cases. Reactions between **114** and *p*-fluorophenyl boronic acid, *o*-tolyl boronic acid, and (*E*)-2-phenylethenyl boronic acid showed incomplete arylation and no naphthofuran could be detected. The analogous reaction with *p*-methoxyphenyl boronic acid gave some of the desired product **326**, but this was isolated in less than 8% yield (Scheme 122).* The reason for this apparent difference in reactivity between phenolic and naphtholic dichlorovinyl ethers is unclear.

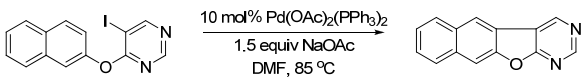
Scheme 122. Attempted synthesis of naphthofuran from dichlorovinyl ether **114** and boronic acids.



114 **326** < 8% yield

Boronic acids are prone to side reactions in the presence of palladium, usually homocoupling and protodeboration;[468] when only 1.05 equivalents of boronic acid are used, if either of these are occurring to any extent, C^1 functionalization obviously cannot go to completion. In our experience, if C^1 functionalization does not go to completion under these conditions intramolecular direct arylation will not occur. For example, all

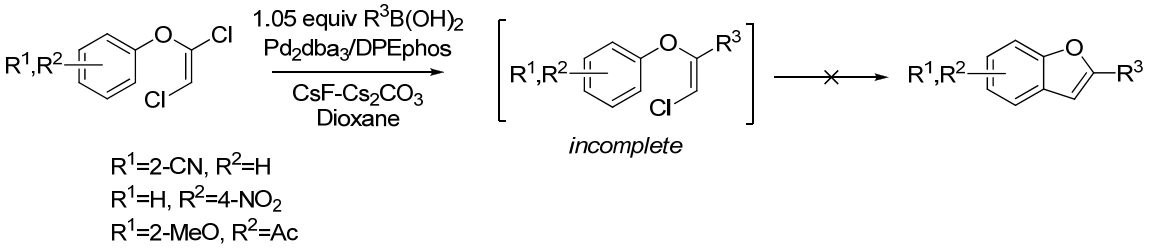
* The full characterization of this compound was never performed. It possible that the material isolated from that reaction was a result of C-H activation at C^1, not C^3 as indicated in Scheme 122. A related reaction (below) was reported to undergo direct arylation at C^3 with moderate success. See Zhang, Y.-M., Razler, T., Jackson, P. F. *Tetrahedron Lett.* **2002**, *43*, 8235-8239.



54%

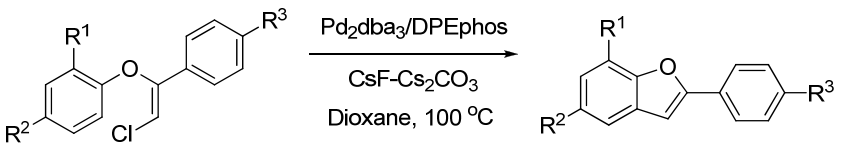
attempts to induce one-pot Suzuki coupling/direct arylation from dichlorovinyl ethers **120**, **126** and **127** were unsuccessful (Scheme 123); Suzuki coupling did not appear to go to completion, and no benzofurans were detected in the ^{1}H NMR of the crude reaction mixtures

Scheme 123. Attempted one-pot Suzuki-coupling/direct arylation of 2-cyanophenol, 4-nitrophenol and acetovanillone derivatives.



To determine whether the problem was deactivation of the palladium catalyst or inefficiency of the first cross-coupling, or simply an intrinsic reactivity problem, the intermediates were isolated and re-subjected to the cyclization conditions (Scheme 124). The *o*-cyano compound **327** was found to be incompletely cyclized after 40 h, and the 7-cyanobenzofuran **328** was isolated in 45% yield with 38% recovered starting material. However, the 5-nitrobenzofuran **330** derived from vinyl chloride **329** was isolated in excellent yield after only 12 h. Curiously, the arylated acetovanillone vinyl chloride synthesized from **127** was isolated unchanged. We are unsure of the cause of this unreactivity.

Scheme 124. Cyclization of arylated materials.



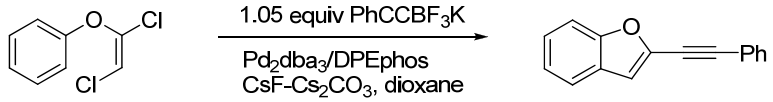
R^1=CN, R^2=H, R^3=Me	**327**	R^1=CN, R^2=H, R^3=Me	**328**	45%
R^1=H, R^2=NO_2, R^3=OMe	**329**	R^1=H, R^2=NO_2, R^3=OMe	**330**	74%
R^1=OMe, R^2=Ac, R^3=OMe	**331**	R^1=OMe, R^2=Ac, R^3=OMe	*No reaction*	

The combination of the results from Scheme 124 and Table 25 suggest that the major restriction is efficiency of the cross-coupling reaction and that individual optimization of the number of equivalents of boronic acid could lead to good yields of the benzofurans in one pot from the dichlorovinyl ethers and boronic acids. As it was noted in Scheme 120, even in the presence of 1.5 equivalents of a boronic acid for a cross-coupling, direct arylation could still compete, albeit at a reduced rate. This suggests that using a slight excess of boronic acid to allow the cross-coupling at C^1 to go to completion will not interfere with the direct arylation to any significant extent and this could be useful in individual optimizations of the one-pot process.

As reported in section 2.3.3, enynes could be formed in high yield by room temperature Sonogashira cross-coupling between the dichlorovinyl ethers and terminal alkynes (Scheme 104). Unfortunately, $Pd(PPh_3)_4$, the palladium catalyst used in the Sonogashira reaction, was not able to induce cyclization and a two-pot procedure was necessary to synthesize 2-alkynyl benzofurans (as reported in Table 22, entry 4). Desiring a direct, one-pot synthesis, we turned to using alkynyl boronic acids and potassium alkynyl trifluoroborate salts as alkyne nucleophiles.[101,106] Application of the Pd/DPEphos conditions to the cross-coupling between dichlorovinyl ether **93** and the boronic acid synthesized from phenyl acetylene was not successful, and **93** was isolated unchanged. The use of the corresponding potassium alkynyl trifluoroborate salt was met with some success, although an unknown black gummy material that developed during the course of the reaction hampered both stirring and product isolation and 2-

alkynylbenzofuran **304** was isolated in only 35% yield. A ^{1}H NMR spectrum of the crude material isolated from the reaction showed signs of decomposition as well. We are not sure of the source of this difference in reactivity and/or possible degradation, and are currently investigating catalytic systems to induce one-pot cross-coupling/direct arylation from terminal alkynes and/or potassium alkynyl trifluoroborates in higher yields. It should be noted that the conditions applied here to the cross-coupling of **93** with a potassium alkynyl trifluoroborate are distinctly different from the typical conditions used in this type of process, most notably by the application of anhydrous conditions, as these are generally done in the presence of water.[101,106]

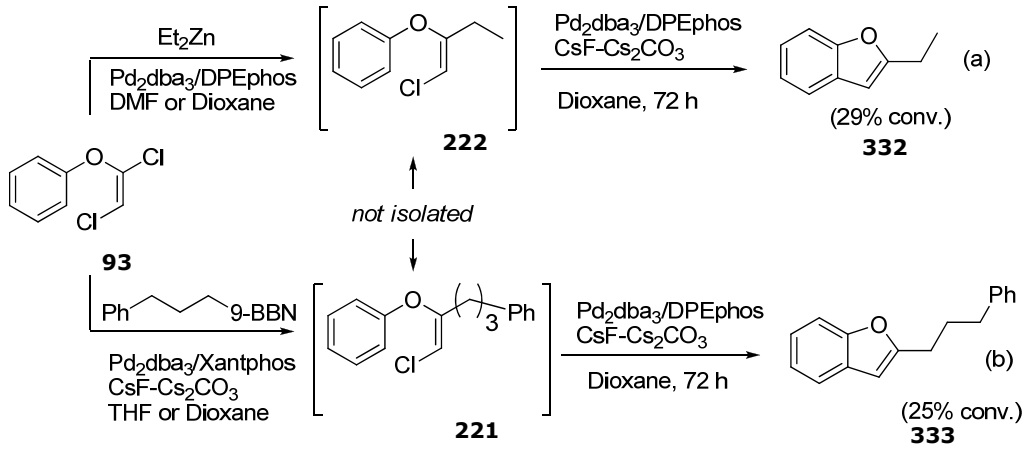
Scheme 125. One-pot synthesis of 2-alkynyl benzofuran.



93 **304** 35%

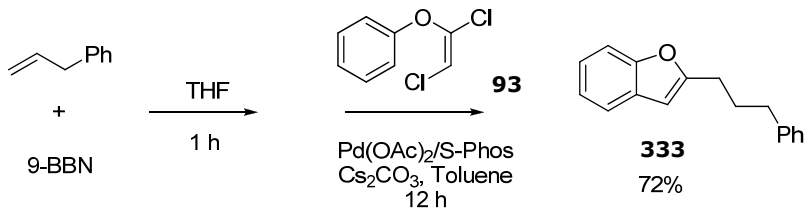
The direct application of the conditions optimized for aryl and alkenyl boronic acids were also not successful in the one-pot cross-coupling/direct arylation of alkyl organometallics. As demonstrated in section 2.3.3, alkyl groups could be installed at C^1 via Negishi coupling with organozinc reagents and Suzuki coupling between alkyl-9-BBN compounds (Table 13). However, attempts to include the alkylation in one-pot routes to benzofurans **332** and **333** were inefficient, and incomplete conversions from the C^1-alkyl compounds to the 2-alkylbenzofurans were observed, even after days of reflux. Subjecting the isolated intermediates **221** and **222** to the same conditions did not improve the result, and conversion to the 2-alkyl benzofurans remained at less than 30% as estimated by analysis of the ^{1}H NMR spectrum of the crude material isolated from the reaction (Scheme 126, equations a and b).

Scheme 126. Attempted one-pot syntheses of 2-alkylbenzofurans using Pd/DPEphos catalytic system.



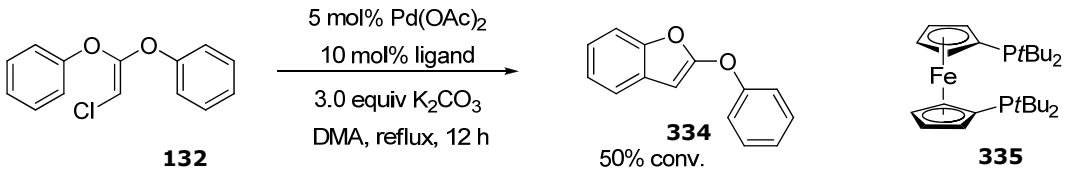
We had noted in the attempts to functionalize the C^2-Cl bond 1-alkyl-2-chloro-1-phenoxyethylenes with a potassium organotrifluoroborates that the rate of C-H activation became competitive with the rate cross-coupling when using the $Pd(OAc)_2$/S-Phos catalytic system (Table 18, entry 2). Therefore, the Pd/S-Phos catalytic system was applied to the cyclization of isolated **221** to benzofuran **333**. The direct arylation of **221** proceeded readily under those conditions, and was complete in under 8 h. Additionally, the C^1 alkylation and direct arylation could be done in one pot under the same conditions to give the 2-alkyl benzofuran **333** in excellent isolated yield from dichlorovinyl ether **93** (Scheme 127). This in fact is a one-pot, three-step procedure, consisting of sequential hydroboration, cross-coupling and direct arylation.

Scheme 127. One-pot route to 2-alkyl benzofuran using Pd/S-Phos catalytic system.



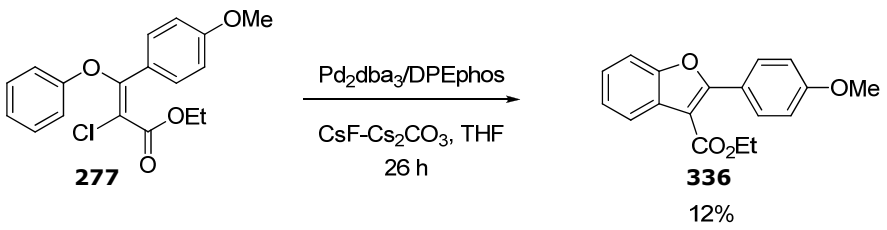
Explorations of the reactivity of other vinyl ethers towards direct arylation conditions were performed. Treating 1,1'-diphenoxy-2-chloroethylene **132** with palladium and electron-rich ferrocene ligand **335** generated 2-(phenoxy)benzofuran **334** in approximately 50% conversion (Scheme 128), as estimated by the ^{1}H NMR of the crude material, though this material was not isolated.

Scheme 128. Cyclization of ketene acetal **132** to 2-phenoxybenzofuran.



Neither the C^2 methylated **270** nor vinyl allyl alcohol **278** could be induced to undergo intramolecular direct arylation using the standard Pd/DPEphos conditions to give the 2,3-disubstituted benzofuran. This was attributed to the inability of the palladium catalyzed to insert into the C^2-Cl bond, as **270** was also unable to act as an electrophile in Suzuki cross-coupling reactions attempted under the same conditions (Table 21). Reasoning that this limitation could be at least in part due to an increase in electron density at C^2-Cl making the oxidative insertion more difficult, the direct arylation was attempted using unsaturated ester **277** as the substrate (Scheme 129). As was observed in the cross-coupling reactions between vinyl chloride **277** and boronic acids (Table 21), reaction did proceed in this case, although the 2,3-disubstituted benzofuran **336** was isolated in only 12% yield. This was partially attributed to solubility problems, however, the reaction proceeded in only 44% conversion from **277** (as estimated by analysis of the ^{1}H NMR spectrum of the unpurified material isolated from the reaction), suggesting that the direct arylation can be sensitive to sterics as well as electronics. The lower isolated yield of **336** was attributed to solubility problems during isolation, as the ^{1}H NMR spectrum of the unpurified material showed only **277** and **336** with no obvious signs of degradation.

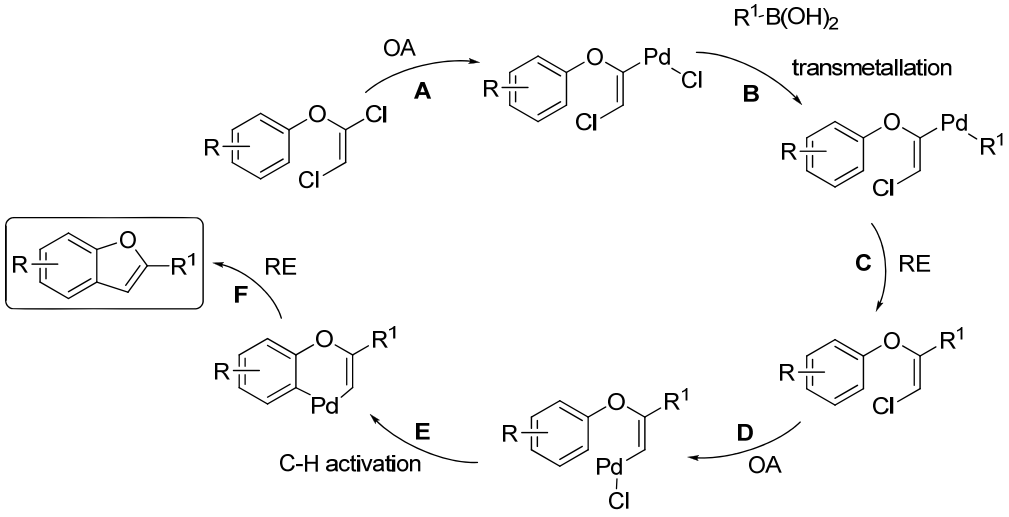
Scheme 129. Synthesis of a 2,3-disubstituted benzofuran from vinyl chloride **277**.



2.5.3 Mechanistic Investigations

At this point, it became clear that a better understanding of the mechanism of the C-H activation step was required. The basic steps of the two processes in our one-pot synthesis of benzofurans are outlined in Scheme 130.

Scheme 130. Hypothesized general steps in the one-pot Suzuki coupling/direct arylation.



The basic mechanism of Suzuki coupling (steps **A**, **B** and **C** in Scheme 130, a more specific example than that presented in Scheme 2) is fairly well known, but direct arylation may proceed via a number of different mechanisms (section 1.2.3). We have assumed that the first step of direct arylation from the vinyl chloride is oxidative insertion

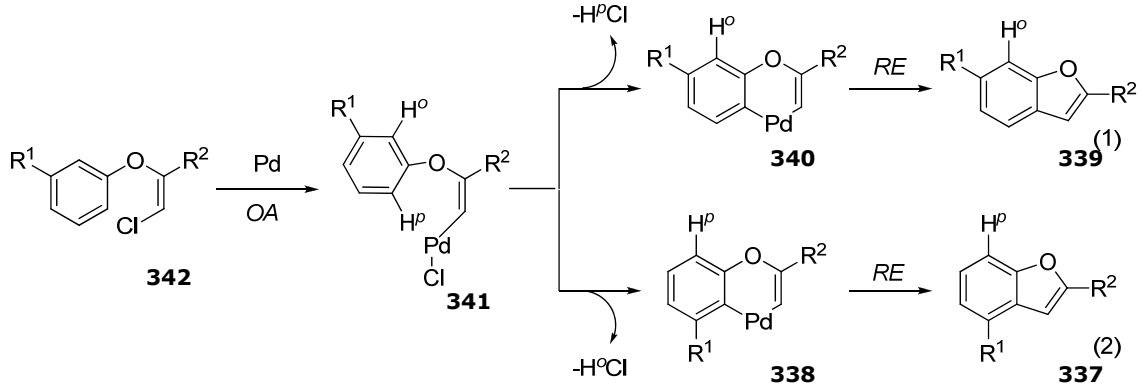
by palladium into the C-Cl bond (step **D**). This is because the alternate route would involve initial oxidative insertion into the C-H bond, which did not seem likely for two reasons. First, this would invoke a Pd(0)-Pd(II)-Pd(IV) catalytic cycle which is not as likely in the absence of obvious oxidants. Second, such an intermolecular C-H insertion in the absence of a directing group and in the presence of *many* different C-H bonds is highly improbable.

To elucidate the mechanism of C-H activation, step **E** in particular, a series of experiments were designed and executed. The results of experiments examining the electronic effects different functional groups have on the reaction, both intramolecularly (section 2.5.3.1) and intermolecularly (section 2.5.3.2) will be discussed first. This section will be concluded with a determination of both inter- and intramolecular kinetic isotope effects to delineate the mechanism of C-H bond cleavage (sections 2.5.3.3 and 2.5.3.4, respectively).

2.5.3.1 Electronic Effects

To probe the influence of electronics on direct arylation, we explored the regioselectivity of C-H activation in unsymmetrically substituted phenol derivatives. When a general aryl chlorovinyl ether **342** synthesized from an unsymmetrical phenol is subjected to the direct arylation procedure, there are two possible products as outlined in Scheme 131. Following palladium oxidative insertion into the C^2-Cl bond, giving **341**, either or both C-H bonds may be cleaved. If H^o (*ortho* with respect to the R^1 substituent) is cleaved, intermediate **338** is formed, and yields 4-substituted benzofurans **337** after reductive elimination. On the other hand, if the H^p bond is cleaved, intermediate **340** results which gives the 6-substituted benzofurans **339**. As the C-H^o and C-H^p bonds are both electronically and sterically different due to the presence of R^1, we reasoned that analyzing the effects different R^1 groups had on the formation of 4- versus 6-benzofurans would give us some insight into the mechanism of C-H functionalization.

Scheme 131. Regioisomeric benzofurans possible from the intramolecular direct arylation of unsymmetrical chlorovinyl aromatic ethers.



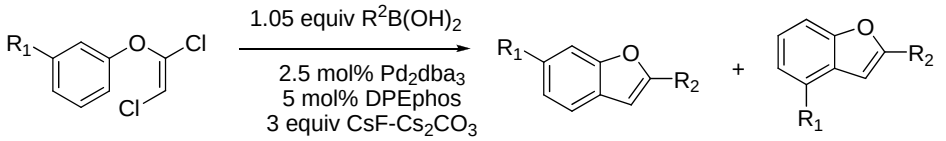
When the dichlorovinyl ether was substituted with the electron-donating 3-methyl group (**111**), one-pot Suzuki coupling/direct arylations with several boronic acids each gave a single product, and the 6-methylbenzofurans **343** - **345** were isolated in good yields (Table 26, entries 1 – 3). In no cases could the 4-methylbenzofuran be detected. Switching to the 3-methoxy analogue **117** as the starting material gave identical results with several different boronic acids and only the 6-methoxybenzofurans **346** - **348** could be detected (entries 4 – 6). Thus, in both cases, only the C-H^p bond was broken.

However, the reaction between *m*-nitrophenol-based **125** and a boronic acid always led to a mixture of 4-nitro and 6-nitro regioisomeric benzofurans, favoring 6-nitrobenzofurans in 3.3:1.0 – 5.9:1.0 ratios, depending on the boronic acid used (Table 26, entries 7 – 9). In contrast to the reactions with *m*-methoxy or –methyl substituted phenolic derivatives, when an *m*-nitro group was present, both the C-H^p and C-H^o bonds were broken, where breakage of C-H^p was favoured.

When the one-pot Suzuki coupling/direct arylation was performed between *m*-cyanophenol **122** and *p*-methoxyphenyl boronic acid, a similar 3.1:1.0 mixture of regioisomers was detected; however, this time, the 4-substituted benzofuran was produced in excess (entry 10). This was the only time we observed preferred

functionalization of the C^o-H bond over the C^p-H bond, showing a switch in regioselectivity.

Table 26. Synthesis of benzofurans from unsymmetrical phenols.



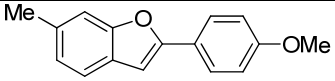
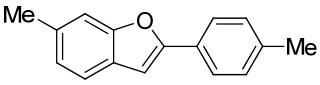
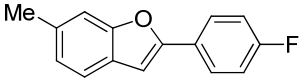
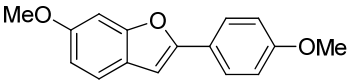
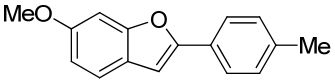
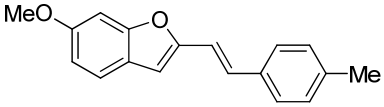
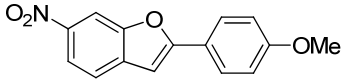
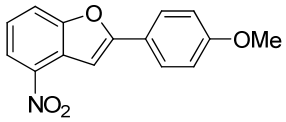
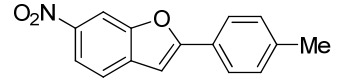
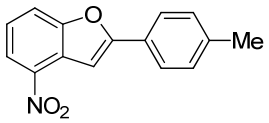
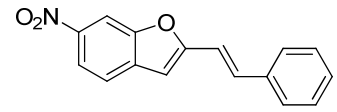
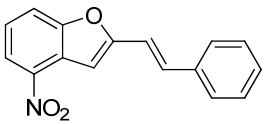
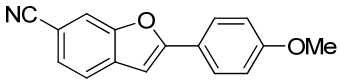
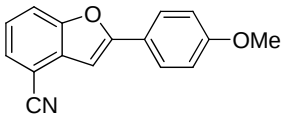
entry	reactants	product(s)	yield[a]	selectivity
1	**111** + 4-OMe-C_6H_4-B(OH)$_2$	 **343**	78%	[b]
2	**111** + 4-Me-C_6H_4-B(OH)$_2$	 **344**	86%	[b]
3	**111** + 4-F-C_6H_4-B(OH)$_2$	 **345**	66%	[b]
4	**117** + 4-OMe-C_6H_4-B(OH)$_2$	 **346**	92%	[b]
5	**117** + 4-Me-C_6H_4-B(OH)$_2$	 **347**	64%	[b]
6	**117** + (*E*)-4-Me-C_6H_4CH=CH-B(OH)$_2$	 **348**	61%	[b]
7	**125** + 4-OMe-C_6H_4-B(OH)$_2$	 **349**  **350**	82%[c]	5.9:1.0[d] (**349:350**)

Table 26 *con't*

entry	reactants	product(s)	yield[a]	selectivity
9	**125** + 4-Me-C_6H_4-$B(OH)_2$	 **351**  **352**	72%[c]	4.5:1.0[d] (**351:352**)
10	**125** + (*E*)-C_6H_5CH=CH-$B(OH)_2$	 **353**  **354**	73%[c]	3.3:1.0[d] (**353:354**)
11	**122** + 4-OMe-C_6H_4-$B(OH)_2$	 **355**  **356**	88%[c]	1.0:3.1[d] (**355:356**)

[a]Isolated yield. [b]Only one isomer was detected by crude ^{1}H NMR. [c]Combined yield of both isomers. [d]Estimated from ^{1}H NMR of the crude material; the isomers were separated and characterized independently (see experimental section).

Both the methyl and methoxy substituents are behaving similarly as electron-donating groups as both produce the 6-substituted benzofuran selectively. It is reasonable to assume that the nitro and cyano substituents exert similar electron-withdrawing effects on the arylation process; the difference in regioselectivity may be a steric one. In other words, it is possible that while both the cyano and nitro groups electronically favour formation of the 4-substituted benzofurans, the larger steric requirement of nitro compared to that of a cyano group forces the formation of the 6-

substituted benzofuran as the major product. It is probably intuitive to the readers that a trivalent nitro group has a larger steric influence that the linear cyano group. Quantitatively, sterics have been described in a couple of different ways. For example, the A value is a measure of the $A^{1,3}$-strain in cyclohexanes, where the A-value of a nitro group is 1.05 compared to the A value of a cyano of 0.21 (H is 0). While the compounds in this thesis are quite different from cyclohexanes, the A values make intuitive sense.

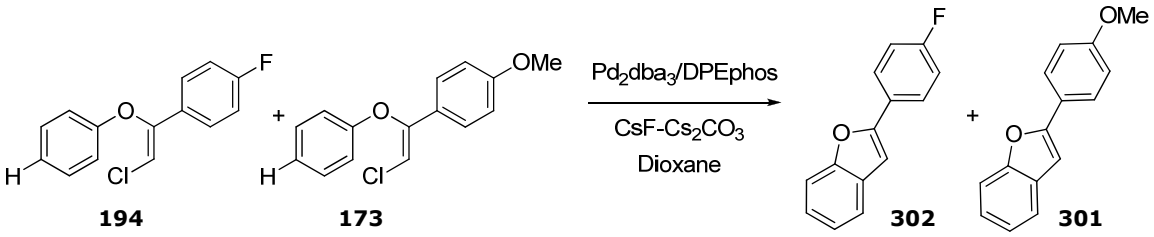
2.5.3.2 Intermolecular Competition Experiments

Toward elucidating the mechanism of C-H functionalization, three competition experiments involving the C-H activation step were performed. The effect of different substituents on the C^1 aryl component or on the phenolic component was each examined. To analyze these electronic effects, an equimolar mixture of two substrates was heated in the presence of the palladium catalyst. After benzofuran formation could be detected by TLC, the reactions were stopped and analyzed by ^{1}H NMR spectroscopy and/or GC-MS. The relative consumption of the starting materials and formation of the corresponding benzofurans were determined. The results of these experiments are described below. It needs to be pointed out that the consumption of the starting materials does not need to match the formation of the corresponding benzofuran. The mass balance was not determined in any of the experiments described. Because of that, the trends observed cannot lead to a solid conclusion. These results will only be interpreted in conjunction with supporting evidence and the difficultly in interpreting the results from these experiments will be specifically highlighted where necessary.

First, we subjected an equimolar mixture of *p*-fluorophenyl derivative **194** and *p*-methoxyphenyl derivative **173** to the cross-coupling conditions to determine if the electronics of the C^1 aryl component had an influence on the reaction. In fact, the fluorinated derivative was both consumed and converted to the corresponding benzofuran fastest, as compared to the methoxy functionalized compound (Scheme 132). This is suggestive of a rate-determining oxidative insertion step, assuming that the relative rates

of subsequent C-H functionalization are similar. However, it is possible that the fluorine substituent, though distant, is still exerting electron-withdrawing effects at that stage in the mechanism. If that is the case, these data would argue against electrophilic aromatic substitution as a mechanism, as the more electron-rich derivative would be expected to undergo arylation faster. It is difficult to deconvolute the individual contributions of oxidative insertion and direct arylation in this, and, in fact, all mechanistic experiments performed in this thesis.

Scheme 132. Intermolecular competition experiments at the C-H activation stage with arylated phenol derivatives.



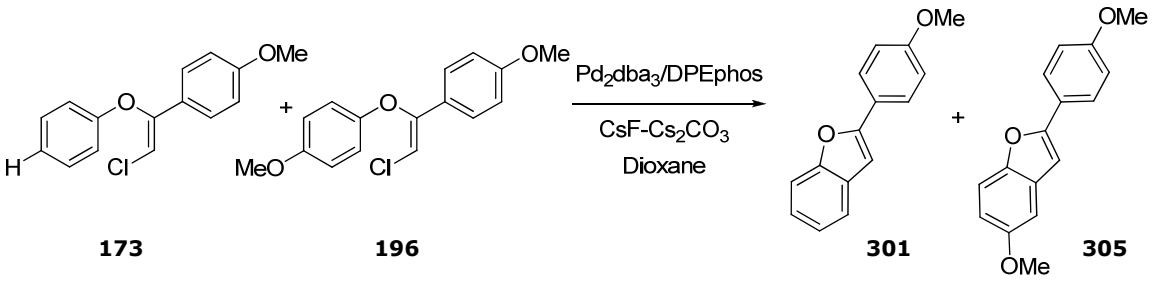
194 **173** **302** **301**

194	:	**173**	:	**302**	:	**301**
1.00	:	2.99	:	5.11	:	2.51

The electronic influence of the phenolic component of the vinyl chloride was examined by varying the substituent from the phenol building block and keeping the C^1 aryl component constant (Schemes 133 and 134). We examined the competition between electron-neutral (**173**) and electron-rich (**196**) (Scheme 133) and electron-poor (**357**) (Scheme 134). We found that a methoxy substituent on the phenol component did not influence consumption of the starting material (**173** versus **196**, Scheme 133), but the cyano-substituted **357** was consumed at approximately three times the rate of **173** (Scheme 134). The consumption of the starting materials could relate to the rate of oxidative addition of Pd into the C-Cl bond. As seen in our competition studies relating to the Suzuki coupling step (Scheme 101), the *p*-cyano compound was consumed fastest

(Scheme 134). However, we found that while there was no difference in consumption of **173** compared to **196**, the benzofuran from **173** (product **301**) was produced in four-fold excess compared to **305** derived from **196**, supportive of a C-H activation mechanism where the less electron-rich arene reacts fastest. Additionally, while the cyano-substituted starting material **357** was consumed at a rate three times that of **173**, the corresponding benzofuran **358** was produced in half the amount that benzofuran **301** was from **173**; again, the consumption of starting material did not correspond to the proportion of product produced, suggesting the possibility of competitive derivative pathways (which is possible in all cases).

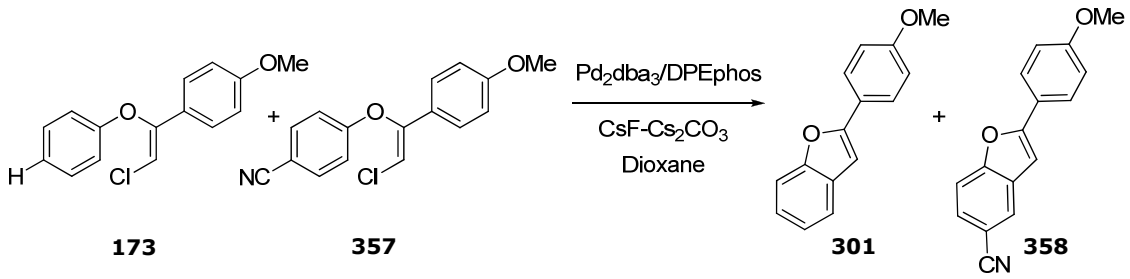
Scheme 133. Intermolecular competition experiments to probe the C-H activation stage with arylated *p*-methoxyphenyl derivatives.



173 **196** **301** **305**

173	:	**196**	:	**301**	:	**305**
3.83	:	3.81	:	4.10	:	1.00

Scheme 134. Intermolecular competition experiments to probe the C-H activation stage with arylated *p*-cyanophenol derivatives.



173 **357** **301** **358**

173	:	**357**	:	**301**	:	**358**
22.12	:	7.21	:	1.96	:	1.00

While the comparison of H, OMe and CN was not performed directly, it appears that arenes substituted with these groups react in the order H > CN > OMe; if the C-H activation was occurring via an electrophilic aromatic substitution mechanism, the order of reactivity would be OMe > H > CN, and it therefore seems that our results are not supportive of EAS (transition state **A**, Scheme 24). Although the regioselective experiments described in Table 26 suggest that methoxy and cyano groups have different electronic contributions, it is still possible that they in fact have the same electronic contribution. A methoxy group is normally considered a π-electron donor. As discussed in section 1.2.3.1, π-electron donors facilitate electrophilic aromatic substitution (EAS) reactions by stabilizing carbocations through π-bond interactions. However, a methoxy group is also a σ-electron-withdrawing group, and is, in fact, a stronger σ-electron-withdrawing group than is a cyano group. If the bond breakage involves σ-bonds rather than π-bonds, the σ-electron withdrawing effect is far more important that the π-electron donating effects. If this is the case, then perhaps the order of reactivity in arylation is related to the electron-withdrawing group and the more electron-rich arene (**173**) reacts fastest, though not via an EAS.

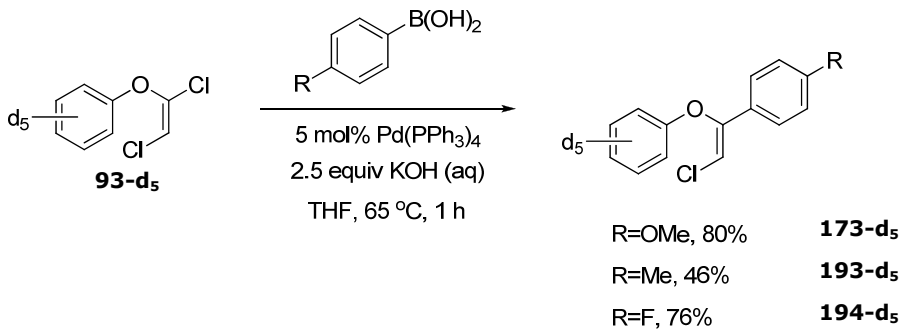
As pointed out in the introduction to this section (and as was observed in our competition experiments), faster consumption of one substrate does not mean that the

corresponding benzofuran is being produced fastest. Similarly, if one particular benzofuran is *not* being produced the fastest, it does not mean the reaction is slower. This may be due to competitive degradative pathways. Ogilvie reported that at refluxing dioxane temperatures, α,β-dihaloesters undergo β-elimination following Pd insertion into the α-C-I bond[174] and Organ observed similar eliminations of vicinal bromides.[276] Organ also looked at leaving group ability of phenoxides in allylic substitution reactions, and found that it is highly pK_a-dependent. An attempted palladium-catalyzed reaction of a allyl-nitrophenoxy substituted alkene led only to loss of the nitrophenol, demonstrating the high leaving ability of β-substituents with electron-withdrawing groups.[272,273,505] This suggests that at higher temperatures, vinyl-Pd species with a leaving group in the β-position are prone to elimination; perhaps at 100°C, β-elimination becomes competitive. Because of this possibility, the direct comparison of the formation of the different substituted benzofurans may not be meaningful. However, the *p*-nitrophenol compound cyclized in good yield – in this case, perhaps direct arylation was occurring at a rate comparable to elimination. The relative rates of formation of different substituted benzofurans as presented in this thesis are somewhat convoluted, but may be interpreted in combination with isotopic labeling experiments described in the following sections.

2.5.3.3 Intermolecular Isotope Effects

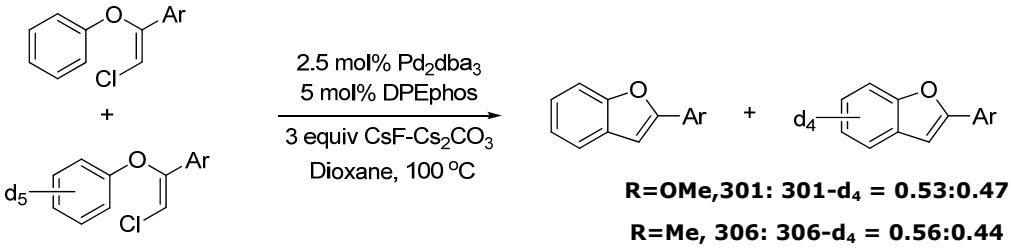
To determine if the C-H bond breakage was occurring at the rate-determining step, we measured the intermolecular kinetic isotope effect. The electronic nature of the C^1 aryl group clearly played a role in the overall rate of the reaction (Scheme 132), so the pentadeuterated C^1 aryl compounds containing a fluoro, methyl or methoxy functional group were all synthesized from **93-d_5** (synthesized from phenol-d_6 and TCE in a similar manner to that shown in Table 2 as described in the experimental section) (Scheme 135). We started from already C^1-arylated compounds in these experiments rather than a one-pot preparation from **93-d_5** so that we could analyzed the kinetic isotope on a single net transformation.

Scheme 135. Synthesis of arylated compounds to study intermolecular isotope effects.



To determine the intermolecular KIE, an equimolar mixture of **173**, **193**, or **194** and **173-d$_5$**, **193-d$_5$**, or **194-d$_5$** were combined in the presence of palladium, and heated until benzofuran formation could be detected by TLC. Each reaction was stopped before it went to completion. As can be seen in Scheme 136, there is no significant KIE in the intermolecular case, showing that the C-H bond breakage is not the rate-determining step. This is consistent with our earlier observation that 2-(4-fluorophenyl)benzofuran **302** forms at a faster rate than 2-(4-methoxyphenyl)benzofuran **301** (Scheme 132), and confirms that oxidative insertion into the C-Cl bond is indeed the rate-determining step. As all three substrates showed no intermolecular KIE, this suggests that the electronics of the system at C^1 may influence the relative rates of reactions but does not significantly change the overall mechanism of reaction.

Scheme 136. Intermolecular kinetic isotope determination.



R=OMe,301: 301-d$_4$ = 0.53:0.47

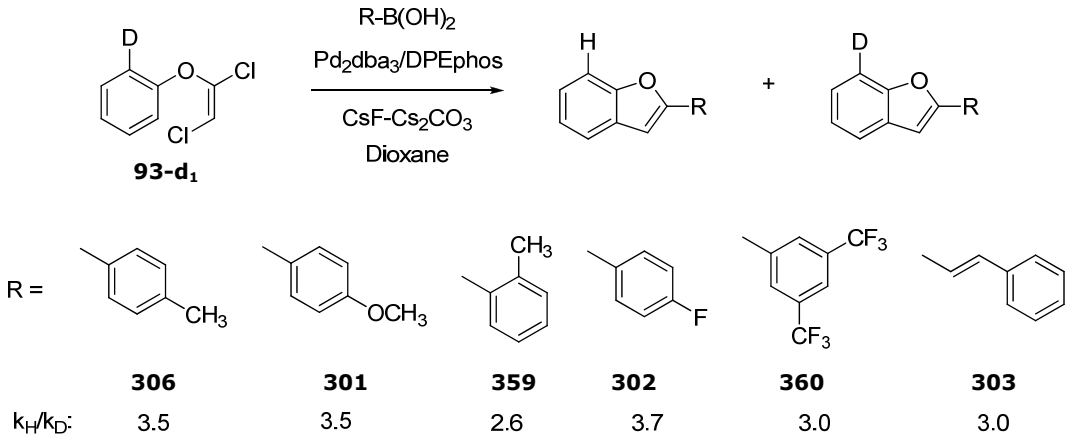
R=Me, 306: 306-d$_4$ = 0.56:0.44

R=F,302: 302-d$_4$ = 0.52:0.48

2.5.3.4 Intramolecular Isotope Effects

The fact that the C-H bond breakage was not involved in the rate-determining step does not indicate that this bond breakage is not involved in the product-determining step. To probe the C-H bond breakage at the product-determining step, the intramolecular KIE was measured in the formation of benzofurans from **93-d_1**, again with several boronic acids. As this is an intramolecular experiment, this reaction was done by using the one-pot procedure as all steps other than the C-H (or C-D) bond breakage are identical.

Scheme 137. Intramolecular KIE measurements.



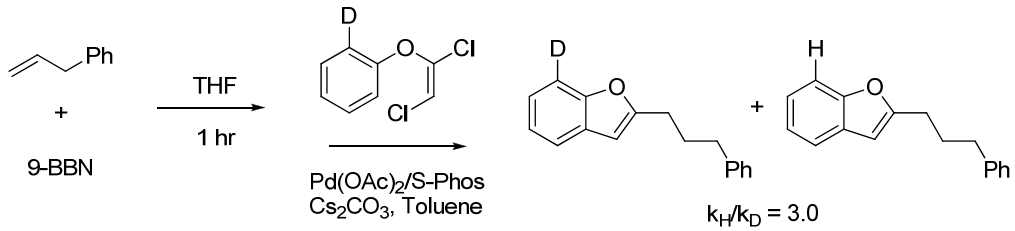
	306	**301**	**359**	**302**	**360**	**303**
k_H/k_D:	3.5	3.5	2.6	3.7	3.0	3.0

The effect of the C^1-functional group was not significant, and the KIE was consistently observed to be about 3. These data are inconsistent with an electrophilic aromatic substitution mechanism, and consistent with a sigma-bond metathesis-like pathway (transition states **B** – **D**, Scheme 24).

As a different catalytic system was used in the synthesis of the 2-alkyl benzofuran **333**, the KIE was measured in that case as well, and found to be on the same order as the Pd/DPEphos system (Scheme 138). This does not necessarily mean that the direct arylations using the Pd/DPEphos and the Pd/S-Phos catalytic systems promote C-H bond cleavage by the same mechanism. Determination of the intermolecular isotope effect as analogous to the reactions examined in Scheme 136 would determine whether the C-H

bond activation was involved in the rate determining step in this case, though this experiment has not been performed.

Scheme 138. KIE determination under Pd/S-Phos catalytic conditions.



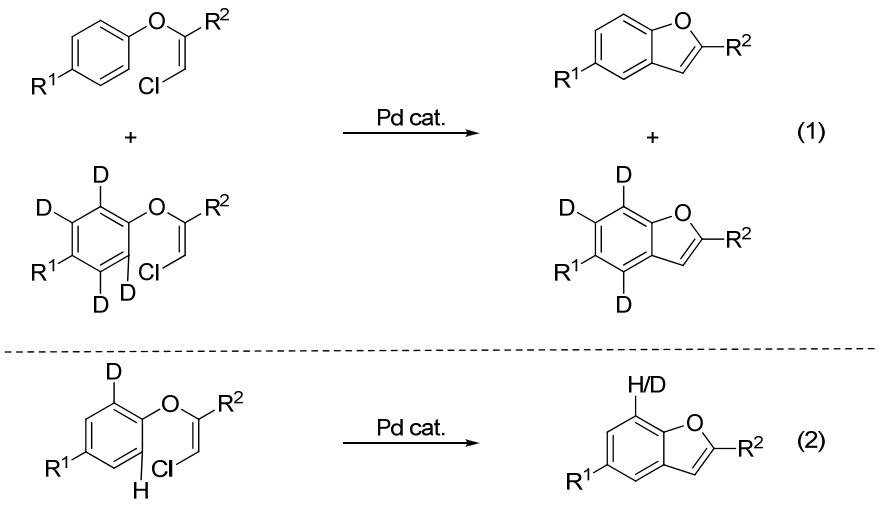
Hennessy and Buchwald found similar inter- and intramolecular KIEs in a similar experiment (Scheme 31);[153] these data suggested that palladation is rapid and reversible as compared to the C-H bond cleavage. As the oxidative insertion into the C-Cl bond is the rate-determining step in our reactions, the observed regioselectivity in the cyclization of the unsymmetrical derivatives (Table 25) could be reflecting the thermodynamic product.

The competition experiments in addition to the observed kinetic isotope effects are clearly unsupportive of a C-H activation occurring via an electrophilic aromatic substitution mechanism. Aryl and other organohalides are, in some cases, capable of oxidizing Pd(II) to Pd(IV) (see Scheme 19 for an example); this requires a mechanism where C-H activation occurs first, followed by intramolecular oxidative addition into the C-Cl bond. As discussed in sections 1.2.2 and 1.2.3, direct insertion into C-H bonds normally requires a directing group.[135] As well, Pd(II)/Pd(IV) catalytic cycles are far more common when reactions are performed in the presence of a strong external oxidant.

To be able to interpret the competition experiments more clearly, isotopic labeling experiments on direct arylation reactions involving substituted phenol derivatives are needed. For example, performing a series of experiments as outlined in Scheme 139

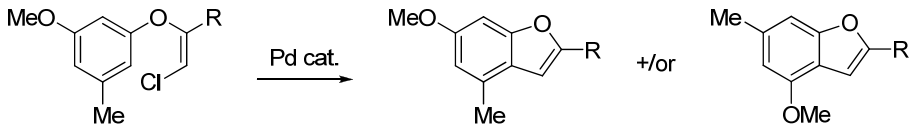
where R^1 = NO_2, CN, Ac, OAc, OMe, Me etc. will examine the influence the substitution in that position has on the rate-determining (Scheme 139, equation 1) and product-determining (Scheme 139, equation 2) steps.

Scheme 139. Proposed experiments to determine the KIE for substituted derivatives.



The *relative* influence of different substituents in the phenolic component on the direct arylation has not yet been determined. For example, while we know that both methoxy and methyl groups promote arylation to form the 6-substituted benzofuran, the relative ability of each group to do so is unknown. However, an arylation reaction performed on the vinyl ether derived from 3-methoxy-5-methylphenol (Scheme 140) would direct probe this effect of methoxy versus methyl groups, and provide more insight into the influence of substituents on the reaction. This experiment, and those with different C^3 and C^5 groups are currently underway in our laboratory.

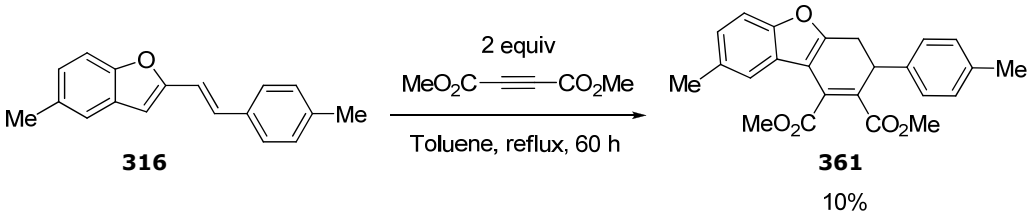
Scheme 140. Proposed arylation experiment with an unsymmetrical 3,5-disubstituted phenol derivative.



2.5.4 Functionalization

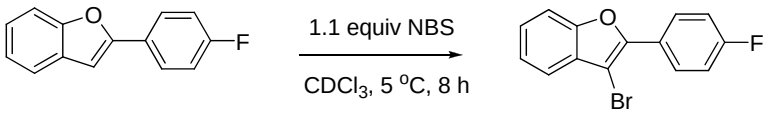
To illustrate the usefulness of these 2-substituted benzofurans, the 2-vinyl species **316** was heated in the presence of dimethyl acetylenedicarboxylate to induce a thermal Diels-Alder reaction (Scheme 141). The adduct was isolated as the substituted benzofuran (or dihydrodibenzofuran) **361**; presumably, the expected Diels-Alder adduct was initially formed, and that intermediate isomerized to the observed product. The low isolated yield could be attributed to the highly conjugated, and therefore not very reactive, starting material. Additionally, all attempts to induce a Diels-Alder between **316** and maleic anhydride failed.

Scheme 141. Diels-Alder cycloaddition between a 2-vinyl benzofuran and an acetylene.



We also briefly examined the C^3 bromination of benzofuran **302**. This general transformation has been performed in the literature using either elemental bromine[506-508] or *N*-bromosuccinimide[509-511] (NBS). We found that treating benzofuran **302** with NBS did produce the corresponding 3-bromo benzofuran **362** in excellent isolated yield (Scheme 142). This compound could obviously be further functionalized by palladium-catalyzed chemistry. Cross-coupling at this position is well-known, and many 2,3-diarylbenzofurans have interesting biological activities.[512]

Scheme 142. C^3 bromination of a 2-aryl benzofuran.



302 **362**

90%

2.5.5 Summary

Much like the syntheses of tri- and tetrasubstituted alkenes from dichlorovinyl ethers, the synthesis of 2-substituted benzofurans was both highly modular and broad in scope. The major limitation is the inability to incorporate heteroaryl moieties at the C^2 position. Additionally, some materials (e.g. 4-nitro- and 2-cyano-based dichlorovinyl ethers) could not be employed as substrates in the one-pot cross-coupling/direct arylations, though the corresponding benzofurans could be isolated following a two-step procedure.

It should be clear that the C^2-Cl functionalization is more complicated that the C^1-Cl functionalization in the sense that cross-coupling will always be in competition with intramolecular C-H activation. Careful choice or optimization of conditions can, however, largely prevent unwanted C-H activation should a cross-coupling be desired. The simple Pd/DPEphos catalytic system proved to be highly general in terms of electronics in both the phenolic component and that of the C^1-functional group. Regioselectivity was good to excellent in examples where unsymmetrical phenols were the starting materials. The Pd/DPEphos system was only shown to fail in the synthesis of 2-alkyl benzofurans, but a simple switch to Pd/S-Phos proved useful, and the reaction could still be carried out in one pot from the dichlorovinyl ether.

The results of the mechanistic experiments argue strongly against an electrophilic aromatic substitution mechanism for the C-H bond breakage event. While it is not entirely conclusive, the absence of both directing groups and external oxidants in the reaction argues against an oxidative addition-based (or Pd(0)/Pd(II)/Pd(IV)) mechanism

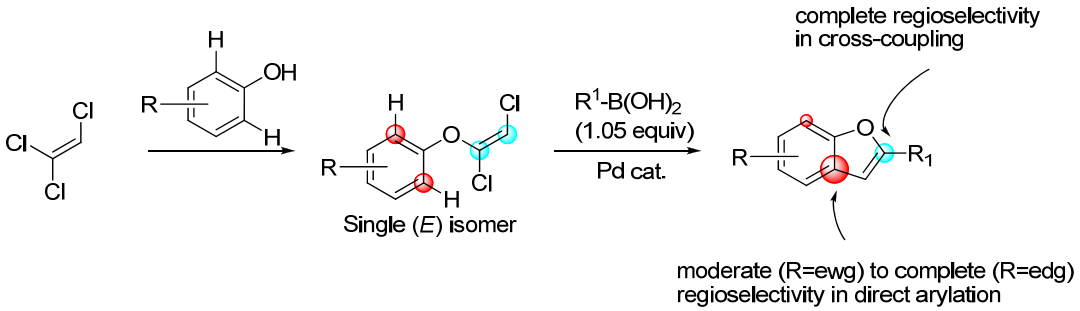
of C-H activation. Therefore, the C-H activation we observe is likely proceeding via a σ-bond metathesis-based pathway (Scheme 24). Where exactly on the continuum of mechanistic possibilities between **B**, **C** or **D** it lies is not clear from these results and may be the subject of further investigations. A computational investigation of possible transition states would be a most useful method to further delineate the mechanism of C-H bond breakage.

The two key C-C bond forming events be carried out in one pot, and the complete synthesis of 2-benzofurans required only 2 steps from inexpensive materials right off the shelf. As discussed in section 1.4.3, benzofurans are most commonly synthesized from 2-iodophenols. While it is likely intuitive that an unactivated phenol is less expensive that an activated phenol, it should be pointed out specifically that while phenol costs only $4.90/mol, 2-iodophenol costs over $1500/mol.[513514]

As a further practical advantage, it should be noted that our synthetic method requires no special purification of any of the starting materials or reagents. While anhydrous dioxane was used in these experiments, a single bottle was used throughout this study over the course of approximately 1.5 years, as was the case with TCE, with no purification. Boronic acids occasionally had to be recrystallized before use, but this was generally only done if there were obvious signs of degradation.

In conclusion, the method developed in this thesis 1) starts from very inexpensive materials; 2) requires only two steps from commercially available compounds; 3) both synthesizes and functionalizes an important biologically active structural motif; 4) is modular and broad in scope; 5) requires no rigorous exclusion of either air or water; and 6) features two highly selective palladium-catalyzed reactions in one pot (Scheme 143).

Scheme 143. Summary of efficiencies in the palladium-catalyzed functionalizations of dichlorovinyl ethers to 2-substituted benzofurans.



2.6 Extension to the Preparation of Other Heterocycles

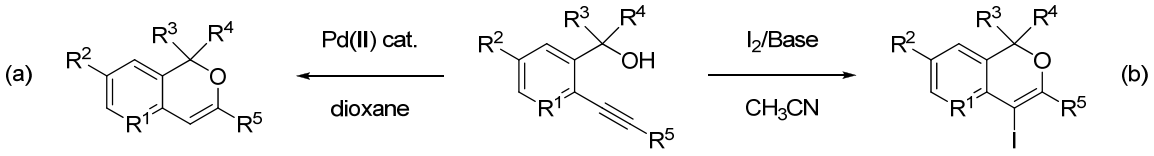
2.6.1 Introduction

Due to ease of both the intramolecular direct arylation of the 1-aryl-2-chlorovinyl ethers to benzofurans and literature reports of addition of other heteroatoms across TCE, examining the syntheses of other heterocycles from different heteroatom-substituted arenes was an obvious extension.

2.6.2 Isochromenes (Benzopyrans)

1*H*-Isochromenes or isobenzopyrans are important heterocycles and have both a wide variety of structures and biological activities.[515-525] Like literature syntheses of benzofurans (section 1.5), existing methods for the construction of the isochromene ring system are hampered by requisite expensive activated precursors. For example, there have been two different reported approaches to the synthesis of isochromenes from *o*-alkynyl benzyl alcohols. A palladium(II) catalyst can yield 3-functionalized isochromenes (Scheme 144, equation a)[526] and iodocyclization[527] gives the 3-functionalized-4-iodo isochromenes (Scheme 144, equation b).

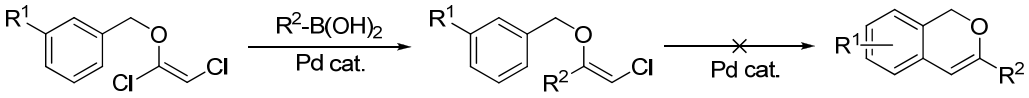
Scheme 144. Synthesis of isochromenes from *o*-alkynyl benzyl alcohols.[526,527]



We attempted the synthesis of 1*H*-benzopyrans from 1,2-dichlorovinyl ethers derived from benzyl alcohols (section 2.2.3, Table 6). Direct application of the conditions used for benzofuran synthesis (Pd/DPEphos, Table 25) was unsuccessful and benzopyrans

364 were unfortunately not formed (Table 27, entries 1 – 3). Surprisingly, however, attempts to isolate the monoaryl intermediate **363** also failed, and unidentified compounds were isolated instead. Attempts to modify our existing standard procedure were also unsuccessful; reactions in xylenes either halted at the monoaryl intermediate **363** (entries 4 and 5) or led to decomposition (entries 6 – 9), depending on the ligand employed.

Table 27. Attempted synthesis of benzopyrans from benzyl alcohol-derived dichlorovinyl ethers.



134 or **136** **363** **364**

entry	sm	R^2	Pd	ligand[a]	base	solvent	result
1	**134**	*p*MeO-C_6H_4-	Pd_2dba_3	**12**	CsF-Cs_2CO_3	THF	**363**
2	**134**	3,4-(OCH_2O)-C_6H_3-	Pd_2dba_3	**12**	CsF-Cs_2CO_3	THF	**363**
3	**134**	*p*F-C_6H_4-	Pd_2dba_3	**12**	CsF-Cs_2CO_3	THF	**363**
4	**136**	*p*Me-C_6H_4-	$Pd(OAc)_2$	**185**	CsF-Cs_2CO_3	Xylenes	**363**
5	**136**	*p*Me-C_6H_4-	$Pd(OAc)_2$	**185**	Cs_2CO_3-Piv	Xylenes	**363**
6	**136**	*p*Me-C_6H_4-	$Pd(OAc)_2$	**186**	CsF-Cs_2CO_3	Xylenes	Decomp.[b]
7	**136**	*p*Me-C_6H_4-	$Pd(OAc)_2$	**186**	Cs_2CO_3-Piv	Xylenes	Decomp.[b]
8	**136**	*p*Me-C_6H_4-	$Pd(OAc)_2$	**184**	CsF-Cs_2CO_3	Xylenes	Decomp.[b]
9	**136**	*p*Me-C_6H_4-	$Pd(OAc)_2$	**184**	Cs_2CO_3-Piv	Xylenes	Decomp.[b]

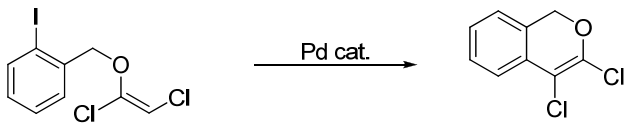
[a]For structures, see Figure 12. [b]No identifiable compounds could be detected in the ^1H NMR of the crude materials isolated from these reactions.

Approaching the problem of efficient benzopyran synthesis from a different direction, we used the 1,2-dichlorovinyl ether derived from *o*-iodobenzyl alcohol (**138**) and treated it with a simple palladium catalyst (Scheme 145). While the reaction was low yielding, the dichlorobenzopyran **365** was isolated in 10% yield, proving the concept.

There were several different compounds produced in this reaction, and **365** was the only identifiable material after separation by column chromatography. The low isolated yield of the desired product likely reflects the fact that vinyl chlorides can be more reactive toward palladium than aryl iodides are (Figure 3). If palladium can insert into both the aryl C-I and alkenyl C^1-Cl at comparable rates, there could be multiple reaction pathways occurring simultaneously. Careful optimization of the reaction conditions could improve the result.

While this route requires a more activated arene, this will in fact create a more functionalized benzopyran than that outlined in Table 27. As the principle of site selectivity dictates that the C^3-Cl should be selectively cross-coupled first, ideally, optimization of chemistry should allow a three-step, one-pot synthesis of disubstituted benzopyrans from 1,2-dichlorovinyl benzyl ethers (Scheme 146).

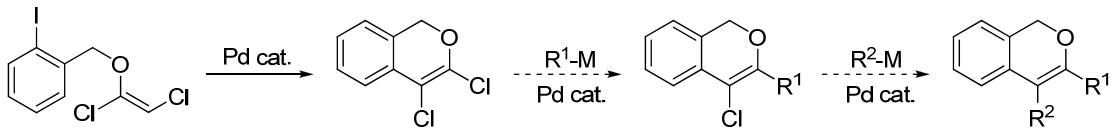
Scheme 145. Heck-type cyclization of dichlorovinyl ethers from *o*-iodobenzyl alcohol.



138 **365**

10% yield

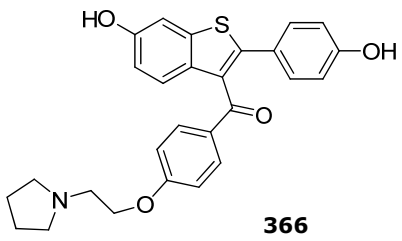
Scheme 146. Proposed synthesis of 3,4-disubstituted benzopyrans via 3 consecutive palladium-catalyzed reactions from **138**.



138 **365**

2.6.3 Benzothiophenes

Benzothiophenes are also very important heterocycles. For example, Raloxifene (**366**, Figure 17), is currently marketed as its hydrochloride salt, and called Evista by Eli Lilly and Company. It was first approved in December 1997, and had 1.2 billion USD in sales in 2006 alone, which placed it in the top 100 selling drugs of that year. It is an oral selective estrogen receptor modulator (SERM) used in the prevention of osteoporosis in postmenopausal women due to estrogenic actions on bone and anti-estrogenic actions on the uterus and breast. Interestingly, however, it has been found that raloxifene is as effective as tamoxifen (**89**) in reducing the incidence of breast cancer in postmenopausal women, but causes fewer cases of uterine cancer than tamoxifen.

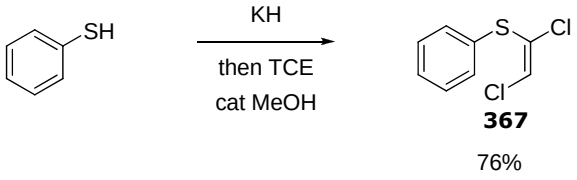


366

Figure 17. Structure of Raloxifene.

Similar to the attempt at the synthesis of isochromenes from benzyl alcohols (section 2.6.2), we imagined that a simple switch from a phenol to a thiophenol donor would provide simple access to the benzothiophene skeleton. Following a literature procedure,[440] the 1,2-dichlorothiovinyl ether **367** was isolated in good yield (Scheme 147).

Scheme 147. Synthesis of 1,2-dichlorovinyl thioether.



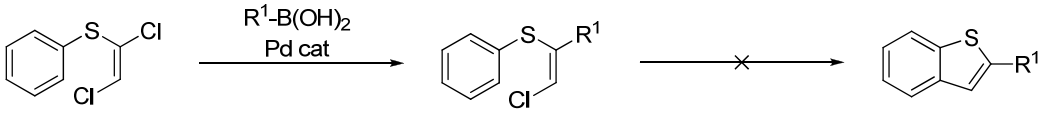
367

76%

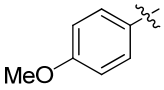
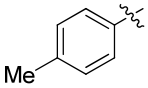
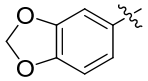
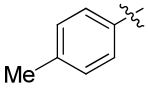
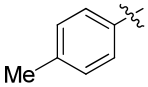
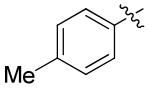
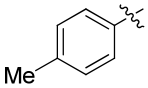
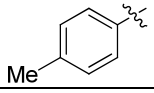
Unfortunately, the attempts at a one-pot preparation of 2-aryl benzothiophenes using our DPEphos system in both THF and dioxane failed (Table 28, entries 1 - 6). The reactions all halted at the monoarylated compounds **368** and no benzothiophene **369** could be detected.

Since the cross-coupling reactions to the monoaryl intermediates **368** went to completion, we reasoned that perhaps by isolating the intermediate and subjecting it to different catalytic conditions, we could get the reaction to go. Several conditions were tried (Table 29). The reaction conditions were based on Fagnou's conditions for heterocycle formation via direct arylation. Unfortunately, the starting material was recovered unchanged and no benzothiophene could be detected.

Table 28. Attempted benzothiophene formation from 1,2-dichlorovinylthioethers and boronic acids.

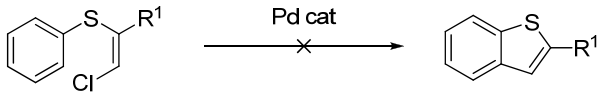


367 **368** **369**

entry	R^1	Pd	ligand	base(s)	solvent	result[a]
1		Pd_2dba_3	DPEphos (**12**)	CsF-Cs_2CO_3	THF	**368**
2					Dioxane	
3		Pd_2dba_3	DPEphos (**12**)	CsF-Cs_2CO_3	THF	**368**
4					Dioxane	
5		Pd_2dba_3	DPEphos (**12**)	CsF-Cs_2CO_3	THF	**368**
6					Dioxane	
7		$Pd(OAc)_2$	**10**	K_2CO_3	Dioxane	N.R.[d]
8		$Pd(OAc)_2$	**10**	Cs_2CO_3	Dioxane	N.R.[d]
9		$Pd(OAc)_2$	**10**	CsF-Cs_2CO_3	Dioxane	N.R.[d]
10		$Pd(OAc)_2$	**10**	K_2CO_3	DMA[b]	Decomp.[e]
11					DMF[c]	
12		$Pd(OAc)_2$	**10**	K_2CO_3-KF	DMA[b]	Decomp.[e]
13					DMF[c]	

[a]As determined by analysis of the ^{1}H NMR spectrum of the crude isolated material. [b]DMA is dimethylacetamide. [c]DMF is dimethylformamide. [d]N.R. = no reaction. [e]No identifiable compounds could be identified in the ^{1}H NMR of the unpurified reaction material

Table 29. Cyclization attempts from isolated aryl intermediates.



368 **369**

entry	Pd	ligand[a]	Base (additive)	Solvent	Result
1	$Pd(OAc)_2$	**185**	K_2CO_3	DMA	N.R.
2	$Pd(OAc)_2$	**185**	K_2CO_3 + piv[b]	DMA	N.R.
3	$Pd(OAc)_2$	**184**	K_2CO_3	DMA	N.R.
4	$Pd(OAc)_2$	**184**	K_2CO_3 + piv[b]	DMA	N.R.

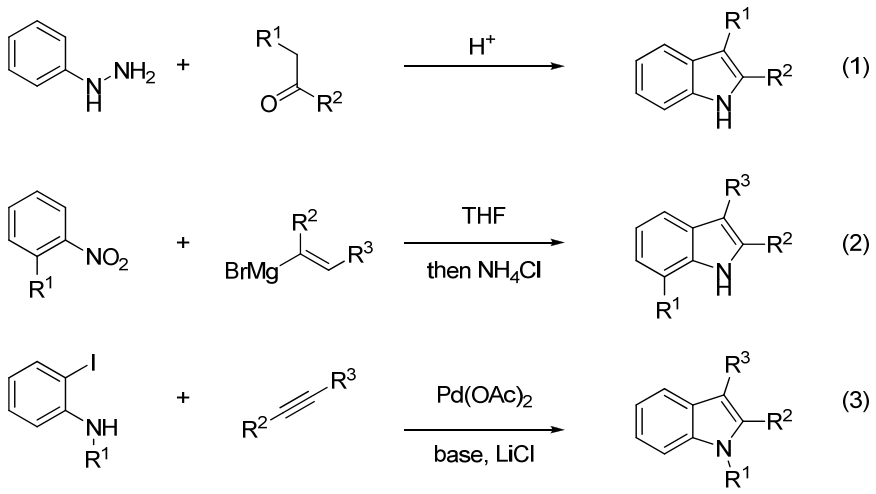
[a]For structures, see Figure 12. [b]Pivalic acid ($(CH_3)_3CCO_2H$)

2.6.4 Indoles

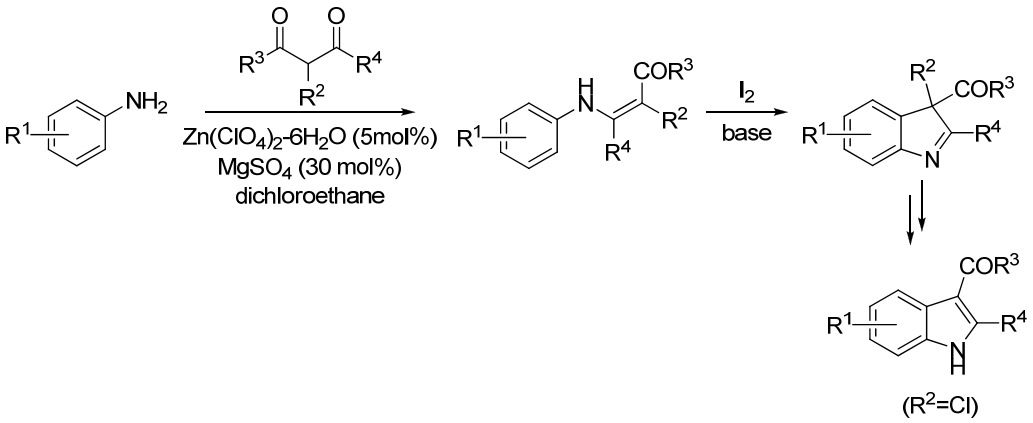
The indole ring system is among the most important heterocyclic substructures present in biologically active compounds. In fact, indoles are so prevalent that they are usually referred to as "privileged scaffolds" by medicinal chemists.[528] Unsurprisingly, there have been numerous different methods for synthesizing these compounds. One of the first syntheses of an indole was reported by Fischer in 1883 (Scheme 148, equation 1). Other common methods of indole synthesis include the Bartoli and Larock syntheses (Scheme 148, equations 2 and 3, respectively).

Recently, a variation of the Fischer indole synthesis was reported by Li and coworkers.[529] This process first generates a 3*H*-indole, which, depending on the substituents on the original carbonyl, may rearrange to form an indole (Scheme 149).

Scheme 148. Traditional methods of indole synthesis.

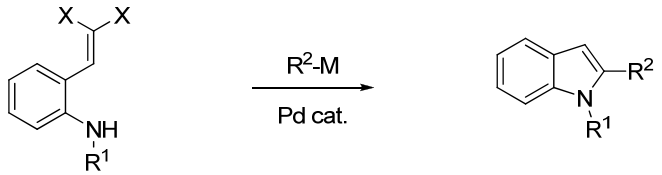


Scheme 149. Synthesis of indoles from enamines.[529]



Lautens and coworkers have published a series of papers on the one-pot preparation of indoles from *o*-(2-dihalovinyl) anilines and a variety of organometallics (Scheme 150).[530-533] This method is both highly general and modular. It is arguably the best method for synthesizing 2-substituted indoles in a diversity-oriented manner, provided the required starting material is available. A review on the general construction of nitrogen heterocycles via C-H activation was recently published.[534]

Scheme 150. Lautens' indole synthesis.[530-533]

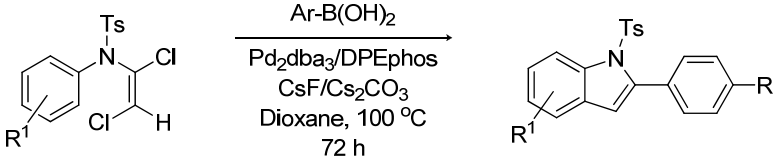


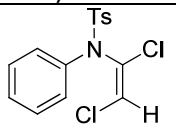
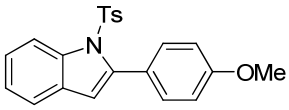
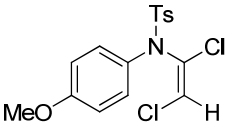
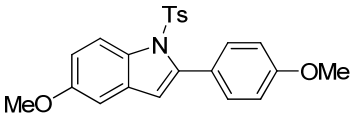
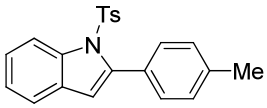
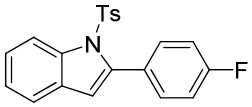
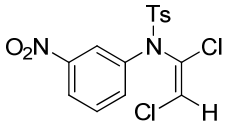
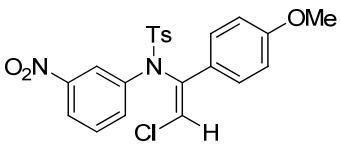
These methods are useful and widely used in the scientific community, but are not without their drawbacks. These include multistep syntheses of starting materials, limiting structural requirements and/or the need for a large excesses of one of the building blocks. Adapting our method for benzofuran synthesis to prepare indoles from the corresponding anilines was an obvious extension. We attempted the synthesis of indoles using both *N*-Boc and *N*-tosyl aniline derivatives (compounds **150** and **153**, for preparation, see Table 7 in section 2.2.4). Not only did the nitrogenous compounds behave differently from the oxygenated ones, but the outcome was dependent on the nitrogen protecting group.

N-Tosyl enamides **153** and **154** underwent palladium-catalyzed one-pot Suzuki coupling and cyclization to indoles **370** - **372** with *p*-methoxyphenyl boronic acid and *p*-tolyl boronic acid (Table 30, entries 1 and 2); unfortunately, after three days at 100°C, the yields of the 2-aryl indoles were only moderate. More significantly, in both cases, the arylated chlorovinyl intermediates **225** and **226** and unreacted starting material were isolated from the reaction mixture in addition to indole, indicating that under these reaction conditions, the sequence of reactions is not as selective as was seen with the oxygenated compounds. When *N*-tosyl aniline **153** was reacted with *p*-fluorophenyl boronic acid, the 2-aryl indole **373** was isolated in only 5% yield (Table 30, entry 4); again, arylated intermediate along with unreacted starting material were identified in the reaction mixture, but the mass recovery of these compounds was very low (<15%), suggesting that degradative pathways may be significantly competing in this case.

The 3-nitro enamide **155** could only undergo Suzuki coupling, and even after 72 h of heating, only monoarylated intermediate **227** could be detected either by TLC or ^{1}H NMR analysis of the crude reaction residue isolated. The significance of this poor reactivity is unclear but could support a mechanism in which arylation is now rate determining.

Table 30. One-pot access to 2-aryl-*N*-tosyl indoles from 1,2-dichlorovinyl amides.

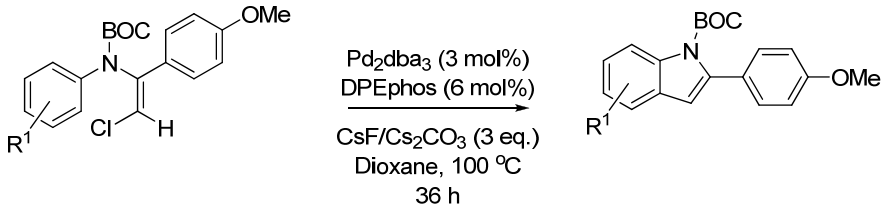


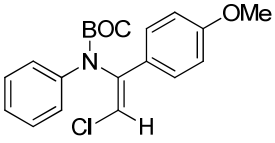
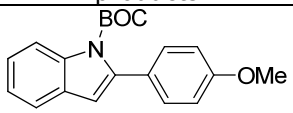
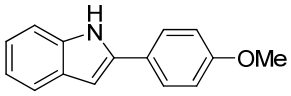
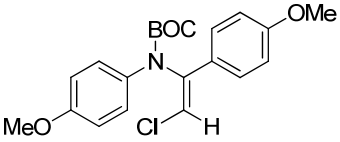
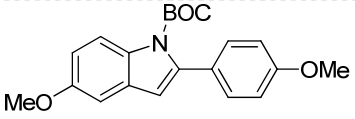
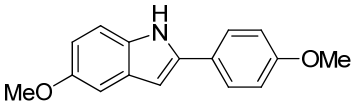
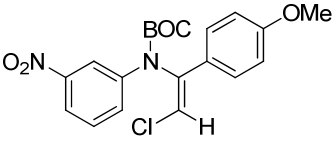
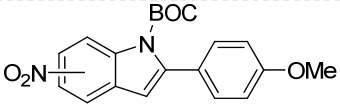
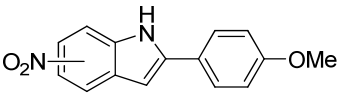
entry	vinyl amide	R	product	yield[a]
1	 **153**	OMe	 **370**	29%[b]
2	 **154**	OMe	 **371**	47%[c]
3	**153**	Me	 **372**	30%
4	**153**	F	 **373**	5%
5	 **155**	OMe	 **227**	79%

[a]Isolated yields. [b]The corresponding arylated intermediate was isolated in 34% yield, and unreacted starting material could be identified. [c]The intermediate was also isolated in 29% yield and 12% of unreacted starting material was recovered.

None of the *N*-Boc anilines could be induced to participate in a one-pot Suzuki-coupling/direct arylation, even after 5 days at 100°C. As we had done with the stubborn phenol derivatives (Scheme 124), the intermediate arylated adducts **228** – **230** were synthesized (Table 14) and separately subjected to the same direct arylation conditions. We were pleased to find that the 2-arylindoles **374** – **379** were isolated in good yields, albeit as a mixture of protected and deprotected compounds (Table 31).

Table 31. Cyclization of *N*-Boc-*N*-(1-aryl-2-chlorovinyl)anilines to give 2-arylindoles.



entry	starting material	products	yield[a]
1	 **228**	 **374**	43%
		 **375**	25%
2	 **229**	 **376**	38%
		 **377**	58%
3	 **230**	 **378**	55%
		 **379**	14%

[a]Isolated yields.

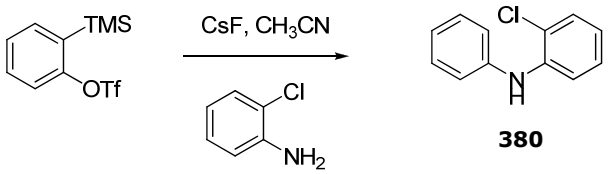
2.6.4.1 Optimization Attempts

Unsatisfied with the efficiency of the indole synthesis from 1,2-dichlorovinyl amides, several alternate reaction conditions were screened in an attempt to improve this process. Several variations of Fagnou's conditions for the synthesis of carbazoles were examined (Scheme 23), reasoning that the indole precursors are electronically and sterically similar to the carbazole precursors. Unfortunately, dozens of different combinations of palladium source, ligand, base and solvent and temperature were not successful, and the results reported in Tables 31 and 32 remain the most successful from these substrates.

2.6.4.2 Evaluation of Protecting Groups

With the failure of Fagnou's conditions to induce indole synthesis, we wondered if the protecting group was influencing the reactivity of these compounds. The protecting group was only in place to maintain geometric stability of the dichlorovinyl compound (section 2.2.4), but as this chemistry did not require this, it seemed reasonable to explore the effect of the group. To examine the effect of the protecting group, we synthesized the corresponding carbazole precursor (Scheme 151), which could then be protected with various groups, and analyzed as the unprotected parent compound **380**. This also would prevent any lability, as the diaryl compounds do not degrade as easily as the enamines.

Scheme 151. Synthesis of 2-chlorophenylaniline.

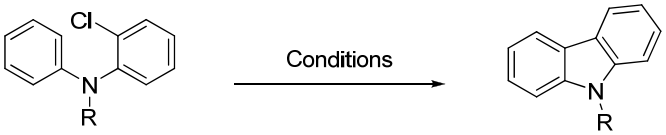


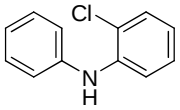
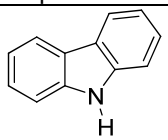
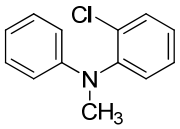
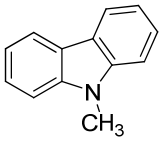
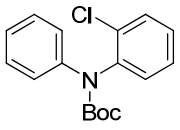
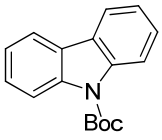
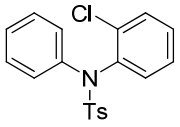
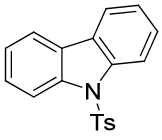
380

Diarylamine **380** was then protected with a methyl, Boc or tosyl group and subjected to both Fagnou's conditions (known to work) and our Pd/DPEphos conditions.

Only the unprotected diaryl amine **380** was able to produce the corresponding carbazole, **381** under Fagnou's conditions (Table 32, entry 1). None of the *N*-functionalized compounds cyclized at all, even under these conditions (entries 3, 5 and 7). Also unfortunately, our Pd/DPEphos conditions were completely unable to promote the desired C-H functionalization, and carbazoles were never detected (entries 2, 4, 6 and 8).

Table 32. Attempts to make carbazole under both Fagnou's and our conditions.



entry	conditions[a]	starting material[b]	product	conv.[c]
1	A	 **380**	 **381**	50%
2	B			N.R.
3	A	 **382**	 **383**	N.R.
4	B			N.R.
5	A	 **384**	 **385**	N.R.
6	B			N.R.
7	A	 **386**	 **387**	N.R.
8	B			N.R.

[a] Conditions A: 5 mol% $Pd(OAc)_2$, 10 mol% P*t*Bu_3·HBF_4, 4 equiv K_2CO_3, DMA (0.1M), 20 h. Conditions B: 2.5 mol% Pd_2dba_3, 5 mol% DPEphos, 3 equiv CsF, 3 equiv Cs_2CO_3, dioxane (0.4M), 22 h. [b]Preparation is described in experimental section. [c]Estimated by ^{1}H NMR of the crude reaction mixture.

The fact that Fagnou's conditions failed to produce carbazoles when the nitrogen was protected suggests that arylation under his conditions requires the availability of the nitrogen lone pairs. The fact that our conditions failed to produce any carbazoles regardless of protecting group likely reflects the increased strength of an aryl C-Cl bond versus an alkenyl C-Cl bond. As pointed out in the introduction (Figure 3), vinyl chlorides are much more reactive towards palladium than aryl chlorides are, and the palladium catalyst formed under our conditions is simply not reactive (or electron-rich) enough to insert into such a bond.

2.6.5 Summary

The syntheses of isochromenes, benzothiophenes and indoles from benzyl alcohols, thiophenols, and anilines were attempted by modification of the now known preparation of benzofurans from phenols. Unfortunately, isochromenes and benzothiophenes were not obtainable under any conditions examined. Indoles were, however, obtainable via this method, although in much lower yields. The reasons for differences in reactivity toward intramolecular direct arylation between phenol, benzyl alcohol, thiophenol and anilines are not obvious and may be the subject of further investigations.

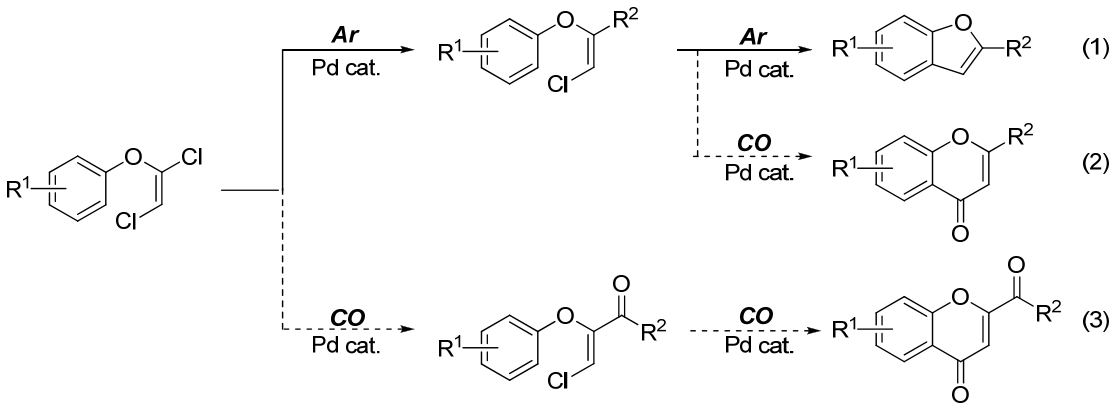
CHAPTER 3 : FUTURE WORK AND CONCLUSIONS

3.1 Future Work

This work has successfully developed conditions for the synthesis of electron-rich alkenes, dienes, enynes, trienes and benzofurans from simple and inexpensive starting materials, using one of three sets of conditions. While the palladium-catalyzed chemistry developed in this thesis was very general, we were unable to directly extend these methods to the preparation of indoles, benzothiophenes, and 1*H*-ischromenes (benzopyrans) (section 2.6). The optimization of the method for the synthesis of these compounds would be very useful as all of these compounds are important medicinally; the extension of the basic method to include the syntheses of these compounds would greatly increase the efficiency of the production of each of these compounds. Therefore, conditions are needed for the simple functionalization of dichlorovinyl ethers derived from anilines, thiophenols and benzyl alcohols.

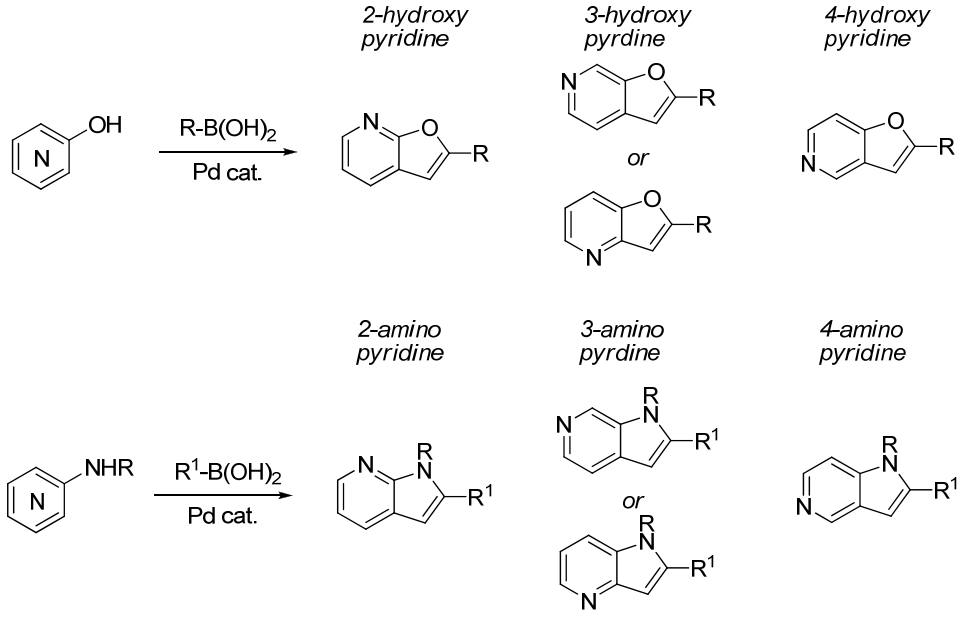
As well, modification of our standard procedures for benzofuran synthesis to a carbonylative palladium-catalyzed process would give flavones (or chromones), an important class of biologically active compounds. This could be as simple as replacing the standard argon atmosphere with a carbon monoxide atmosphere.[535] For example, if the first cross-coupling was performed in an argon atmosphere, and then the direct arylation under a carbon monoxide atmosphere, 2-aryl chromones (or flavones) would be the result (Scheme 152, equation 2). However, if both the cross-coupling and direct arylation were performed under a carbon monoxide atmosphere, 2-carbonyl chromones would result (Scheme 152, equation 2).

Scheme 152. Standard carbonylative cross-coupling and/or direct arylation to yield chromones from phenols, TCE and boronic acids. Ar = argon atmosphere, CO = carbon monoxide atmosphere. Dashed reaction bonds indicate proposed reactions.



In addition to the heterocycles above, using pyridine-based starting materials could lead to an even wider array of heterocycles (Scheme 153) and this would provide simple access to azaindoles[536] and azabenzofurans, medicinally important compounds, in only two steps.

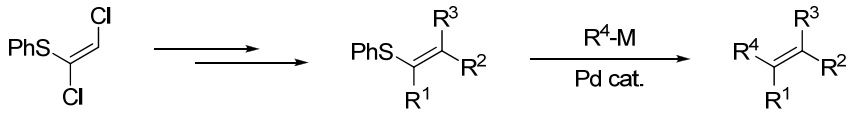
Scheme 153. Proposed synthesis of azaheterocycles from heteroatom-substituted pyridines.



The two pot synthesis of tetrasubstituted alkenes from commercially available materials reported in this thesis also can benefit from further development and optimization. Additionally, if the tetrasubstituted alkenes were built around a thiophenol platform, fully carbon-substituted alkenes should be easily accessible.

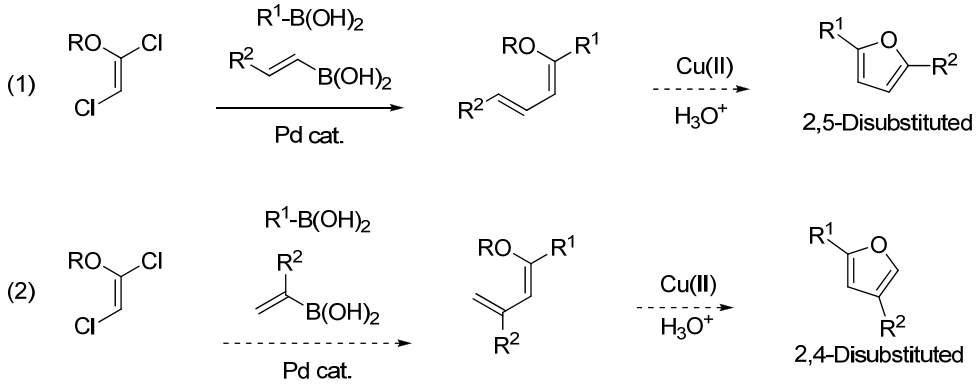
Extending the chemistry developed in section 2.4.2 to thiophenol-based substrates should give the tetrasubstituted thioalkene in analogy to the oxygen-substituted alkenes. However, thiobenzene may also act as an electrophile in palladium-catalyzed cross-coupling,[292] and thus the tetrasubstituted vinyl thioether may be further functionalized to give the fully carbon-substituted alkene in a highly modular manner (Scheme 154).

Scheme 154. Proposed synthesis of fully carbon substituted alkenes from dichlorovinyl thioethers.

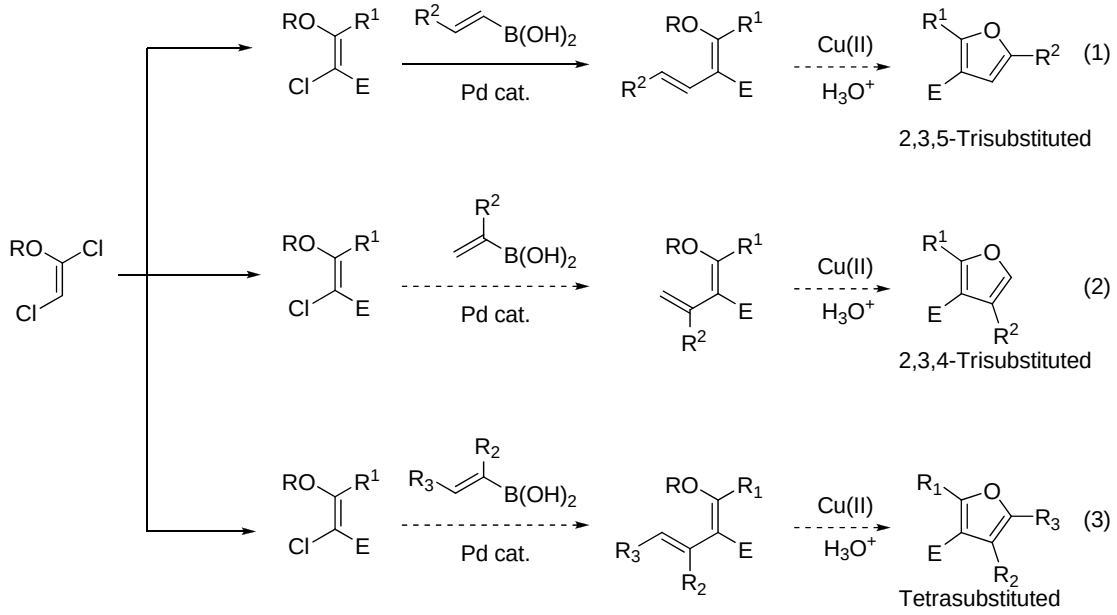


The synthetic method presented in this thesis is capable of synthesizing a very diverse array of 1-phenoxy-1,3-butadienes (for example, see Table 15 and Table 21). Symmetrically substituted 1-alkoxy-1,3-butadienes (derived from an alcohol and two equivalents of an aryl alkyne) were recently demonstrated to be useful in the synthesis of symmetrical 2,5-disubstituted furans.[307] Using the method developed in this thesis, simply changing the boronic acids that go into the reaction to make trisubstituted alkenes, both unsymmetrical 2,5-disubstituted (equation 1) and 2,4-disubstituted (equation 2) furans could be easily made (Scheme 155). Similarly, by modifying the boronic acids that go into the synthesis of tetrasubstituted alkenes, 2,3,5-trisubstituted (equation 1), 2,3,4-trisubstituted (equation 2) and tetrasubstituted (equation 3) furans are potentially as easily accessible (Scheme 156).

Scheme 155. Proposed three-step synthesis of disubstituted furans from a dichlorovinyl ether.



Scheme 156. Proposed routes to polysubstituted furans from a dichlorovinyl ether.

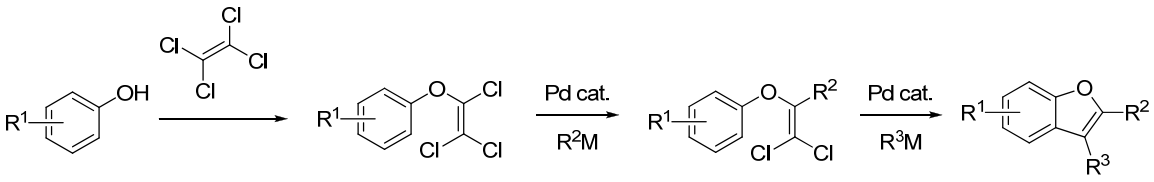


As the conditions for the copper(II)-catalyzed oxidation do not conflict with the palladium-catalyzed step prior to it, it is possible that a one-pot synthesis could be developed. This would constitute the most simple, general and diverse synthesis of polysubstituted furans and would yield furans difficult or impossible to access otherwise.

We are not the first to demonstrate that multiply halogenated alkenes can be useful building blocks in organic synthesis. As discussed in the introduction, Organ has successful employed 2,3-dihalopropenes and (*E*)-2-chloro-1-iodoethene as simple linchpins in sequential palladium-catalyzed cross-coupling chemistries (Scheme 55). We have shown that trichloroethylene may also be viewed as a useful template. This work opens the door for the application of other polyhalogenated alkenes in synthesis. Much like trichloroethylene, tetrachloroethylene is readily available and very inexpensive. However, directly replacing trichloroethylene with tetrachloroethylene is not likely to be feasible. Kende and coworkers demonstrated that enolates are sufficiently nucleophilic to react with polyhalogenated compounds.[436] It is not immediately clear if phenols will be

nucleophilic enough to react with tetrachloroethylene in an addition-elimination mechanism (in opposite order to the elimination-addition reaction of phenols with trichloroethylene, Scheme 91). If phenols cannot react with tetrachloroethylene in this manner, a Buchwald-Hartwig cross-coupling[537] could be used to synthesize trichlorovinyl ethers. Subsequent cross-coupling reactions from trichlorovinyl ethers could then generate 2,3-disubstituted benzofurans in a highly efficient manner (Scheme 157).

Scheme 157. Proposed application of tetrachloroethylene in the synthesis of 2,3-disubstituted benzofurans.



3.2 Conclusions

The work presented in this thesis has successfully demonstrated that trichloroethylene is highly useful synthetic template, or linchpin, for use in organic synthesis. A highly site selective monofunctionalization of dichlorovinyl ethers, obtained from reaction between trichloroethylene and phenols, via cross-coupling chemistry has been developed. The simple catalyst $Pd(PPh_3)_4$ was sufficiently active for the installation of aryl, heteroaryl, alkenyl and alkynyl organometallics at C^1-Cl. Additionally, the catalyst derived from Pd/DPEphos could cross-couple a dichlorovinyl ether and an aryl boronic acid in as little as one hour, and the catalyst derived from Pd/P*t*Bu_3 was found to be useful for room temperature Suzuki coupling.

Following the installation of an organic group at C^1, a second organometallic reagent could be introduced, generating a wide variety of trisubstituted alkenes, dienes, trienes and enynes. The two cross-coupling reactions were most often done in two discrete steps, but may also be done in one pot.

The synthesis of tetrasubstituted alkenes and dienes required four steps from similar simple materials. After the synthesis of the dichlorovinyl ether starting materials and a site selective cross-coupling reaction with an organometallic reagent, the adducts could be deprotonated and quenched with a variety of electrophiles, then further reacted with palladium in the presence of a second organometallic nucleophile to give the tetrasubstituted alkenes. The method developed here is not only very general, but is the most modular method in the literature for synthesizing electron-rich alkenes. Moreover, a single catalytic system for the functionalization of a C^2-Cl was developed that could install all of alkyl, alkenyl, alkynyl and aryl organometallics with no optimization of the conditions required.

When the adducts from the initial site selective cross-coupling were heated in the presence of palladium, an intramolecular C-H activation occurred, yielding 2-substituted benzofurans. In fact, the cross-coupling/direct arylation could be performed in one pot, demonstrating a highly general and modular synthesis of these biologically important compounds. All of alkyl, alkenyl, alkynyl and aryl-substituted benzofurans could be synthesized using one of two catalytic systems. To date, we have been unable to identify conditions that could successfully cross-couple heteroaryl boronic acids with a dichlorovinyl ether that also permits subsequent intramolecular direct arylation from the cross-coupled adduct.

The synthesis of alkenes was executed in two to four steps from inexpensive, commercially available materials. These syntheses were highly efficient; via simple change of organometallic reagent, diverse arrays of highly functionalized compounds were accessed using one of three different catalytic systems in a predictable fashion. While the alkenes themselves are very useful compounds, the true power of the methods developed in this thesis also lies beyond the target alkenes. The reactions proposed in the future work section highlight the advantage this method has over any of the methods for the synthesis of electron-rich alkenes in the current literature as numerous different flavours of compounds are easily generated by simple choice of reagents with no other modification to the conditions. No significant structural limitations in regards to the nature of the organometallic reagent have been encountered to date.

Trichloroethylene is quite toxic,[538-540] and this may perhaps be perceived as a disadvantage. The recent results that show a link between trichloroethylene exposure and Parkisonism[539] and general neurodegeneration[540] also showed that these conditions were due to a chronic and direct exposure to trichloroethylene. These findings are perhaps not as relevant in a chemical and synthetic environment, where the material in question is contained and exposure is minimal. The methods developed in this thesis are ideal for use in discovery chemistry, where a large number of related compounds are required for identification of lead compounds towards new pharmaceuticals and

modularity in synthesis is key.[541] This is in contrast to process chemistry, where the goal is to synthesize a single compound very well.[542] Therefore, the toxicity of trichloroethylene would not be relevant if it was used as a starting material to identify a lead compound through discovery chemistry and not as the starting material for an active pharmaceutical ingredient in process chemistry.

This thesis began with a general introduction to synthetic method development within the context of an ideal synthesis. A fully 'unactivated' organic molecule (i.e. hydrocarbon) is the ideal starting material. In the context of benzofuran synthesis, this would require starting from an aryl vinyl ether, for which a number of different approaches have been published. For example, Blouin and Frenette developed a copper-mediated coupling of tetravinyl tin and phenols.[543] McKinley and O'Shea reported a similar copper-mediated reaction between a vinyl boron reagent and phenols.[544] Ishii and coworkers reported an iridium-catalyzed coupling between phenols and vinyl acetate.[545,546] Solinas et al. used a two-step procedure to couple 1,2-dibromoethane and phenols.[547] These routes use stoichiometric metals, expensive or elaborate reagents and/or require multiple steps. In contrast, the methods employed in this thesis use inexpensive reagents and require only one step. In terms of 'atom economy',[2] 'step ecomony'[3] and 'redox economy'[4], the method in this thesis is more efficient. However, there is still room for improving the overall efficiency of the production of benzofurans in that the method as presented requires a stoichiometric amount of an organometallic reagent for cross-coupling. It would be more efficient to synthesize a 1-chloro-2-aryl vinyl ether by a direct reaction between an unactivated arene and 1,2-dichlorovinyl ether, and this is useful future work. While not perfect, the method presented here certainly points in the direct of achieving a truly general and ideal synthesis of complex materials from simple ones.

CHAPTER 4 : EXPERIMENTAL PROCEDURES

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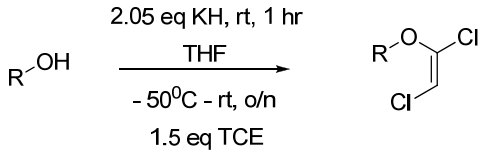
4.1 General Considerations

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded in $CDCl_3$ solution, unless otherwise noted. Chemical shifts for ^{1}H and ^{13}C are reported in parts per million (ppm) down field from TMS, using residual $CDCl_3$ (7.27 ppm and triplet at 77.0 ppm, respectively) as an internal standard. Atom connectivity and assignment for ^{1}H and ^{13}C were determined using combinations of standard gradient ^{1}H-COSY, ^{1}H,^{13}C-HSQC and ^{1}H,^{13}C-HMBC techniques where appropriate, though these spectra are not included here. Flash chromatography was performed using Silicycle Silica-P flash silica gel (230-400mesh). R_f values refer to TLC on pre-coated (0.2 mm) Alugram® Sil G/UV silica gel plates obtained using the eluant indicated and visualized by UV unless otherwise indicated. All glassware was oven dried at 140 ^{o}C overnight and cooled in a desiccator before use. All reactions were carried out under argon using standard syringe techniques. THF was purified by passage through two columns of activated alumina under argon pressure[548] and degassed via sparging with argon before use. Anhydrous dioxane was purchased from Sigma Aldrich and was degassed via sparging with argon before use. Boronic acids were purchased from Sigma Aldrich, Strem Chemicals or

Combi-Blocks; aryl boronic acids were used as received, but *trans*-2-phenylvinylboronic acid and 2-thiophene boronic acid were recrystallized before use. Alkynes were purchased from Sigma Aldrich and were generally used as purchased, except phenylacetylene which was passed through a short column of activated alumina first. Iodomethane and iodoethane were passed through a short column of activated alumina immediately before use. All palladium reagents and phosphine ligands were used as purchased from Strem Chemicals. Cesium fluoride and cesium carbonate were used as received from Sigma Aldrich.

4.2 Compounds from Section 2.2 – Dichlorovinyl Starting Materials

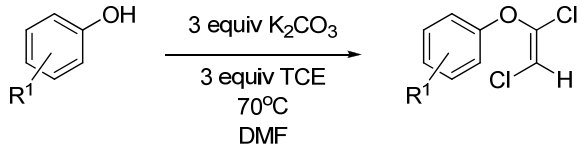
General Procedure I: Synthesis of 1,2-dichlorovinyl ethers using KH in THF



This procedure is based on similar reactions reported by Greene.[409] KH (2.05 equiv) was weighed into a round-bottom flask and washed with 3 portions of either pentane or petroleum ether. The KH was then suspended in THF (ca. 2.4 mL per mmol of KH). A solution of the phenol (1.0 equiv) in THF (ca. 1.25 mL per mmol of phenol) was added drop wise (vigorous gas evolution was noted) and the reaction was allowed to stir for 30 to 120 min. The suspension was cooled to approximately −50 ºC ($CHCl_3/CO_2$(s) bath). Trichloroethylene (1.1 – 1.5 eq) was then added drop wise. The reaction was allowed to warm gradually to room temperature overnight. The reaction was diluted with petroleum ether and quenched with ice-cold water. The phases were separated and the aqueous phase was extracted once more with petroleum ether. The organic layers were combined, dried with sodium sulfate, filtered and concentrated to give a yellow to dark

brown oil. The crude oil was applied to a silica column pre-treated with triethylamine (ca. 2.5 vol% with respect to the volume of dry silica) and eluted with an appropriate solvent to give a colourless oil or solid.

General Procedure II: Synthesis of 1,2-dichlorovinyl ethers using K_2CO_3 in DMF

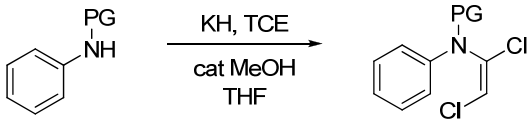


This procedure is based on similar reactions reported by Sales and Mani.[435] Phenol and freshly ground anhydrous potassium carbonate (3 equiv) were combined in an oven-dried round bottom flask. Anhydrous DMF (1.4M with respect to the phenol) was added to the mixture, which was then heated to 60°C. Three equiv of TCE was dropwise and the reaction mixture was heated at 70 °C overnight. After approximately 12 h, the reaction was cooled to room temperature, and the material was partitioned between water and ethyl acetate. The layers were separated and the organic layer was concentrated. If the crude material was a solid, it was recrystallized from an appropriate solvent. Liquid or oily crude materials were applied to a silica gel column pretreated with 2.5 volume% triethylamine and eluted with an appropriate solvent.

Synthesis of protected anilines

N-Acetanilide was used as received from Sigma Aldrich. *N*-Tosylaniline was purchased from Alfa Aesar and used as received. *N*-*tert*-Butoxycarbonylaniline,[549] *N*-*tert*-butoxycarbonyl-4-methoxyaniline (*N*-Boc p-anisidine),[550] *N*-*tert*-butoxycarbonyl-3-nitroaniline,[551] 4-methyl-*N*-(4-methoxyphenyl)-benzenesulfonamide,[552] and 4-methyl-*N*-(3-nitrophenyl)benzenesulfonamide[553] were synthesized according to literature procedures. All ^{1}H and ^{13}C NMR spectra were in accordance with literature values. *N*-*tert*-Butoxycarbonylaniline is also commercially available from Sigma Aldrich.

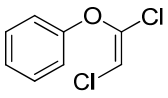
General Procedure III: Synthesis of 1,2-dichlorovinyl amides



The general procedure was modified from Greene's synthesis of ynethiol ethers.[440] KH (1.5 equiv) was weighed into a round-bottom flask and washed with 3 portions of either pentane or petroleum ether before being suspended in THF (5 mL per mmol of KH). A solution of the anilide (1.0 equiv) in THF (3.1 mL per mmol of anilide) was added drop wise (vigorous gas evolution was noted) and the reaction was then allowed to stir for 30 to 120 min. The suspension was cooled to approximately −15 ºC (ethylene glycol/CO_2(s) bath). Trichloroethylene (1.1 eq) was added drop wise followed by addition of methanol (5-40 μL). The reaction was allowed to warm gradually to room temperature overnight. In the case of *N*-tosyl anilides, the reaction required further refluxing for 2 days. The reaction was diluted with diethyl ether and quenched with ice-cold water. The phases were separated and the aqueous phase was extracted once more with diethyl ether. The organic layers were combined, dried with sodium sulfate, filtered and concentrated to give a yellow to dark brown oil or gummy solid. The crude material was applied to a silica gel column (pre-treated with triethylamine as previously described) and eluted with an appropriate solvent to give a colourless oil (*N*-Boc derivatives) or solid (*N*-acetyl and *N*-tosyl derivatives).

4.2.1 Compound Characterization Data

(*E*)-(1,2-Dichlorovinyloxy)benzene (93)



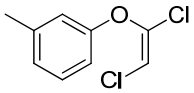
This compound is a clear oil and was prepared on up to a 20 mmol scale according to General Procedure I. The product was purified via flash chromatography using petroleum ether as an eluant to give 2.93 g of **93**. The ^{1}H NMR was consistent with published data.[407]

R_f = 0.75 (2.5% triethylamine in pentane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.36 (m, 2H), 7.22-7.17 (m, 1H), 7.13-7.08 (m, 2H), 5.97 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 140.1, 129.8, 124.5, 117.1, 103.7.

(*E*)-1-(1,2-Dichlorovinyloxy)-3-methylbenzene (111)



This compound is a clear oil and was prepared on an 11.5 mmol scale according to General Procedure I. The product was purified via flash chromatography using petroleum ether as an eluant to give 2.21 g of **111**.

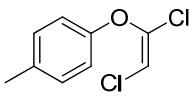
R_f = 0.66 (hexanes).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.27 (m, 1H), 7.06-7.02 (m, 1H), 6.96-6.91 (m, 2H), 6.00 (s, 1H), 2.43 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 140.1, 129.5, 125.3, 117.7, 114.0, 103.6, 21.4.

HRMS: Calculated for $C_9H_8Cl_2O$: 201.9952, Found: 201.9946.

(*E*)-1-(1,2-Dichlorovinyloxy)-4-methylbenzene (113)



This compound is a clear oil and was prepared on an 11.5 mmol scale according to General Procedure I. The product was purified via flash chromatography using petroleum ether as an eluant to give 2.27 g of **113**.

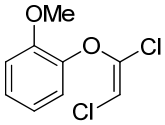
R_f = 0.68 (hexanes).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (m, 2H), 6.99 (m, 2H), 5.94 (s, 1H), 2.34 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 140.4, 134.2, 130.3, 117.0, 103.2, 20.7.

HRMS: Calculated for $C_9H_8Cl_2O$: 201.9952, Found: 201.9949.

(*E*)-1-(1,2-Dichlorovinyloxy)-2-methoxybenzene (115)



This compound is a clear oil and was prepared on a 13.6 mmol scale according to General Procedure I. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give approximately 200 mg of **115**.

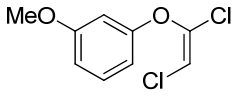
R_f = 0.38 (9:1 hexanes:ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18-7.12 (m, 1H), 7.06-6.91 (m, 3H), 5.85 (s, 1H), 3.90 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 142.7, 140.6, 125.6, 120.8, 118.4, 113.0, 101.5, 56.2.

HRMS: Calculated for $C_9H_8Cl_2O_2$: 217.9901, Found: 217.9906.

(*E*)-1-(1,2-Dichlorovinyloxy)-3-methoxybenzene (117)



This compound is a clear oil and was prepared on an 11 mmol scale according to General Procedure I. The product was purified via flash chromatography using 9:1 petroleum ether: dichloromethane as an eluant to give 2.36 g of **117**.

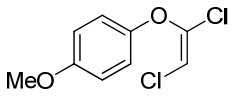
R_f = 0.55 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (t, 1H), 6.78-6.67 (m, 3H), 6.00 (s, 1H), 3.84 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 154.9, 140.0, 130.2, 110.2, 109.0, 104.0, 103.4, 55.5.

HRMS: Calculated for $C_9H_8Cl_2O_2$: 217.9901, Found: 217.9900.

(*E*)-1-(1,2-Dichlorovinyloxy)-4-methoxybenzene (110)



This compound is a clear oil and was prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography using 9:1 petroleum ether: dichloromethane as an eluant to give 2.04 g of **110**.

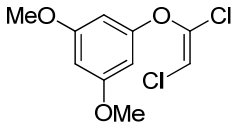
R_f = 0.64 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (d, 2H), 6.89 (d, 2H), 5.89 (s, 1H), 3.80 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 147.6, 140.8, 118.6, 114.8, 102.5, 55.7.

We were unable to obtain satisfactory mass spectra of this compound. However, it was converted to the known benzofuran natural product Corsifuran C (**305**) (see below).

(*E*)-1-(1,2-Dichlorovinyloxy)-3,5-dimethoxybenzene (112)



This compound is a clear oil and was prepared on a 6.42 mmol scale according to General Procedure I. The product was purified via flash chromatography using petroleum ether as an eluant to give 913.8 mg of **112**.

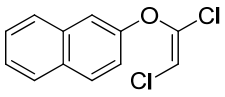
R_f = 0.48 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.30 (t, 1H), 6.27 (d, 2H), 5.99 (s, 1H), 3.81 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 155.5, 139.8, 104.3, 96.6, 95.7, 55.5.

HRMS: Calculated for $C_{10}H_{10}Cl_2O_3$: 248.0007, Found: 248.0004.

(*E*)-2-(1,2-Dichlorovinyloxy)naphthalene (114)



This compound is a clear oil and was prepared on a 6.9 mmol scale according to General Procedure I. The product was purified via flash chromatography using petroleum ether as an eluant to give 1.22 g of **114**.

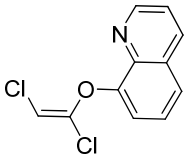
R_f = 0.24 (petroleum ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89-7.80 (m, 3H), 7.55-7.43 (m, 3H), 7.30 (dd, 1H, J^1 = 3 Hz, J^2 = 9 Hz), 6.05 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 151.6, 140.1, 133.9, 130.8, 130.1, 127.9, 127.4, 127.0, 125.3, 117.9, 112.6, 104.1.

HRMS: Calculated for $C_{12}H_8Cl_2O$: 237.9952, Found: 237.9945.

(*E*)-8-(1,2-Dichlorovinyloxy)quinoline (116)



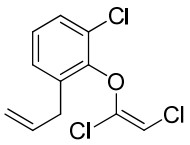
This compound is a colourless oil and was prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography using 9:1 petroleum ether: ethyl acetate as an eluant to give 672.2 mg of **116**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.99 (dd, J^1 = 1.8 Hz, J^2 = 4 Hz, 1H), 8.16 (dd, J^1 = 1.7 Hz, J^2 = 8 Hz, 1H), 7.63-7.59 (m, 1H), 7.51-7.49 (m, 2H), 7.29 (dd, , J^1 = 1.2 Hz, J^2 = 8 Hz, 1H), 6.07 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5, 149.3, 140.1, 139.9, 135.9, 129.8, 126.1, 123.9, 122.1, 113.9, 104.3.

No HRMS was acquired for this compound.

((E)-1-allyl-3-chloro-2-(1,2-Dichlorovinyloxy)benzene (119)



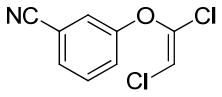
This compound is a colourless oil and was prepared on a 5 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using petroleum ether as an eluant to give 838.5 mg of **119**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.27 (m, 1H), 7.16-7.13 (m, 2H), 6.01-5.88 (m, 1H), 5.63 (s, 1H), 5.18-5.15 (m, 1H), 5.13-5.11 (m, 1H), 3.43 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 140.3, 135.7, 135.1, 128.7, 128.5, 128.1, 126.9, 117.1, 96.2, 34.2.

No HRMS was acquired for this compound.

(*E*)-3-(1,2-dichlorovinyloxy)benzonitrile (122)



This compound is a clear oil and was prepared on 8.3 mmol scale according to General Procedure I. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant to give 1.61 g of **122**.

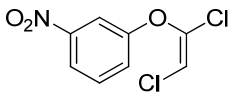
R_f = 0.43 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.46 (m, 2H), 7.35-7.29 (m, 2H), 6.08 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 139.0, 130.9, 128.2, 121.7, 120.2, 117.8, 113.9, 105.7.

HRMS: Calculated for $C_9H_5Cl_2NO$: 212.9748, Found: 212.9742

(E)-1-(1,2-Dichlorovinyloxy)-3-nitrobenzene (125)



This compound is a colourless oil and was prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography using 9:1 petroleum ether: dichloromethane as an eluant to give 2.28 g of **125**.

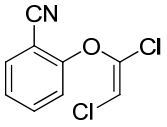
R_f = 0.44 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (dt, 1H), 7.92 (t, 1H), 7.58 (t, 1H), 7.42 (ddd, 1H), 6.11 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 149.3, 139.0, 130.5, 123.1, 119.4, 112.1, 105.9.

HRMS: Calculated for $C_8H_5Cl_2NO_3$: 232.9647, Found: 232.9652.

(*E*)-2-(1,2-dichlorovinyloxy)benzonitrile (128)



This compound is a clear oil and was prepared on a 8.31 mmol scale according to General Procedure II. The product was purified via recrystallization from hexanes to give 1.21 g of **128**.

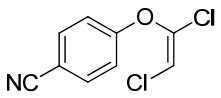
R_f = 0.35 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71-7.59 (m, 2H), 7.28 (t, 1H, *J* = 6.6 Hz), 7.14 (d, 1H, *J* = 8 Hz), 6.11 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 138.6, 134.4, 134.1, 124.7, 116.0, 114.9, 106.9, 103.8.

HRMS: Calculated for $C_9H_5Cl_2NO$: 212.9748, Found: 212.9747.

(*E*)-4-(1,2-dichlorovinyloxy)benzonitrile (129)



This compound is a clear oil and was prepared on a 10 mmol scale according to General Procedure II. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 2.01 g of **129**.

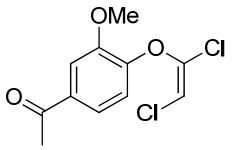
R_f = 0.45 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 8 Hz), 7.15 (d, 2H *J* = 8 Hz), 6.08 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.9, 138.7, 134.3, 118.3, 117.4, 108.2, 106.1.

HRMS: Calculated for $C_9H_5Cl_2NO$: 212.9748, Found: 212.9741.

(*E*)-1-(4-(1,2-dichlorovinyloxy)-3-methoxyphenyl)ethanone (130)



This compound is a clear oil and was prepared on a 9.03 mmol scale according to General Procedure II. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 1.89 g of **130**.

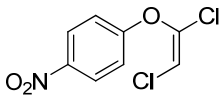
R_f = 0.26 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, 1H, *J* = 2 Hz), 7.55 (dd, 1H, J^1 = 2 Hz, J^2 = 8 Hz), 7.05 (d, 1H, *J* = 8 Hz), 5.96 (s, 1H), 3.95 (s, 3H), 2.58 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 150.1, 146.5, 139.6, 134.4, 122.2, 116.8, 111.9, 103.6, 56.3, 26.4.

HRMS: Calculated for $C_{11}H_{10}Cl_2O_3$: 260.0007, Found: 260.0006.

(*E*)-1-(1,2-dichlorovinyloxy)-4-nitrobenzene (131)



This compound is a clear oil and was prepared on a 7.2 mmol scale as described in General Procedure II, but modified by adding 10 µL of methanol after the addition of TCE. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 1.47 g of **131**.

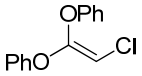
R_f = 0.53 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, 2H, *J* = 9 Hz), 7.18 (d, 2H, *J* = 9 Hz), 6.13 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 144.3, 138.6, 126.0, 116.9, 106.4.

HRMS: Calculated for $C_8H_5Cl_2NO_3$: 232.9646, Found: 232.9638.

1-(2-chloro-1-phenoxyvinyloxy)benzene (132)



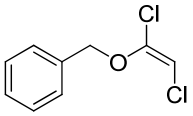
KH (1.34 g, 10.0 mmol, 5.0 equiv) was weighed into a round-bottom flask and washed with 3 portions of either pentane or petroleum ether. The KH was then suspended in THF (6 mL). A solution of the phenol (0.4753 g, 5.00 mmol, 2.5 equiv) in 10 mL THF was added drop wise (vigorous gas evolution was noted) and the reaction was allowed to stir for 60 min at room temperature. The suspension was cooled to approximately −50 ºC ($CHCl_3/CO_2$(s) bath). Trichloroethylene (0.18 mL, 2 mmol, 1 equiv) was then added drop wise. The reaction was allowed to warm gradually to room temperature over two h, then heated to reflux for 12 h. The reaction was diluted with petroleum ether and quenched with ice-cold water. The phases were separated and the aqueous phase was extracted once more with petroleum ether. The organic layers were combined, dried with sodium sulfate, filtered and concentrated to give a yellow to dark brown oil. The crude oil was applied to a silica column pre-treated with triethylamine (ca. 2.5 vol% with respect to the volume of dry silica) and eluted with an appropriate solvent to give **132** as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.28 (m, 4H), 7.15-7.03 (m, 6H), 5.58 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 154.1, 153.3, 129.7, 129.6, 124.3, 123.9, 117.8, 117.2, 91.5.

HRMS was not acquired for this compound.

(*E*)-1-((1,2-dichlorovinyloxy)methyl)benzene (134)



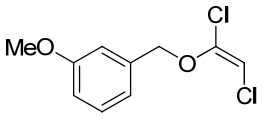
This compound is a colourless liquid prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using hexanes as an eluant to give 1.00 g of **134**. The ^{1}H and ^{13}C NMR were consistent with those reported in literature.[554]

R_f = 0.55 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-7.37 (m, 5H), 5.53 (s, 1H), 5.07 (s, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4, 134.7, 128.8, 128.6, 128.6, 98.9, 73.4.

(*E*)-1-((1,2-dichlorovinyloxy)methyl)-3-methoxybenzene (136)



This compound is a colourless liquid prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using petroleum ether as an eluant to give 1.61 g of **136**.

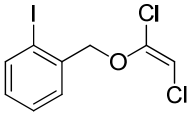
R_f = 0.61 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.30 (m, 1H), 7.05-7.02 (m, 2H), 6.96-6.91 (m, 1H), 5.55 (s, 1H), 5.06 (s, 2H), 3.86 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 143.4, 136.2, 129.6, 120.6, 114.6, 113.7, 98.8, 73.2, 55.3.

HRMS: Calculated for $C_{10}H_{10}Cl_2O_2$ 232.0058, Found: 232.0044.

(*E*)-1-((1,2-dichlorovinyloxy)methyl)-2-iodobenzene (138)



This compound is a colourless liquid prepared on a 5 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using petroleum ether as an eluant to give 1.11 g of **138**.

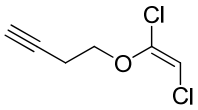
$\mathbf{R_f}$ = 0.82 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, 1H), 7.53 (m, 1H), 7.39 (m, 1H), 7.05 (m, 1H), 5.57 (s, 1H), 5.09 (s, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 139.5, 137.5, 130.2, 129.5, 128.4, 99.0, 97.9, 76.9.

HRMS was not acquired for this compound.

(*E*)-4-(1,2-Dichlorovinyloxy)but-1-yne (140)



This compound is a colourless liquid prepared on a 6.61 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using petroleum ether as an eluant to give 126.0 mg of **140**. This compound has been previously reported, but no characterization data were given.[413]

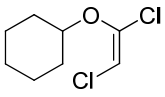
$\mathbf{R_f}$ = 0.60 (9:1 hexanes: ethyl acetate, visualized by staining with permanganate and heating).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55 (s, 1H), 4.12 (t, 2H, J = 7 Hz), 2.62 (dt, 2H, J^1 = 7 Hz), J^2 = 2.6 Hz), 2.04 (t, 1H, J = 2.6 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0, 98.9, 79.2, 70.5, 69.2, 19.2.

HRMS was not acquired for this compound.

(E)-(1,2-Dichlorovinyloxy)cyclohexane (142)

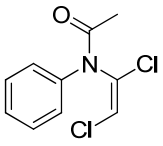


This compound is a clear liquid prepared on a 5 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using petroleum ether as an eluant to give 838.5 mg of **142**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52 (s, 1H), 4.28 (m, 1H), 1.95-1.76 (m, 4H), 1.64-1.47 (m, 3H), 1.39-1.24 (m, 4H).

HRMS was not acquired for this compound.

(*E*)-*N*-(1,2-dichlorovinyl)-*N*-phenylacetamide (149)



Pale yellow solid and was prepared on a 10 mmol scale according to General Procedure III. The product was purified via flash chromatography using petroleum ether as an eluant to give 996.8 mg of **149**.

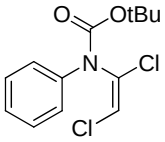
R_f = 0.31 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.39 (m, 5H), 6.43 (br s, 1H), 2.26 (br s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) All signals very broad and of low intensity due to hindered rotation.

HRMS: Calculated for $C_{10}H_9Cl_2NO$: 229.0061, Found: 229.0047.

(*E*)-*tert*-Butyl (1,2-dichlorovinyl(phenyl)carbamate (150).



This compound is a clear oil and was prepared on a 5.17 mmol scale according to General Procedure III. The product was purified via flash chromatography using a gradient from hexanes to 9:1 hexanes: ethyl acetate as an eluant to give 1.24 g of **150**.

R_f = 0.56 (9:1 hexanes: ethyl acetate).

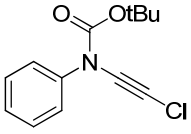
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.38 (m, 4H), 7.33-7.26 (m, 1H), 6.33 (s, 1H), 1.55 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 138.6, 132.1, 129.0, 127.1, 125.8, 115.9, 82.8, 28.1.

HRMS: Calculated for $C_{13}H_{15}Cl_2NO_2$: 287.0480, Found: 287.0469.

In the reaction perfomed in the absence of methanol, ynamide **157** was isolated as a byproduct.

tert-Butyl 2-chloroethynyl(phenyl)carbamate (157)



This compound is a colourless oil isolated from the reaction between *N*-Boc aniline and trichloroethylene on a 10 mmol scale reaction preformed according to General Procedure III but in the absence of methanol. The product was purified via flash chromatography using a gradient from hexanes to 9:1 hexanes: ethyl acetate as an eluant to give 0.4222 g of **157**.

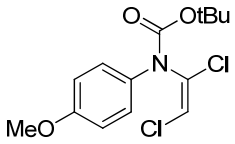
R_f = 0.59 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.37 (m, 4H), 7.31-7.25 (m, 1H), 1.56 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 139.2, 128.9, 126.9, 124.8, 83.8, 63.9, 51.2, 28.0.

HRMS was not acquired for this compound.

tert-Butyl 2-chloroethynyl(4-methoxyphenyl)carbamate (151)



This compound is a clear oil and was prepared on a 2 mmol scale according to General Procedure III. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 402.7 mg of **151**.

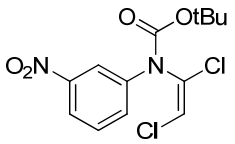
R_f = 0.44 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, 2H), 6.91 (d, 2H), 6.27 (s, 1H), 3.82 (s, 3H), 1.53 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 138.6, 132.1, 128.9, 129.0, 127.1, 125.8, 115.9, 82.8, 29.6.

HRMS: Calculated for $C_{14}H_{17}Cl_2NO_3$: 317.0585, Found: 317.0572.

tert-Butyl 2-chloroethynyl(3-nitrophenyl)carbamate (152)



This compound is a clear oil and was prepared on a 2.10 mmol scale according to General Procedure III. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 580.6 mg of **152**.

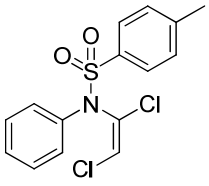
R_f = 0.43 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (t, 1H), 8.13 (ddd, 1H), 7.74 (ddd, 1H), 7.56 (t, 1H), 6.43 (s, 1H), 1.56 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 148.6, 139.7, 131.0, 130.7, 129.69, 129.65, 121.4, 120.0, 117.6, 82.0, 28.0.

HRMS: Calculated for $C_{13}H_{14}Cl_2N_2O_4$: 332.0331, Found: 332.0337.

(*E*)-(*N*-1,2-dichlorovinyl)-4-methyl-*N*-phenylbenzenesulfonamide (153)



This compound is a colourless solid and was prepared on a 6.06 mmol scale according to General Procedure III. The product was purified via flash chromatography using 4:1 hexanes: dichloromethane as an eluant to give 1.26 g of **153**.

R_f = 0.33 (9:1 hexanes: ethyl acetate).

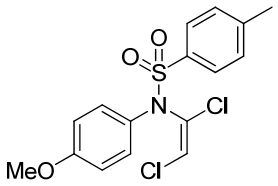
Also prepared on a 8.1 mmol scale according to General Procedure II. The product was purified via recrytalization from hexanes and ethyl acetate to give 1.88 g **153**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, 2H), 7.42-7.33 (m, 5H), 7,27 (m, 2H), 6.47 (s, 1H), 2.44 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 137.7, 135.6, 130.7, 129.4, 129.4, 129.1, 128.7, 128.6, 120.5, 21.7.

HRMS: Calculated for $C_{15}H_{13}Cl_2NO_2S$: 341.0044, Found: 341.0046.

(*E*)-*N*-(1,2-dichlorovinyl) *N*-(4-methoxyphenyl)-4-methyl-benzenesulfonamide (154)



This compound is a clear oil and was prepared on a 5.41 mmol scale according to General Procedure III. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 1.29 g of **154**.

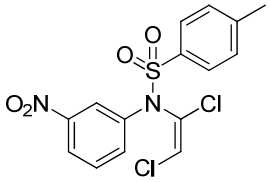
R_f = 0.42 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, 2H), 7.27 (app. d, 4H), 6.84 (m, 2H), 6.43 (s, 1H), 3.82, (s, 3H), 2.45 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 144.5, 135.6, 130.0, 130.6, 130.1, 129.4, 128.7, 119.9, 114.5, 55.5, 21.7.

HRMS: Calculated for $C_{16}H_{15}Cl_2NO_3S$: 371.0150, Found: 371.0154.

(*E*)-*N*-(1,2-dichlorovinyl) *N*-(3-nitrophenyl)-4-methyl-benzenesulfonamide (155)



This compound is a colourless solid and was prepared on a 3.4 mmol scale according to General Procedure III. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 385.0 mg of **155**.

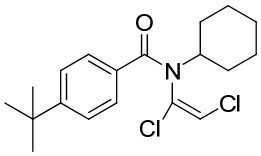
R_f = 0.32 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25-8.17 (m, 2H), 7.81 (m, 1H), 7.71 (d, 2H), 7.58 (t, 1H), 7.31 (d, 2H), 6.57 (d, 1H, *J* = 0.6Hz), 2.46 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6, 145.5, 138.9, 134.9, 133.9, 130.2, 129.8, 129.8, 128.6, 123.4, 122.5, 122.0, 21.7

HRMS: Calculated for $C_{15}H_{12}Cl_2N_2O_4S$: 385.9895, Found: 385.9897.

(*E*)-4-*tert*-Butyl-*N*-cyclohexyl-*N*-(1,2-dichlorovinyl)-benzamide (156)



This compound is a colourless gummy solid and was prepared on a 0.96 mmol scale according to General Procedure III. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant to give 223.7 mg of **156**.

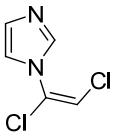
R_f = 0.56 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, 2H), 7.36 (d, 2H), 6.03 (s, 1H), 4.40 (m, 1H), 2.07-1.59 (m, 8H), 1.43-1.16 (m, 12H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 153.9, 133.1, 132.5, 126.8, 124.7, 117.6, 56.9, 34.9, 31.6, 31.3, 29.6, 26.1, 26.03, 26.00, 25.96, 25.5.

No HRMS was acquired for this compound.

(*E*)-1-(1,2-Dichlorovinyl)-1*H*-imidazole (159)



This compound is a colourless liquid prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using 4:1 hexanes: ethyl acetate as an eluant to give 1.38 g of **159**. ^{1}H and ^{13}C NMR

spectra are consistent with data reported by Kende,[555] but inconsistent with spectral data reported by Pielichowski.[454,556]

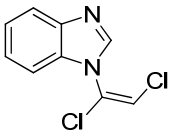
R_f = 0.15 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (m, 1H), 7.15 (m, 1H), 7.08 (m, 1H), 6.33 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2, 129.9, 125.2, 118.8, 111.3.

HRMS: Calculated for $C_5H_4Cl_2N_2$: 161.9751, Found: 161.9754.

(*E*)-1-(1,2-Dichlorovinyl)-1*H*-benzo[*d*]imidazole (161)



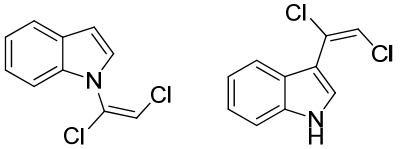
This compound is a colourless liquid prepared on a 10 mmol scale according to General Procedure I. The product was purified via solid-phase extraction on TEA-treated silica using 4:1 hexanes: ethyl acetate as an eluant to give 1.35 g of **161**. ^{1}H and ^{13}C NMR spectra are consistent with recently acquired spectral data published by Kerwin,[557] but inconsistent with spectral data published by Pielichowski.[454]

R_f = 0.21 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (s, 1H). 7.83 (m, 1H), 7.46-7.41 (m, 1H), 7.37-7.32 (m, 2H), 6.60 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 141.9, 132.1, 124.8, 124.4, 123.7, 120.9, 115.5, 111.3.

(*E*)-1-(1,2-Dichlorovinyl)-1*H*-indole (163) and (*E*)-3-(1,2-dichlorovinyl)-1*H*-indole (164)



This compound is a colourless liquid prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using hexanes as an eluant to give 1.28 g of **163** and **164**.

$\mathbf{R_f}$ = 0.71, 0.77 (9:1 hexanes: ethyl acetate).

Mixture:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (m, 1H), 7.69 (m, 2.7H), 7.45-7.25 (m, 13H), 7.21 (m, 2.7H), 6.73 (m, 2.7H), 6.60 (s, 1H), 6.57 (s, 2.7H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 135.2, 134.5, 130.8, 129.1, 128.9, 128.2, 127.1, 127.0, 124.4, 123.2, 122.5, 121.7, 121.4, 120.5, 114.9, 113.7, 111.8, 111.9, 106.1, 101.3.

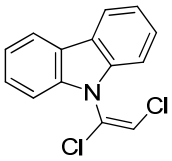
*Single Isomer (**163**): (NMR contains a small amount of **164**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (m, 1H), 7.47-7.27 (m, 3H), 7.23 (m, 1H), 6.75 (m, 1H), 6.58 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 135.3, 128.9, 128.2, 127.1, 123.3, 121.7, 121.4, 113.7, 111.6, 106.2.

HRMS: Calculated for: $C_{10}H_7Cl_2N$: 210.9955, Found: 210.9951.

(*E*)-9-(1,2-Dichlorovinyl)-9*H*-carbazole (166)



This compound is a colourless solid and was prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using hexanes as an eluant to give 877.6 mg of **166**. This compound has been previously reported, though our spectral data are not consistent with literature values.[443,452,453,558,559]

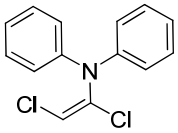
$\mathbf{R_f}$ = 0.23 (hexanes).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (m, 2H), 7.55-7.34 (m, 6H), 6.83 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 127.3, 126.5, 124.5, 121.7, 120.6, 117.5, 111.1.

HRMS: Calculated for: $C_{14}H_9Cl_2N$: 261.0112, Found: 261.0116.

(*E*)-*N*-(1,2-Dichlorovinyl)-*N*-phenylbenzenamine (168)



(*E*)-*N*-(1,2-dichlorovinyl)-*N*-phenylbenzenamine

This compound is a colourless oil and was prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using 9:1 petroleum ether: ethyl acetate as an eluant to give 1.48 g of **168**.

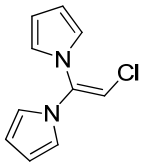
R_f = 0.24 (hexanes).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.36 (m, 4H), 7.24-7.16 (m, 6H), 6.31 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3, 135.5, 129.4, 124.1, 122.0, 113.3.

No HRMS wasa acquired for this compound.

1-(2-Chloro-1-(1*H*-pyrrol-1-yl)vinyl)-1*H*pyrrole (170)



This compound is a colourless liquid prepared on a 10 mmol scale according to General Procedure I. The product was purified via flash chromatography on TEA-treated silica using pentane as an eluant to give 58.1 mg of **170**.

R_f = 0.54 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.87 (t, 2H, *J* = 2.2Hz), 6.70 (t, 2H, *J* = 2.3Hz), 6.33 (t, 2H, *J* = 2.2Hz), 6.28 (t, 2H, *J* = 2.3Hz), 6.04 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 136.6, 121.6, 120.6, 111.0, 110.3, 99.7.

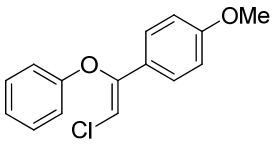
No HRMS was acquired for this compound.

4.3 Compounds from Section 2.3 – Site Selective Cross-Coupling

Initial Cross-Coupling - Scheme 97

Dichlorovinyl ether (0.1680 g, 0.89 mmol, 1 equiv), *p*-methoxyphenylboronic acid (0.2026 g, 1.3 mmol, 1.5 equiv), $Pd(PPh_3)_4$ (0.1028 g, 0.089 mmol, 10 mol%) were placed in a oven-dried round-bottom flask to which 3.5 mL of anhydrous THF was added, followed by 2.6 mL of a 1.0M aqueous solution of KOH. The solution was brought to reflux. After 48 h, the reaction was cooled to room temperature, diluted with diethyl ether and the layers were separated. The aqueous layer was extracted twice more with diethyl ether. The organic layers were combined and dried with magnesium sulfate, filtered and concentrated. The crude residue was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 0.1041 g of **173** and 0.1527 g of **175**.

(*Z*)-1-(2-Chloro-1-(4-methoxyphenyl)vinyloxy)benzene (173)



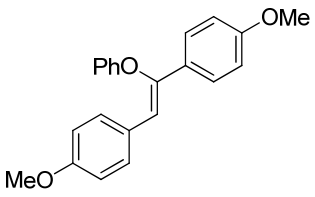
R_f = 0.39 in 9:1 hexanes: ethyl acetate.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, 2H), 7.28-7.21 (m, 2H), 7.00-6.95 (m, 3H), 6.83 (d, 2H), 6.30 (s, 1H), 3.78 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 156.1, 151.1, 129.6, 127.7, 127.1, 125.7, 122.2, 115.9, 114.2, 105.1, 55.3.

HRMS: Calculated for $C_{15}H_{13}ClO_2$: 260.0604, Found: 260.0606.

(Z)-1,2-bis(4-methoxyphenyl)-1-phenoxyethene (175)



R_f = 0.24 in 9:1 hexanes: ethyl acetate.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (m, 2H), 7.51 (m, 2H), 7.27-7.21 (m, 2H), 7.04 (m, 2H), 6.98-6.92 (m, 1H), 6.86-6.82 (m, 4H), 6.54 (s, 1H), 3.78 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 158.6, 156.5, 147.8, 130.1, 129.6, 128.7, 127.8, 127.1, 121.8, 116.2, 114.6, 113.99, 113.96, 55.3, 55.2.

HRMS was not obtained for this compound.

Procedure for Ligand Screen (Figure 12)

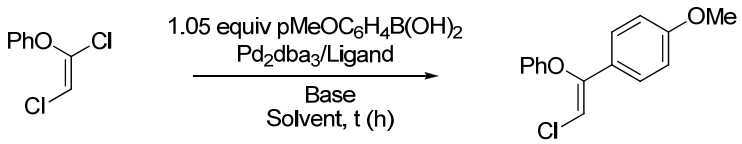
To each of 11 oven-dried test tubes were added *p*-methoxyphenyl boronic acid (16.1 mg, 0.104 mmol, 1.05 equiv), Cs_2CO_3 (97.2 mg, 0.30 mmol, 3 equiv), Pd_2dba_3 (2.2 mg, 2.4 μmmol, 2.5 mol%) and the ligand (see table below for amounts). The test tubes were sealed with rubber septa and purged with argon for 10 min. To each test tube was added 0.5 mL of a 0.2M solution of dichlorovinyl either **93** in THF (18.8 mg, 99.5 μmmol, 1 equiv) and the solutions were heated at 65 °C for 4 h.

ligand	equiv	μmmol	mass
P*t*Bu$_3$·HBF$_4$ (**183**)	7.5 mol%	7.4	2.2 mg
PCy$_3$·HBF$_4$ (**184**)	7.5 mol%	7.4	2.7 mg
PhDavePhos (**185**)	7.5 mol%	7.4	1.9 mg
JohnPhos (**186**)	5 mol%	4.9	2.3 mg
S-Phos (**187**)	5 mol%	4.9	2.1 mg
DPPE (**188**)	5 mol%	4.9	2.0 mg
DPPB (**189**)	5 mol%	4.9	2.1 mg

DPPF (**190**)	5 mol%	4.9	2.8 mg
*t*Bu-Xantphos (**191**)	5 mol%	4.9	2.5 mg
DPEphos (**12**)	5 mol%	4.9	2.7 mg
Xantphos (**192**)	5 mol%	4.9	2.9 mg

After 4 h, the test tubes were cooled to room temperature and each was diluted with ethyl acetate (5 mL) and were filtered through a Pasteur pipette packed with silica, and washed with an additional 5 mL ethyl acetate. The samples were then analyzed by GC-MS and the results are reported in Figure 12.

General Procedure IV: Study of the effect of base (Figure 14)



To 9 different test tubes were added dichlorovinyl ether **93** (1 equiv), *p*-methoxyphenyl boronic acid (1.05 equiv), Pd_2dba_3 (2.5 mol%), ligand (Xantphos or DPEphos, 5 mol%) and base (3 equiv each) (the scales on which these were performed are in the tables below). The test tubes were sealed with septa, purged with argon for 10 min, then the appropriate solvent was added. After the length of time indicated, the test tubes were cooled to room temperature and diluted with dichloromethane. After water was added, the layers were separated and the aqueous layer was extracted twice more with dichloromethane. The organic layers were combined, dried with magnesium sulfate, filtered and concentrated. The crude residues were purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant, and yields for each reaction are reported below.

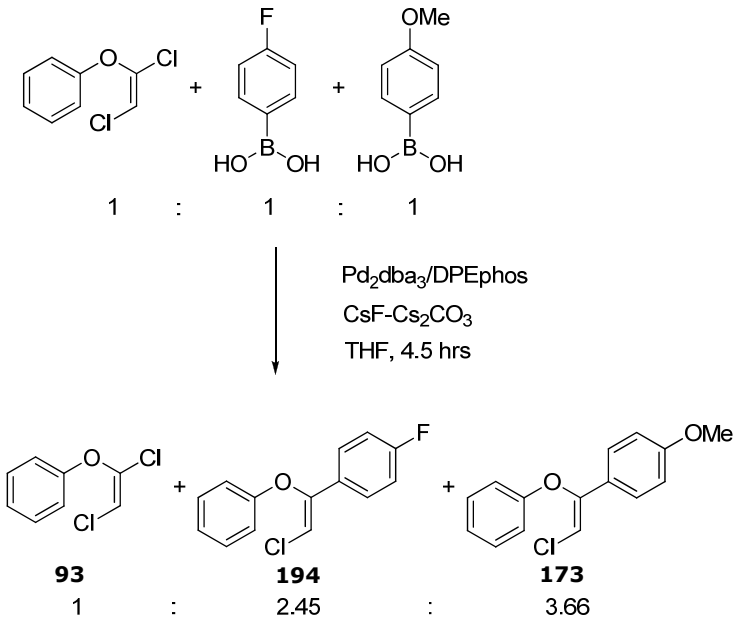
ligand	solvent	CsF (equiv)	Cs_2CO_3 (equiv)	scale (mmol)[a]	time	yield[b]
Xantphos	Dioxane	3	-	0.39	1 hr	68%

Xantphos	Dioxane	-	3	0.38	1 hr	67%
Xantphos	Dioxane	3	3	0.34	1 hr	95%
DPEphos	Dioxane	3	-	0.34	1 hr	71%
DPEphos	Dioxane	-	3	0.37	1 hr	62%
DPEphos	Dioxane	3	3	0.32	1 hr	72%
DPEphos	THF	3	-	0.34	6 hrs	86%
DPEphos	THF	-	3	0.33	6 hrs	76%
DPEphos	THF	3	3	0.47	6 hrs	88%

[a]The amount of **93** submitted to the reaction conditions reported in mmoles. The amounts of the other reagents were scaled appropriately. [b]Isolated yields.

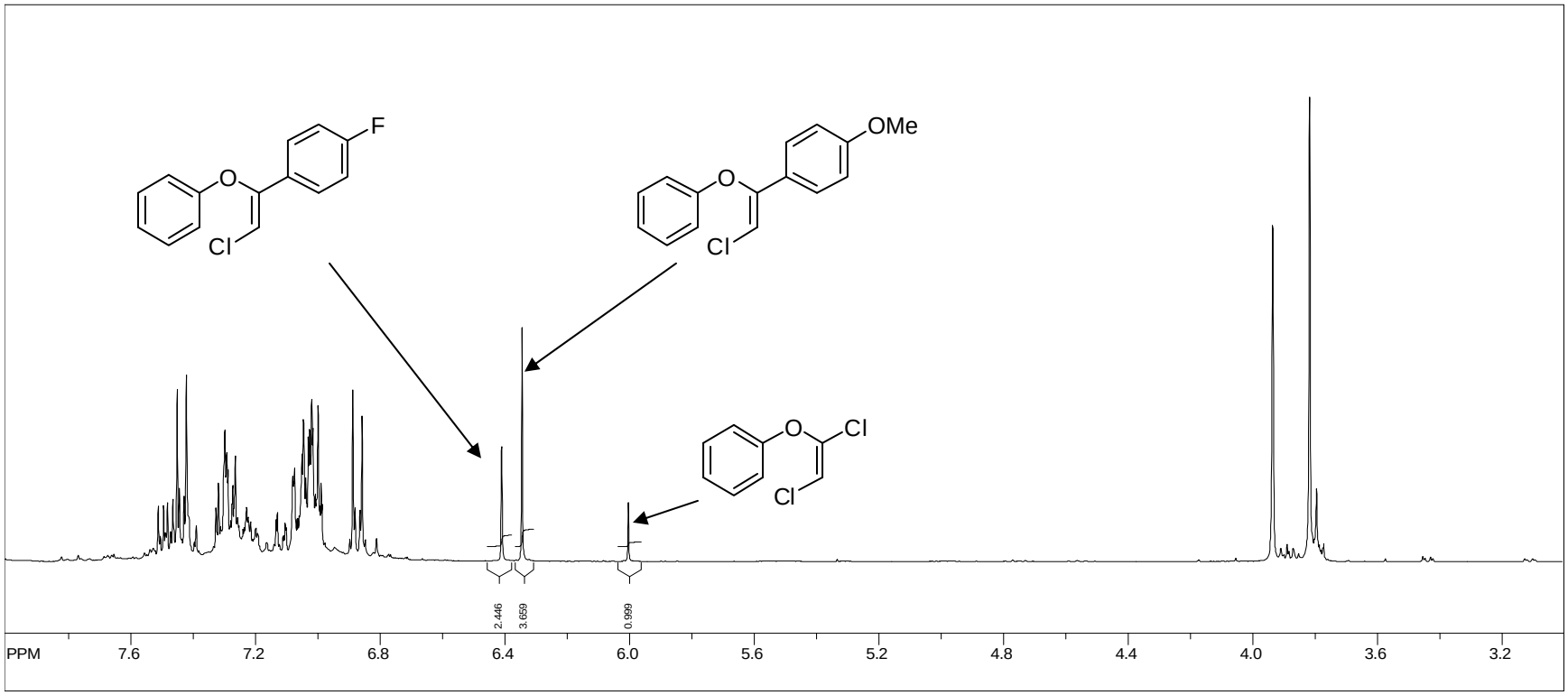
Intermolecular Competition Experiments

C1 Arylation: varying the boronic acid



Both boronic acids (0.405 mmol, 1 equiv each), Pd_2dba_3 (9.2 mg, 2.5 mol%), DPEphos (11.1 mg, 5mol%), CsF (184 mg, 3 equiv) and Cs_2CO_3 (396 mg, 3 equiv) were placed into a one piece round bottom flask/condenser, sealed with a septum and purged with argon for 20-30 min. 1,2-Dichlorovinyl ether **93** (1.0 mL, 0.405 M, 1 equiv) in dioxane was added. The solution was vigorously stirred and brought to reflux. After 4.5 h, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and evaporated. The residue was characterized by crude NMR (data below).

SpinWorks 2.5: dichlorophenol ether:pMeOPhB(OH)2:pFPhB(OH)2



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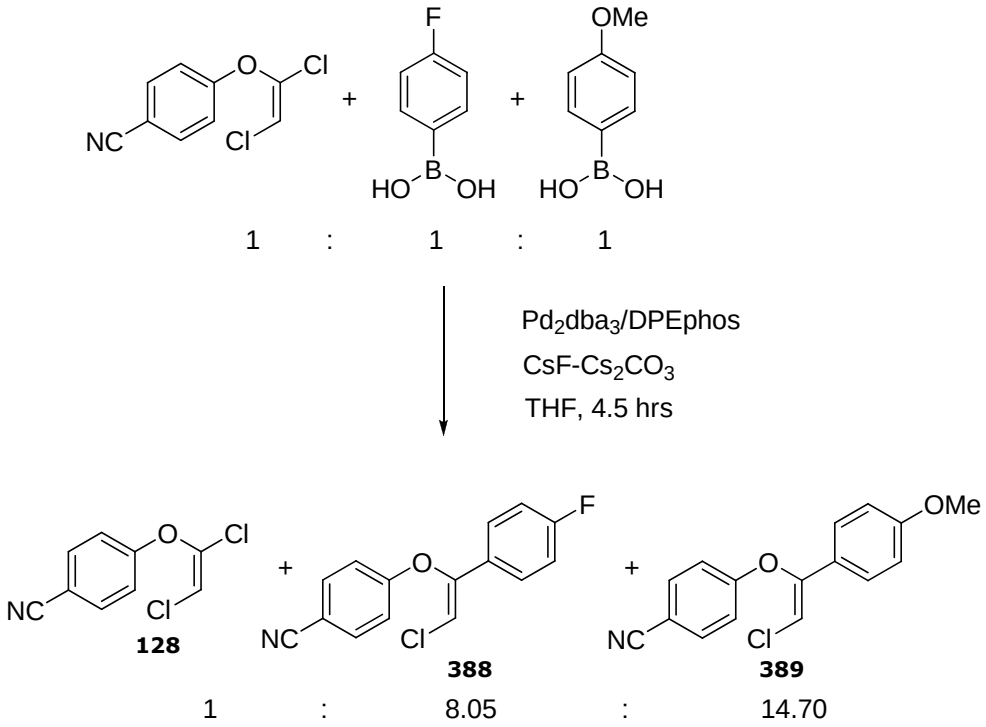
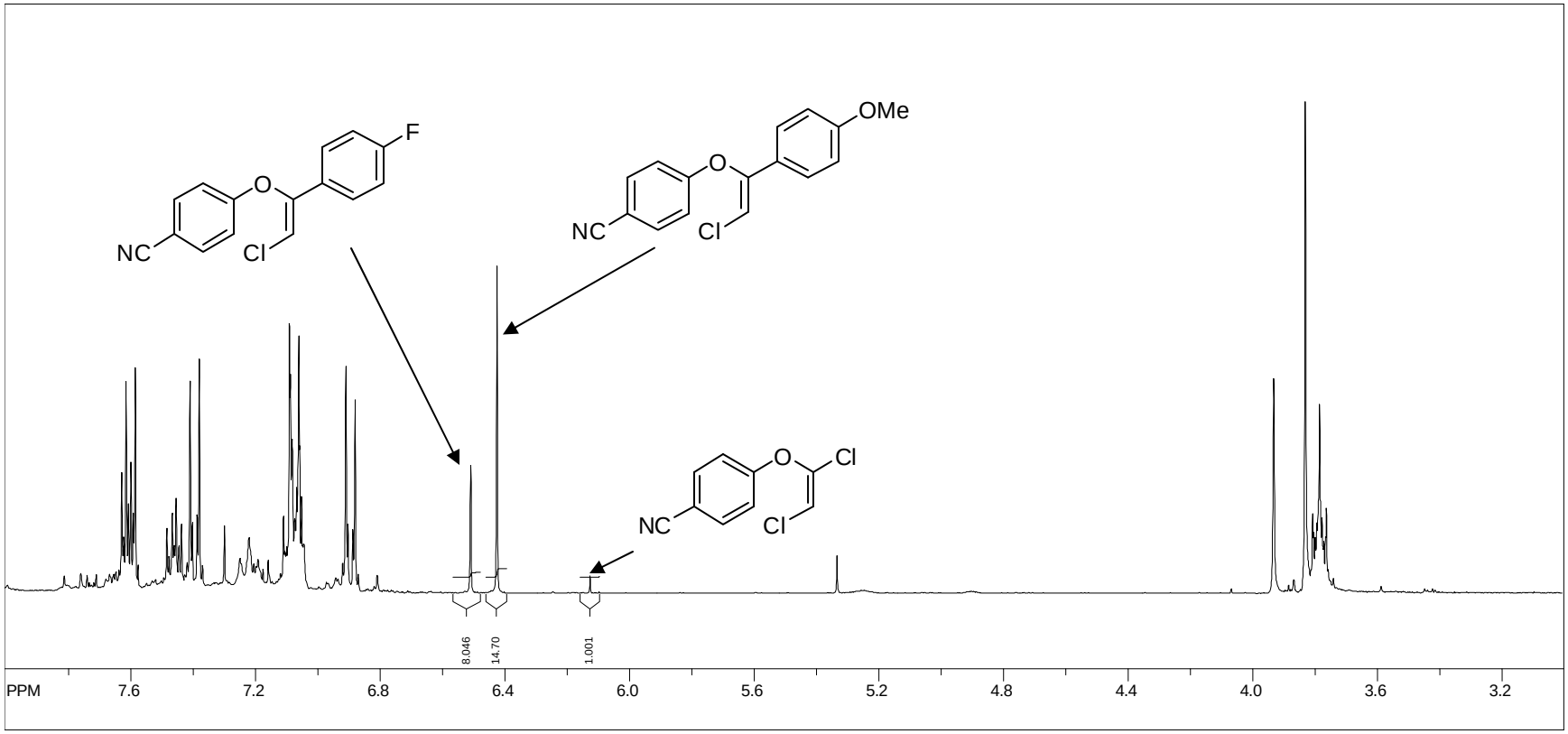
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 6

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000



Both boronic acids (0.393 mmol, 1 equiv each), Pd_2dba_3 (9.0 mg, 2.5 mol%), DPEphos (10.8 mg, 5mol%), CsF (179 mg, 3 equiv) and Cs_2CO_3 (385 mg, 3 equiv) were placed into a one piece round bottom flask/condenser, sealed with a septum and purged with argon for 20-30 min. 1,2-Dichlorovinyl ether **128** (1.0 mL, 0.41 M, 1 equiv) in dioxane was added. The solution was vigorously stirred and brought to reflux. After 4.5 h, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and evaporated. The residue was characterized by crude NMR (data below).

SpinWorks 2.5: pCNdichlorophenol ether: pMeOPh(BOH)2: pFPhB(OH)2



file: Z:\Laina\lmgxvi\lmgxvi_46\1\fid expt: <zg30>
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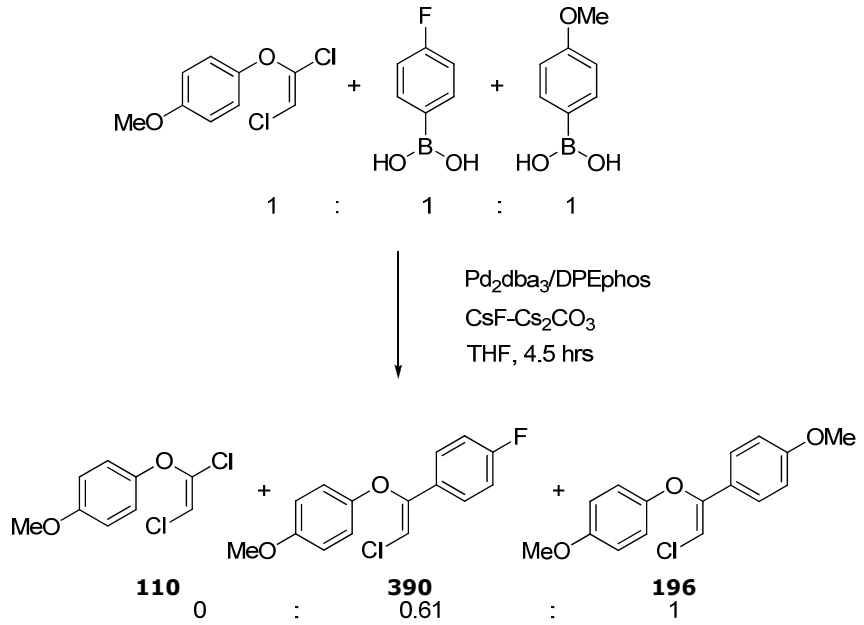
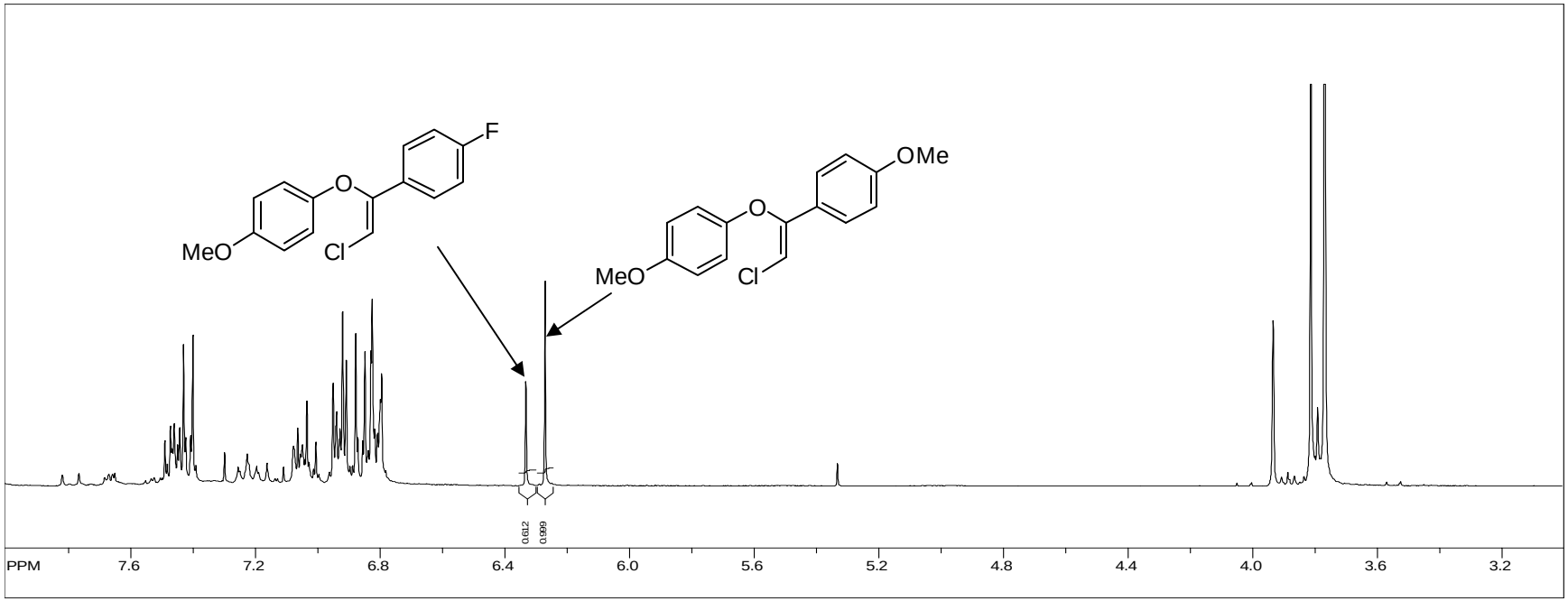
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000



Both boronic acids (0.405 mmol, 1 equiv each), Pd_2dba_3 (9.2 mg, 2.5 mol%), DPEphos (11.1 mg, 5mol%), CsF (185 mg, 3 equiv) and Cs_2CO_3 (396 mg, 3 equiv) were placed into a one piece round bottom flask/condenser, sealed with a septum and purged with argon for 20-30 min. 1,2-Dichlorovinyl ether **110** (1.0 mL, 0.405 M, 1 equiv) in dioxane was added. The solution was vigorously stirred and brought to reflux. After 4.5 h, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and evaporated. The residue was characterized by crude NMR (data below).

SpinWorks 2.5: pOMedichlorophenol ether: pMeOPh(BOH)2: pFPhB(OH)2



file: Z:\Laina\lmgxw\lmgxwi_47\1\fid expt: <zg30>
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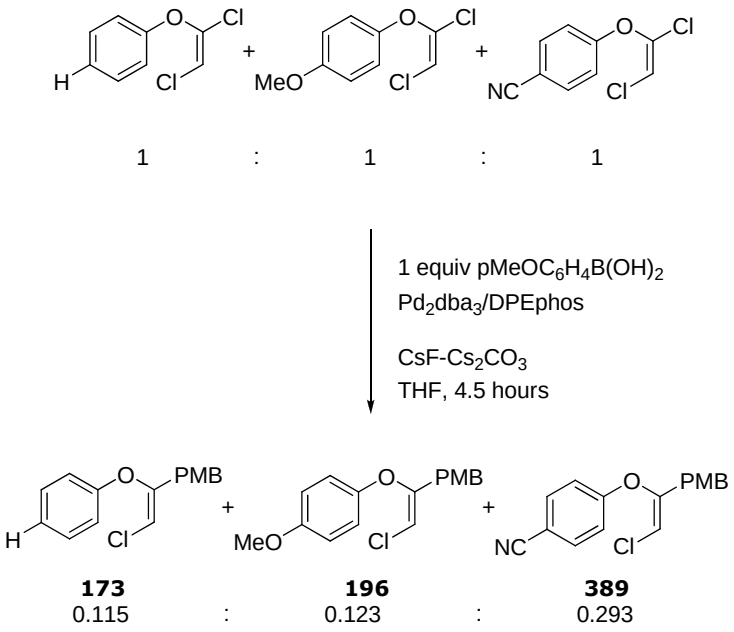
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

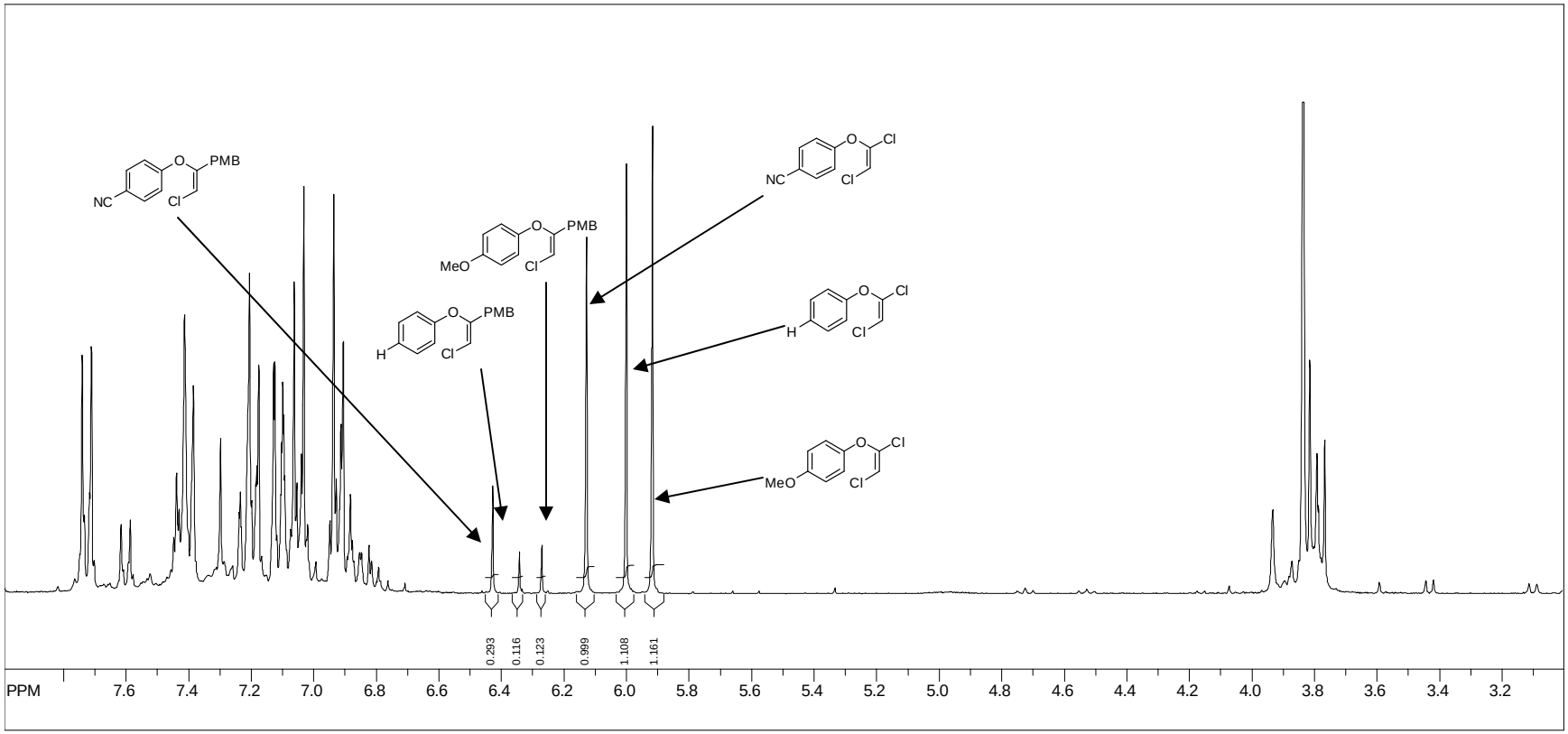
freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

C1 Arylation: varying the vinyl chloride



Pd_2dba_3 (4.5 mg, 4.9 μmol, 0.025 equiv), DPEphos (5.4 mg, 9.8 μmol, 0.05 equiv), CsF (89.6 mg, 0.59 mmol, 3 equiv), Cs_2CO_3 (192.2 mg, 0.59 mmol, 3 equiv) and 29.8 mg of $pMeOC_6H_4B(OH)_2$ (0.196 mmol, 1 equiv) were added to an oven-dried round bottom flask with an attached condenser and the headspace was purged with argon for 20 min. To this was added 0.49 mL of a 0.405M solution of **93** in dioxane (0.196 mmol), 0.49 mL of a 0.405M solution of **110** in dioxane (0.196 mmol) and 0.50 mL of a 0.393M solution of **129** in dioxane (0.196 mmol). The suspension was brought to reflux and monitored for consumption of the boronic acid. When complete, the reaction was cooled to room temperature and diluted with dichloromethane. The organic layer was separated, dried with magnesium sulphate, filtered and evaporated. The residue was analyzed by ^1H NMR (results below).

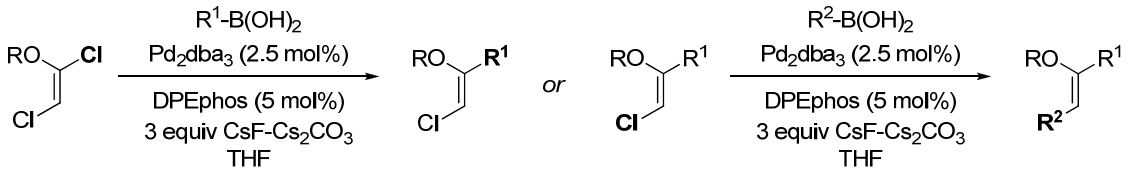
SpinWorks 2.5: pMeOPh(BOH)2:pCNPhO:pMeOPhO:PhO



file: Z:\Laina\lmgxvi\lmgxvi_44\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

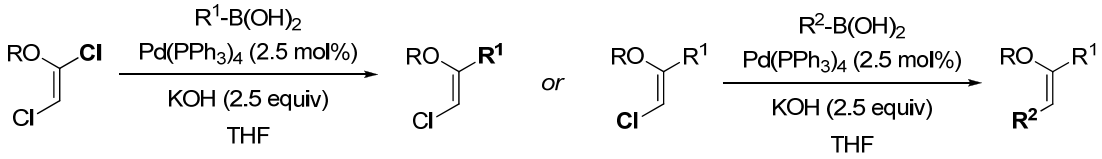
freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

General Procedure V: Pd/DPEphos catalyzed Suzuki cross-coupling



The dichloroethylene or chloroethylene (1 equiv), boronic acid (1.05 equiv for C^1 functionalization and 1.5 equiv for C^2 functionalization), Pd_2dba_3 (2.5 mol%), DPEphos (5 mol%), CsF (3 equiv), and Cs_2CO_3 (3 equiv) were placed into a one-piece round bottom flask/condenser, sealed with a septum and purged with argon for 20 – 30 min. THF was added (0.25 – 0.5 M with respect to dichloroethylene). The solution was vigorously stirred and brought to reflux. When complete (5 – 25 h), the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were washed with brine, dried with sodium sulfate, filtered, concentrated and purified via flash chromatography.

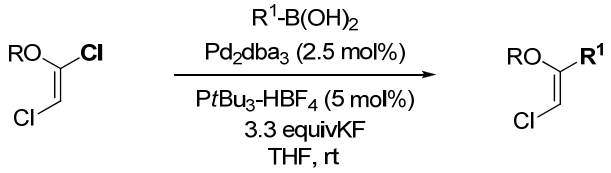
General Procedure VI: $Pd(PPh_3)_4$ catalyzed Suzuki cross-coupling



The dichloroethylene or chloroethylene (1 equiv), boronic acid (1.05 equiv for C^1 functionalization and 1.5 equiv for C^2 functionalization), and tetrakis(triphenylphosphine)palladium (0) (5 mol%) were placed into a a one-piece round bottom flask/condenser, sealed with a septum and purged with argon for 20 min. THF was added (0.25 – 0.5 M with respect to dichloroethylene). A degassed 1.0 M aqueous solution of KOH (2.1 equivalents) was added. The solution was vigorously stirred and brought to reflux. When complete (1 – 30 h), the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer

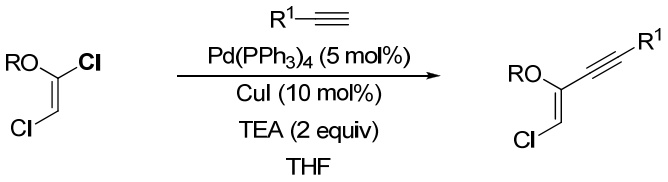
was extracted with dichloromethane once more. The combined organic layers were washed with brine, dried with sodium sulfate, filtered, concentrated and purified via flash chromatography.

General Procedure VII: Room temperature Suzuki cross-coupling



The dichloroethylene **93** (1 equiv), boronic acid (1.05 equiv), Pd_2dba_3 (2.5 mol%), $PtBu_3 \cdot HBF_4$ (5 mol%), and KF (3.3 equiv) %) were placed into an oven-dried one-piece round bottom flask/condenser, sealed with a septum and purged with argon for 20 min. THF was added (0.45 M with respect to dichloroethylene), and the reactions were stirred at room temperatures for the times indicated in Table 11. After the specified length of time passed, the reactions were diluted with ethyl acetate and filtered through silica. The solutions were concentrated and analyzed by ^1H NMR spectroscopy, and the conversions from **93** to the respective functionalized vinyl ethers are given in Table 11. The crude reaction materials were not purified. All reactions were performed on a 0.23 mmol scale with respect to **93**.

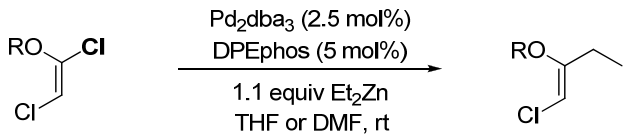
General Procedure VIII: Sonogashira cross-coupling



The $Pd(PPh_3)_4$ (5 mol%) and CuI (10 mol%) were placed into an oven-dried one-piece round bottom flask/condenser, sealed with a septum and purged with argon for 20 min. A 0.4 M solution of dichlorovinyl ether in THF was added, followed by TEA (2.0 equiv) and acetylene (1.1 equiv). The solution was stirred at room temperature for 12 – 14 h, after

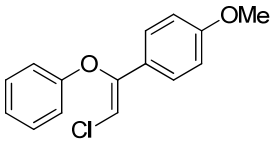
which it was diluted with ethyl acetate, filtered through silica, concentrated and purified via flash chromatography.

General Procedure IX: Negishi cross-coupling



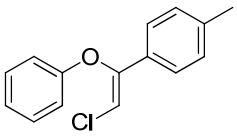
The Pd_2dba_3 (2.5 mol%) and DPEphos (5 mol%) were placed into an oven-dried one-piece round bottom flask/condenser, sealed with a septum and purged with argon for 20 min. A 0.2 M solution of dichlorovinyl ether in THF or DMF was added, followed by diethyl zinc (1.1 equiv) and the reaction was stirred at room temperature for 12 h. At the end of the reaction, water and diethyl ethere were added. The layers were separated and the aqueous layer was extracted once more with diethyl ether. The organic layers were combined, washed with brine, concentrated and purified by flash chromatography.

(Z)-1-(2-Chloro-1-(4-methoxyphenyl)vinyloxy)benzene (173)



Prepared according to General Procedure V in up to a 8.5 mmol scale.. The product was purified via flash chromatography using 14:1 hexanes: dichloromethane as an eluant to give 1.26 g of **173**.

(Z)-1-(2-Chloro-1-(4-methylphenyl)vinyloxy)benzene (193)



This compound is a clear oil and was prepared on a 5.4 mmol scale according to General Procedure V. The product was purified via flash chromatography using 14:1 hexanes: dichloromethane as an eluant to give 1.26 g of **193**.

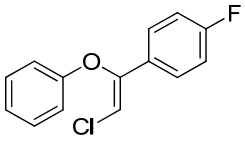
R_f = 0.32 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, 2H, *J* = 8Hz), 7.34-7.29 (m, 2H), 7.19 (d, 2H, *J* = 8Hz), 7.08-7.02 (m, 3H), 6.54 (s, 1H), 2.38 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 151.4, 139.3, 130.4, 129.6, 129.5, 125.6, 122.3, 116.0, 106.2, 21.3.

HRMS: Calculated for $C_{15}H_{13}ClO$: 244.0655: Found, 244.0659.

(Z)-1-(2-Chloro-1-(4-fluorophenyl)vinyloxy)benzene (194)



This compound was a colourless solid and was prepared according to General Procedure V to give 0.1067 g **194**. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant.

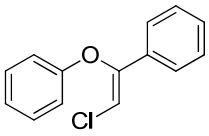
R_f = 0.5 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (m, 2H), 7.31 (m, 2H), 7.07-7.00 (m, 5H), 6.41 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 161.5, 155.9, 150.5, 129.7, 129.4, 122.5, 116.1, 115.9, 115.8, 106.8, 106.8.

HRMS: Calculated for $C_{14}H_{10}ClFO$: 248.0404, Found: 248.0394.

(*Z*)-1-(2-Chloro-1-phenoxyvinyl)benzene (195)

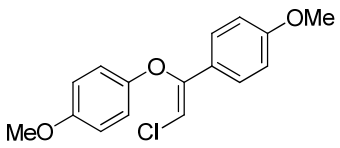


This compound is a viscous, colourless oil and was prepared on a 0.38 mmol scale according to General Procedure V. The product was purified via flash chromatography on TEA-treated silica using 9:1 hexanes: dichloromethane as an eluant to give 75.5 mg of **195**. This compound was only characterized by ^{1}H NMR, but was transformed into a known compound (2-phenylbenzofuran).

R_f = 0.57 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52-7.49 (m, 2H), 7.36- 7.25 (m, 5H), 7.04-7.00 (m, 3H), 6.47 (s, 1H).

(*Z*)-1-(2-Chloro-1-(4-methoxyphenoxy)vinyl)-4-methoxybenzene (196)



This compound is a clear oil, prepared on a 0.43 mmol scale according to General Procedure V and a 1.11 mmol scale according to General Procedure VI. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant.

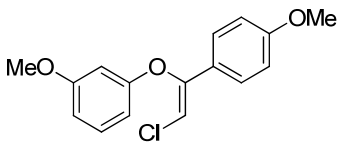
R_f = 0.41 (9:1 in hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, 2H), 6.93 (d, 2H), 6.85 (d, 2H), 6.80 (d, 2H), 6.26 (s, 1H), 3.80 (s, 3H), 3.75 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 154.9, 151.7, 127.3, 125.8, 117.0, 114.7, 114.2, 104.6, 55.6, 55.3.

We were unable to obtain satisfactory mass spectra of this compound, but it was converted to the known benzofuran natural product Corsifuran C (**305**).

(*Z*)-1-(2-Chloro-1-(3-methoxyphenoxy)vinyl)-4-methoxybenzene (197)



This compound was prepared on a 0.50 mmol scale according to General Procedure V and is a clear oil. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant.

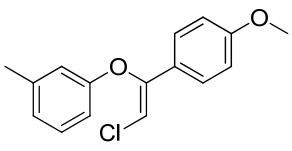
R_f = 0.37 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, 2H), 7.16 (dt, 1H), 6.86 (d, 2H), 6.61-6.56 (m, 3H), 6.33 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 160.4, 157.3, 151.1, 130.0, 127.0, 125.7, 114.2, 107.8, 108.2, 105.2, 102.4, 55.3 (×2).

We were unable to obtain satisfactory mass spectra for this compound, but it was successfully converted to the known benzofuran **346**.

(*Z*)-1-(2-Chloro-1-(3-methylphenoxy)vinyl)-4-methoxybenzene (198)



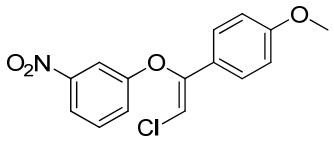
This compound was a colourless oil and was prepared on a 0.98 mmol scale according to General Procedure V. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant. The product is contaminated with a small amount of 4,4'-dimethoxybiphenyl **211**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (m, 2H), 7.16 (t, 1H), 6.89-6.79 (m, 5H), 6.34 (s, 1H), 3.81 (s, 3H), 2.33 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 156.2, 151.1, 139.8, 129.3, 127.8, 127.1, 125.8, 123.2, 116.7, 114.2, 112.8, 105.1, 55.3, 21.5.

HRMS was not obtained for this compound.

(*Z*)-1-(2-Chloro-1-(3-nitrophenoxy)vinyl)-4-methoxybenzene (199)



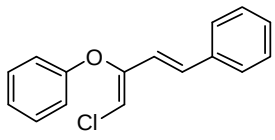
This compound was a viscous oil and was prepared on a 0.48 mmol scale according to General Procedure V. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90-7.79 (m, 2H), 7.47-7.31 (m, 4H), 6.88 (m, 2H), 6.41 (s, 1H), 3.81 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 156.7, 150.6, 130.3, 127.2, 127.0, 124.6, 122.2, 120.0, 117.3, 114.5, 111.0, 106.0, 55.4.

HRMS was not obtained for this compound.

1-((1*E*,3*Z*)-4-Chloro-3-phenoxybuta-1,3-dienyl)benzene (200)



This compound is a clear oil, prepared on a 0.43 mmol scale according to General Procedure Vand a 1.11 mmol scale according to General Procedure VI.

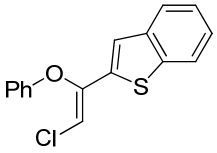
R_f = 0.49 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.27 (m, 7H), 7.12-7.06 (m, 3H), 6.83 (d, 1H, *J* = 16Hz), 6.72 (d, 1H, *J* = 16Hz), 6.22 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.5, 151.1, 136.0, 131.1, 129.7, 128.8, 128.5, 126.9, 122.3, 120.3, 115.2, 110.6.

HRMS: Calculated for $C_{16}H_{13}ClO$: 256.0655, Found: 256.0665.

(Z)-2-(2-Chloro-1-phenoxyvinyl)benzo[b]thiophene (201)

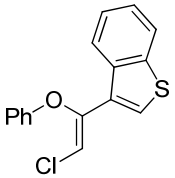


This compound is a viscous, colourless oil and was prepared on a 1.65 mmol scale according to General Procedure VI. The product was purified via flash chromatography on TEA-treated silica using 14:1 hexanes: dichloromethane as an eluant to give 0.50 g of **201**. We were unable to obtain this compound in high purity, but the ^{1}H and ^{13}C NMR spectra are included in Appendix 1.

R_f = 0.65 (9:1 hexanes: diethyl ether).

HRMS: Calculated for $C_{16}H_{11}ClOS$: 286.0219, Found: 286.0227.

(Z)-3-(2-Chloro-1-phenoxyvinyl)benzo[b]thiophene (202)



This compound is a viscous, colourless oil and was prepared on a 1.59 mmol scale according to General Procedure VI. The product was purified via flash chromatography on TEA-treated silica using 14:1 hexanes: dichloromethane as an eluant to give 0.31 g of **202**.

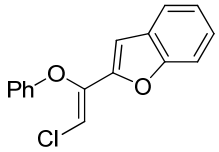
R_f = 0.53 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, 1H, *J* = 8Hz), 7.86 (d, 1H, *J* = 8Hz), 7.62 (s, 1H), 7.51-7.38 (m, 2H), 7.30-7.22 (m, 2H), 7.07 (m, 2H), 7.00 (m, 1H), 6.44 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8, 147.9, 140.4, 136.2, 129.7, 129.6, 127.2, 125.0, 123.1, 123.0, 122.7, 116.3, 107.8.

HRMS: Calculated for $C_{16}H_{11}ClOS$: 286.0219, Found: 286.0207.

(Z)-2-(2-Chloro-1-phenoxyvinyl)benzofuran (203)



This compound is a viscous, colourless oil and was prepared on a 1.62 mmol scale according to General Procedure VI. The product was purified via flash chromatography on TEA-treated silica using 14:1 hexanes: dichloromethane as an eluant to give 175.8 mg of **203**.

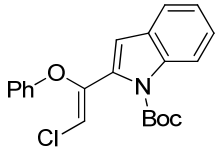
R_f = 0.28 (14:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70-7.59 (m, 1H), 7.51 (m, 2H), 7.41-7.33 (m, 4H), 7.28-7.22 (m, 1H), 7.13-7.08 (m, 3H), 6.90 (s, 1H), 6.71 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 155.0, 149.5, 143.2, 129.8, 128.6, 128.1, 125.5, 125.1, 123.4, 123.4, 122.8, 121.6, 121.4, 115.3, 111.3, 111.2, 109.7, 105.2, 103.7.

HRMS: Calculated for $C_{16}H_{11}ClO_2$: 270.0448, Found: 270.0447.

(Z)-*tert*-Butyl 2-(2-chloro-1-phenyloxyvinyl)-1*H*-indole-1-carbonxylate (204)



This compound is a viscous, colourless oil and was prepared on a 2.75 mmol scale according to General Procedure VI. The product was purified via flash chromatography on TEA-treated silica using 4:1 hexanes: dichloromethane as an eluant to give 524.5 mg of **204**.

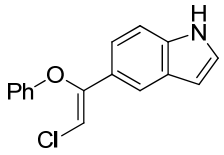
$\mathbf{R_f}$ = 0.36 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, 1H, *J* = 8Hz), 7.56 (d, 1H, *J* = 7.5Hz), 7.41-7.34 (m, 2H), 7.25 (m, 3H), 7.03 (m, 3H), 6.80 (s, 1H), 6.28 (s, 1H), 1.78 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 149.4, 146.2, 137.4, 131.3, 129.4, 128.0, 125.6, 123.2, 123.1, 121.0, 117.2, 115.4 (x2), 114.2, 108.0, 84.4, 28.0.

HRMS: Calculated for $C_{21}H_{20}ClNNaO_3$: 392.1024, Found: 392.0989.

(Z)-5-(2-Chloro-1-phenoxyvinyl)-1*H*-indole (205)



This compound is a viscous, colourless oil and was prepared on a 0.53 mmol scale according to General Procedure VI. The product was purified via flash chromatography on TEA-treated silica using 4:1 hexanes: ethyl acetate as an eluant to give 65.7 mg of **205**.

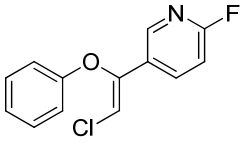
$\mathbf{R_f}$ = 0.15 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.80 (s, 1H), 7.35-7.23 (m, 4H), 7.20 (t, 1H, *J* = 2.8Hz), 7.07 (m, 2H), 6.98 (m, 1H), 6.54 (br t, 1H, *J* = 2.4Hz), 6.39 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 152.6, 136.2, 129.6, 127.9, 125.2, 125.2, 122.1, 120.0, 118.8, 116.1, 111.4, 104.6, 103.3.

HRMS was not obtained for this compound.

(*Z*)-5-(2-Chloro-1-phenoxyvinyl)-2-fluoropyridine (206)



This compound is a clear oil and was prepared on a 0.53 mmol scale according to General Procedure VI.

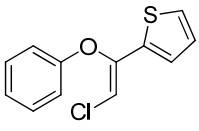
R_f = 0.10 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, 1H, *J* = 2Hz), 7.85 (ddt, 1H, *J* = 1Hz, 2Hz, 7Hz), 7.32-7.26 (m, 2H), 7.04 (dt, 1H, *J* = 1Hz, 7Hz), 6.97 (dd, 1H, *J* = 1Hz, 8Hz), 6.90 (dd, 1H, *J* = 3Hz, 8Hz), 6.46 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 162.1, 155.4, 148.0, 145.3, 145.1, 138.4, 138.3, 129.9, 127.6, 127.5, 123.0, 116.0, 110.1, 109.6, 108.41, 108.39.

HRMS: Calculated for $C_{13}H_9ClFNO$: 249.0357, Found: 249.0357.

(*Z*)-2-(2-Chloro-1-phenoxyvinyl)thiophene (207)



This compound was prepared on a 0.53 mmol scale according to General Procedure VI. However, it decomposes at room temperature over several h and thus we have been unable to obtain satisfactory ^{13}C NMR spectra.

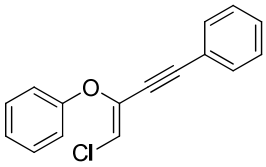
R_f = 0.56 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.24 (m, 3H), 7.13 (m, 1H), 7.07-7.02 (m, 3H), 6.96 (m, 1H), 6.42 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1, 146.7, 136.4, 129.7, 127.6, 126.2, 125.9, 122.6, 115.8, 106.1 (also contains a small amount of decomposed material).

HRMS: Calculated for $C_{12}H_9ClOS$: 236.0063, Found: 236.0083.

(*Z*)-1-(4-Chloro-3-phenoxybut-3-en-1-ynyl)benzene (214)



This compound is a clear oil and was prepared on a 4.95 mmol scale according to General Procedure VIII.

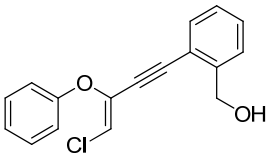
R_f = 0.48 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.26 (m, 7H), 7.18-7.13 (m, 3H), 6.21 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 136.5, 131.5, 129.4, 129.2, 128.4, 123.8, 121.4, 118.4, 111.3, 94.0, 81.3.

HRMS: Calculated for $C_{16}H_{11}ClO$: 254.0498, Found: 254.0492.

(*Z*)-(2-(4-Chloro-3-phenoxybut-3-en-1-ynyl)phenyl)methanol (215)



This compound is a viscous, colourless oil and was prepared on a 0.8 mmol scale according to General Procedure VIII. The product was purified via flash chromatography on TEA-treated silica using hexanes as an eluant to give 171.8 mg of **215**.

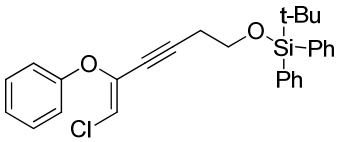
R_f = 0.33 (hexanes).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.32 (m, 5H), 7.28-7.16 (m, 4H), 6.22 (s, 1H), 4.39 (s, 2H), 1.57 (br s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 142.8, 136.5, 132.1, 129.64, 129.56, 127.4, 127.2, 124.2, 119.3, 118.8, 111.2, 91.7, 85.7, 63.2.

HRMS: Calculated for $C_{17}H_{13}ClO_2$: 284.0604, Found: 284.0601.

(*Z*)-*tert*-Butyl(6-chloro-5-phenoxyhex-5-en-3-ynyloxy)diphenylsilane (216)



O-*tert*-Butyldiphenylsilyl-3-butyn-1-ol was synthesized from 3-butyn-1-ol using a literature procedure.[560] 3-Butyn-1-ol, *t*butyldiphenylsilyl chloride (1.1 equiv) and imidazole (1.1 equiv) were combined in dichloromethane (0.6 mL per mmol of 3-butyn-1-ol) and stirred at room temperature overnight. After approximately 12 hours, the reaction was diluted with diethylether and washed with saturated aqueous NaCl. The organic layer was dried with magnesium sulfate, filtered and concentrated. The crude oil was purified by flash chromatography prior to use in Sonogashira cross-coupling.

Compound **216** is a colourless oil and was prepared according to General Procedure VIII.

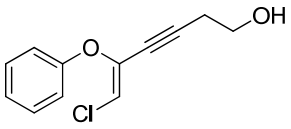
R_f = 0.61 (9:1 hexane: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72-7.67 (m, 4H), 7.51-7.40 (m, 6H), 7.34-7.28 (m, 2H), 7.12-7.05 (m, 3H), 6.04 (s, 1H), 3.71 (t, 2H), 2.51 (t, 2H), 1.09 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 136.2, 135.63, 135.60, 133.5, 129.8, 129.3, 127.8, 123.5, 117.9, 111.0, 92.8, 74.0, 61.8, 26.8, 23.4, 19.2.

We were unable to obtain a satisfactory mass spectrum of this compound.

(*Z*)-6-Chloro-5-Phenoxyhex-5-en-3-yn-1-ol (217)



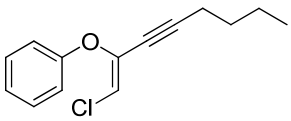
This compound is a colourless oil and according to General Procedure VIII. The compound decomposed on standing at room temperature, thus we could not obtain satisfactory HRMS.

R_f = 0.17 (9:1 hexane: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.32 (m, 2H), 7.17-7.12 (m, 1H), 7.10-7.05 (m, 2H), 6.04 (s, 1H), 3.56 (t, 2H), 2.47 (t, 2H), 1.61 (br s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 136.3, 129.3, 123.9, 118.5, 110.5, 92.4, 74.7, 60.5, 23.6.

(*Z*)-1-(1-Chlorooct-1-en-3-yn-2-yloxy)benzene (218)



This compound is a colourless oil and was prepared according to General Procedure VIII.

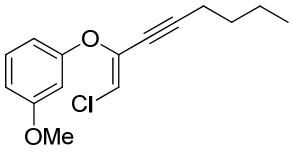
R_f = 0.63 (9:1 hexane: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.31 (m, 2H), 7,15-7.06 (m, 3H), 6.01 (s, 1H), 2.22 (t, 2H), 1.44-1.34 (m, 2H), 1.30-1.18 (m, 2H), 0.84 (t, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 136.5, 129.2, 123.5, 118.3, 109.9, 95.9, 72.9, 30.0, 21.7, 18.8, 13.5.

We were unable to obtain a satisfactory mass spectrum of this compound.

(*Z*)-1-(1-Chlorooct-1-en-2-yn-2-yloxy)-3-methoxybenzene (219)



This compound is a colourless oil and was prepared on 0.60 mmol scale according to General Procedure VIII.

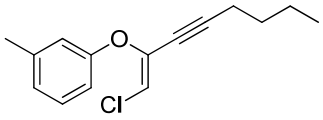
R_f = 0.56 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (t, 1H), 6.70-6.63 (m, 3H), 6.01 (s, 1H), 3.82 (s, 3H), 2.24 (t, 2H), 1.46-1.36 (m, 2H), 1.33-1.20 (m, 2H), 0.86 (t, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.6, 156.3, 136.3, 129.6, 110.6, 109.3, 104.1, 95.7, 73.0, 55.4, 30.0, 21.7, 18.9, 13.5.

HRMS: Calculated for $C_{15}H_{17}ClO_2$: 264.0917, Found: 264.0916.

(*Z*)-1-(1-Chlorooct-1-en-2-yn-2-yloxy)-3-methylbenzene (220)



This compound is a clear oil and was prepared on a 1.0 mmol scale according to General Procedure VIII. The product was purified via flash chromatography on TEA-treated silica using a gradient of hexanes to 20:1 hexanes: ethyl acetate as an eluant to give 153.4 mg of **220**.

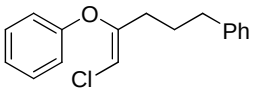
R_f = 0.39 (hexanes).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (t, 1H, *J* = 8Hz), 6.96-6.88 (m, 3H), 6.01 (s, 1H), 2.39 (s, 3H), 2.24 (t, 2H, *J* = 7Hz), 1.45-1.36 (m, 2H), 1.32-1.22 (m, 2H), 0.86 (t, 3H, *J* = 7Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 139.3, 136.6, 128.9, 124.3, 118.9, 115.2, 109.8, 95.7, 73.1, 30.0, 21.7, 21.4, 18.9, 13.5.

HRMS was not obtained for this compound.

(Z)-1-(5-Chloro-4-phenoxypent-4-enyl)benzene (221)



An oven-dried one piece round bottom flask/condenser was sealed with a septum and purged with argon for 20-30 min. Allyl benzene (0.64 mL, 4.8 mmol, 1.2 equiv) was added, followed by 9.6 mL of a 0.5M solution of 9-BBN in THF (4.8 mmol, 1.2 equiv) and the mixture was stirred at room temperature. After one hour, Pd_2dba_3 (91.5 mg, 5 mol%), Xantphos (115.7 mg, 10mol%), CsF (1.82 g, 12 mmol, 3 equiv) and Cs_2CO_3 (3.91 g, 12 mmol, 3 equiv) were added, followed by 16 mL of THF. The suspension was brought to reflux and was stirred at that temperature for 12 h. When complete, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated onto silica gel. The product was purified via flash chromatography using 14:1 hexanes: diethyl ether to give 900 mg of **221** as a colourless liquid.

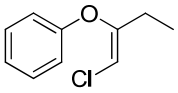
R_f = 0.71 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.32 (m, 4H), 7.30-7.26 (m, 3H), 7.17-7.10 (m, 1H), 7.08-7.02 (m, 2H), 5.81 (m, 1H), 2.70 (t, 2H, *J* = 7 Hz), 2.33 (t, 2H, *J* = 7Hz), 1.90 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 152.9, 141.5, 129.7, 128.5, 126.0, 122.7, 116.7, 104.3, 35.0, 31.0, 27.9.

HRMS Calculated for $C_{17}H_{17}ClO$: 272.0968, Found: 272.0956.

(Z)-1-(1-Chlorobut-1-en-2-yloxy)benzene (222)



This compound is a colourless oil and was prepared on a 0.67 mmol scale according to General Procedure IX. The product was purified via flash chromatography on TEA-treated silica using hexanes as an eluant to give 83.9 mg of **222**.

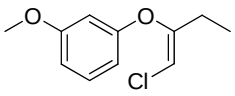
R_f = 0.56 (hexanes).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.31 (m, 2H), 7.11-7.05 (m, 1H), 7.03-6.99 (m, 2H), 5.77 (t, 1H, J = 1.2Hz), 2.28 (dd, 2H, J^1 = 7.5 Hz, J^2 = 1.2Hz), 1.11 (t, 3H, J = 7.5Hz)

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 154.7, 129.6, 122.6, 116.7, 103.4, 24.9, 11.2.

HRMS was not obtained for this compound.

(Z)-1-(1-Chlorobut-1-en-2-yloxy)-3-methoxybenzene (223)

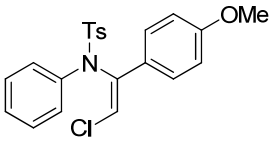


This compound is a colourless oil and was prepared on a 0.56 mmol scale according to General Procedure IX. The product was purified via flash chromatography on TEA-treated silica using hexanes as an eluant to give 117.7 mg of **223**.

R_f = 0.31 (hexanes). This compound was characterized by ^{1}H NMR only.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (m, 1H), 6.64-6.54 (m, 3H), 5.75 (t, 1H, J = 1.1Hz), 3.81 (s, 3H), 2.26 (dd, 2H, J^1 = 7.5Hz, J^2 = 1.1Hz), 1.09 (t, 3H, J = 7.5Hz).

(Z)-N-(2-Chloro-1-(4-methoxyphenyl)vinyl)-4-methyl-*N*-phenylbenzenesulfonamide (225)



This compound was prepared on a 0.22 mmol scale according to General Procedure VII. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 44.3 mg of **225**.

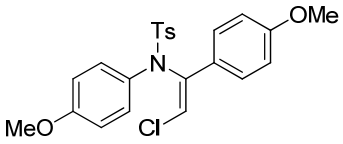
R_f = 0.15 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (m, 2H), 7.50-7.41 (m, 4H), 7.29-7.18 (m, 6H), .6.87 (m, 2H), 6.58 (s, 1H), 3.83 (s, 3H), 2.41 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 143.8, 141.8, 139.6, 137.3, 129.13, 129.09, 128.6, 128.5, 128.2, 126.7, 125.9, 118.0, 114.1, 55.4, 21.6.

HRMS: Calculated for $C_{22}H_{20}ClNO_3S$: 413.0852, Found: 413.0845.

(Z)-N-(2-Chloro-1-(4-methoxylphenyl)vinyl)*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide (226)



This compound was prepared on a 0.24 mmol scale according to General Procedure VII. The product was purified via flash chromatography using 6:1 hexanes: ethyl acetate as an eluant to give 65.4 mg of **226**.

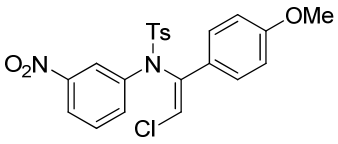
R_f = 0.18 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7,62 (m, 2H), 7.48 (m, 2H),7.33-7.17 (m, 6H), 6.87 (m, 2H), 6.75 (m, 2H), 6.48 (s, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 2.41 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 158.8, 143.5, 142.3, 137.3, 131.8, 129.7, 129.0, 128.8, 128.5, 128.2, 117.1, 114.2, 114.0, 55.3 (2), 21.6.

HRMS was not acquired for this sample.

(Z)-N-(2-Chloro-1-(4-methoxylphenyl)vinyl)*N*-(3-nitrophenyl)-4-methylbenzenesulfonamide (227)

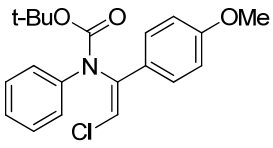


This compound was prepared on a 0.22 mmol scale according to General Procedure VII. The product was purified via flash chromatography using 6:1 hexanes: ethyl acetate as an eluant to give 78.3 mg of **227**. This compound was characterized by ^{1}H NMR only.

R_f = 0.19 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (m, 1H), 8.00 (m, 1H), 7.80-7.77 (m, 3H), 7.48-7.40 (m, 3H), 7.26 (m, 2H), 6.89 (m, 2H), 6.70 (s, 1H), 3.83 (s, 3H), 2.42 (s, 3H).

(Z)-tert-Butyl 2-chloro-1-(4-methoxyphenyl)vinyl(phenyl)carbamate (228)



This compound is a colourless oil and was prepared according to General Procedure VI.

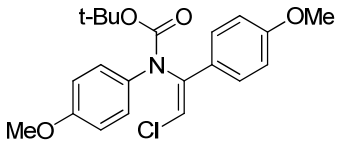
R_f = 0.29 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 4H), 7.29 (m, 3H), 7.11 (m, 1H), 6.88 (d, 2H), 6.45 (s, 1H), 3.81 (s, 3H), 1.43 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 152.9, 141.8, 140.4, 128.6, 127.1, 127.4, 125.1, 124.4, 114.3, 114.2, 81.5, 55.3, 20.1.

HRMS: Calculated for $C_{20}H_{22}ClNO_3$: 359.1288, Found: 359.1300.

(Z)-tert-Butyl 2-chloro-1-(4-methoxyphenyl)vinyl(4-methylphenyl)carbamate (229)



This compound is a colourless oil and was prepared according to General Procedure VI.

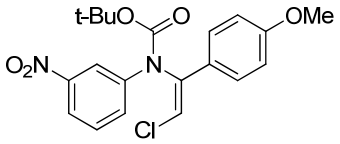
R_f = 0.32 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 2H), 7.27 (m, 2H), 6.87 (m, 2H), 6.81 (m, 2H), 6.40 (s, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 1.43 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 157.1, 153.2, 142.0, 133.4, 128.7, 127.4, 126.2, 114.2, 114.1, 113.8, 55.4, 55.3, 21.8.

ESI-HRMS: Calculated for $C_{21}H_{24}ClNO_4Na$: 412.1286, Found: 412.1287.

(Z)-tert-Butyl 2-chloro-1-(4-methoxyphenyl)vinyl(3-nitrophenyl)carbamate (230)



This compound is a pale yellow oil and was prepared according to General Procedure VI.

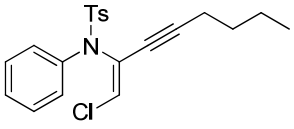
R_f = 0.23 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (t, 1H, *J* = 2.5 Hz), 7.96 (ddd, 1H, *J* = 1Hz, 2.5Hz, 8Hz), 7.72 (dd, 1H, *J* = 1Hz, 8Hz), 7.44 (t, 1H), 7.35 (d, 2H), 6.89 (d, 2H), 6.54 (s, 1H), 3.82 (s, 3H), 1.42 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 152.4, 148.5, 141.7, 141.0, 129.3, 129.3, 127.8, 127.1, 119.5, 118.5, 115.2, 114.4, 82.6, 55.4, 28.0.

HRMS: Calculated for $C_{20}H_{21}ClN_2O_5$: 404.1139, Found: 404.1134.

(Z)-*N*-(1-Chlorooct-1-en-3-yn-2-yl)-4-methyl-*N*-phenylbenzenesulfonamide (231)



This compound is a clear oil and was prepared on a 0.22 mmol scale according to General Procedure VIII. The product was purified via flash chromatography on TEA-treated silica using 9:1 hexanes: dichloromethane as an eluant to give 42.8 mg of **231**.

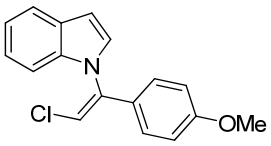
R_f = 0.30 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (m, 2H), 7.42-7.29 (m, 5H), 7.22 (m, 2H), 6.53 (s, 1H), 2.42 (s, 3H), 2.25 (t, 2H, *J* = 6.5 Hz), 1.49-1.33 (m, 4H), 0.92 (t, 3H, *J* = 7.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 139.3, 136.3, 129.0, 128.9, 128.5, 128.3, 128.2, 128.0, 124.8, 94.6, 75.7, 30.1, 22.0, 21.6, 19.1, 13.6.

No HRMS was acquired for this compound.

(Z)-1-(2-Chloro-1-(4-methoxyphenyl)vinyl)-1*H*-indole (232)



This compound was a colourless solid and was prepared on a 0.57 mmol scale according to General Procedure VI. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 8.4 mg **232**

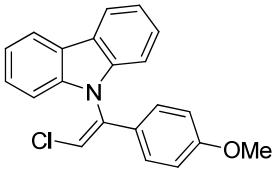
R_f = 0.38 (19:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (m, 2H), 7.24-7.17 (m, 3H), 7.10 (m, 2H), 7.01 (m, 1H), 6.87 (m, 2H), 6.74 (m, 1H), 6.64 (s, 1H), 3.82 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 139.3, 135.8, 128.6, 128.4, 128.1, 127.7, 122.2, 120.9, 120.4, 114.3, 111.9, 111.5, 103.7, 55.4.

HRMS: Calculated for $C_{17}H_{14}ClNO$: 283.0764, Found: 283.0762.

(Z)-9-(2-Chloro-1-(4-methoxyphenyl)vinyl)-9*H*-carbazole (233)



This compound was a colourless solid and was prepared on a 0.5 mmol scale according to General Procedure VI. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 25.0 mg **233**.

R_f = 0.33 (9:1 hexanes: ethyl acetate).

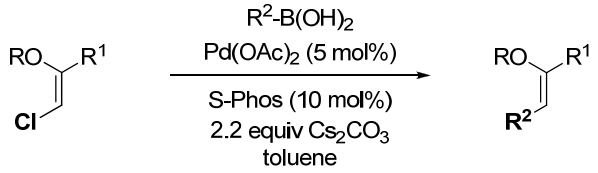
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (m, 2H), 7.43 (m, 2H), 7.33 (m, 2H), 7.19-7.12 (m, 4H), 6.95 (s, 1H), 6.83 (m, 2H), 3.81 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.6, 139.5, 137.3, 127.4, 127.2, 126.0, 123.6, 120.3, 120.1, 114.8, 114.4, 111.0, 55.3.

HRMS: Calculated for $C_{21}H_{16}ClNO$: 333.0920, Found: 333.0921.

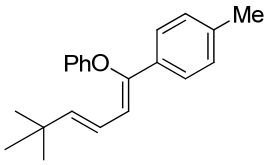
4.4 Compounds from Section 2.4.2 – Trisubstituted Alkenes

General Procedure X: Pd/S-Phos Catalyzed Suzuki Coupling



The boronic acid (1.5 equiv), $Pd(OAc)_2$ (5 mol%), SPhos (10 mol%) and Cs_2CO_3 (2.2 equiv) were placed in a one-piece round bottom flask/condenser, sealed with a septum and purged with argon for 20 min. A 0.2M solution of the vinyl chloride in toluene was added and the suspension was refluxed overnight. When complete, the reaction was cooled, partitioned between dichloromethane and water. The layers were separated, and the water layer extracted twice more with dichloromethane. The organic layers were combined, dried with magnesium sulphate, filtered and concentrated onto silica gel, which was applied to a silica gel column and eluted with an appropriate solvent.

1-((1*Z*,3*E*)-5,5-dimethyl-1-phenoxyhexa-1,3-dienyl-4-methylbenzene (234)



This compound is a colourless solid and was prepared according to General Procedure X on a 0.26 mmol scale. The product was purified via flash chromatography using 14:1 hexanes: dichloromethane to give 66.7 mg of **234**.

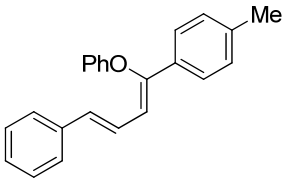
R_f = 0.25 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, 2H), 7.29 (t, 2H), 7.14 (d, 2H), 7.06-6.97 (m, 3H), 6.48-6.34 (m, 2H), 5.96 (d, 1H), 2.36 (s, 3H), 1.08 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 147.7, 147.0, 137.9, 132.5, 129.5, 129.3, 125.3, 121.5, 119.2, 116.9, 115.9, 33.6, 29.6, 21.2.

HRMS: Calculated for $C_{21}H_{24}O$: 292.1827, Found: 292.1827.

1-Methyl-4-((1*Z*,3*E*)-1-phenoxy-4-1,3-dienyl)benzene (235)



This compound is a colourless solid and was prepared according to General Procedure X on a 0.26 mmol scale. The product was purified via flash chromatography using 14:1 hexanes: dichloromethane to give 53.1 mg of **235**.

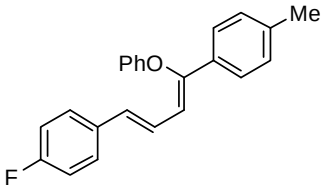
R_f = 0.10 (14:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.43 (m, 2H), 7.36-7.14 (m, 8H), 7.09-6.98 (m, 3H), 6.78-6.66 (m, 2H), 2.37 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 149.8, 138.4, 137.5, 132.7, 132.0, 129.7, 129.4, 128.6, 127.6, 126.5, 125.5, 123.2, 121.8, 116.6, 115.2, 21.3.

HRMS: Calculated for $C_{23}H_{20}O$: 312.1514, Found: 312.1517.

1-((1*Z*,3*E*)-4-(4-fluorophenyl)-1-phenoxybuta-1,3-dienyl)-4-methylbenzene (236)



This compound is a colourless solid and was prepared according to General Procedure X on a 0.26 mmol scale. The product was purified via flash chromatography using 14:1 hexanes: dichloromethane to give 12.7 mg of **236**.

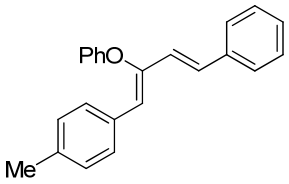
$\mathbf{R_f}$ = 0.10 (14:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, 2H), 7.38 (m, 2H), 7.31-7.25 (m, 3H), 7.15 (d, 2H), 7.09-6.97 (m, 6H), 6.71-6.62 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 160.7, 157.9, 149.8, 138.9, 133.7, 132.0, 131.4, 129.7, 129.4, 128.0, 127.9, 125.5, 122.89, 122.86, 121.8, 116.42, 116.41, 115.9, 115.7, 115.4, 21.3.

HRMS: Calculated for $C_{23}H_{19}FO$: 330.1420, Found: 330.1427.

1-((1*E*,3*Z*)-3-phenoxy-4-*p*-tolylbuta-1,3-dienyl)benzene (237)



This compound is a pale yellow solid and was prepared according to General Procedure V on a 0.38 mmole scale. The product was purified via flash chromatography using 14:1 hexanes: dichloromethane as an eluant to give 64.7 mg of **237**.

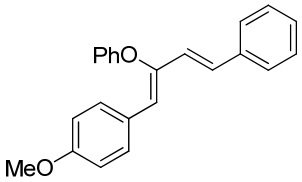
$\mathbf{R_f}$ = 0.14 (14:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, 2H, *J* = 8Hz), 7.42 (m, 2H), 7.38-7.24 (m, 5H), 7.16-7.10 (m, 4H), 7.03 (m, 1H), 6.87 (d, 1H, *J* = 16Hz), 6.71 (d, 1H, *J* = 16Hz), 6.40 (s, 1H), 2.34 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.5, 148.5, 137.6, 136.7, 131.8, 130.1, 129.7, 129.3, 129.1, 128.7, 127.8, 126.7, 124.6, 121.8, 121.3, 115.4, 21.3.

HRMS: Calculated for $C_{23}H_{20}O$: 312.1514, Found: 312.1514.

1-Methoxy-4-((1*Z*,3*E*)-2-phenoxy-4-phenylbuta-1,3-dienyl)benzene (238)



This compound is a pale yellow solid and was prepared according to General Procedure V on a 0.38 mmole scale. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 100.4 mg of **238**.

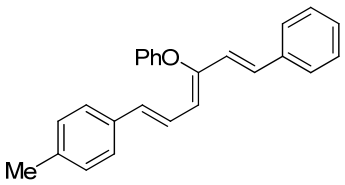
R_f = 0.38 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, 2H, *J* = 8Hz), 7.43-7.23 (m, 7H), 7.14 (d, 2H, *J* = 8Hz), 7.03 (t, 1H), 6.86 (m, 3H), 6.68 (d, 1H, *J* = 16Hz), 6.37 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 156.5, 147.5, 136.8, 130.6, 129.8, 129.5, 128.6, 127.7, 127.4, 126.6, 124.6, 121.8, 120.9, 115.3, 114.1, 55.2.

HRMS: Calculated for $C_{23}H_{20}O_2$ 328.1463, Found: 328.1465.

1-((1*E*,3*Z*,5*E*)-3-phenoxy-6-*p*-tolylhexa-1,3,5-trienyl)benzene (239)



This compound is a colourless solid and was prepared according to General Procedure V on a 0.21 mmole scale. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 27.7 mg of **239**.

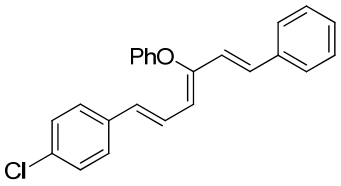
R_f = 0.50 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.17 (m, 13H), 7.09 (m, 2H), 7.04-6.98 (m, 2H), 6.81-6.62 (m, 3H), 6.28 (d, 1H, *J* = 11Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 149.7, 137.3, 136.6, 133.3, 130.3, 129.7, 128.6, 128.6, 127.9, 127.8, 126.7, 123.3, 122.9, 122.1, 121.8, 115.3.

HRMS: Calculated for $C_{25}H_{22}O$: 338.1671, Found: 338.1672.

1-((1*E*,3*Z*,5*E*)-6-(4-Chlorophenyl)-3-phenoxy-1,3,5-trienyl)benzene (240)



This compounds is a pale yellow solid and was prepared according to General Procedure V on a 0.19 mmole scale. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant to give 44.6 mg of **240**.

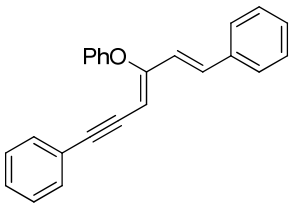
R_f = 0.14 (hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.25 (m, 12H), 7.13-6.98 (m, 4H), 6.83-6.70 (m, 2H), 6.62 (d, 1H, *J* = 16Hz), 6.29 (d, 1H, *J* = 11Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 150.2, 136.5, 135.8, 133.3, 131.8, 130.7, 129.8, 128.8, 128.7, 128.1, 127.7, 126.8, 123.5, 123.2, 121.9, 121.7, 115.3.

HRMS: Calculated for $C_{24}H_{19}ClO$: 358.1124, Found: 358.1126.

(1*E*,3*Z*)-3-phenoxy-1,6-diphenylhexa-1,3-dien-5-yn (241)



This compound is a pale yellow solid and was prepared according to General Procedure V on a 0.19 mmol scale. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant to give 13.2 mg of **241**.

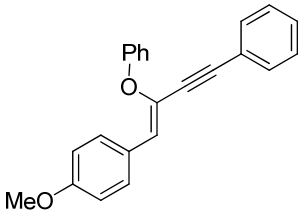
$\mathbf{R_f}$ = 0.10 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.41-7.06 (m, 14H), 7.02 (d, 1H, *J* = 16Hz), 6.84 (d, 1H, *J* = 16Hz), 5.70 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 157.3, 136.1, 132.0, 131.3, 129.5, 128.8, 128.5, 128.1, 127.1, 123.3, 123.0, 122.2, 116.4, 99.7, 98.9, 85.5

HRMS: Calculated for $C_{24}H_{18}O$: 322.1358, Found: 322.1373.

(*Z*)-1-Methoxy-4-(2-phenoxy-4-phenylbut-1-en-3-ynyl)benzene (242)



This compound is a colourless solid and was prepared on a 0.28 mmol scale according to General Procedure V. The product was purified via flash chromatography using 20:1 hexanes: ethyl acetate to give 75.9 mg of **242**.

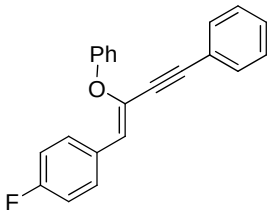
$\mathbf{R_f}$ = 0.43 (20:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (m, 2H), 7.45-7.38 (m, 2H), 7.33-7.25 (m, 7H), 7.17 (m, 2H), 6.92 (m, 2H), 6.45 (s, 1H), 3.84 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 155.6, 132.8, 131.5, 130.7, 129.4, 128.6, 128.3, 127.5, 123.3, 122.3, 121.9, 118.3, 114.1, 91.6, 85.7, 55.3.

HRMS was not acquired for this compound.

(*Z*)-1-(4-(4-Fluorophenyl)-3-phenoxybut-3-en-1-ynyl)benzene (243)



This compound is a colourless solid and was prepared on a 0.28 mmol scale according to General Procedure V. The product was purified via flash chromatography using 20:1 hexanes: ethyl acetate to give 68.7 mg of 243.

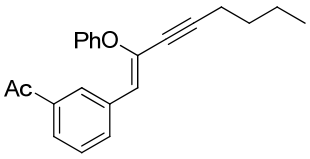
R_f = 0.60 (20:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (m, 2H), 7.42 (m, 2H), 7.35-7.23 (m, 7H), 7.22-7.16 (m, 1H), 7.06 (m, 2H), 6.41 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 160.4, 155.4, 134.34, 134.31, 131.5, 131.0, 130.9, 129.4, 128.8, 128.4, 123.7, 122.1, 120.3, 118.7, 115.7, 115.4, 92.3, 85.2.

No HRMS was acquired for this compound.

(*Z*)-1-(3-(2-Phenoxyoct-1-en-3-ynyl)phenyl)ethanone (245)



This compound is a colourless solid and was prepared according to General Procedure V on a 85 μmol scale. The product was purified via flash chromatography using 10:1 hexanes: ethyl acetate to give 11.3 mg of **245**.

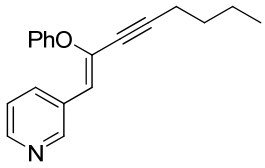
R_f = 0.19 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (m, 1H), 7.84 (m, 1H), 7.78 (m, 1H), 7.40-7.31 (m, 3H), 7.14-7.08 (m, 3H), 6.23 (s, 1H), 2.54 (s, 3H), 2.23 (t, 2H, *J* = 6.5 Hz), 1.42-1.32 (m, 2H), 1.29-1.17 (m, 2H), 0.82 (t, 3H, *J* = 7.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 155.3, 137.3, 135.8, 135.2, 133.2, 129.3, 129.0, 128.7, 126.8, 123.4, 118.9, 118.5, 94.4, 76.3, 30.1, 26.6, 21.7, 18.9, 13.5.

HRMS: Calculated for $C_{22}H_{22}O_2$: 318.1620, Found: 318.1625.

(*Z*)-3-(2-Phenoxyoct-1-en-3-ynyl)pyridine (246)



This compound is a colourless oil and was prepared according to General Procedure VI on 0.28 mmol scale. The product was purified via flash chromatography on TEA-treated silica using 4:1 hexanes: ethyl acetate as an eluant.

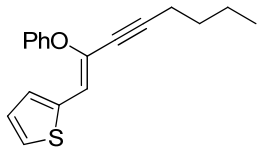
R_f = 0.33 (2:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (d, 1H, *J* = 2.2 Hz), 8.44 (dd, 1H, J^1 = 1.5 Hz, J^2 = 5 Hz), 8.08 (dt, 1H, J^1 = 2 Hz, J^2 = 8 Hz), 7.40-7.34 (m, 2H), 7.25-7.21 (m, 1H), 7.18-7.12 (m, 2H), 6.17 (s, 1H), 2.26 (t, 2H, *J* = 7 Hz), 1.44-1.35 (m, 2H), 1.31-1.19 (m, 2H), 0.85 (t, 2H, *J* = 7 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 150.0, 147.9, 137.0, 135.4, 130.9, 129.2, 123.7, 123.4, 118.8, 115.8, 94.9, 76.0, 30.1, 21.7, 18.9, 13.5.

HRMS: Calculated for $C_{19}H_{19}NO$: 277.1467, Found: 277.1476.

(*Z*)-2-(2-Phenoxyoct-1-en-3-ynyl)thiophene (247)



This compound is a colourless oil and was prepared according to General Procedure VI on a 0.28 mmole scale. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant to give 23.2 mg of **247**.

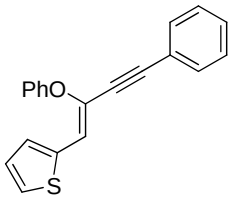
R_f = 0.18 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.32 (m, 2H), 7.28-7.25 (m, 1H), 7.18-7.09 (m, 4H), 7.02-6.98 (m, 1H), 6.58 (s, 1H), 2.27 (t, 2H, *J* = 6.8 Hz), 1.47-1.37 (m, 2H), 1.34-1.23 (m, 2H), 0.85 (t, 3H, *J* = 7.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 137.4, 132.4, 129.2, 127.1, 126.9, 126.5, 123.2, 118.1, 115.1, 94.9, 75.9, 30.2, 21.7, 19.0, 13.5.

HRMS: Calculated for $C_{18}H_{18}OS$: 282.1078, Found: 282.1072.

(*Z*)-2-(2-Phenoxy-4-phenylbut-1-en-3-ynyl)thiophene (248)



This compound is a colourless solid and was prepared according to General Procedure VI on a 0.28 mmol scale. The product was purified via flash chromatography using 20:1 hexanes: dichloromethane to give 24.3 mg of **248**.

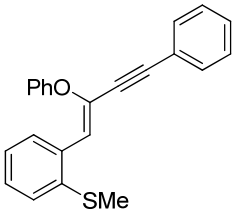
R_f = 0.55 (20:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.36 (m, 2H), 7.33-7.13 (m, 11H), 7.04 (m, 1H), 6.77 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 137.2, 132.2, 131.4, 129.3, 128.7, 128.3, 127.8, 127.6, 126.6, 123.5, 122.1, 118.3, 116.4, 93.4, 84.6.

We were unable to obtain satisfactory HRMS of this compound.

(*Z*)-Methyl(2-(2-phenoxy-4-phenylbut-1-en-3-ynyl)phenyl)sulfane (244)



This compound is a colourless solid and was prepared according to General Procedure V on a 0.20 mmol scale. The product was purified via flash chromatography using 3% diethyl ether in hexanes to give 27.7 mg of **244**.

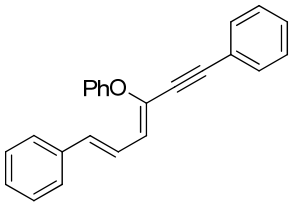
R_f = 0.26 (24:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (m, 1H), 7.43-7.14 (m, 13H), 6.89 (s, 1H), 2.55 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.6, 137.1, 135.4, 133.2, 131.5, 129.8, 129.3, 128.7, 128.3, 128.1, 127.2, 125.5, 123.5, 118.7, 117.8, 92.4, 85.2, 16.9.

We were unable to obtain satisfactory HRMS of this compound.

(1*E*,3*Z*)-3-Phenoxy-1,6-diphenylhexa-1,3-dien-5-yne (249)



This compound is a pale yellow solid and was prepared according to General Procedure V on a 0.18 mmol scale. The product was purified via flash chromatography using 20:1 hexanes: dichloromethane as an eluant to give 45.2 mg of **249**.

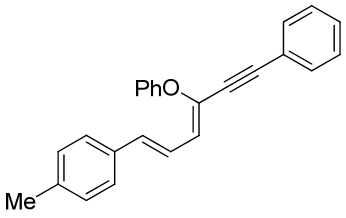
R_f = 0.10 (20:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.43-7.12 (m, 14H), 6.71 (d, 1H, *J* = 16Hz), 6.41 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 137.2, 134.0, 133.2, 131.5, 129.4, 128.7, 128.7, 128.4, 128.0, 126.8, 123.8, 123.2, 122.1, 118.1, 93.3, 85.2.

HRMS: Calculated for $C_{24}H_{18}O$: 322.1358, Found: 322.1359.

1-((3*Z*,5*E*)-3-Phenoxy-6-*p*-tolylhexa-3,5-dien-1-ynyl)benzene (250)



This compound is a pale yellow solid and was prepared according to General Procedure V on a 0.18 mmol scale. The product was purified via flash chromatography using 20:1 hexanes: dichloromethane as an eluant to give 39.1 mg of **250**.

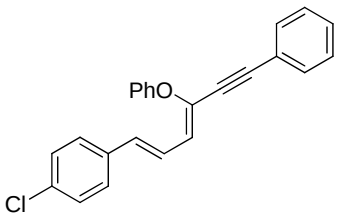
R_f = 0.10 (20:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.35 (m, 4H), 7.32-7.25 (m, 6H), 7.22-7.11 (m, 5H), 6.68 (d, 1H, *J* = 16Hz), 6.40 (m, 1H), 2.37 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 138.0, 134.4, 133.5, 133.3, 131.5, 129.4, 129.4, 128.7, 128.3, 126.7, 124.2, 123.1, 122.2, 121.2, 118.0, 93.1, 85.3, 21.4.

HRMS: Calculated for $C_{25}H_{20}O$: 336.1514, Found: 336.1515.

1-((3*Z*,5*E*)-6-(4-Chlorophenyl)-3-phenoxyhexa-3,5-dien-1-ynyl)benzene (251)



This compound is a pale yellow solid and was prepared according to General Procedure V on a 0.18 mmol scale. The product was purified via flash chromatography using 20:1 hexanes: dichloromethane as an eluant to give 29.5 mg of **251**.

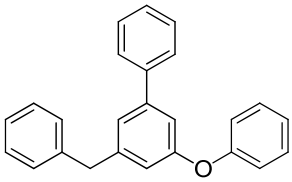
$\mathbf{R_f}$ = 0.40 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.12 (m, 15H), 6.63 (d, 1H, *J* = 16Hz), 6.36 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 135.7, 134.5, 133.5, 131.6, 131.5, 129.4, 128.9, 128.8, 128.4, 127.9, 123.3, 123.2, 122.7, 122.0, 118.2, 93.6, 85.0.

HRMS: Calculated for $C_{24}H_{17}ClO$: 356.0968, Found: 356.0962.

(3-Benzyl-5-phenoxy)biphenyl (253)



This compound is a colourless solid and was prepared according to General Procedure V on a 0.18 mmol scale. The product was purified via flash chromatography using 20:1 hexanes: dichloromethane as an eluant to give 25.7 mg of **253**.

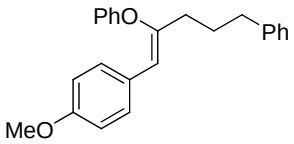
$\mathbf{R_f}$ = 0.13 (20:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.25 (m, 8H), 7.20-7.06 (m, 5H), 7.03-6.98 (m, 2H), 6.95-6.90 (m, 3H), 4.05 (s, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 155.7, 144.7, 141.3, 141.3, 129.9, 129.7, 129.4, 128.4, 128.1, 128.0, 127.2, 127.1, 125.48, 125.45, 123.0, 118.5, 117.9, 33.0.

HRMS: Calculated for $C_{25}H_{20}O$: 336.1514, Found: 336.1517.

(*Z*)-1-Methoxy-4-(2-phenoxy-5-phenylpent-1-enyl)benzene (254)



This compound is a colourless oil and was prepared according to General Procedure X on a 0.34 mmole scale. The product was purified via flash chromatography using 24:1 hexanes: ethyl acetate as an eluant to give 48.3 mg of **254**.

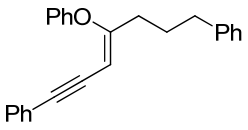
R_f = 0.18 (24:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.37-7.28 (m, 5H), 7.25-7.18 (m, 3H), 7.10-7.04 (m, 3H), 6.84 (m, 2H), 5.94 (s, 1H), 3.81 (s, 3H), 2.70 (t, 2H, *J* = 8.2 Hz), 2.36 (t, 2H, II = 7.7 Hz), 1.92 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 155.5, 150.5, 142.1, 129.7, 128.5, 128.3, 127.8, 125.8, 122.2, 117.0, 115.1, 113.8, 55.2, 35.1, 32.7, 28.7.

We were unable to obtain satisfactory HRMS of this compound.

(*Z*)-4-Phenoxy-1,7-diphenylhept-3-en-1-yne (255)



This compound is a colourless oil and was prepared according to General Procedure X on a 0.34 mmol scale using 1.5 equiv of $PhCCBF_3K$.[106] The product was purified via flash chromatography using 24:1 hexanes: ethyl acetate as an eluant to give 27.8 mg of **255**.

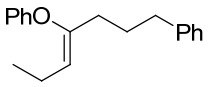
R_f = 0.28 (20:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.05 (m, 15H), 5.32 (d, 1H, *J* = 0.6 Hz), 2.72 (t, 2H, *J* = 7.5 Hz), 2.37 (t, 2H, *J* = 7.5 Hz), 1.94 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 156.0, 141.7, 131.3, 129.4, 128.44, 128.40, 127.7, 125.9, 123.6, 122.8, 118.0, 94.3, 93.1, 84.3, 35.1, 33.2, 28.4.

We were unable to obtain satisfactory HRMS of this compound.

(*Z*)-1-(1-Phenylhept-4-en-4-yloxy)benzene (257)



This compound is a colourless oil and was prepared according to General Procedure X on a 0.34 mmol scale using 1.5 equiv of Et_2Zn and no boronic acid. The product was purified via flash chromatography using a gradient of hexanes to 4:1 hexanes: dichloromethane as an eluant to give 30.2 mg of **257**.

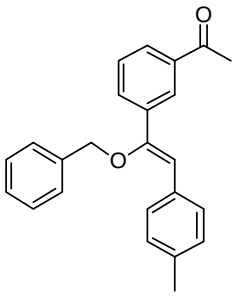
R_f = 0.20 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.29 (m, 4H), 7.24-7.19 (m, 3H), 7.05-6.98 (m, 3H), 5.08 (t, 1H, *J* = 7.2 Hz), 2.67 (t, 2H, *J* = 7.6 Hz), 2.22 (t, 2H, *J* = 8 Hz), 2.09 (t, 2H, *J* = 7 Hz), 1.84 (m, 2H), 1.00 (t, 3H, *J* = 8 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 149.7, 142.2, 129.5, 128.5, 128.3, 125.8, 121.4, 118.3, 115.9, 35.2, 31.9, 28.5, 18.7, 14.1.

We were unable to obtain satisfactory HRMS of this compound.

(*Z*)-1-(3-(1-Benzyloxy)-2-*p*-tolylvinyl)phenyl)ethanone (258)



This compound is a colourless solid and was prepared on scale according to a modification of General Procedure XV; when the first cross-coupling with *m*-

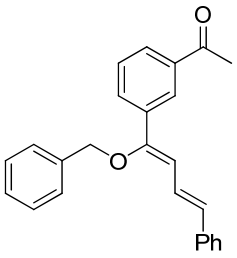
acetylphenylboronic acid was deemed complete by TLC, the reaction was cooled to room temperature, and 1.5 equiv of *p*-methylphenyl boronic acid was added as a solid. The reaction was re-sealed and brough to reflux, and treated as described in.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.34 (m, 7H), 7.26-7.22 (m, 2H), 5.87 (s, 1H), 4.88 (s, 2H), 2.43 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 139.2, 136.9, 130.8, 129.4, 128.5, 128.4, 128.1, 126.6, 102.2, 72.4, 21.3.

HRMS: Calculated for $C_{24}H_{22}O_2$: 342.1620, Found: 342.1622

1-(3-(1*Z*,3*E*)-1-(Benzyloxy)-4-phenylbuta-1,3-dienyl)phenyl)ethanone (259)



This compound is a colourless solid and was prepared on a 0.13 mmol scale according to a modification of General Procedure XV; when the first cross-coupling with *m*-acetylphenylboronic acid was deemed complete by TLC, the reaction was cooled to room temperature, and 1.5 equiv of *p*-methylphenyl boronic acid was added as a solid. The reaction was re-sealed and brough to reflux, and treated as described in. The product was purified via flash chromatography using 10:1 hexanes: ethyl acetate as an eluant to give 21.8 mg of **259**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (m, 1H), 7.93 (m, 1H), 7.80 (m, 1H), 7.54-7.18 (m, 10H), 6.64 (d, 1H, *J* = 16Hz), 6.33 (d, 1H, *J* = 10Hz), 4.86 (s, 2H), 2.64 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9, 153.7, 137.7, 137.6, 137.1, 136.4, 132.1, 130.4, 129.0, 128.63, 128.61, 128.3, 128.2, 128.1, 127.5, 126.4, 125.9, 123.4, 116.7, 73.8, 26.7.

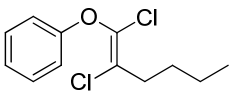
HRMS was not acquired for this compound.

4.5 Compounds from Section 2.4.3.2 – Tetrasubstituted Alkenes

Lithiation and electrophilic quenching in the presence of HMPA

This procedure is based on similar reactions reported by Greene.[479] A solution of the dichlorovinyl ether (0.1379 g, 0.73 mmol in 4 mL THF) was cooled to -78°C. *n*BuLi (0.36 mL of 2.0M solution in cyclohexane, 1.13 equiv) was added dropwise and stirred for 5 min. Iodomethane (91 μL, 1.46 mmol, 2.0 equiv) was added, followed immediately be 1 mL HMPA. The solution was allowed to stir at -78 °C for 30 min then removed from the cold bath and allowed to warm to room temperature. The reaction was quenched with water and extracted twice with diethyl ether, dried with magnesium sulphate, filtered and concentrated. The crude residue was applied to a silica gel column pretreated with 2.5 volume% of triethylamine and eluted with the indicated solvent to yield a colourless oil. This material was characterized by ^{1}H NMR only. The characterization of the second component isolated (methylated **261**) is provided below.

(*E*)-1-(1,2-Dichlorohex-1-enyloxy)benzene (260)

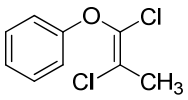


^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 2H), 7.14 (m, 1H), 7.03 (m, 2H), 2.57 (t, 2H, *J* = 7.5Hz), 1.71-1.61 (m, 2H), 1.50-1.37 (m, 2H), 0.99 (t, 2H, *J* = 7.5Hz).

General Procedure XI: Lithiation and Electrophilic Quenching of Dichlorovinyl Ether

This procedure is modified from similar reactions reported by Greene.[479] A solution of the dichlorovinyl ether (0.2 M in THF) was cooled to -78°C. *n*BuLi (either a 1.6M solution in hexanes or a 2.0M solution in cyclohexane, 1.13 equiv) was added dropwise and stirred for 5 min. The electrophile (1.5 – 2.5 equiv) was added dropwise. The solution was allowed to stir at -78 °C for 1 hour and allowed to warm to room temperature. The reaction was quenched with NH_4Cl and extracted twice with dichloromethane, dried with magnesium sulphate, filtered and concentrated. The crude residue was applied to a silica gel column pretreated with 2.5 volume% of triethylamine and eluted with the indicated solvent to yield a colourless oil.

(*E*)-1-(1,2-Dichloroprop-1-enyloxy)benzene (261)



This compound is a clear oil and was prepared according to General Procedure XI on a 0.79 mmol scale using 2.0 equivalents of iodomethane passed through a plug of activated alumina immediately before use. The product was purified via flash chromatography using hexanes as an eluant to give 121.3 mg of **261** (76% yield).

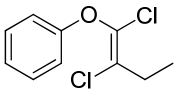
R_f = 0.7 (9:1 hexanes:ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.34 (m, 2H), 7.19-7.13 (m, 1H), 7.09-7.04 (m, 2H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.5, 134.9, 129.7, 124.0, 116.6, 116.5, 21.6.

HRMS: Calculated for $C_9H_8Cl_2O$: 201.9952, Found: 201.9944.

(*E*)-1-(1,2-Dichlorobut-1-enyloxy)benzene (264)



This compound is a clear oil and was prepared according to General Procedure XI on a 1.01 mmol scale using 2.0 equivalents of iodoethane passed through a plug of activated alumina immediately before use. This material was not purified.

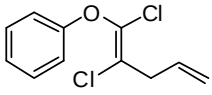
R_f = 0.69 (9:1 hexanes:ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (m, 2H), 7.15 (m, 1H), 7.05 (m, 2H), 2.60 (q, 2H, *J* = 7Hz), 1.24 (t, 3H, *J* = 7Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 129.7, 123.9, 122.7, 117.5, 116.4, 28.2, 11.6.

HRMS was not acquired for this compound.

(*E*)-1-(1,2-Dichloropenta-1,4-dienyloxy)benzene (265)



This compound is a clear oil and was prepared according to General Procedure XI on a 0.80 mmol scale using 2.5 equiv allyl bromide. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant to give 107.11 mg of **265** (66% yield).

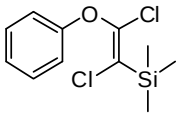
R_f = 0.55 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.34 (m, 2H), 7.19-7.13 (m, 1H), 7.08-7.03 (m, 2H), 5.97-5.83 (m, 1H), 5.32-5.22 (m, 2H), 3.33 (dd, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 135.5, 129.8, 124.1, 118.7, 118.1, 116.5, 39.0.

We were unable to obtain satisfactory HRMS for this compound.

(*E*)-(1,2-Dichloro-2-phenoxyvinyl)trimethylsilane (266)



This compound is a clear oil and was prepared according to General Procedure XI on a 0.88 mmol scale using 2 equiv chlorotrimethylsilane. The product was purified via flash chromatography using 17:1 hexanes: ethyl acetate as an eluant to give 205.8 mg of **266** (89% yield).

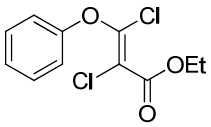
$\mathbf{R_f}$ = 0.55 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.36 (m, 2H), 7.21-7.15 (m, 1H), 7.09-7.05 (m, 2H), 0.41 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 143.6, 129.8, 124.2, 117.9, 117.0, -0.97.

HRMS: Calculated for $C_{11}H_{14}Cl_2OSi$: 260.0191, Found: 260.0194.

(E)-Ethyl 2,3-dichloro-3-phenoxyacrylate (267)



This compound is a clear oil and was prepared according to General Procedure XI on 1.2 mmol scale using 2.5 equiv of ethylchloroformate. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant to give 174.4 mg of **267** (56% yield).

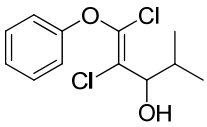
$\mathbf{R_f}$ = 0.50 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.35 (m, 2H), 7.25-7.19 (m, 1H), 7.09-7.04 (m, 2H), 4.35 (m, 2H), 1.38 (t, 3H, *J* = 7Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 153.4, 145.7, 129.9, 125.4, 118.6, 109.8, 62.6, 14.1.

HRMS: Calculated for $C_{11}H_{10}Cl_2O_3$: 260.0007, Found: 260.0006.

(*E*)-1,2-Dichloro-4-methyl-1-phenoxypent-1-en-3-ol (268)



This compound is a clear oil and was prepared according to General Procedure XI on a 0.83 mmol scale using 2 equiv isobutyraldehyde. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 200.1 mg of **268** (92% yield).

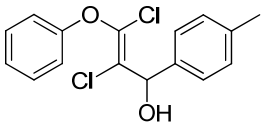
R_f = 0.21 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.33 (m, 2H), 7.19-7.13 (m, 1H), 7.07-7.02 (m, 2H), 4.43 (m, 1H), 2.07 (br d, 1H), 2.04-1.94 (m, 1H), 1.16 (d, 3H, *J* = 6.6 Hz), 0.98 (d, 3H, *J* = 6.9 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 136.5, 129.8, 124.3, 122.3, 116.9, 76.3, 32.8, 19.0, 18.5.

HRMS: Calculated for $C_{12}H_{14}Cl_2O_2$: 260.0371, Found: 260.0362.

(*E*)-2,3-Dichloro-3-phenoxy-1-*p*-tolylprop-2-en-1-ol (265)



This compound is a clear oil and was prepared according to General Procedure XI on a 0.70 mmol scale using 1.5 equiv *p*-tolualdehyde. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 203.1 mg of **265** (94% yield).

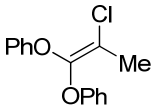
R_f = 0.18 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.38 (m, 4H), 7.28 (d, 2H, *J* = 8 Hz), 7.25-7.19 (m, 1H), 7.12-7.08 (m, 2H), 6.11 (br s, 1H), 2.61 (br s, 1H), 2.43 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 138.1, 136.7, 136.5, 129.9, 129.4, 125.6, 124.5, 122.5, 117.0, 71.5, 21.2.

HRMS: Calculated for $C_{16}H_{14}Cl_2O_2$: 308.0371, Found: 308.0373.

1-(2-chloro-1phenoxy-1-enyloxy)benzene (270)



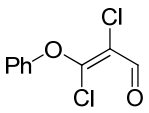
This compound is a colourless liquid prepared on a 0.23 mmol scale according to a modification of General Procedure XI starting from ketene acetal **132** using 1.5 equivalents iodomethane.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 4H), 7.10-7.00 (m, 6H), 2.20 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 154.7, 146.7, 129.6, 129.5, 123.4, 123.4, 116.7, 116.4, 107.2, 29.8.

HRMS was not acquired for this compound.

(*E*)-2,3-Dichloro-3-phenoxyacrylaldehyde (271)



This compound is a colourless oil and was prepared on a 3.89 mmol scale according to General Procedure XI using 5 equivalents DMF. The reaction was quenched with aqueous NH_4Cl after 5 minutes at -78 ^{o}C and then allowed to warm to room temperature. This compound was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 301.1 mg of **271** as a viscous oil.

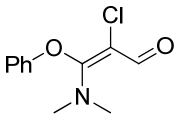
R_f =- 0.4 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.05-7.44 (m, 2H), 7.37-7.31 (m, 1H), 7.17-7.13 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 183.1, 153.8, 152.8, 130.0, 126.5, 119.9, 116.1

HRMS was not acquired for this compound.

2-Chloro-3-(dimethylamino)-3-phenoxyacrylaldehyde (272)



This compound is a colourless oil and was prepared on a 5.28 mmol scale according to General Procedure XI.. The reaction was quenched with 5 equivalents DMF and allowed to warm to room temperature before quenching with aqueous NH_4Cl. This compound was purified via flash chromatography using 2:1 hexanes: ethyl acetate as an eluant to give 980.5 mg of **271** as a viscous oil.

R_f = 0.15 (2:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.41-7.35 (m, 2H), 7.19-7.13 (m, 1H), 6.99-6.94 (m, 2H), 3.03 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 181.6, 164.2, 155.9, 130.3, 124.5, 116.4, 40.4.

HRMS was not acquired for this compound.

One-pot synthesis and C^2-H functionalization of dichlorovinyl ether 93

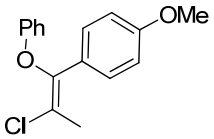
KH (2.74 g, 20.5 mmol, 2.05 equiv) was weighed into a round-bottom flask and washed with 3 5 mL portions of either pentane or petroleum ether. The KH was then suspended in 20 mL THF. A solution of the phenol 0.9411 g, 10 mmol, 1.0 equiv) 5 mL in THF was added drop wise (vigorous gas evolution was noted) and the reaction was allowed to stir for 60 min. The suspension was cooled to approximately −50 ºC ($CHCl_3/CO_2$(s) bath). Trichloroethylene (1.35 mL, 15 mmol, 1.5 equiv) was then added drop wise. The reaction was allowed to warm gradually to room temperature overnight. In the morning, the crude solution of the dichlorovinyl ether was cooled to -78°C. *n*BuLi (7.5 mL of 1.6M

solution in hexanes, 1.13 equiv) was added dropwise and stirred for 5 min. The ethyl chloroformate (2.0 mL, 20 mmol, 2.0 equiv) was added dropwise. The solution was allowed to stir at -78 ^{o}C for 1 hour and allowed to warm to room temperature. The reaction was quenched with NH_4Cl and extracted twice with dichloromethane, dried with magnesium sulphate, filtered and concentrated. The crude residue was applied to a silica gel column pretreated with 2.5 volume% of triethylamine and eluted with the indicated solvent to yield a 51% of **267**. ^{1}H, ^{13}C and HRMS data are listed above.

Cross-coupling between vinyl chloride 261 and *p*-methoxyphenyl boronic acid

This reaction was performed according to on a 0.37 mmol scale. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluant to give 54.1 mg (*Z*)-**276** and 4.0 mg (*E*)-**276**.

(Z)-1-(2-Chloro-1-(4-methoxyphenyl)prop-1-enyloxy)benzene ((Z)-276)



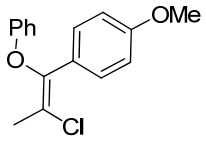
R_f = 0.48 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (m, 2H), 7.24-7.18 (m, 2H), 6.97-6.92 (m, 3H), 6.84 (m, 2H), 3.77 (s, 3H), 2.32 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 156.2, 145.4, 130.5, 129.4, 125.8, 122.1, 119.5, 116.5, 113.8, 55.2, 22.1.

HRMS: Calculated for $C_{16}H_{15}ClO_2$: 274.0761, Found: 274.0767.

(*E*)-1-(2-Chloro-1-(4-methoxyphenyl)prop-1-enyloxy)benzene ((E)-276)



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.26 (m, 5H), 7.09-7.04 (m, 1H), 7.02-6.98 (m, 1H), 6.80 (m, 2H), 3.76 (s, 3H), 2.24 (s, 3H).

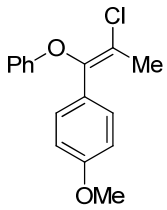
^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 155.3, 135.2, 130.5, 130.4, 129.5, 129.4, 128.8, 116.7, 113.5, 55.2, 20.2.

HRMS was not obtained for this compound.

General Procedure XII: Functionalization of 1-Aryl-2-Chlorovinyl ethers - Lithiation

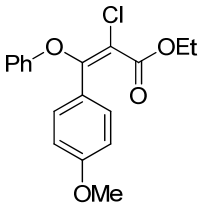
This procedure is similar to General Procedure XI. A solution of the chlorovinyl ether (0.2 M in THF) was cooled to -78 °C. *n*BuLi (either a 1.6M solution in hexanes or a 2.0M solution in cyclohexane, 1.13 equiv) was added dropwise and stirred for 30 min. The electrophile (2.5 equiv) was then added dropwise. The solution was allowed to stir at -78 °C for 10 mins and quenched with water. It was then extracted twice with dichloromethane, dried with magnesium sulphate, filtered and concentrated. The crude residue was applied to a silica gel column pretreated with 2.5 volume% of triethylamine and eluted with the indicated solvent to yield a colourless oil.

(Z)-1-Phenoxy-1-(4-methoxyphenyl)-2-chloropropene (276)



This compound is a clear oil and was prepared on a 3.06 mmol scale according to General Procedure XII. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 832.1 mg of **276**. NMR and HRMS data are listed above.

(*Z*)-Ethyl 2-chloro-3-(4-methoxyphenyl)-3-phenoxyacrylate (277)



This compound is a clear oil and was prepared on a 3.06 mmol scale according to General Procedure XII. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant to give 938.8 mg of **277**.

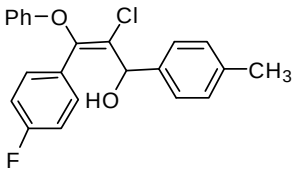
R_f = 0.25 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 2H), 7.21 (m, 2H), 6.98 (m, 1H), 6.92 (m, 2H), 6.80 (m, 2H), 4.15 (q, 2H), 3.77 (s, 3H), 1.13 (t, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1. 160.9, 158.8, 155.0, 131.1, 129.5, 124.9, 123.4, 118.5, 113.5 (x2), 110.7, 61.9, 55.2, 13.8.

HRMS: Calculated for $C_{18}H_{17}ClO_4$: 332.7782, Found: 332.0815.

(*Z*)-2-Chloro-3-(4-fluorophenyl)-3-phenoxy-1-*p*-tolylprop-2-en-1-ol (278)



This compound is a clear oil and was prepared on a 1.75 mmol scale according to General Procedure XII. The product was purified via flash chromatography using a gradient of 9:1 to 4:1 hexanes: ethyl acetate as an eluant to give 338.8 mg of **278**.

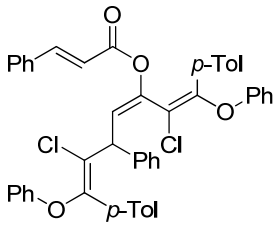
$\mathbf{R_f}$ = 0.18 (9:1 petroleum ether: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (m, 2H), 7.37 (m, 2H), 7.28-7.21 (m, 4H), 7.05-6.97 (m, 5H), 5.78 (br s, 1H), 2.40 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 161.5, 155.5, 148.3, 137.9, 137.6, 131.3, 131.2, 129.6, 129.3, 128.9, 128.8, 126.0, 125.3, 122.9, 117.2, 116.0, 115.8, 72.0, 21.2.

No HRMS was acquired for this compound.

(1*Z*,3*E*,6*Z*)-2,6-Dichloro-1,7-diphenoxy)-5-phenyl-1,7-di*p*-tolylhepta-1,3,6-trien-3-yl cinnamate (279)



This compound is a gummy, colourless solid and was prepared on a 2.6 mmol scale according to the General Procedure XII. The product was purified via flash chromatography using a gradient of 24:1 – 6:1 hexanes: ethyl acetate as an eluant on silica pretreated with 2.5 vol% triethylamine to give 682.4 mg of **279**.

$\mathbf{R_f}$ = 0.23 (6:1 hexanes: ethyl acetate).

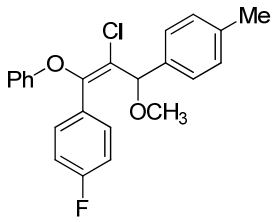
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, 2H, *J* = 8 Hz), 7.46-6.96 (m, 27H), 6.02 (d, 1H, *J* = 16 Hz), 5.82 (d, 1H, *J* = 9.5 Hz), 5.30 (d, 1H, *J* = 9.5 Hz), 2.27 (s, 3H), 1.98 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 156.1, 155.6, 150.0, 148.2, 146.3, 143.5, 139.5, 139.20, 139.16, 134.0, 130.8, 130.6, 130.3, 129.9, 129.5, 129.4, 129.3, 129.2, 129.0,

128.9, 128.6, 128.3, 127.6, 127.1, 123.6, 123.1, 122.6, 122.3, 117.3, 116.8, 116.1, 44.0, 21.4, 21.0.

HRMS: Calculated for $C_{48}H_{38}Cl_2NaO_4$: 771.2044, Found: 771.2039.

(*Z*)-2-Chloro-1-(4-fluorophenyl)-3-methoxy-3-*p*-tolylprop-1-enyloxy)benzene (284)



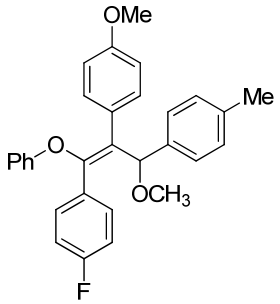
Compound **278** (0.3403 g, 0.92 mmol, 1 equiv) was dissolved in 9 mL THF and cooled to 0 °C. NaH (55 mg, 1.38 mmol. 1.5 equiv) was added as a solid and stirred for 30 min. Methyl iodide (0.17 mL, 2.7 mmol, 3 equiv) was added and the reaction was stirred at 0 °C for 1.5 h. The reaction was quenched with water and extracted with three portions of ethyl acetate. The organic layers were combined and concentrated then purified via flash chromatography using 4:1 petroleum ether:dichloromethane as an eluant to give 338.8 mg of **284**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.34 (m, 2H), 7.26-7.19 (m, 4H). 7.08-6.92 (m, 5H), 5.21 (s, 1H), 3.40 (s, 3H), 2.38 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 161.5, 155.4, 149.3, 137.8, 135.4, 131.5, 131.3, 129.5, 129.1, 126.7, 124.0, 122.9, 117.3, 116.0, 115.7, 80.3, 56.3, 21.2.

HRMS was not acquired for this compound.

(*E*)-1-(3-(4-Fluorophenyl)-1-methoxy-2-(4-methoxyphenyl)-3-phenoxyallyl)-4-methylbenzene (285)



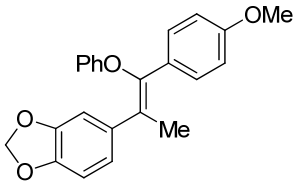
$PdCl_2(CH_3CN)_2$ (1.2 mg, 4.8 μmol, 5 mol%), S-Phos (3.9 mg, 9.6 μmol, 10 mol%), *p*-methoxyphenylboronic acid (17.8 mg, 0.116 mmol, 1.2 equiv) and Cs_2CO_3 (78.7 mg, 0.24 mmol, 2.5 equiv) were placed into an oven-dried test tube, sealed with a septum and purged with argon for 20 min. A solution of **284** (37.0 mg, 96.6 μmol) in 0.4 mL dioxane was added, and the reaction was heated at 100 °C for 24 h, after which it was cooled to room temperature, diluted with ethyl acetate and filtered through celite. The crude material was purified via flash chromatography using 18:1 hexanes: ethyl acetate to give 30.7 mg of **285**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (m, 2H), 7.18-7.03 (m, 10H), 6.90-6.85 (m, 3H), 6.71 (m, 2H), 5.30 (s, 1H), 3.74 (s, 3H), 3.39 (s, 3H), 2.32 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 161.0, 158.4, 156.4, 149.4, 137.0, 136.7, 132.0, 131.9, 130.9, 130.80, 130.75, 129.2, 128.7, 128.3, 127.6, 126.7, 122.0, 117.7, 115.6, 115.3, 112.9, 81.1, 56.1, 55.0.

HRMS was not acquired for this compound.

(*Z*)-5-(1-(4-Methoxyphenyl)-1-phenoxyprop-1-en-2-yl)benzo[*d*][1,3]dioxole (286)



This compound was prepared according to General Procedure X on a 0.30 mmol scale. The product was purified via flash chromatography using 11:1 hexanes to ethyl acetate as an eluant to give 83.6 mg of **286**.

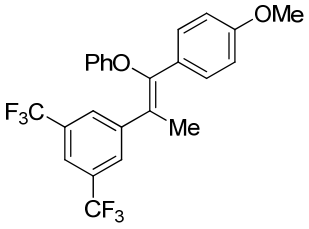
R_f = 0.24 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.17 (t, 2H, *J* = 7.5 Hz), 7.05-6.85 (m, 7H), 6.77 (m, 1H), 5.93 (s, 2H), 3.81 (s, 3H), 2.22 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 157.3, 147.2, 146.2, 145.0, 134.5, 131.0, 129.2, 128.0, 122.5, 121.3, 121.2, 117.0, 113.5, 108.6, 108.0, 100.8, 55.18, 20.2.

HRMS: Calculated for $C_{23}H_{20}O_4$: 360.1362, Found: 360.1362.

(Z)-1-((2-3,5-bis(Trifluoromethyl)phenyl)-1-(4-methoxyphenyl)prop-1-enyloxy)benzene (287)



This compound was prepared according to General Procedure X on a 0.30 mmol scale. The product was purified via flash chromatography using 14:1 hexanes to ethyl acetate as an eluant to give 115.2 mg of **287**.

R_f = 0.32 (14:1 hexanes: ethyl acetate).

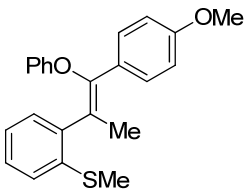
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 2H), 7.72 (s, 1H), 7.50 (m, 2H), 7.16 (m, 2H), 6.95-6.82 (m, 5H), 3.83 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 156.7, 147.7, 142.7, 131.3, 131.0, 129.3, 128.34, 128.29, 126.9, 125.3, 121.9, 121.6, 120.31, 120.25, 119.8, 116.7, 113.7, 55.2, 19.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.92.

HRMS: Calculated for $C_{24}H_{18}F_6O_2$: 452.1211, Found: 452.1216.

(*Z*)-(2-(1-Methoxyphenyl)-1-phenoxyprop-1-en-2-yl)phenyl)(methyl)sulfane (288)



This compound was prepared according to General Procedure X on a 0.30 mmol scale. The product was purified via flash chromatography using 12:1 hexanes to ethyl acetate as an eluant to give 78.5 mg of **288**.

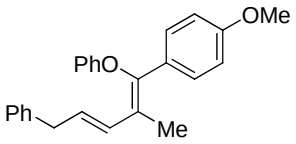
R_f = 0.31 (12:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.23-7.04 (m, 6H), 6.90-6.84 (m, 4H), 6.79 (m, 1H), 3.80 (s, 3H), 2.48 (s, 3H), 2.18 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 157.3, 146.3, 140.3, 136.7, 130.9, 128.8, 128.5, 127.4, 127.3, 125.5, 124.7, 122.7, 121.1, 117.3, 113.5, 55.2, 19.6, 15.9.

HRMS: Calculated for $C_{23}H_{22}O_2S$: 362.1341, Found: 362.1348.

1-Methoxy-4-((1*Z*,3*E*)-2-methyl-1-phenoxy-5-phenylpenta-1,3-dienyl)benzene (289)



This compound was prepared according to General Procedure X on a 0.30 mmol scale. The product was purified via flash chromatography using a gradient of neat hexanes to 14:1 hexanes to ethyl acetate as an eluant to give 100.9 mg of **289**.

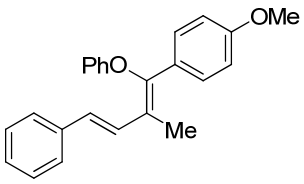
R_f = 0.34 (14:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (m, 2H), 7.36-7.31 (m, 7H), 7.00-6.84 (m, 7H), 6.03-5.92 (m, 1H), 3.81 (s, 3H), 3.52 (d, 2H, *J* = 7.7 Hz), 2.04 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 157.5, 146.0, 140.8, 131.0, 129.6, 129.4, 128.59, 128.55, 128.5, 128.3, 127.7, 126.1, 121.5, 121.0, 116.7, 113.4, 55.3, 39.9, 14.5.

We were unable to acquire satisfactory HRMS for this compound.

1-((1*Z*,3*E*)-1-(4-methoxyphenyl)-2-methyl-4-phenylbuta-1,3-dienyloxyl)benzene (290)



This compound was prepared according to General Procedure X on a 0.30 mmol scale. The product was purified via flash chromatography using a gradient of neat hexanes to 9:1 hexanes to ethyl acetate as an eluant to give 78.5 mg of **290**.

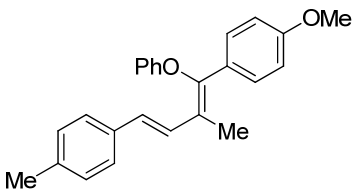
R_f = 0.25 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, 1H, *J* = 16Hz), 7.47-7.41 (m, 4H), 7.34-7.28 (m, 2H), 7.25-7.19 (m, 3H), 7.00-6.83 (m, 5H), 6.71 (d, 1H, *J* = 16Hz), 3.80 (s, 3H), 2.16 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 157.5, 147.9, 138.0, 131.2, 129.4, 128.7, 128.6, 127.6, 127.3, 126.5, 126.1, 121.8, 121.2, 117.0, 113.5, 55.2, 14.6.

HRMS: Calculated for $C_{24}H_{22}O_2$: 342.1620, Found: 342.1625.

1-((1*Z*,3*E*)-(4-methoxyphenyl)-2-methyl-4-*p*-tolylbuta-1,3-dienyloxy)benzene (291)



This compound was prepared according to General Procedure X on a 0.30 mmol scale. The product was purified via flash chromatography using a gradient of neat hexanes to 9:1 hexanes to ethyl acetate as an eluant to give 78.5 mg of **291**.

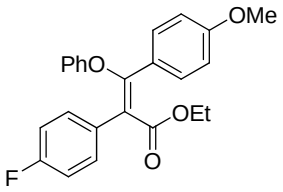
R_f = 0.25 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-6.81 (m, 14H) 6.68 (d, 1H, *J* = 16Hz),3.79 (s, 3H), 2.34 (s, 3H), 2.14 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 157.6, 147.5, 137.1, 135.2, 131.1, 129.6, 129.4, 129.3, 128.7, 127.7, 126.4, 125.1, 121.7, 121.3, 117.0, 113.5, 55.2, 21.2, 14.4.

HRMS: Calculated for $C_{25}H_{24}O_2$: 356.1776, Found: 356.1780.

(E)-Ethyl 2-(4-fluorophenyl)-3-(4-methoxyphenyl)-3-phenoxyacrylate (292)



This compound was prepared according to and General Procedure X and purified via flash chromatography using a gradient of 12:1 to 9:1 hexanes to ethyl acetate as an eluant.

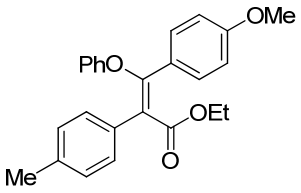
R_f = 0.35 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.36 (m, 4H), 7.19-7.13 (m, 2H), 7.00-6.86 (m, 5H), 6.82-6.78 (m, 2H), 4.10 (q, 2H, *J* = 7.2 Hz), 3.77 (s, 3H), 1.06 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 163.7, 160.5, 156.2, 154.6, 130.6, 130.4, 129.4, 126.8, 122.6, 121.0, 117.9, 115.4, 115.1, 113.7, 61.2, 55.2, 13.9.

HRMS: Calculated for $C_{24}H_{21}FO_4$: 392.1424, Found: 392.1437.

(E)-Ethyl 3-(4-methoxyphenyl)-3-phenoxy-2-*p*-tolylacrylate (293)



This compound was prepared according to General Procedure X. The product was purified via flash chromatography using a 10:1 hexanes to ethyl acetate.

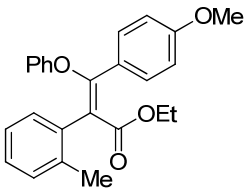
R_f = 0.36 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (m, 2H), 7.35 (m, 2H), 7.23-7.11 (m, 4H), 6.97-6.92 (m, 3H), 6.83 (m, 2H), 4.14 (q, 2H, *J* = 7.2 Hz), 3.80 (s, 3H), 2.35 (s, 3H), 1.11 (t, 3H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 160.3, 156.5, 153.5, 137.4, 131.6, 130.3, 129.3, 129.0, 128.4, 127.1, 122.4, 122.3, 118.0, 113.7, 61.1, 55.2, 21.3, 13.9.

HRMS: Calculated for $C_{25}H_{24}O_4$: 388.1675, Found: 388.1674.

(E)-Ethyl 3-(4-methoxyphenyl)-3-phenoxy-2-*o*-tolylacrylate (294)



This compound was prepared according to and General Procedure X. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate.

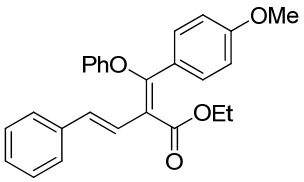
R_f = 0.36 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, 2H), 7.30 (m, 1H), 7.19-7.07 (m, 5H), 6.89-6.79 (m, 5H), 4.08 (q, 2H, *J* = 7 Hz), 3.80 (s, 3H), 2.35 (s, 3H), 1.06 (t, 3H, *J* = 7 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 160.5, 157.8, 156.3, 137.1, 134.8, 130.9, 130.0, 129.9, 129.1, 127.7, 126.8, 125.5, 122.4, 120.5, 118.3, 113.5, 60.8, 55.3, 20.0, 13.9.

HRMS: Calculated for $C_{25}H_{24}O_4$: 388.1675, Found: 388.1676.

(2*E*,3*E*)-Ethyl 2-((4-methoxypheny)(phenoxy)methylene)-4-phenylbut-3-enoate (295)



This compound was prepared according to General Procedure X. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluant.

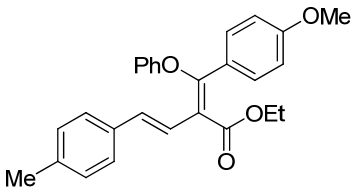
R_f = 0.38 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.40 (m, 4H), 7.33-7.19 (m, 7H), 7.01-6.94 (m, 3H), 6.82-6.72 (m, 2H), 4.21 (q, 2H, *J* = 7.1 Hz), 3.78 (s, 3H), 1.12 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 160.4, 156.6, 152.1, 137.4, 130.8, 130.0, 129.6, 128.6, 127.7, 126.7, 122.6, 122.4, 121.2, 117.5, 113.8, 61.3, 55.2, 13.9.

HRMS: Calculated for $C_{26}H_{24}O_4$: 400.1675, Found: 400.1674.

(2*E*,3*E*)-Ethyl 2-((4-methoxyphenyl)(phenoxy)methylene)-4-*p*-tolylbut-3-enoate (296)



This compound was prepared according to General Procedure X. The product was purified via flash chromatography using 7:1 hexanes: ethyl acetate as an eluant.

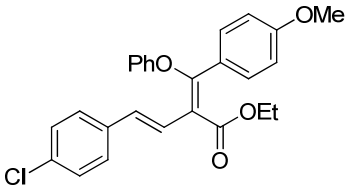
R_f = 0.38 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (m, 2H), 7.31-7.12 (m, 6H), 7.02-6.87 (m, 6H), 6.64 (d, 1H, *J* = 16 Hz), 4.33 (q, 2H, *J* = 7.2 Hz), 3.83 (s, 3H), 2.37 (s, 3H), 1.21 (t, 3H, *J* = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 160.4, 156.8, 151.6, 137.6, 134.5, 131.6, 131.1, 129.4, 129.2, 126.4, 125.1, 122.6, 122.4, 121.3, 117.8, 113.9, 61.2, 55.3, 21.3, 14.1.

HRMS: Calculated for $C_{27}H_{26}O_4$: 414.1831, Found: 414.1835.

(2*E*,3*E*)-Ethyl 4-(4-chlorophenyl)-2-((4-methoxyphenyl)(phenoxy)methylene)but-3-enoate (297)



This compound was prepared according to and General Procedure X. The product was purified via flash chromatography using 7:1 hexanes: ethyl acetate as an eluant.

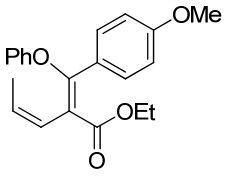
R_f = 0.35 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (m, 2H), 7.32-7.28 (m, 5H), 7.21 (m, 3H), 7.00-6.88 (m, 6H), 6.60 (d, 1H, *J* = 16 Hz), 4.33 (q, 2H, *J* = 7.1 Hz), 3.83 (s, 3H), 1.21 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 160.6, 156.6, 152.8, 135.8, 133.2, 131.6, 129.6, 129.2, 128.8, 127.6, 124.8, 122.9, 122.5, 122.1, 117.9, 114.0, 61.2, 55.3, 14.1.

HRMS: Calculated for $C_{26}H_{23}ClO_4$: 434.1285, Found: 434.1287.

(2*E*,3*Z*)-Ethyl 2-((4-methoxyphenyl)(phenoxy)methylene)pent-3-enoate (298)



This compound was prepared according to General Procedure X on a 0.30 scale. The product was purified via flash chromatography using 7:1 hexanes: ethyl acetate as an eluant to give 81.4 mg of **298**.

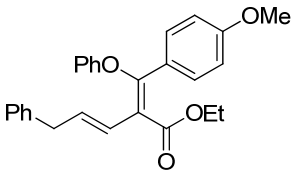
R_f = 0.35 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 2H), 7.24-7.18 (m, 2H), 7.00-6.91 (m, 3H), 6.81 (m, 2H), 6.24 (m, 1H), 5.78-5.67 (m, 1H), 4.14 (q, 2H, J = 7.2 Hz), 3.79 (s, 3H), 1.70 (dd, 3H, J^1 = 2Hz, J^2 = 7Hz), 1.14 (t, 3H, J = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 160.4, 156.0, 154.4, 130.4, 129.4, 128.9, 126.5, 122.5, 122.4, 119.3, 117.6, 113.6, 61.1, 55.2, 14.9, 13.8.

HRMS: Calculated for $C_{21}H_{22}O_4$: 338.1518, Found: 338.1527.

(2*E*,3*E*)-Ethyl 2-((4-methoxyphenyl)(phenoxy)methylene)-5-phenylpent-3-enoate (299)



This compound was prepared according to General Procedure X on a 0.30 scale. The product was purified via flash chromatography using a gradient of 9:1 to 7:1 hexanes: ethyl acetate as an eluant to give 81.4 mg of **299**.

R_f = 0.28 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.19 (m, 10H), 7.02-6.93 (m, 3H), 6.82 (m, 2H). 6.66 (m, 2H), 6.09-5.98 (m, 1H), 4.15 (q, 2H, J = 7.2 Hz), 3.79 (s, 3H), 3.52 (d, 2H, J = 7.2 Hz), 1.09 (t, 3H, J = 7.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 160.3, 156.6, 150.8, 140.0, 132.1, 130.7, 129.9, 129.5, 128.6, 128.5, 126.8, 126.2, 126.1, 123.7, 122.4, 122.0, 117.9, 113.7, 113.3, 61.1, 55.2, 39.7, 13.9.

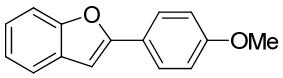
HRMS: Calculated for $C_{27}H_{26}O_4$: 414.1831, Found: 414.1828.

4.6 Compounds from Section 2.5 – Benzofurans

General Procedure XIII: Cyclization of 1,1'-disubstituted-2-chloroethylenes

The vinyl chloride, Pd_2dba_3, DPEphos, CsF and Cs_2CO_3 were placed into a test tube, sealed with a septum and purged with argon for 20 – 30 min. Dioxane was added (0.25 – 0.5 M with respect to dichloroethylene). The solution was vigorously stirred and brought to reflux. When complete, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were washed with brine, dried with sodium sulfate, filtered and concentrated.

2-(4-Methoxyphenyl)-benzofuran (301)



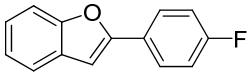
This compound was synthesized according to General Procedure XIII. ^{1}H and ^{13}C NMR data were consistent with published values.[372]

R_f = 0.47 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, 2H), 7.61-7.53 (m, 2H), 7.32-7.23 (m, 2H), 7.01 (d, 2H), 6.91 (s, 1H), 3.89 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 156.1, 154.8, 129.6, 126.5, 123.8, 122.9, 120.6, 114.3, 111.0, 99.7, 55.4.

2-(4-Fluorophenyl)-benzofuran (302)



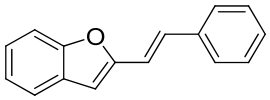
This material was synthesized according to General Procedure XIII. ^{1}H and ^{13}C NMR spectral data were consistent with literature values.[358]

R_f = 0.5 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90-7.83 (m, 2H), 7.61 (m, 1H), 7.55 (m, 1H), 7.35-7.24 (m, 2H), 7.17 (m, 2H), 6.98 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 161.3, 155.1, 154.9, 129.2, 126.9, 126.8, 124.3, 123.1, 120.9, 116.1, 115.8, 111.2, 101.0.

2-(*trans*-2-Phenylethenyl)benzofuran (303)



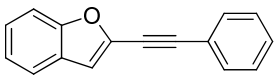
This compound was synthesized according to General Procedure XIII. ^{1}H and ^{13}C NMR data were consistent with published values.[561]

R_f = 0.44 (11:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61-7.51 (m, 4H), 7.46-7.40 (m, 2H), 7.37-7.33 (m, 2H), 7.32-7.24 (m, 1H), 7.06 (d, 1H, *J* = 16 Hz), 6.72 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 155.0, 136.7, 130.3, 129.2, 128.9, 128.2, 126.8, 124.7, 123.0, 120.9, 116.5, 111.0, 105.3.

2-(2-Phenylethynyl)benzofuran (304)



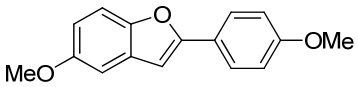
This compound was synthesized according to General Procedure XIII. ^{1}H and ^{13}C NMR data were consistent with published values.[202]

R_f = 0.61 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.59 (m, 3H), 7.51 (m, 1H), 7.34-7.42 (m, 4H), 7.26-7.31 (m, 1H), 7.03 (d, 1H, *J* = 1Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.0, 138.8, 131.7, 129.2, 128.5, 127.8, 125.6, 123.3, 121.9, 121.2, 111.5, 111.3, 95.1, 79.7.

2-(4-Methoxyphenyl)-5-methoxy-benzofuran (Corsifuran C) (305)



This compound was synthesized according to General Procedure XIII. ^{1}H NMR data were consistent with published values acquired in C_6D_6.[326]

R_f = 0.33 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, C_6D_6) δ 7.75 (d, 2H), 7.30 (d, 1H), 6.95 (d, 2H, *J* = 2.5Hz), 6.83 (dd, 1H, *J* = 2.5Hz, 9Hz), 6.78 (d, 2H), 6.60 (s, 1H), 3.43 (s, 3H), 3.26 (s, 3H).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, 2H), 7.40 (d, 1H, *J* = 9Hz), 7.04 (d, 1H, *J* = 2.5Hz), 6.99 (d, 2H), 6.88 (dd, 1H, *J* = 2.5Hz, 9Hz), 6.85 (s, 1H), 3.88 (s, 3H), 3.87 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 156.9, 156.1, 149.8, 130.1, 126.4, 123.5, 114.3, 112.3, 111.4, 103.2, 99.9, 55.9, 55.4.

General Procedure XIV: Ligand screening for one-pot Suzuki-coupling/direct arylation

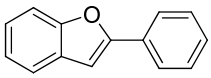
The boronic acid, Pd_2dba_3, Ligand, CsF and Cs_2CO_3 bases were placed into a one piece round bottom flask/condenser. This was sealed at the top with a septum and the headspace was purged with argon for 20-30 min. A 0.4 M solution of the 1,2-dichlorovinyl ether in dioxane was added. The solution was vigorously stirred and brought to reflux. When complete as judged by tlc (note that the benzo[b]furan product spots fluoresced under 254 nm UV illumination), the reaction was cooled and partitioned

between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated and analyzed by ^{1}H NMR spectroscopy.

General Procedure XV: Pd/DPEphos catalyzed one-pot Suzuki coupling/direct arylation

The boronic acid, Pd_2dba_3, DPEphos, CsF and Cs_2CO_3 bases were placed into a one piece round bottom flask/condenser. This was sealed at the top with a septum and the headspace was purged with argon for 20-30 min. A 0.4 M solution of the 1,2-dichlorovinyl ether in dioxane was added. The solution was vigorously stirred and brought to reflux. When complete as judged by tlc (note that the benzo[b]furan product spots fluoresced under 254 nm UV illumination), the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated onto silica gel, applied to a column and eluted with the appropriate solvent.

2-Phenylbenzofuran (310)



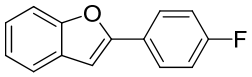
This compound was synthesized according to General Procedure XV. ^{1}H and ^{13}C NMR were consistent with published values.[372]

R_f = 0.56 (11:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (m, 2H), 7.66-7.57 (m, 2H), 7.53-7.48 (m, 2H), 7.44-7.38 (m, 1H), 7.35-7.27 (m, 2H), 7.07 (s, 1H).

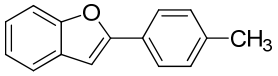
^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 155.0, 130.6, 129.3, 128.9, 128.6, 125.0, 124.3, 123.0, 121.0, 111.3, 101.4.

2-(4-Fluorophenyl)-benzofuran (302)



This material was synthesized according to General Procedure XV. ^{1}H and ^{13}C NMR spectral data were consistent with literature values[358] and listed above.

2-(4-Methylphenyl)benzofuran (306)



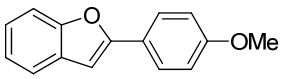
This compound was synthesized according to General Procedure XV. ^{1}H and ^{13}C NMR were consistent with published values.[372]

R_f = 0.45 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, 2H), 7.60 (m, 1H), 7.55 (m, 1H), 7.33-7.22 (m, 4H), 7.00 (s, 1H), 2.43 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 154.8, 138.6, 129.5, 129.4, 127.8, 124.9, 124.0, 122.9, 120.8, 111.1, 100.6, 21.4.

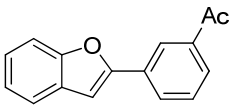
2-(4-Methoxyphenyl)benzofuran (301)



This compound was synthesized according to General Procedure XV. ^{1}H and ^{13}C NMR data were consistent with published values[372] and are listed above.

R_f = 0.47 (9:1 hexanes: ethyl acetate).

2-(3-Acetylphenyl)benzofuran (311)



This compound is a pale yellow solid and was prepared on a 0.40 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: diethyl ether as an eluent to give 46.9 mg of **311**.

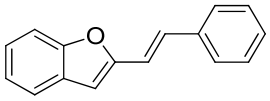
$\mathbf{R_f}$ = 0.20 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (br s, 1H), 8.08 (dd, 1H, J^1 = 0.7 Hz, J^2 = 8 Hz), 7.96 (dd, J^1 = 0.8 Hz, J^2 = 8 Hz), 7.67-7.55 (m, 3H), 7.38-7.26 (m, 2H), 7.15 (s, 1H), 2.72 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 155.0, 154.8, 137.7, 131.1, 129.2, 129.2, 129.0, 128.2, 124.8, 124.6, 123.2, 121.2, 111.3, 102.4, 26.8.

HRMS: Calculated for $C_{16}H_{12}O_2$: 236.0837, Found: 236.0832.

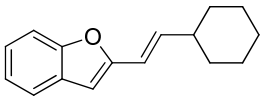
2-(*trans*-2-Phenylethenyl)benzofuran (303)



This compound was synthesized according to General Procedure XV. ^{1}H and ^{13}C NMR data were consistent with published values[561] and are listed above.

$\mathbf{R_f}$ = 0.44 (11:1 hexanes: dichloromethane).

(*E*)-2-(2-Cyclohexylvinyl)benzofuran (312)



This compound is a colourless oil and was prepared on a 0.26 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluent to give 35.5 mg of **312**.

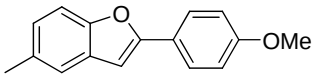
$\mathbf{R_f}$ = 0.52 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, 1H), 7.47 (d, 1H), 7.30-7.19 (m, 2H), 6.55-6.47 (m, 2H), 6.34 (d, 1H, *J* = 16 Hz), 2.28-2.15 (m, 1H), 1.94-1.70 (m, 5H), 1.47-1.18 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5, 154.6, 139.3, 129.2, 123.9, 122.6, 120.6, 116.3, 110.8, 102.8, 41.0, 32.7, 26.2, 26.0.

HRMS: Calculated for $C_{16}H_{18}O$: 226.1358, Found: 226.1361.

2-(4-Methoxyphenyl)-5-methylbenzofuran (313)



This compound is a colourless solid and was prepared on a 0.32 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluent to give 66.5 mg of **313**.

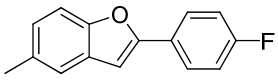
R_f = 0.46 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (m, 2H), 7.43-7.37 (m, 2H), 7.11 (m, 1H), 7.01 (m, 2H), 6.85 (s, 1H), 3.90 (s, 3H), 2.48 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 156.2, 153.2, 132.2, 129.6, 126.4, 125.0, 123.6, 120.5, 114.3, 110.5, 99.5, 55.4, 21.4.

HRMS: Calculated for $C_{16}H_{14}O_2$: 238.0994, Found: 238.0996.

2-(4-Fluorophenyl)-5-methylbenzofuran (314)



This compound is a colourless solid and was prepared on a 0.32 mmol scale according to General Procedure XV. The product was purified via flash chromatography using a gradient of hexanes to 14:1 hexanes: diethyl ether as an eluent to give 55.3 mg of **314**.

R_f = 0.44 (9:1 hexanes: ethyl acetate).

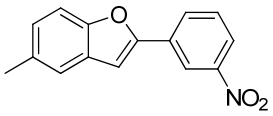
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (m, 2H), 7.45-7.39 (m, 2H), 7.21-7.12 (m, 3H), 6.92 (s, 1H), 2.50 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 161.2, 155.1, 153.4, 132.5, 129.3, 127.02, 126.98, 126.8, 126.7, 125.6, 120.8, 116.0, 115.7, 110.7, 100.8, 100.8, 21.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ-112.58.

HRMS: Calculated for $C_{15}H_{11}FO_2$: 226.0794, Found: 226.0788.

2-(3-Nitrophenyl)-5-methylbenzofuran (315)



This compound is a colourless solid and was prepared on 0.32 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 14:1 hexanes: diethyl ether as an eluent to give 10.6 mg of **315**.

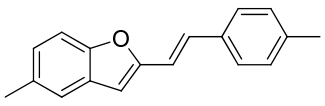
R_f = 0.34 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72 (t, 1H, *J* = 2 Hz), 8.19 (m, 2H). 7.65 (t, 1H, *J* = 8 Hz), 7.49-7.44 (m, 2H), 7.20 (m, 1H), 7.15 (s, 1H), 2.50 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 153.2, 148.8, 133.0, 132.3, 130.2, 129.8, 128.8, 126.7, 122.7, 121.2, 119.6, 110.9, 103.4, 21.4.

HRMS: Calculated for $C_{15}H_{11}NO_3$: 253.0739, Found: 253.0738.

2-(2-*trans*-(4-Methylphenyl)ethenyl)-5-methylbenzofuran (316)



This compound is a colourless solid and was prepared on a 0.32 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 50:1 petroleum ether: diethyl ether as an eluent to give 56.5 mg of **316**.

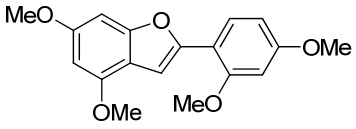
R_f = 0.18 (hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.21 (m, 7H), 7.19-7.11 (m, 1H), 7.05-6.97 (m, 1H), 6.63 (s, 1H), 2.50 (s, 3H), 2.43 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5, 153.4, 138.1, 139.9, 132.3, 130.0, 129.5, 129.4, 126.7, 125.8, 120.7, 115.7, 110.4, 104.7, 21.4 (x2).

HRMS: Calculated for $C_{18}H_{16}O_2$: 248.1201, Found: 248.1209.

2-(2,4-Dimethoxyphenyl)-4,6-dimethoxy-benzofuran (317)



This compound is a colourless solid and was prepared according to General Procedure XV.

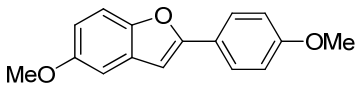
R_f = 0.25 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, 1H, *J* = 9Hz), 7.23 (s, 1H), 6.72 (s, 1H), 6.62 (dd, 1H, *J* = 2Hz, 9Hz), 6.57 (d, 1H, *J* = 2Hz). 6.35 (d, 1H, *J* = 1.5Hz), 3.97 (s, 3H), 3.95 (s, 3H), 3.88 (s, 3H), 3.87 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 158.7, 157.2, 155.4, 153.4, 150.3, 127.2, 113.8, 113.2, 104.7, 101.6, 98.7, 94.0, 88.1, 55.8, 55.6, 55.5, 55.4.

HRMS: Calculated for $C_{18}H_{18}O_5$: 314.1154, Found: 314.1138.

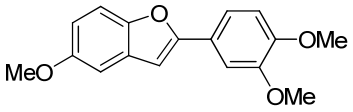
2-(4-Methoxyphenyl)-5-methoxy-benzofuran (Corsifuran C) (305)



This compound was synthesized according to General Procedure XV. ^{1}H NMR data were consistent with published values acquired in C_6D_6[326] and reported above.

R_f = 0.33 (9:1 hexanes: ethyl acetate).

2-(3,4-Dimethoxyphenyl)-5-methoxybenzofuran (318)



This compound is a colourless solid and was prepared on 0.30 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 4:1 hexanes: ethyl acetate as an eluent to give 76.9 mg of **318**.

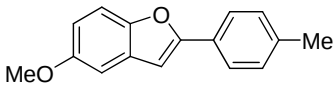
R_f = 0.30 (4:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.39 (m, 3H), 7.05 (d, 1H, *J* = 2.5 Hz), 6.96 (d, 1H, *J* = 8 Hz), 6.92-6.87 (m, 2H), 4.02 (s, 3H), 3.96 (s, 3H), 3.89 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 156.1, 149.8, 149.6, 149.2, 130.1, 123.7, 117.9, 112.4, 111.4, 108.1, 103.3, 100.2, 56.03, 56.01, 55.9.

HRMS: Calculated for $C_{17}H_{16}O_4$: 284.1049, Found: 284.1048.

2-(4-Methylphenyl)-5-methoxybenzofuran (319)



This compound is a colourless solid and was prepared on a 0.20 mmol scale according to General Procedure XV. The product was purified via flash chromatography using a gradient of 9:1 hexanes: dichloromethane to 4:1 hexanes: dichloromethane as an eluent to give 18.7 mg of **319**.

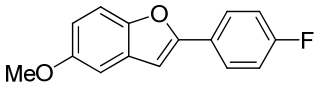
R_f = 0.34 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, 2H, *J* = 8 Hz), 7.42 (d, 1H, *J* = 9 Hz), 7.27 (d, 2H, *J* = 8 Hz), 7.06 (d, 1H, *J* = 2.5 Hz), 6.93 (s, 1H), 6.90 (dd, 1H, J^1 = 2.5 Hz, J^2 = 9 Hz), 3.88 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.1, 156.1, 149.9, 138.6, 129.9, 129.5, 127.9, 124.9, 112.8, 111.5, 103.3, 100.8, 55.9, 21.4.

HRMS: Calculated for $C_{16}H_{14}O_2$: 238.0994, Found: 238.0990.

2-(4-Fluorophenyl)-5-methoxybenzofuran (320)



This compound is a colourless solid and was prepared on a 0.20 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluent to give 33.0 mg of **320**. ^{1}H NMR has been previously reported in acetone.[562]

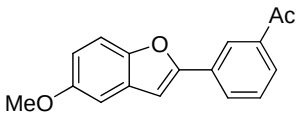
R_f = 0.38 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (m, 2H), 7.42 (d, 1H, *J* = 9 Hz), 7.15 (m, 2H), 7.05 (d, 1H, *J* = 2.5 Hz), 6.92 (dd, 1H, J^1 = 9 Hz, J^2 = 2.5 Hz), 6.90 (s, 1H), 3.88 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 161.2, 156.2, 155.8, 149.9, 129.8, 126.94, 126.89, 126.8, 126.7, 116.0, 115.7, 113.0, 111.6, 103.4, 101.2, 55.9.

HRMS: Calculated for $C_{15}H_{11}FO_2$: 242.0743, Found: 242.0748.

2-(3-Acetylphenyl)-5-methoxybenzofuran (321)



This compound is a colourless solid and was prepared on 0.20 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluent to give 11.4 mg of **321**.

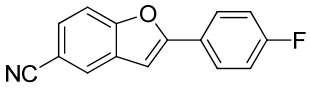
R_f = 0.27 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (m, 1H), 8.00 (m, 2H), 7.57 (t, 1H, *J* = 7 Hz), 7.46 (d, 1H, *J* = 8 Hz), 7.07 (m, 1H), 6.96 (dd, 1H, J^1 = 2.5 Hz, J^2 = 9 Hz), 6.82 (s, 1H), 3.90 (s, 3H), 2.71 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9, 156.4, 155.6, 150.1, 137.6, 131.1, 129.6, 129.1, 128.1, 124.6, 116.1, 114.9, 113.6, 111.8, 103.4, 102.5, 55.9, 26.8.

HRMS: Calculated for $C_{17}H_{14}O_3$: 266.0943, Found: 266.0951.

2-(4-Fluorophenyl)-5-cyanobenzofuran (322)



This compound is a colourless solid and was prepared on a 0.14 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluent to give 27.4 mg of **322**.

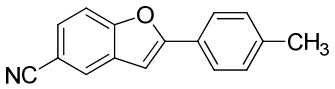
R_f = 0.29 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (m, 1H), 7.86 (m, 2H), 7.60-7.56 (m, 2H), 7.19 (m, 2H), 7.00 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 161.8, 159.5, 157.5, 156.4, 134.3, 130.7, 130.6, 129.9, 128.0, 127.6, 127.5, 127.3, 127.2, 125.8, 125.7, 125.6, 119.4, 116.9, 116.4, 116.2, 116.1, 116.0, 115.6, 112.3, 107.1, 100.5.

HRMS: Calculated for $C_{15}H_8FNO$: 237.0590, Found: 237.0607.

2-(4-Methylphenyl)-5-cyanobenzofuran (323)



This compound is a colourless solid and was prepared on a 0.20 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluent to give 39.6 mg of **323**.

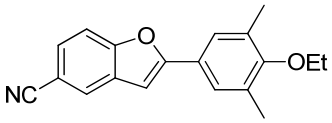
R_f = 0.29 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (m, 1H), 7.80 (m, 2H), 7.59 (m, 2H), 7.32 (m, 2H), 7.03 (s, 1H), 2.46 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 156.4, 139.8, 130.1, 129.7, 127.7, 126.6, 125.6, 125.2, 119.6, 112.2, 106.8, 100.0.

HRMS: Calculated for $C_{16}H_{11}NO$: 233.0841, Found: 233.0846.

2-(4-Ethoxy-3,5-dimethylphenyl)-5-cyanobenzofuran (324)



This compound is a colourless solid and was prepared on a 0.39 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluent to give 109.3 mg of **324**.

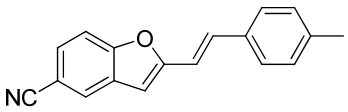
R_f = 0.20 (9:1 hexane: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (m, 1H), 7.55-7.50 (m, 3H), 6.92 (s, 1H), 3.90 (q, 2H, *J* = 7 Hz), 2.36 (s, 6H), 1.46 (t, 3H, *J* = 7 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 157.5, 156.4, 131.9, 130.1, 127.5, 125.9, 125.5, 124.6, 119.6, 112.1, 106.8, 99.8, 68.2, 16.5, 15.8.

HRMS Calculated for: $C_{19}H_{17}NO_2$: 291.1259, Found: 291.1273.

2-(2-*trans*-(4-Methylphenyl)ethenyl)-5-cyanobenzofuran (325)



This compound is a colourless solid and was prepared on a 0.14 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 14:1 hexanes: ethyl acetate as an eluant to give 25.2 mg of **325**. We were unable to obtain this compound in a highly pure form.

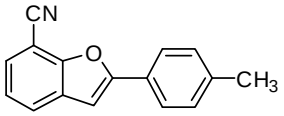
R_f = 0.25 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (m, 1H), 7.57 (m, 1H), 7.49-7.23 (m, 6H), 6.99 (d, 1H, *J* = 16Hz), 6.71 (s, 1H), 2.42 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6, 156.5, 139.0, 133.2, 132.5, 129.6, 128.0, 126.9, 125.5, 119.5, 114.4, 111.9, 106.8, 103.7, 21.4.

Preparation of Arylated Vinyl Chlorides and Procedure for the Cyclization to Benzofurans

2-(4-Methylphenyl)-7-cyanobenzofuran (328)



The boronic acid, Pd_2dba_3, DPEphos, CsF and Cs_2CO_3 bases were placed into a one piece round bottom flask/condenser, which was sealed with a septum and purged with argon for 20-30 min. A 0.4 M solution of the 1,2-dichlorovinyl ether in dioxane was added. The solution was vigorously stirred and brought to reflux. When TLC showed that no further change was occurring, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated onto silica gel, applied to a column and eluted with 9:1 petroleum ether: ethyl acetate. The arylated vinyl chloride (**327**) was obtained as a colourless solid which was characterized by ^{1}H and ^{13}C NMR (data below) before subjecting it to direct arylation conditions.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (dd, 1H, J^1 = 1.5 Hz, J^2 = 7.7 Hz), 7.46-7.39 (m, 3H), 7.19 (d, 2H, *J* = 7.7 Hz), 7.10 (dt, 1H, J^1 = 1.0 Hz, J^2 = 7.7 Hz), 6.89 (m, 1H), 6.51 (s, 1H), 2.38 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 150.8, 140.0, 134.4, 133.9, 129.8, 129.3, 125.3, 122.6, 115.9, 114.9, 107.4, 102.6, 21.3.

The aryl vinyl ether **327** prepared above (13.0 mg, 0.045 mmol), Pd_2dba_3 (1.0 mg, 2.5mol%), DPEphos (1.3 mg, 5mol%), CsF (20.7 mg, 3 equiv) and Cs_2CO_3 (44.5 mg, 3 equiv) were placed into a one piece round bottom flask/condenser, sealed with a septum and purged with argon for 20-30 min, then 0.45 mL of dioxane was added. The solution was vigorously stirred and brought to reflux. When complete, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated onto silica gel, applied to a column and eluted with 10:1 petroleum ether: ethyl acetate to give 5.1 mg of **328**.

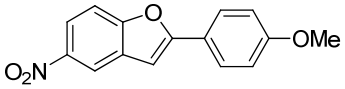
R_f = 0.36 (10:1 petroleum ether: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.80 (m, 3H), 7.58 (m, 1H), 7.36-7.29 (m, 3H), 7.05 (s, 1H), 2.46 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 154.4, 139.8, 130.5, 129.7, 127.8, 126.4, 125.6, 125.3, 123.2, 115.3, 110.3, 96.1, 21.5.

We were unable to acquire satisfactory HRMS for this compound.

2-(4-Methoxyphenyl)-5-nitro-benzofuran (330)



The boronic acid, Pd_2dba_3, DPEphos, CsF and Cs_2CO_3 bases were placed into a one piece round bottom flask/condenser, sealed with a septum and purged with argon for 20-30 min. A 0.4 M solution of the 1,2-dichlorovinyl ether in dioxane was added. The solution was vigorously stirred and brought to reflux. When complete, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the

aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated onto silica gel, applied to a column and eluted with a gradient of 9:1 to 4:1 hexanes: ethyl acetate to give compound as a colourless solid. This material (**329**) was characterized by ^{1}H and ^{13}C NMR (data below) before subjecting to direct arylation conditions.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, 1H, *J* = 1.7 Hz), 7.43 (m, 3H), 6.87 (m, 2H), 6.82 (d, 1H, *J* = 8.6 Hz), 6.34 (s, 1H), 3.81 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 160.8, 150.4, 142.8, 126.8, 126.0, 124.5, 116.0, 114.5, 106.1, 55.4.

The aryl vinyl ether **329** prepared above (54.9 mg, 0.17 mmol), Pd_2dba_3 (4.1 mg, 2.5mol%), DPEphos (4.9 mg, 5mol%), CsF (81.7 mg, 3 equiv) and Cs_2CO_3 (175.4 mg, 3 equiv) were placed into a one piece round bottom flask/condenser, sealed with a septum and purged with argon for 20-30 min, then 0.45 mL of dioxane was added. The solution was vigorously stirred and brought to reflux. When complete, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated onto silica gel, applied to a column and eluted with a 6:1 hexanes: ethyl acetate to give 35.7 mg of compound **330** as a colourless solid.

R_f = 0.39 (6:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, 1H, *J* = 2.3Hz), 8.22 (dd, 1H, J^1 = 2.3Hz, J^2 = 8.8Hz), 7.85 (m, 2H), 7.59 (d, 1H, *J* = 8.8 Hz), 7.05 (m, 2H), 7.02 (s, 1H), 3.92 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 159.5, 157.5, 144.3, 130.0, 126.9, 122.0, 119.7, 116.9, 114.5, 111.2, 99.9, 55.5.

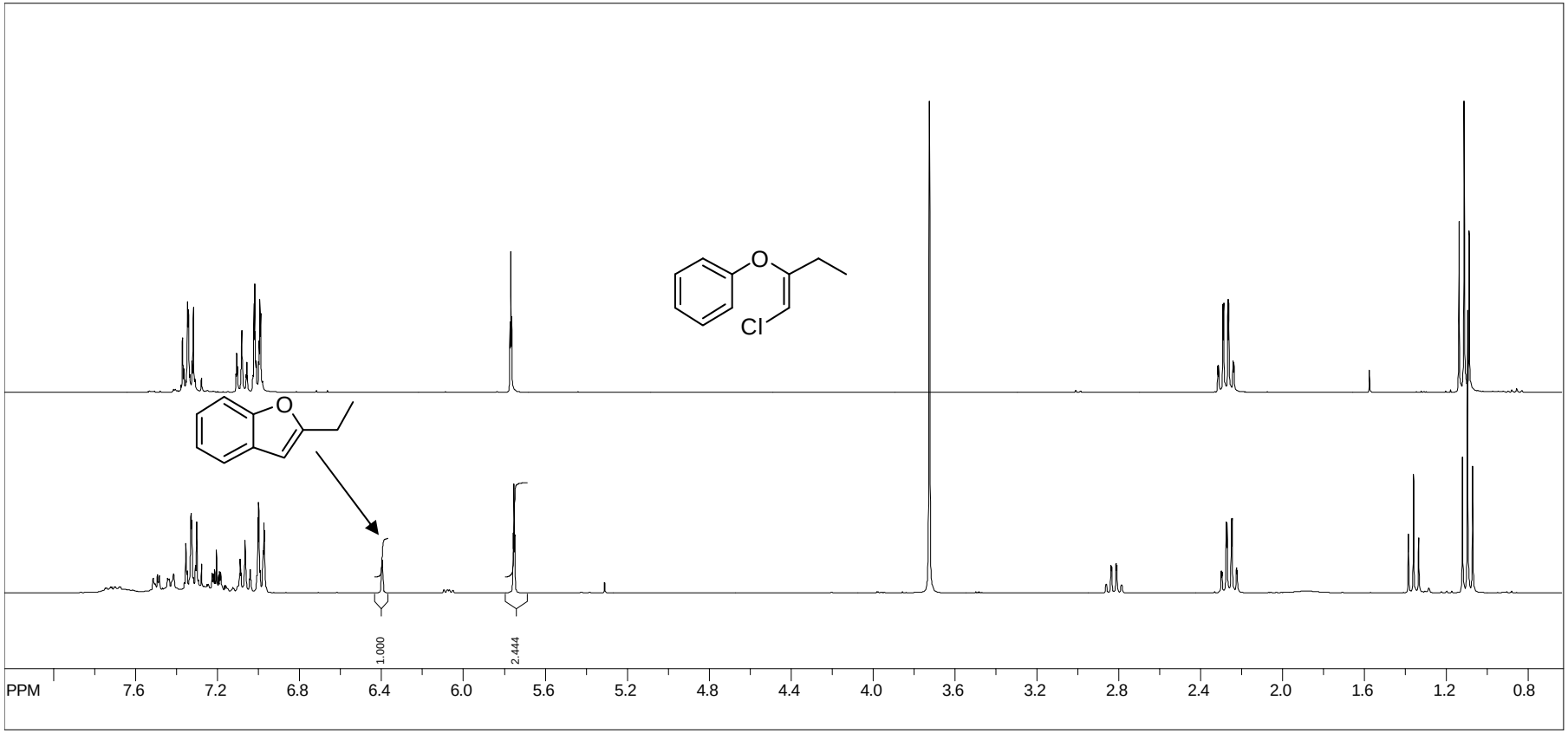
HRMS Calculated for $C_{15}H_{11}NO_4$: 269.0688, Found: 269.0700.

Synthesis of 2-alkyl benzofurans

2-Ethylbenzofuran (332)

Alkyl vinyl ether **222** (34.3 mg, 0.18 mmol), Pd_2dba_3 (5.1 mg, 5.6 μmol, 0.03 equiv), DPEphos (6.2 mg, 11.2 μmol, 0.06 equiv), CsF (85.5 mg, 0.563 mmol, 3 equiv) and Cs_3CO_3 (183.4 mg, 0.563 mmol, 3 equiv) were placed into an oven-dried test tube, sealed with a septum and purged with argon for 15 min. Anhydrous and degassed dioxane (0.8 mL) was added, and the suspension was brought to reflux. After 72 h (TLC still indicated starting material), the reaction was cooled to room temperature, diluted with dichloromethane and water was added. The layers were separated and the organic layer was dried with magnesium sulphate, filtered and concentrated. Compound **332** was identified by comparing the crude ^{1}H NMR spectrum to literature data for the known compound.[342] Integration of the vinylic ^{1}H signals from the starting material and the product indicated only 29% conversion to 2-ethylbenzofuran.

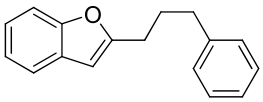
SpinWorks 2.5: cyclization of x_23



file: Z:\Laina\lmgx\lmgx_65\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(3-Phenylpropyl)benzofuran (333)



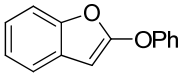
An oven-dried one piece round bottom flask/condenser was sealed with a septum and purged with argon for 20-30 min. Allyl benzene (37 μL, 0.27 mmol, 1.2 equiv) was added, followed by 0.56 mL of a 0.5 M solution of 9-BBN in THF (0.27 mmol, 1.2 equiv) and the solution was stirred at room temperature. After one hour, Pd $(OAc)_2$ (2.6 mg, 5 mol%), SPhos (9.5 mg, 10 mol%), Cs_2CO_3 (333.0 mg, 1.02 mmol, 4.4 equiv) were added, followed by 1.5 mL of a 0.15M solution of dichlorophenol ether **93**. The suspension was brought to reflux and stirred for 17.5 h. When complete, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated onto silica gel. The product was purified via flash chromatography to give 39.5 mg of **333** as a colourless viscous oil. Proton and carbon NMR were consistent with published data.[344]

R_f = 0.20 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (m, 1H), 7.48 (m, 1H), 7.39-7.23 (m, 8H), 6.45 (m, 1H), 2.86 (t, 2H, *J* = 7.5 Hz), 2.78 (t, 2H, *J* = 7.9 Hz), 2.15 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 154.7, 141.8, 129.0, 128.6, 128.4, 126.0, 123.2, 122.5, 120.3, 110.8, 102.2, 35.3, 29.3, 27.9.

2-Phenoxybenzofuran (334)



Ketene acetal **132** (88.6 mg, 0.36 mmol, 1 equiv), $Pd(OAc)_2$ (12.1 mg, 0.018 mmol, 5 mol%), *t*Bu-ferrocene **345** (17.4 mg, 0.036 mmol, 10 mol%) and K_2CO_3 (0.1489 g,

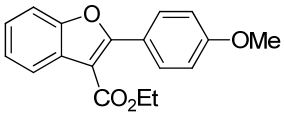
1.077 mmol, 3 equiv) were placed in an oven-dried test tube, sealed with a septum and purged with argon for 20 min. To this was added 1.8 mL DMA and the reaction was heated at 135 °C for 11 h, at which time the reaction was concentrated. NMR data below has an approximately equal mixture of **132** and **334**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.02 (m, 23H). 5.84 (s, 1.1H, **334**), 5.58 (s, 1H, **132**)

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 155.7, 154.6, 154.1, 153.3, 149.6, 129.9, 129.7, 129.6, 128.9, 124.8, 124.3, 123.9, 123.2, 122.8, 121.3, 120.0, 118.2, 117.8, 117.2, 110.7, 91.4, 83.9.

334 ^{13}C NMR (75 MHz, $CDCl_3$, signals from **132** removed) δ 160.1, 155.7, 149.6, 129.9, 128.9, 124.8, 123.2, 122.8, 121.3, 120.0, 118.2, 110.7, 83.9.

Ethyl 2-(4-methoxyphenyl)benzofuran-3-carboxylate (336)



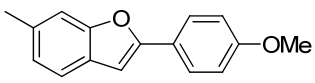
This compound was a colourless solid and was prepared on a 0.16 mmol scale according to General Procedure XIII. This material was characterized by ^{1}H NMR only.

R_f = 0.33 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (m, 3H), 7.55-7.52 (m, 1H), 7.38-7.33 (m, 2H), 7.03 (m, 2H), 4.44 (q, 2H, *J* = 7Hz), 3.19 (s, 3H), 1.45 (t, 3H, *J* = 7Hz).

Synthesis of benzofurans from unsymmetrical dichlorovinyl phenol ethers

2-(4-Methoxyphenyl)-6-methylbenzofuran (343)



This compound is a colourless solid and was prepared on 0.40 mmol scale according to General Procedure XV. The product was purified via flash chromatography using a gradient of hexanes to 9:1 hexanes: ethyl acetate as an eluent to give 74.9 mg of **343**.

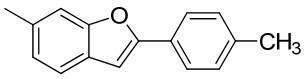
R_f = 0.49 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (m, 2H), 7.48 (d, 2H, *J* = 8 Hz), 7.37 (s, 1H), 7.10 (d, 1H, *J* = 8 Hz), 7.02 (m, 2H), 6.88 (s, 1H), 3.90 (s, 3H), 2.53 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 155.5, 155.2, 134.0, 127.0, 126.3, 124.2, 123.6, 120.1, 114.3, 111.3, 99.6, 55.4, 21.8.

HRMS: Calculated for $C_{16}H_{14}O_2$: 238.0994, Found: 238.0998.

2-(4-Methylphenyl)-6-methylbenzofuran (344)



This compound is a colourless solid and was prepared on 0.40 mmol scale according to General Procedure XV. The product was purified via flash chromatography using a gradient of hexanes to 19:1 hexanes: ethyl acetate as an eluent to give 77.5 mg of **344**.

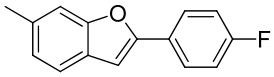
R_f = 0.65 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, 2H, *J* = 8 Hz), 7.51 (d, 1H, *J* = 8 Hz), 7.40 (s, 1H), 7.13 (d, 2H, *J* = 8 Hz), 7.12 (d, 1H, *J* = 8 Hz), 6.98 (s, 1H), 2.56 (s, 3H), 2.47 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 155.3, 138.3, 134.3, 129.5, 128.0, 126.9, 124.8, 124.3, 120.3, 111.4, 100.5, 21.8, 21.4.

HRMS: Calculated for $C_{16}H_{14}O$: 222.1045, Found: 222.1048.

2-(4-Fluorophenyl)-6-methylbenzofuran (345)



This compound is a colourless solid and was prepared on a 0.40 mmol scale according to General Procedure XV. The product was purified via flash chromatography using a gradient of hexanes to 19:1 hexanes: ethyl acetate as an eluent to give 62.8 mg of **345**.

$\mathbf{R_f}$ = 0.63 (9:1 hexanes: ethyl acetate).

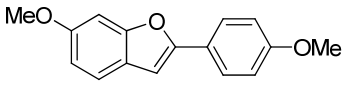
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (m, 2H), 7.50 (d, 1H, *J* = 8 Hz), 7.37 (s, 1H), 7.21-7.09 (m, 3H), 6.94 (s, 1H), 2.54 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 161.1, 155.3, 154.5, 150.8, 134.6, 127.1, 127.0, 126.7, 126.6, 126.5, 124.5, 120.4, 116.0, 115.7, 111.4, 100.93, 100.91, 21.8.

^{19}F NMR (282 MHz, $CDCl_3$) δ -112.78.

HRMS: Calculated for $C_{15}H_{11}FO_2$: 226.0794, Found: 226.0782.

2-(4-Methoxyphenyl)-6-methoxybenzofuran (346)



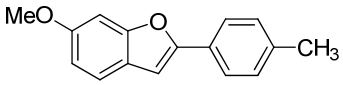
This compound was synthesized according to General Procedure XV. ^{1}H NMR data were consistent with published values.[563]

$\mathbf{R_f}$ = 0.38 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, 2H), 7.43 (d, 1H, *J* = 9Hz), 7.08 (d, 1H, *J* = 2Hz), 6.99 (d, 2H), 6.88 (dd, 1H, *J* = 2Hz, 9Hz), 6.83 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 157.7, 155.7, 155.3, 126.0, 123.7, 122.9, 120.7, 114.3, 111.7, 99.5, 96.0, 55.8, 55.4.

2-(4-Methylphenyl)-6-methoxybenzofuran (347)



This compound is a colourless solid and was prepared on a 0.29 mmol scale according to General Procedure XV. The product was purified via flash chromatography using a gradient of hexanes to 9:1 hexanes: diethylether as an eluent to give 44.4 mg of **347**.

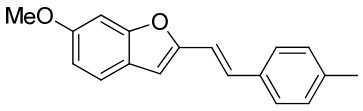
R_f = 0.15 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (m, 2H), 7.48 (dd, 1H, J^1 = 1 Hz, J^2 = 9 Hz), 7.29 (d, 2H, J = 8 Hz), 7.13 (m, 1H), 6.96-6.90 (m, 2H), 3.92 (s, 3H), 2.45 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 155.8, 155.5, 138.1, 129.5, 128.0, 124.5, 122.7, 120.9, 111.9, 100.4, 95.9, 55.8, 21.4.

HRMS Calculated for $C_{16}H_{14}O_2$: 238.0994, Found: 238.0990.

2-(2-*trans*-(4-Methylphenyl)ethenyl)-6-methylbenzofuran (348)



This compound is a colourless solid and was prepared on a 0.29 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 3:2 hexanes: dichloromethane as an eluent to give 46.9 mg of **348**.

R_f = 0.43 (3:2 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, 2H, J = 8 Hz), 7.31-7.10 (m, 5H), 6.96 (d, 1H, J = 16 Hz), 6.76 (s, 1H), 6.66 (d, 1H, J = 8 Hz), 3.96 (s, 3H), 2.39 (s, 3H).

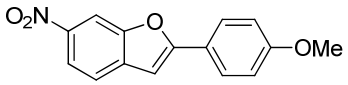
^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 154.1, 153.3, 138.1, 134.0, 129.7, 129.5, 126.6, 125.2, 119.5, 115.6, 104.2, 103.4, 102.3, 55.6, 21.3.

We were unable to obtain satisfactory HRMS from this compound.

Reaction between 3-nitrophenol 125 and *p*-methoxyphenyl boronic acid

This reaction was performed on a 0.32 mmol scale according to General Procedure XV, to give a mixture of **349** and **350** which were separated via flash chromatography using 9:1 hexanes: dichloromethane as an eluant.

2-(4-Methoxyphenyl)-6-nitro-benzofuran (349)



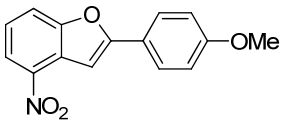
R_f = 0.26 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.18 (dd, 1H, *J* = 2Hz, 9Hz), 7.85 (d, 2H), 7.61 (d, 1H, *J* = 9Hz), 7.03 (d, 2H), 6.98 (s, 1H), 3.90 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ161.7, 161.2, 153.3, 144.3, 135.7, 127.2, 121.9, 120.0, 119.0, 114.6, 107.4, 99.7, 55.5.

We were unable to obtain satisfactory mass spectra of this compound.

2-(4-Methoxyphenyl)-4-nitro-benzofuran (350)



R_f = 0.37 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, 1H, *J* = 8Hz), 7.90 (d, 2H), 7.80 (d, 1H, *J* = 8Hz), 7.65 (s, 1H), 7.35 (t, 1H), 7.04 (d, 2H), 3.91 (s, 3H).

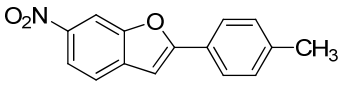
^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 160.3, 155.9, 140.1, 127.4, 125.8, 122.7, 121.8, 119.7, 117.0, 114.6, 99.9, 55.5.

HRMS: Calculated for $C_{15}H_{11}NO_4$: 269.0688, Found: 269.0690.

Reaction between 3-nitrophenol 125 and *p*-methylphenyl boronic acid

This reaction was performed on a 0.42 mmol scale according to to General Procedure XV, to give a mixture of **351** and **352** which were separated via flash chromatography using 14:1 hexanes: diethyl ether as an eluant.

2-(4-Methylphenyl)-6-nitro-benzofuran (351)



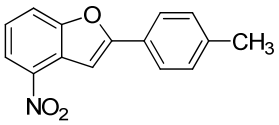
$\mathbf{R_f}$ = 0.29 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (m, 1H), 8.17 (m, 1H), 7.79 (d, 2H, *J* = 8 Hz), 7.62 (m, 1H), 7.31 (d, 2H, *J* = 8 Hz), 7.04 (s, 1H), 2.44 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 153.3, 144.5, 140.5, 135.5, 129.8, 126.4, 125.5, 120.3, 118.9, 107.5, 100.6, 21.5.

HRMS: Calculated for $C_{15}H_{11}NO_3$: 253.0739, Found: 253.0737.

2-(4-Methylphenyl)-4-nitro-benzofuran (352)



$\mathbf{R_f}$ = 0.41 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (m, 1H), 7.89-7.80 (m, 3H), 7.73 (s, 1H), 7.40-7.27 (m, 4H), 2.45 (s, 3H).

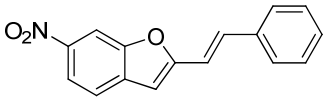
^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 155.9, 140.5, 129.8, 126.4, 125.7, 125.6, 123.0, 119.7, 117.2, 100.8, 21.6.

HRMS: Calculated for $C_{15}H_{11}NO_3$: 253.0739, Found: 253.0742.

Reaction between 3-nitrophenol 125 and *trans*-styryl boronic acid

This reaction was performed on a 0.42 mmol scale according to to General Procedure XV, to give a mixture of **353** and **354** which were separated via flash chromatography using 14:1 hexanes: diethyl ether as an eluant.

2-(trans-2-Phenylethenyl)-6-nitro-benzofuran (353)



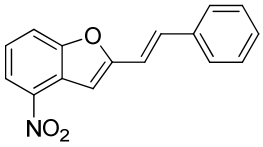
R_f = 0.21 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (m, 1H), 8.15 (m, 1H), 7.61-7.55 (m, 3H), 7.48-7.34 (m, 4H), 7.02 (d, 1H, *J* = 16 Hz), 6.76 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 153.5, 144.9, 135.8, 135.2, 133.9, 129.1, 129.0, 127.2, 120.3, 119.0, 115.3, 107.2, 104.7.

HRMS: Calculated for $C_{16}H_{11}NO_3$: 265.0739, Found: 265.0734.

2-(trans-2-Phenylethenyl)-4-nitro-benzofuran (354)



R_f = 0.34 (9:1 hexanes: diethyl ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (m, 1H), 7.76 (m, 1H), 7.57 (m, 1H), 7.50-7.32 (m, 7H), 7.07 (d, 1H, *J* = 16Hz).

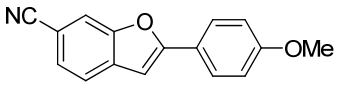
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 156.0, 140.3, 135.8, 133.9, 132.8, 129.1, 129.0, 128.7, 127.2, 126.4, 125.3, 123.6, 119.7, 116.9, 115.4, 104.9.

HRMS: Calculated for $C_{16}H_{11}NO_3$: 265.0739, Found: 265.0725.

Reaction between 3-cyanophenol 122 and *p*-methoxyphenyl boronic acid

This reaction was performed on a 0.28 mmol scale according to to General Procedure XV, to give a mixture of **355** and **356** which were separated via flash chromatography using 14:1 hexanes: diethyl ether as an eluant.

2-(4-Methoxyphenyl)-6-cyano-benzofuran (355)



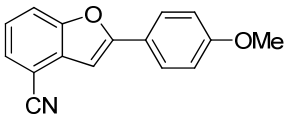
R_f = 0.16 (9:1 hexanes: ethyl acetate). ^{1}H NMR spectra in DMSO-d_6 of this compound has been previously reported.[564]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.82 (m, 3H), 7.65 (m, 1H), 7.52 (m, 1H), 7.05 (m, 2H), 6.97 (s, 1H), 3.92 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 159.8, 153.4, 134.0, 127.1, 126.8, 122.0, 121.2, 119.7, 115.0, 114.5, 106.2, 99.7, 55.5.

HRMS Calculated for $C_{16}H_{11}NO_2$: 249.0790, Found: 249.0799.

2-(4-Methoxyphenyl)-4-cyano-benzofuran (356)



R_f = 0.26 (9:1 hexanes: ethyl acetate).

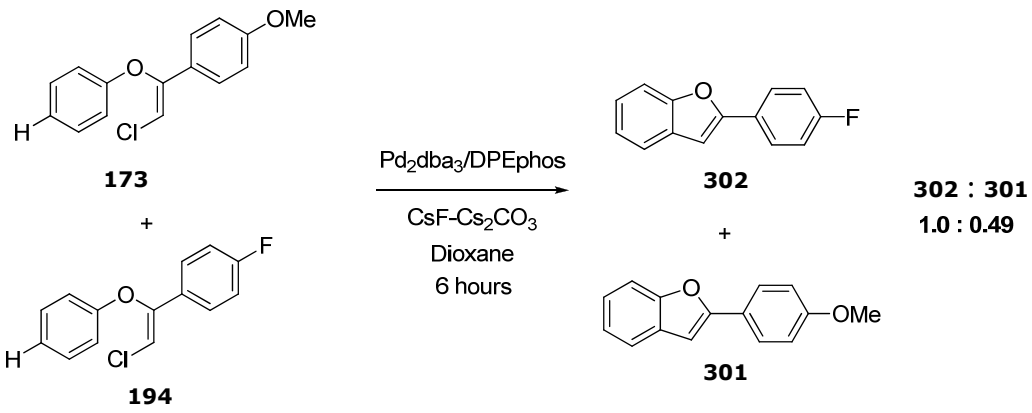
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (m, 2H), 7.70 (m, 1H), 7.54 (m, 1H), 7.30 (m, 1H), 7.08 (s, 1H), 7.01 (m, 2H), 3.89 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 159.0, 154.1, 132.5, 127.5, 127.1, 123.6, 121.9, 117.8, 115.4, 114.5, 103.1, 98.3, 55.5.

HRMS Calculated for $C_{16}H_{11}NO_2$: 249.0790, Found: 249.0783.

4.6.1 Procedures from Section 2.6.3 – Mechanistic Investigations

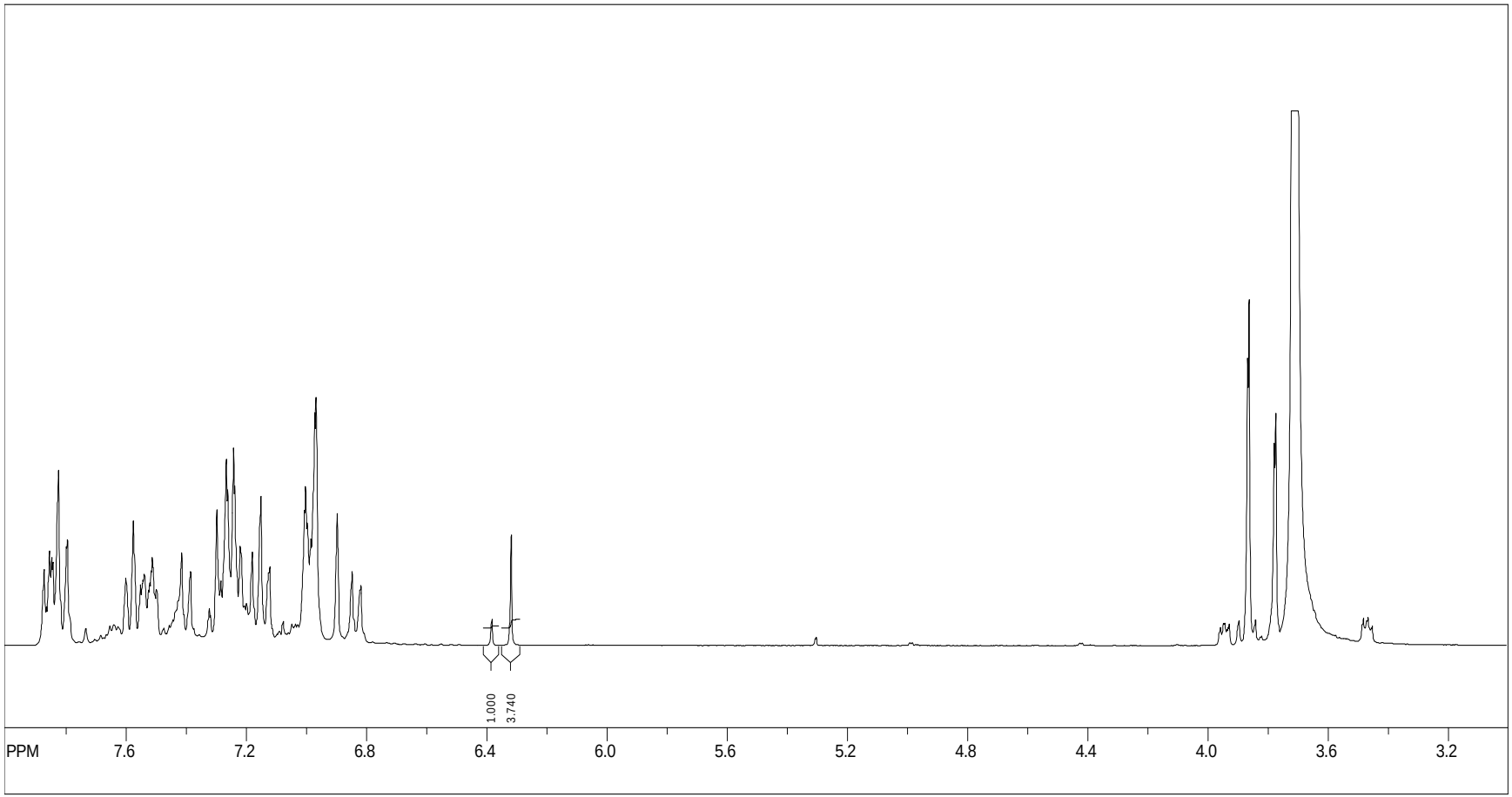
Intramolecular Direct Arylation Competition Experiment



Pd_2dba_3 (5.3 mg, 2.5mol%), DPEphos (6.5 mg, 5mol%), CsF (107 mg, 3 equiv) and Cs_2CO_3 (230 mg, 3 equiv) were placed into a one piece round bottom flask/condenser, sealed with a septum and purged with argon for 20-30 min. A 0.39 M solution of arylchloroethylene **173** in dioxane (0.6 mL, 0.23 mmol, 1 equiv), arylchloroethylene **194** (61.2 mg, 0.23 mmol, 1 equiv) and an additional 0.6 mL of dioxane were added. The solution was vigorously stirred and brought to reflux. After 6 h, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and evaporated. The residual material was characterized by crude NMR and GCMS.

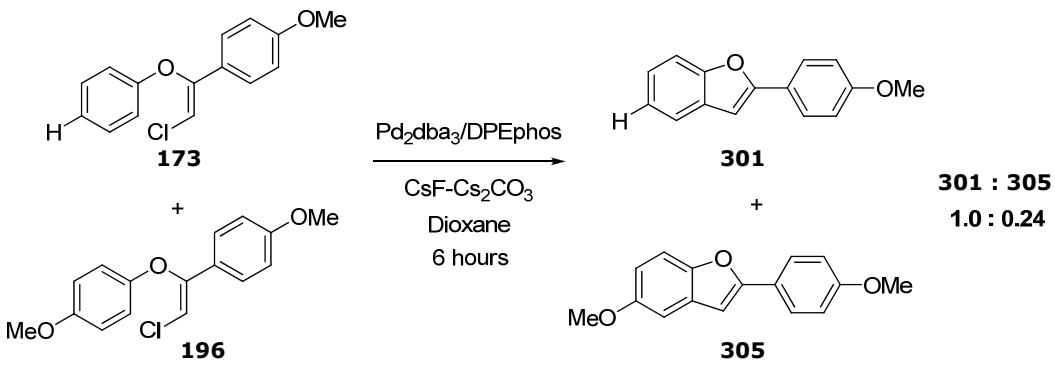
The consumption of the arylchloroethylenes can be measured using ^1H NMR; after 6 h, the ratio of **173**:**194** was 3.76:1.0 (see spectrum below). A similar ratio (3:1) was found by integrating GCMS peaks. Formation of the benzo[b]furans cannot accurately be determined by NMR due to overlap of the signals, so only GCMS data was used. 2-(4-Fluorophenyl)benzofuran was formed at approximately twice the rate that 2-(4-methoxyphenyl)benzofuran was formed.

SpinWorks 2.5: C1 aryl variation: pF vs pMeO



file: Z:\Laina\lmgxvi\lmgxvi_25\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

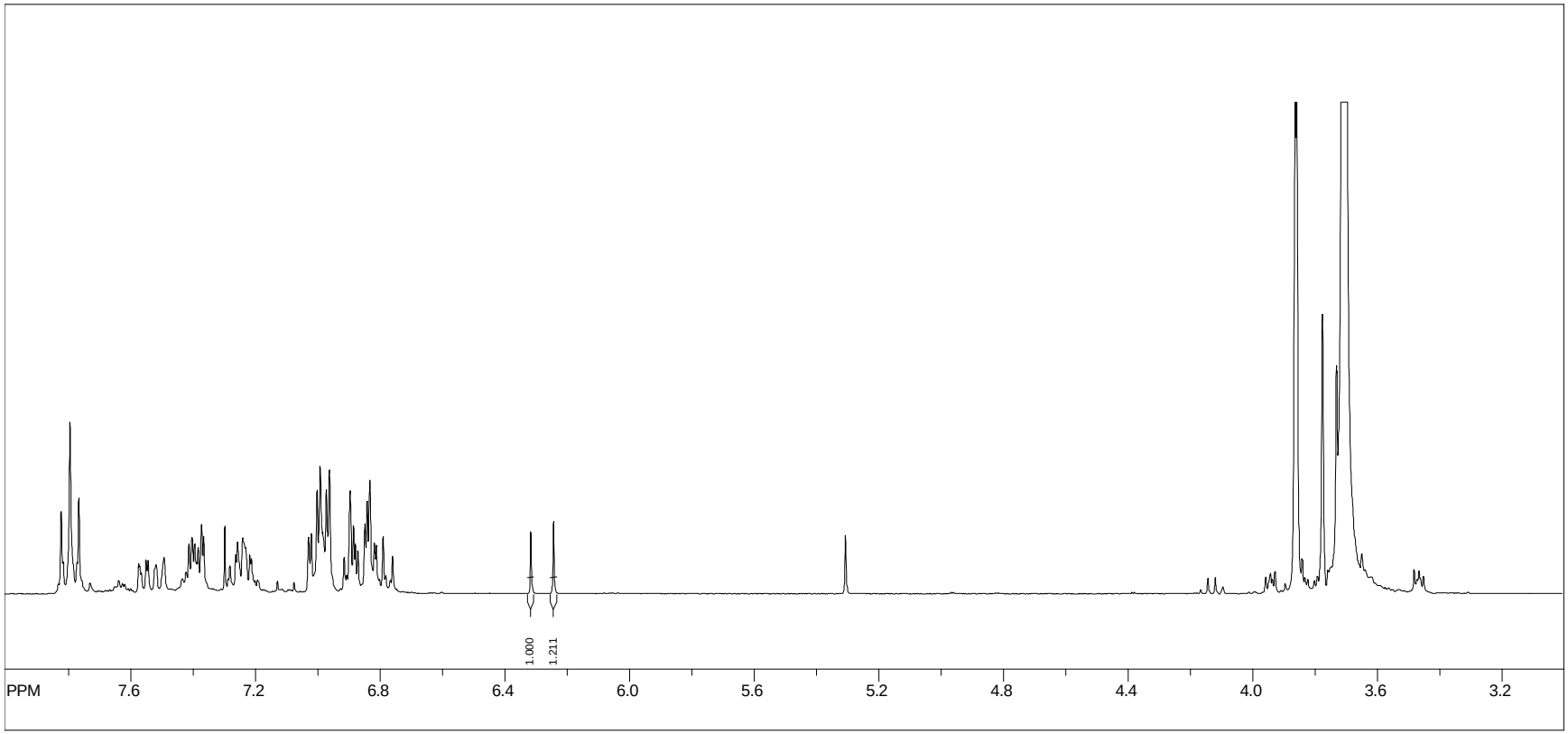
freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000



Pd_2dba_3 (3.8 mg, 2.5mol%), DPEphos (4.6 mg, 5mol%), CsF (76.5 mg, 3 equiv) and Cs_2CO_3 (164.1 mg, 3 equiv) were placed into a one piece round bottom flask/condenser, sealed with a septum and the headspace was purged with argon for 20-30 min. A 0.42 M solution of arylchloroethylene **196** in dioxane (0.5 mL, 0.17 mmol, 1 equiv), arylchloroethylene **173** (43.7 mg, 0.17 mmol, 1 equiv) and an additional 0.6 mL of dioxane were added. The solution was vigorously stirred and brought to reflux. After 6 h, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and evaporated. The residual material was characterized by crude NMR and GCMS.

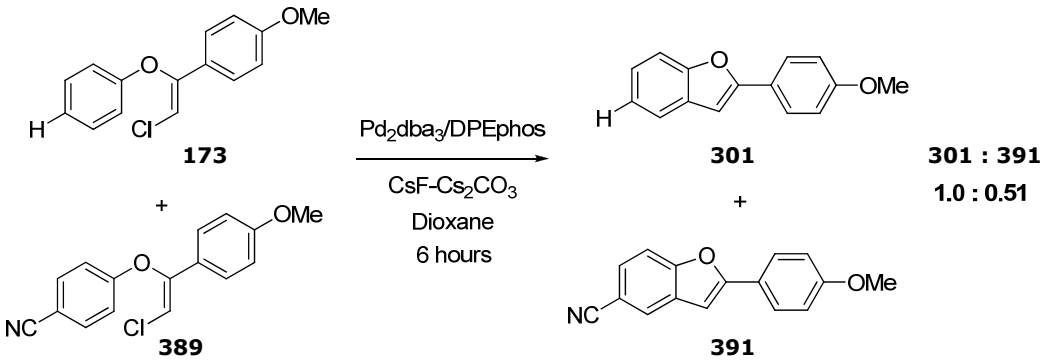
The consumption of the arylchloroethylenes can be identified via crude NMR; after 6 h, the ratio of **173**:**196** was 1.0:1.21 (see spectrum below).

SpinWorks 2.5: phenoxy variation: H vs pMeO



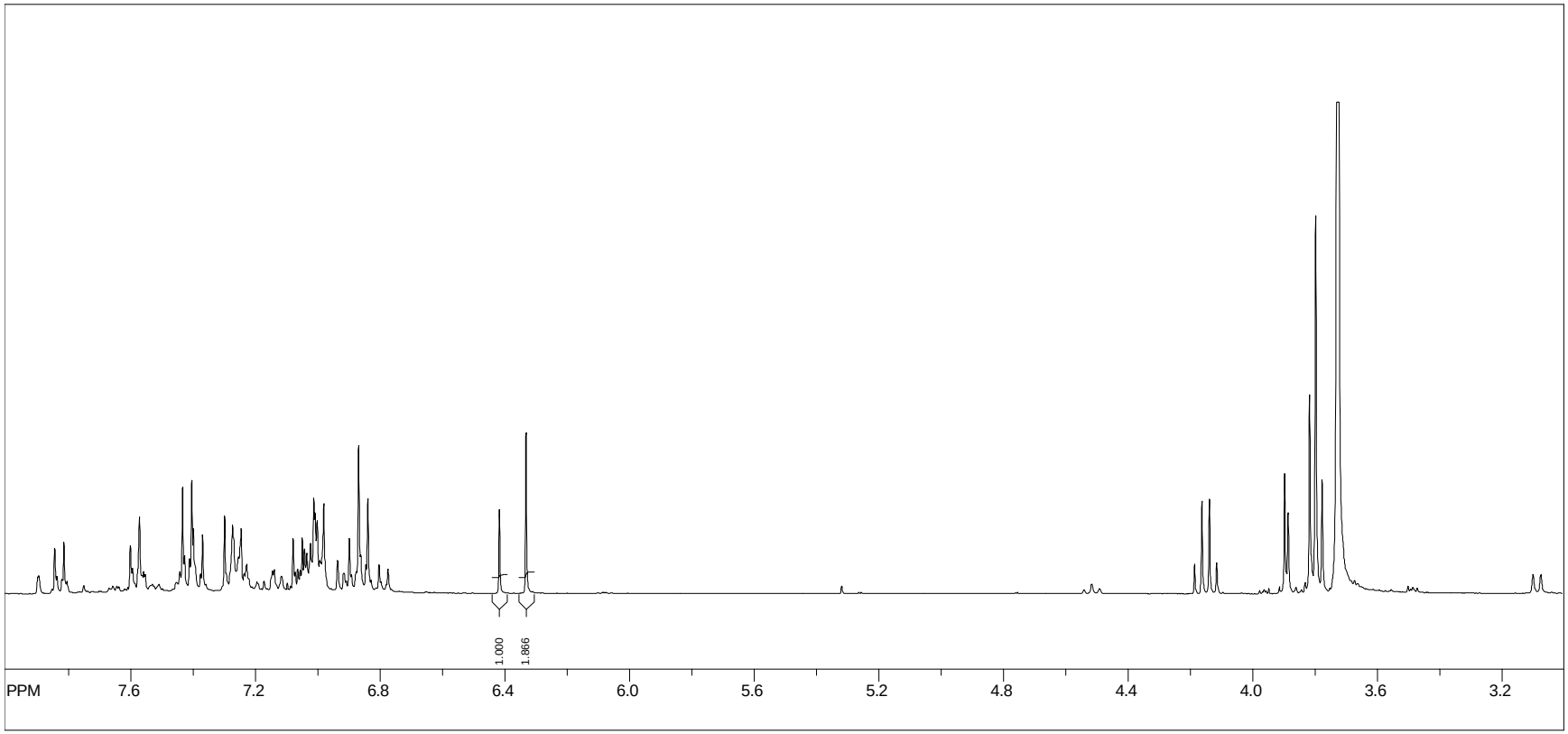
file: Z:\Laina\lmgxvi\lmgxvi_26\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000



Pd_2dba_3 (5.3 mg, 2.5mol%), DPEphos (6.5 mg, 5mol%), CsF (107 mg, 3 equiv) and Cs_2CO_3 (230 mg, 3 equiv) were placed into a one piece round bottom flask/condenser, sealed with a septum and the headspace was purged with argon for 20-30 min. A 0.1744 M solution of arylchloroethylene **389** (1.4 mL, 0.23 mmol, 1 equiv) in dioxane and arylchloroethylene **173** (61.3 mg, 0.17 mmol, 1 equiv) were added. The solution was vigorously stirred and brought to reflux. After 6 h, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and evaporated. The residual material was characterized by crude NMR and GCMS.

SpinWorks 2.5: phenoxy variation: H vs pCN



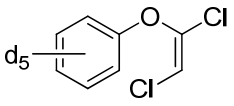
file: Z:\Laina\lmgxvi\lmgxvi_27\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

Synthesis of Deuterated Benzofurans and Determination of KIEs

Intermolecular Isotope Effects

(E)-(1,2-Dichlorovinyloxy)pentadeuterobenzene (93-d_5)

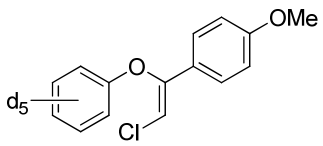


KH (1.4 g, 10.2 mmol, 2.05 equiv) was weighed into a round-bottom flask and washed with 3 portions of either pentane or petroleum ether. The KH was then suspended in 20 mL THF. A solution of hexadeuterophenol (0.500 g, 5 mmol, 1.0 equiv) in 5 mL THF was added drop wise (vigorous gas evolution was noted) and the reaction was allowed to stir for 30 min. The suspension was cooled to approximately −50 ºC ($CHCl_3/CO_2$(s) bath). Trichloroethylene (0.68 mL, 7.5 mmol, 1.5 equiv) was then added drop wise. The reaction was allowed to warm gradually to room temperature overnight. The reaction was diluted with petroleum ether and quenched with ice-cold water. The phases were separated and the aqueous phase was extracted once more with petroleum ether. The organic layers were combined, dried with sodium sulfate, filtered and concentrated to give a yellow to dark brown oil. The crude oil was applied to a silica column pre-treated with triethylamine (ca. 2.5 vol% with respect to the volume of dry silica) and eluted with petroleum ether to give 0.8213 g of **93-d_5** (85%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.01 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 140.1, 129.6, 129.3, 129.0, 124.3, 124.0, 123.7, 117.1, 116.7, 116.4, 103.8.

(Z)-1-(2-Chloro-1-(4-methoxyphenyl)vinyloxy)-2,3,4,5,6-pentadeuterobenzene (173-d_5)



Prepared via an analogous method to **173**. The product was purified by flash chromatography using 12:1 hexanes: ethyl acetate as an eluent to give 511.0 mg of 45-d.

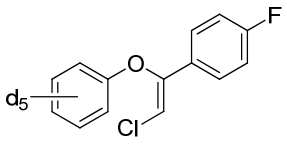
Rf = 0.27 (14:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, CDCl3) δ 7.45 (m, 2H), 6.88 (m, 2H), 6.35 (s, 1H), 3.82 (s, 3H).

^{13}C NMR (75 MHz, CDCl3) δ 160.4, 156.1, 151.2 129.1, 128.8, 127.1, 125.7, 115.9, 115.6, 115.3, 114.2, 105.1, 55.3.

HRMS: Calculated for $C_{15}H_8D_5ClO_2$: 265.0918, Found: 265.0904.

(Z)-1-(2-Chloro-1-(4-fluorophenyl)vinyloxy)-2,3,4,5,6-pentadeuterobenzene (194-d_5)



Prepared via an analogous method to **194**. The product was purified via flash chromatography using 14:1 hexanes: ethyl acetate as an eluent to give 479.0 mg of **194-d_5**.

R_f = 0.12 (14:1 hexanes: dichloromethane).

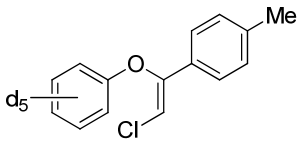
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.45 (m, 2H), 7.06-6.99 (m, 2H), 6.39 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 161.6, 155.9, 150.6, 129.53, 129.45, 129.4, 129.2, 128.9, 128.5, 127.7, 127.6, 116.1, 115.9, 115.7, 115.6, 115.3, 106.82, 106.79.

^{19}F NMR (282 MHz, $CDCl_3$) δ -113.34.

HRMS: Calculated for $C_{14}H_5D_5ClFO$: 253.0718, Found: 253.0710.

(Z)-1-(2-Chloro-1-(4-methylphenyl)vinyloxy)-2,3,4,5,6-pentadeuterobenzene (193-d_5)



Prepared via an analogous method to **193**. The product was purified via flash chromatography using 9:1 hexanes: ethyl acetate as an eluent to give 264.8 mg of **193-d_5**.

R_f = 0.13 (14:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, 2H, *J* = 8Hz), 7.18 (d, 2H, *J* = 8Hz), 6.45 (s, 1H), 2.38 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1, 151.4, 139.3, 130.4, 129.5, 129.1, 128.8, 125.9, 125.6, 125.5, 125.2, 122.1, 121.8, 121.5, 115.9, 115.6, 115.3, 106.2, 21.3.

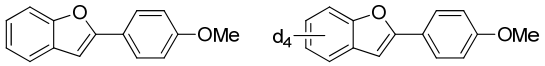
HRMS: Calculated for $C_{15}H_8D_5ClO$: 249.0968, Found: 249.0975.

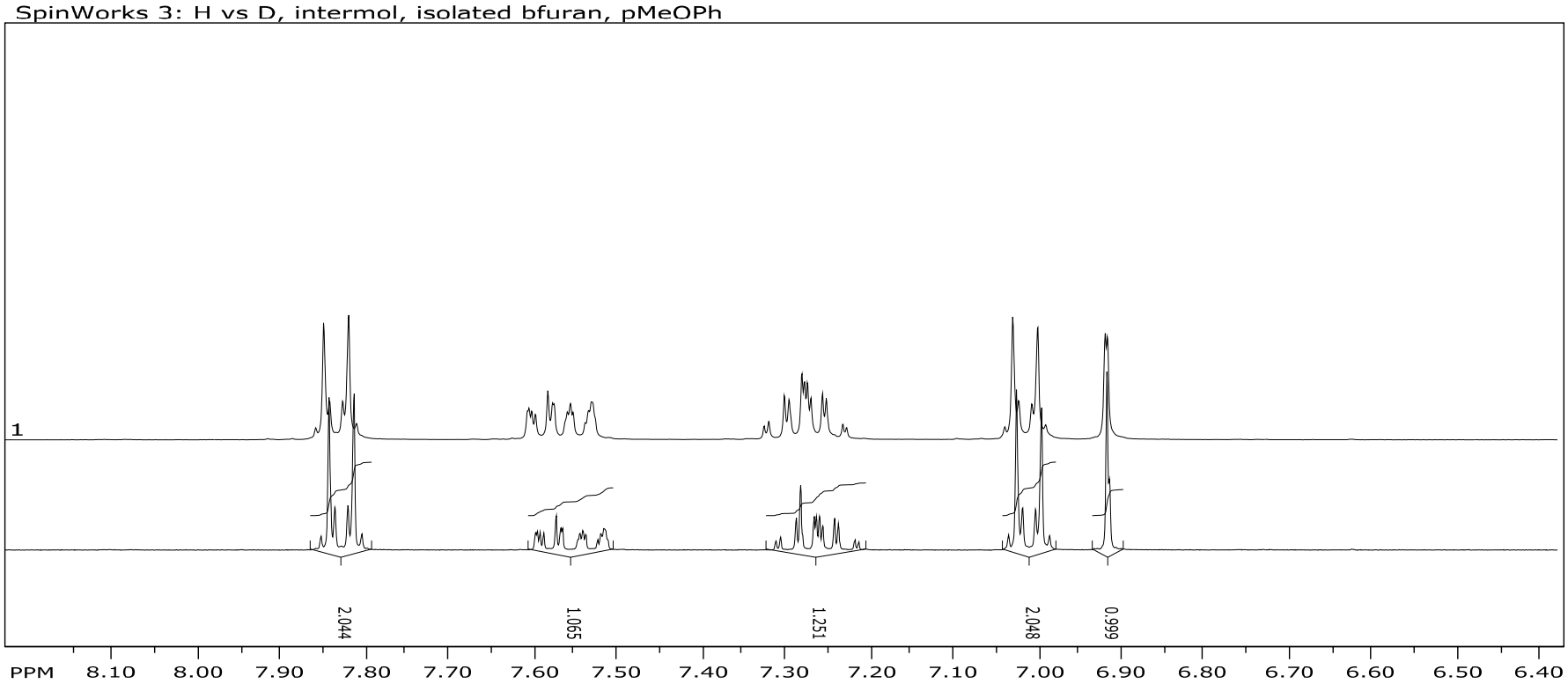
Intermolecular Competition Experiments

An equimolar mixture of hydrogenated and deuterated aryl vinyl ethers as stock solutions in degassed dioxane (0.14M) were added to an oven-dried round bottom flask purged of oxygen and containing Pd_2dba_3, DPEphos, CsF and Cs_2CO_3. The reactions were monitored by tlc until there was evidence of benzo[b]furan formation, at which point the reactions were removed from the heat, diluted with dichloromethane and quenched with water. The layers were separated, and the aqueous layer was extracted again with dichloromethane. The organic layers were combined, dried with magnesium sulfate, filtered and concentrated onto silica gel to apply to a column. The unreacted starting

materials were separated from the benzo[b]furans, and the benzo[b]furan mixture was analyzed by ^{1}H NMR. For all spectra, the upper trace is a copy of the hydrogenated material that can also be found in the NMR section.

2-(4-methoxyphenyl)benzofuran: 301: 301-d_4 = 0.53:0.47





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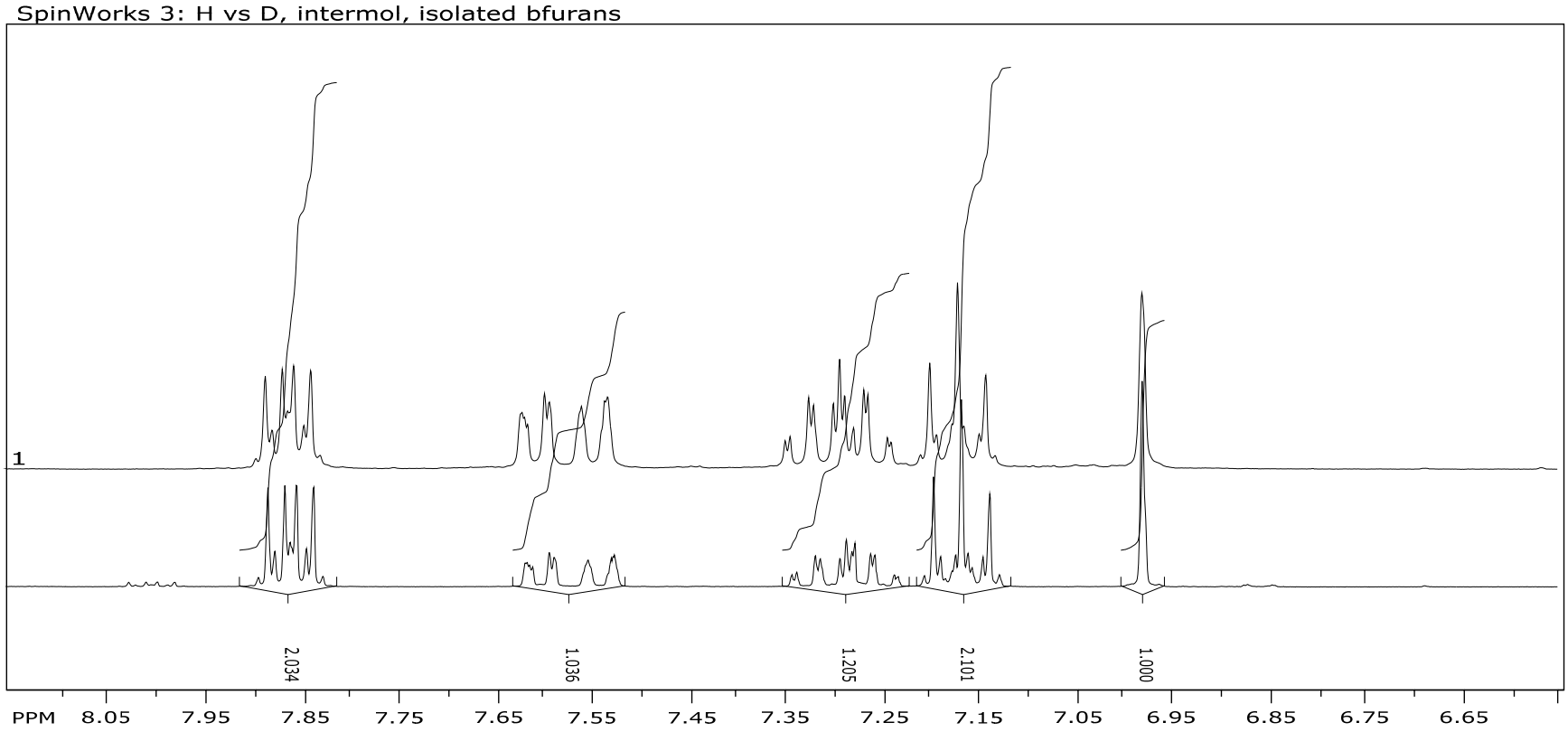
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 6

freq. of 0 ppm: 300.130005 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 22.275 ppm/cm: 0.07422

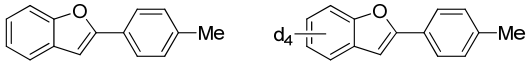
2-(4-fluorophenyl)benzofuran: 302: 302-d_4 = 0.52:0.48

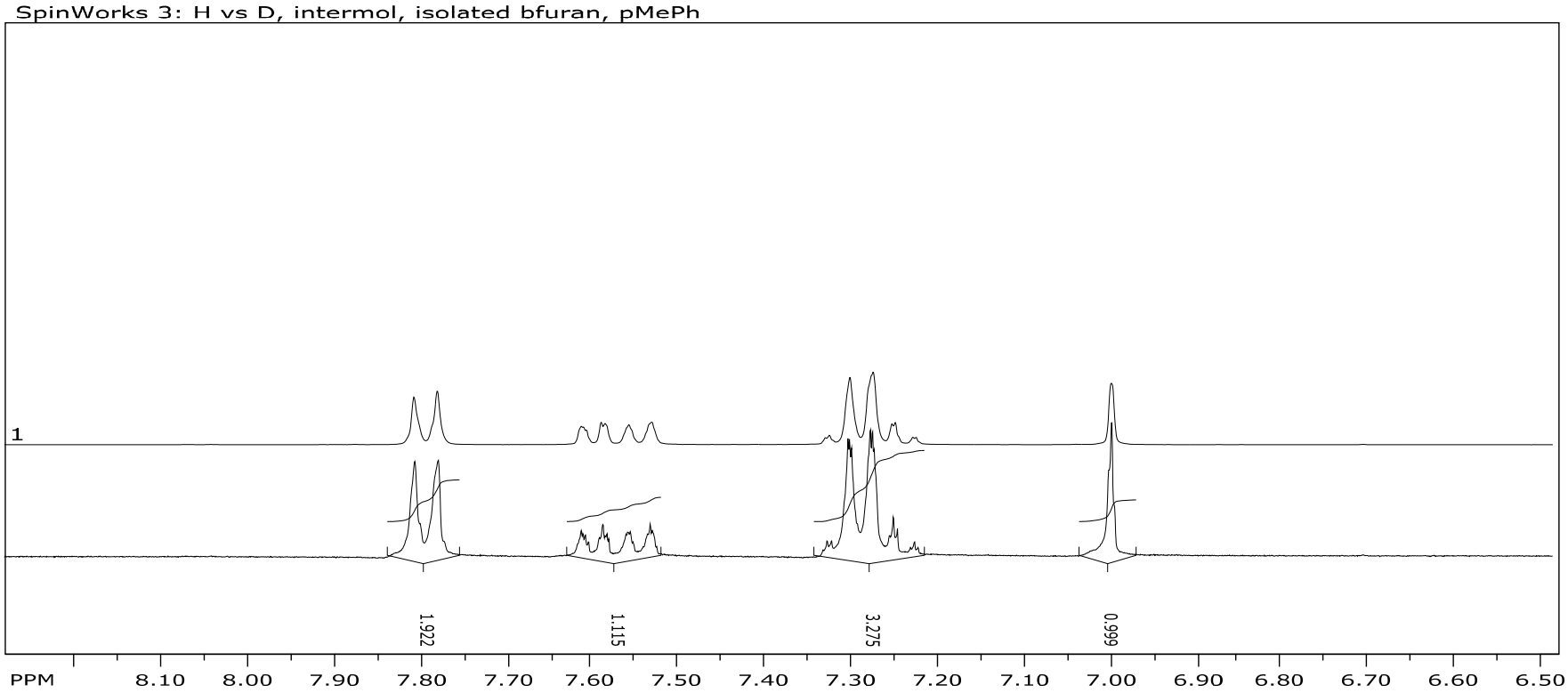


file: Z:\Laina\lmgxvi\lmgxvi_55a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 15

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 19.333 ppm/cm: 0.06441

2-(4-methylphenyl)benzofuran: 306: 306-d_4 = 0.56:0.44



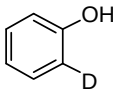


file: Z:\Laina\lmgxvi\lmgxvi_56a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 21.644 ppm/cm: 0.07212

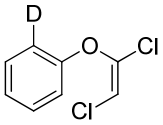
Intramolecular Isotope Effects

o-Deuteriophenol



Prepared from 2-bromophenol according to a published procedure[54] on a 14.8 mmol scale to give 1.29 g of the title compound. ^{1}H and ^{13}C were consistent with literature values.

(E)-(1,2-Dichlorovinyloxy)-2-deuteriobenzene (93-d)



This compound is a colourless oil and was prepared on a 10.3 mmol scale according to General Procedure I. The product was purified via flash chromatography using petroleum ether as an eluent to give 1.34 g **93-d**.

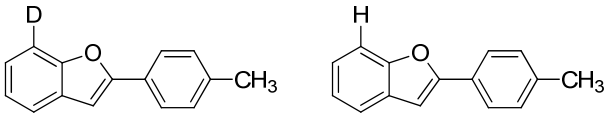
R_f = 0.33 (petroleum ether).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.40 (m, 2H), 7.27-7.26 (m, 1H), 7.16-7.11 (m, 1H), 6.01 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 140.1, 129.8, 129.7, 124.5, 117.1, 116.8, 116.5, 103.8.

HRMS: Calculated for $C_8H_5DCl_2O$: 188.9858, Found: 188.9866.

2-(4-Methylphenyl)benzofuran (306) and 2-(4-Methylphenyl)-7-deuteriobenzofuran (306-d)



This compound is a colourless solid and was prepared on a 0.36 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane to give 58.2 mg of a mixture of **306** and **306-d**.

R_f = 0.36 (9:1 hexanes: dichloromethane).

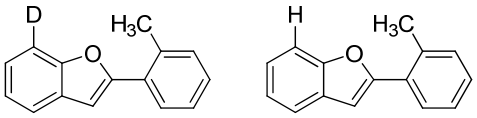
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (m, 2H), 7.65 (m, 1H), 7.60 (m, 0.27H), 7.37-7.28 (m, 5H), 7.03 (s, 1H), 2.48 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 154.9, 154.8, 138.6, 129.6, 129.5, 127.8, 125.0, 124.1, 124.0, 122.9, 120.8, 111.3, 111.2, 110.9, 110.6, 100.6, 21.4.

KIE from ^{1}H NMR:

k_H/k_D = (1.00-0.22)/.22 = 3.5.

2-(2-Methylphenyl)benzofuran (359) and 2-(2-Methylphenyl)-7-deuteriobenzofuran (359-d)



This compound is a colourless solid and was prepared on a 0.36 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluent to give 53.7 mg of a mixture **359** and **359-d**.

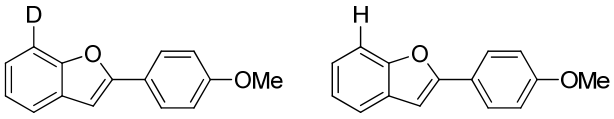
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97-7.93 (m, 1H), 7.72-7.68 (m, 1H), 7.65-7.60 (m, 0.24H), 7.43-7.30 (m, 5H), 6.98 (s, 1H), 2.67 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 154.5, 154.4, 135.9, 131.3, 130.0, 129.3, 128.6, 128.2, 126.2, 124.3, 124.2, 122.9, 121.0, 111.3, 111.2, 110.9, 110.6, 22.0.

KIE from ^{1}H NMR:

k_H/k_D = (1-.24)/.24 = 3.2.

2-(4-Methoxyphenyl)benzofuran (301) and 2-(4-methoxyphenyl)-7-deuteriobenzofuran (301-d)

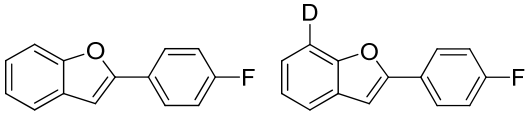


This compound is a colourless solid and was prepared on a 0.64 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 14:1 hexanes: ethyl acetate as an eluent to give 100.3 mg of a mixture **301** and **301-d**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (m, 2H), 7.62-7.53 (m, 1.22H), 7.32-7.24 (m, 2H), 7.03 (m, 2H), 6.93 (s, 1H), 3.91 (s, 3H).

KIE from ^{1}H NMR:

k2-(4-Fluorophenyl)benzofuran (302) and 2-(4-fluorophenyl)-7-deuteriobenzofuran (302-d)



This compound is a colourless solid and was prepared on a 0.36 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluent to give 53.2 mg of a mixture of **302** and **302-d**.

R_f = 0.30 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (m, 2H), 7.63 (m, 1H), 7.57 (m, 0.22H), 7.37-7.26 (m, 2H), 7.23-7.16 (m, 2H), 7.00 (s 1H).

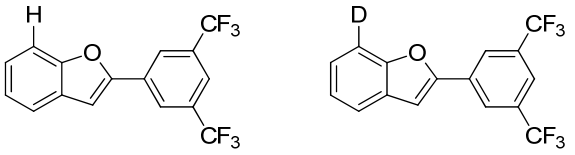
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 161.3, 155.1, 154.9, 154.9, 129.3, 126.9, 126.9, 126.8, 126.8, 124.3, 124.2, 123.1, 120.9, 116.1, 115.8, 111.3, 111.2, 110.9, 110.6, 101.1, 101.0.

^{19}F NMR (282 MHz, $CDCl_3$) δ -112.33.

KIE from ^{1}H NMR:

k_H/k_D = (1-0.20)/.2 = 4.0.

2-[3,5-Bis(trifluoromethyl)phenyl]benzofuran (360) and 2-[3,5-bis(trifluoromethyl)phenyl]-7-deuteriobenzofuran (360-d)



This compound is a colourless solid and was prepared on a 0.36 mmol scale according to General Procedure XV. The product was purified via flash chromatography using hexanes as an eluent to give 51.9 mg of a mixture of **360** and **360-d**.

R_f = 0.45 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (s, 2H), 7.87 (s, 1H), 7.67 (d, 2H), 7.60 (d, 0.23H), 7.44-7.39 (m, 1H), 7.36-7.29 (m, 1H), 7.23 (s, 1H).

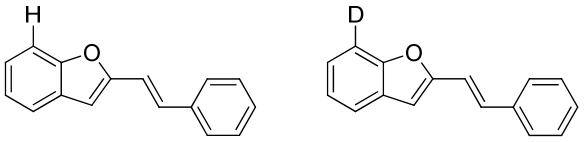
^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 152.5, 133.0, 132.6, 132.5, 132.1, 131.7, 128.5, 125.7, 125.6, 125.0, 124.5, 123.6, 121.7, 121.62, 121.58, 121.53, 121.48, 121.4, 111.5, 104.2.

^{19}F NMR (282 MHz, $CDCl_3$) δ -63.09.

KIE from ^{1}H NMR:

k_H/k_D = (1-.23)/.23 = 3.3.

2-(trans-2-Phenylethenyl)benzofuran (303) and 2-(trans-2-Phenylethenyl)-7-deuteriobenzofuran (303-d)



This compound is a colourless solid and was prepared on a 0.36 mmol scale according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: dichloromethane as an eluent to give 39.8 mg of a mixture of **303** and **303-d**. R_f = 0.26 (9:1 hexanes: dichloromethane).

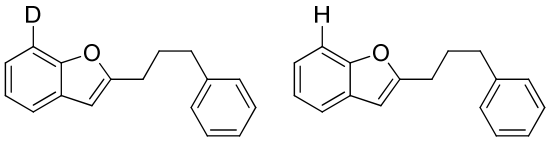
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.57 (m, 3.25H), 7.47-7.26 (m, 6H). 7.08 (d, 1H, *J* = 16 Hz), 6.74 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 155.0, 154.9, 136.7, 132.9, 130.3, 129.3, 129.2, 128.8, 128.7, 128.2, 127.6, 126.8, 126.5, 124.7, 124.6, 122.9, 120.9, 116.5, 111.1, 111.0, 110.7, 110.4, 105.3.

KIE from ^{1}H NMR:

k_H/k_D = (1-.25)/.25 = 3.0.

2-(3-Phenylpropyl)benzofuran (333) and 2-(3-Phenylpropyl)-7-deuteriobenzofuran (333-d)



Prepared according to procedure above for non-deuterated benzofuran.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57-7.45 (m, 1.20H), 7.38-7.20 (m, 7H), 6.45 (m, 1H), 2.88-2.67 (m, 5H), 2.19-2.09 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 141.8, 129.6, 129.5, 129.0, 128.54, 128.52, 128.4, 128.3, 126.0, 123.1, 122.4, 120.2, 112.7, 102.1, 35.2, 29.3, 27.9.

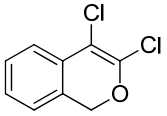
KIE from ^{1}H NMR:

k_H/k_D = (1-.20)/.20 = 4.0.

4.7 Compounds from Section 2.6 – Other Heterocycles

4.7.1 Isochromene

3,4-Dichloro-1*H*-isochromene (365)



This procedure was modified from a literature procedure.[565] Dichlorovinyl ether **138** (0.2267 g, 0.69 mmol, 1 equiv), Pd_2dba_3 (31.5 mg, 0.034 mmol, 5 mol%), and P(*o*-Tol)$_3$ (42.8 mg, 0.14 mmol, 20 mol%) were placed in an oven-dried test tube, sealed with a septum and purged with argon. TEA (0.39 mL, 2.7 mmol, 4.1 equiv) and CH_3CN (4.9 mL) were added and heated at reflux for 2 h. After that time, the reaction was cooled to room temperature and diluted with ethyl acetate. The solution was then sequentially washed with 10% aqueous citric acid, saturated aqueous $NaHCO_3$ then brine, dried with magnesium sulfate, filtered and concentrated. The crude residue was purified via flash chromatography using petroleum ether as the eluant to give 10.6 mg of **365**.

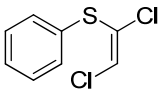
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (m, 1H), 7.49 (m, 1H), 7.36 (m, 1H), 7.01 (m, 1H), 4.68 (s, 2H). NMR contaminated with a small amount of starting material (see appendix).

^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9, 139.5, 130.2, 130.1, 128.8, 99.5, 98.9, 51.0.

HRMS was not acquired for this compound.

4.7.2 Benzothiophenes

(*E*)-(1,2-Dichlorovinyl)(phenyl)sulfane (367)

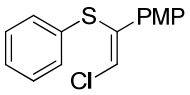


This compound is a colourless, viscous oil and was prepared on a 20 mmol scale according to General Procedure III. The product was purified via flash chromatography using petroleum ether as an eluant to give 3.11 g **367**. ^{1}H NMR was consistent with literature values.[407]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.47 (m, 2H), 7.42-7.37 (m, 3H), 6.60 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 132.63, 130.69, 130.15, 129.30, 128.71, 120.56.

(*Z*)-(2-Chloro-1-(4-methoxyphenyl)vinyl)(phenyl)sulfane (368)

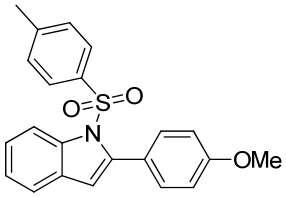


This material was a colourless solid and was prepared according to General Procedure V, and was characterized by ^{1}H NMR only.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 2H), 7.26-7.11 (m, 5H), 6.78 (m, 2H), 6.57 (s, 1H), 3.78 (s, 3H).

4.7.3 Indoles

2-(4-Methoxyphenyl)-1-Tosyl-1*H*-indole (370)



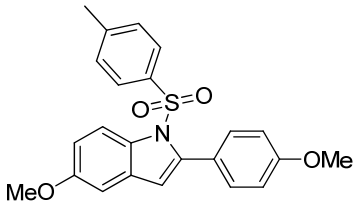
This compound was prepared according to General Procedure XV. ^{1}H and ^{13}C were consistent with published data.[566]

R_f = 0.30 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, 1H, *J* = 8.8Hz), 7.44 (m, 3H), 7.36 (dt, 1H, *J* = 1Hz, 7Hz), 7.30-7.25 (m, 3H), 7.05 (d, 2H, *J* = 7Hz), 6.97 (m, 2H), 6.49 (s, 1H), 3.91 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 144.5, 142.1, 138.2, 134.8, 131.7, 130.7, 129.2, 126.8, 124.8, 124.5, 124.3, 120.5, 116.7, 113.0, 112.9, 55.3, 21.5.

5-Methoxy-2-(4-methoxyphenyl)-1-tosyl-1*H*-indole (371)



This compound was prepared according to General Procedure XV.

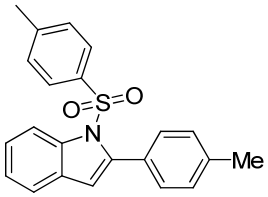
R_f = 0.18 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, 1H, *J* = 9Hz), 7.45 (d, 2H), 7.25 (m, 2H), 7.05 (d, 2H), 6.99-6.94 (m, 3H), 6.88 (d, 1H, *J* = 2.5Hz), 6.43 (s, 1H), 3.90 (s, 3H), 3.83 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 157.1, 144.4, 143.1, 134.4, 132.8, 131.9, 131.6, 129.1, 126.8, 124.8, 117.8, 113.1, 113.1, 113.0, 103.1, 55.6, 55.3, 21.5.

HRMS: Calculated for $C_{23}H_{21}NO_4S$: 407.1191, Found: 407.1196.

2-*p*-Tolyl-1-tosyl-1*H*-indole (372)



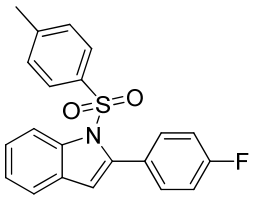
This compound was prepared according to General Procedure XV. The product was purified via flash chromatography using 9:1 hexanes: diethyl ether as an eluant. ^{1}H and ^{13}C were consistent with published data.[567]

R_f = 0.27 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (m, 1H), 7.47-7.24 (m, 9H), 7.06 (m, 2H), 6.53 (s, 1H), 2.47 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.5, 142.3, 138.6, 138.3, 134.7, 130.7, 130.2, 129.6, 129.2, 128.3, 126.8, 124.6, 124.3, 120.6, 116.7, 113.3, 21.54, 21.47.

2-(4-Fuorophenyl)-1-tosyl-1*H*-indole (373)

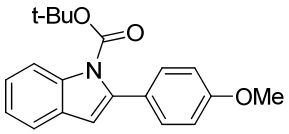


This compound was prepared according to General Procedure XV. The product was purified via flash chromatography using a gradient of 9:1 to 4:1 hexanes: diethyl ether as an eluant. This material was characterized by ^{1}H NMR only.

R_f = 0.30 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (m, 1H), 7.52-7.26 (m, 9H), 7.18-7.00 (m, 6H), 6.56 (s, 1H), 2.33 (s, 3H).

tert-Butyl 2-(4-methoxyphenyl)-1*H*-indole-1-carboxylate (374)

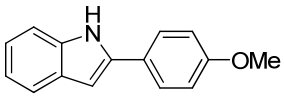


This compound was synthesized according to General Procedure XIII. ^{1}H and ^{13}C NMR data were consistent with published values.[568]

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, 1H, *J* = 9 Hz), 7.56 (d, 1H, *J* = 8 Hz), 7.39 – 7.23 (m, 4H), 6.96 (m, 2H), 6.53 (s, 1H), 3.88 (s, 3H), 1.39 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 150.3, 140.4, 137.3, 129.9, 129.3, 127.5, 124.1, 122.3, 115.2, 113.3, 109.5, 83.4, 55.4, 27.7.

2-(4-Methoxyphenyl)-1*H*-indole (375)

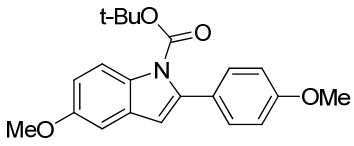


This compound was isolated with **374**. ^{1}H and ^{13}C NMR data were consistent with published values.[569]

^{1}H NMR (300 MHz, DMSO-d_6) δ 11.39 (s, 1H), 7.79 (m, 2H), 7.49 (d, 1H, *J* = 7.5 Hz), 7.37 (dd, 1H, J_1 = 8 Hz, J_2 = 0.6 Hz), 7.09 – 6.94 (m, 4H), 6.75 (dd, 1H, J_1 = 2.1 Hz, J_2 = 0.6 Hz), 3.80 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 158.8, 137.7, 136.9, 128.8, 126.3, 124.9, 121.0, 119.7, 119.2, 114.3, 111.0, 97.3, 55.2.

tert-Butyl 5-methoxy-2-(4-methoxyphenyl)-1*H*-indole-1-carboxylate (376)

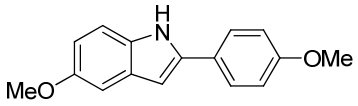


This compound was synthesized according to General Procedure XIII. ^{1}H and ^{13}C NMR data were consistent with published values.[570]

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, 1H, *J* = 9 Hz), 7.35 (m, 2H), 7.02 (d, 1H, *J* = 3 Hz), 6.97 – 6.92 (m, 3H), 6.45 (s, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 1.37 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 156.0, 150.3, 141.1, 132.1, 130.1, 129.9, 116.1, 113.3, 112.7, 109.5, 102.9, 83.2, 55.7, 55.4, 27.7.

5-Methoxy-2-(4-methoxyphenyl)-1*H*-indole (377)



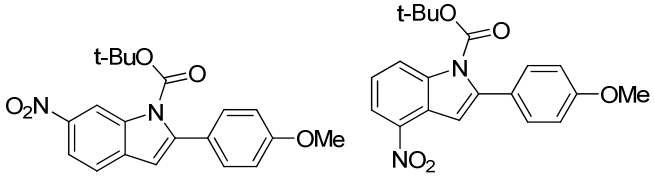
This compound was isolated with **376**. ^{1}H NMR data in $CDCl_3$ were consistent with published values.[571]

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (br s, 1H), 7.59 (m, 2H), 7.29 (d, 1H), 7.09 (d, 1H, *J* = 2.2 Hz), 6.99 (m, 2H), 6.84 (dd, 1H, J_1 = 9 Hz, J_2 = 2.2 Hz), 6.66 (dd, 1H, J_1 = 2.2 Hz, J_2 = 0.7 Hz), 3.88 (s, 3H), 3.87 (s, 3H).

^{1}H NMR (300 MHz, DMSO-d_6) δ 11.22 (br s, 1H), 7.75 (m, 2H), 7.25 (d, 1H, *J* = 8.6 Hz), 7.02 (m, 2H), 6.99 (d, 1H, *J* = 2.5 Hz), 6.71 – 6.66 (m, 2H), 3.80 (s, 3H), 3.75 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 158.7, 153.5, 138.3, 132.0, 129.2, 126.2, 125.0, 114.3, 111.7, 111.0, 101.4, 97.2, 55.22, 55.16.

tert-Butyl 2-(4-methoxylphenyl)-6-nitro-1*H*-indole-1-carboxylate (378) and *tert*-Butyl 2-(4-methoxylphenyl)-4-nitro-1*H*-indole-1-carboxylate (378')



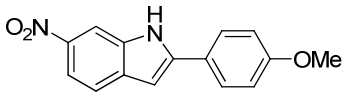
This compound was synthesized according to General Procedure XIII. The two isomers could not be separated and are present in an approximately 16:1 ratio as judged by NMR integration.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (t, 1H, J = 2 Hz), 7.96 (ddd, 1H, J_1 = 8 Hz, J_2 = 2.2 Hz, J_3 = 0.9 Hz), 7.72 (dd, 1H, J_1 = 8 Hz, J_2 = 1.4 Hz), 7.72 (dd, 1H, J_1 = 8 Hz, J_2 = 1.4 Hz), 7.57 (m 0.13H), 7.44 (t, 1H, J_1 = 8 Hz), 7.36 (m, 2H), 6.89 (m, 2H), 6.54 (s, 1H), 6.36 (s, 0.06H),3.83 (s, 0.24H), 3.82 (s, 3H), 1.42 (s, 3H), 1.38 (s, 0.77H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 152.3, 148.5, 141.7, 141.0, 130.6, 130.0, 129.9, 129.42, 129.35, 129.3, 127.8, 127.1, 119.5, 118.6, 118.5, 115.2, 114.4, 113.8, 113.8, 82.8, 82.6, 67.1, 55.4, 55.3, 28.0.

We were unable to obtain satisfactory mass spectra for this mixture of compounds.

2-(4-Methoxyphenyl)-6-nitro-1*H*-indole (379)

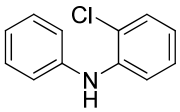


This compound was isolated with **378** and **378'** and this isomer is the major product. ^{1}H and ^{13}C NMR data were consistent with published values.[572]

^{1}H NMR (300 MHz, DMSO-d_6) δ 12.22 (br s, 1H), 8.25 (d, 1H, J = 2 Hz), 7.88 (m, 3H), 7.66 (d, 1H, J = 9 Hz), 7.37 (m, 0.5H), 7.28 (m, 0.6H), 7.10 (m, 2H), 7.03 (d, 1H, J = 2 Hz), 6.94 (m, 0.7H), 3.83 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d6) δ 159.9, 150.1, 148.7, 144.5, 141.4, 135.3, 134.0, 129.9, 127.3, 123.3, 119.9, 119.6, 114.8, 114.6, 109.7, 107.5, 106.9, 98.6, 55.3.

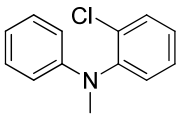
2-Chloro-*N*-phenylbenzamine (380)



This procedure was based on a literature protocol for a similar reaction.[573] A 250 mL round bottom flask was sealed with a septum andpurged with argon for 10 min. 2-Chloroaniline (1.16 mL, 11 mmol, 1.1 equiv), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2.5 mL, 10 mmol, 1 equiv) were added to the flask, followed by 160 mL dry CH_3CN, then CsF (3.34 g, 22 mmol, 2.2 equiv) was added as a solid. The reaction was stirred at room temperature for 24 h, then washed with brine and dried with sodium sulfate. The solution was concentrated and purified via flash chromatography using 100:0 – 4:1 petroleum ether:dichloromethane as an eluant to give 1.99 g **380** (98% yield). ^{1}H NMR was consistent with literature values.[574]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.30 (m, 4H), 7.24-7.06 (m, 4H), 6.88-6.82 (m, 1H), 6.14 (br s, 1H).

2-Chloro-*N*-methyl-*N*-phenylbenzamine (382)



This procedure was based on a literature procedure.[575] The diarylamine **380** (0.3532 g, 1.7 mmol, 1 equiv) was dissolved in DMF and cooled to 0°C. NaH (0.1734 g, 4.3 mmol, 2.5 equiv) was added as a solid and the reaction was stirred for 15 min. Iodomethane (0.12 mL, 1.9 mmol, 1.1 equiv) freshly passed through activated alumina was added and the reaction was allowed to warm to room temperature overnight. After 14 h, the reaction was diluted with diethylether, washed with brine, dried with sodium sulfate and concentrated. The crude oil was purified via flash chromatography using a gradient of hexanes to 9:1 hexanes: dichloromethane as an eluant to give 0.33 g of **382** (87% yield).

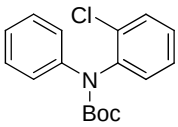
R_f = 0.22 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.38-7.24 (m, 5H), 6.84 (m, 1H), 6.68 (m, 1H), 3.33 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.7, 145.4, 133.7, 131.0, 130.2, 129.0, 128.2, 127.4, 117.9, 113.6, 39.0.

HRMS: Calculated for $C_{13}H_{13}ClN$: 218.0736, Found: 218.0731.

tert-Butyl 2-chlorophenyl(phenyl)carbamate (384)



This procedure was adapted from a literature procedure.[576] Diarylamine **380** (0.2585 g, 1.27 mmol. 1 equiv), Boc_2O (0.3047 g, 1.4 mmol, 1.1 equiv) and DMPA (31.0 mg, 0.25 mmol, 20 mol%) were combined in 2.0 mL THF and stirred at 65 ^{o}C for 24 h. The reaction was then cooled to room temperature, filtered and concentrated. The crude oil was purified via flash chromatography using 9:1 hexanes: diethyl ether as an eluant to give 0.2659 g **384** (69% yield).

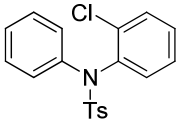
R_f = 0.42 (9:1 hexanes: ethyl acetate).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.49 (m, 1H), 7.35-7.26 (m, 7H), 7.20-7.15 (m, 1H), 1.50 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 142.1, 140.2, 133.6, 130.6, 130.2, 128.6, 128.5, 127.7, 125.3, 81.4, 28.2.

HRMS: Calculated for $C_{17}H_{18}ClNNaO_2$: 326.0924, Found: 326.0918.

N-(2-chlorophenyl)-4-methyl-*N*-phenylbenzenesulfonamide (386)



This procedure was based on a literature protocol.[577] KOH (92 mg, 1.6 mmol, 1.5 equiv) was powdered and added to DMF (16 mL) at 0^{o}C. A solution of diarylamine **380** (0.2217

g, 1.1 mmol) in 2.5 mL DMF was added to the KOH suspension dropwise and stirred for 25 min, then a solution of tosyl chloride (0.2283 g, 1.2 mmol, 1.1 equiv) was added to the above solution and the reaction was stirred for another 2.5 h. After this time, the reaction was diluted with water and extracted with three portions of ethyl acetate. The organic layers were combined, washed with two portions of water and dried with magnesium sulfate and filtered. The crude oil was purified via flash chromatography using 4:1 hexanes: ethyl acetate as an eluant to give 0.2743 g **386** (70% yield).

R_f = 0.26 (9:1 hexanes: dichloromethane).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (m, 2H), 7.49-7.25 (m, 11H), 2.47 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8, 140.3, 138.3, 137.4, 135.4, 131.8, 131.0, 129.8, 129.5, 129.0, 128.1, 127.9, 127.5, 127.3, 21.6.

HRMS: Calculated for $C_{19}H_{16}ClNNaO_2S$: 380.0488, Found: 380.0482.

General Procedure XVI – Attempted synthesis of Carbazoles (Table 32)

This method is based on Fagnou's conditions for carbazole synthesis.[144,150] Palladium acetate (1.0 mg, 4.5 μmol, 5 mol%), P*t*Bu$_3$·HBF$_4$ (2.6 mg, 8.9 μmol, 10 mol%), and K_2CO_3 (49.3 mg, 0.36 mmol, 4 equiv) were placed into an oven-dried one-piece round bottom flask/condenser, sealed with a septum and purged with argon for 20 min A stock solution of either **380**, **382**, **384** or **386** (89.1 μmol) in DMA (0.8 mL) was added, and the reaction was heated at 135 ^oC for 19 h. After that time, the reaction was removed from heat, diluted with ethyl acetate, filtered through celite and analysed by ^{1}H NMR.

Similarly, the conversions of **380**, **382**, **384** or **386** to **381**, **383**, **385** or **387**, respectively were performed on approximately 0.13 mmol scales according to General Procedure XIII. No reaction was observed during 22 h of heating.

CHAPTER 5 : REFERENCES

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(514) Costs per gram as estimated from Sigma Alrich in Canadian dollars on June 16, 2010.

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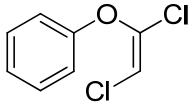
CHAPTER 6 : NMR SPECTRA

Table of Contents

6.1: Section 2.2 – 1,2-Dichlorovinyl Starting Materials

((*E*)-(1,2-Dichlorovinyloxy)benzene (93)



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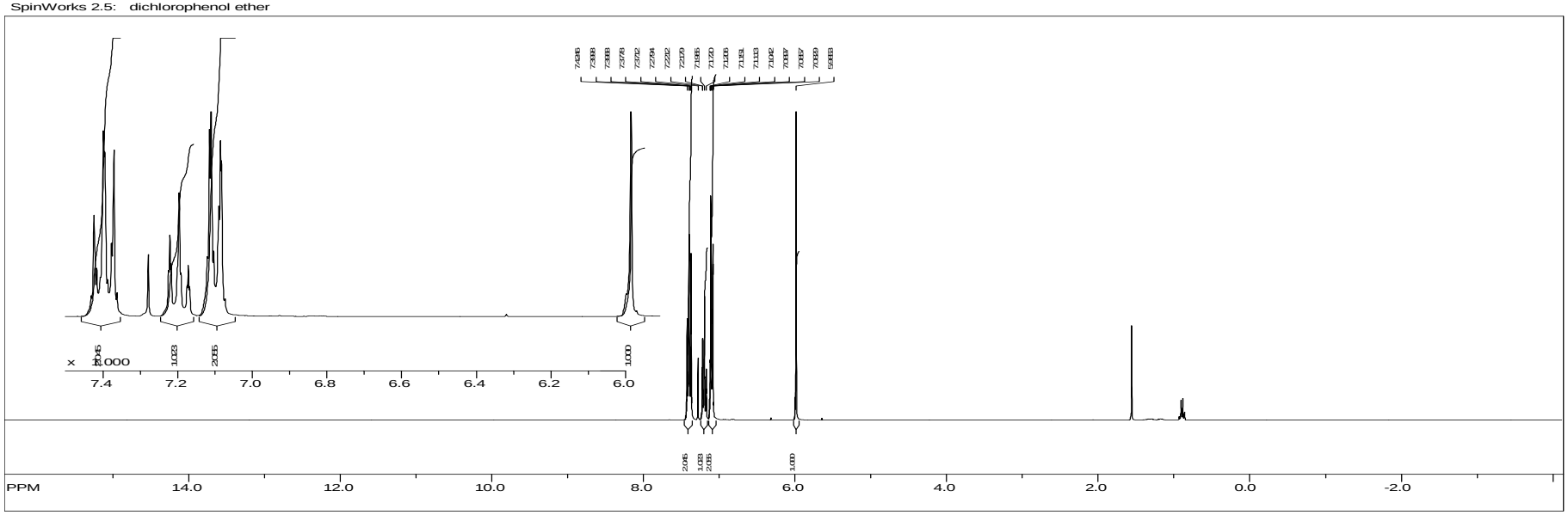

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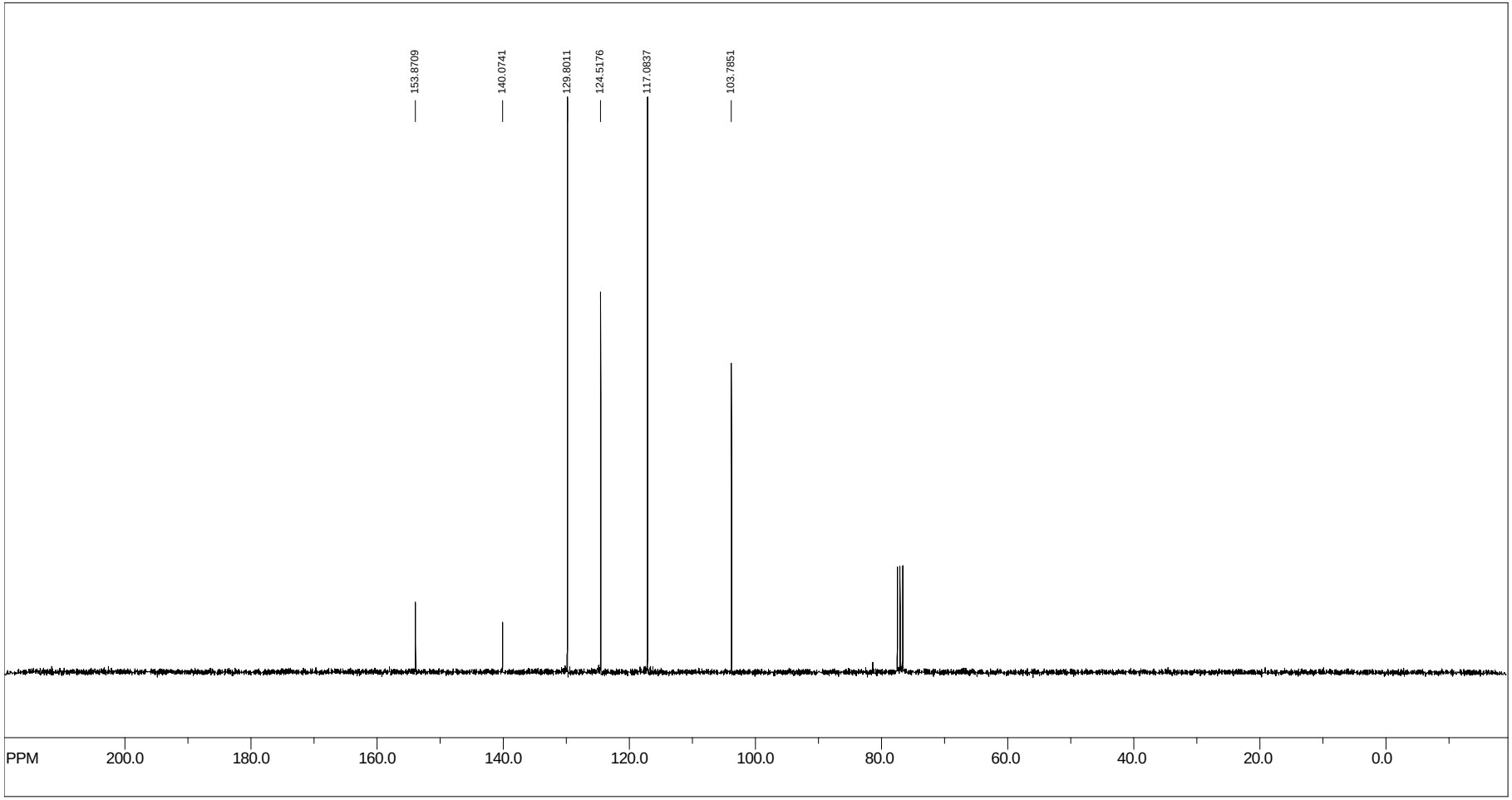

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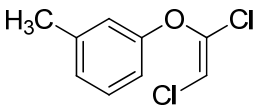

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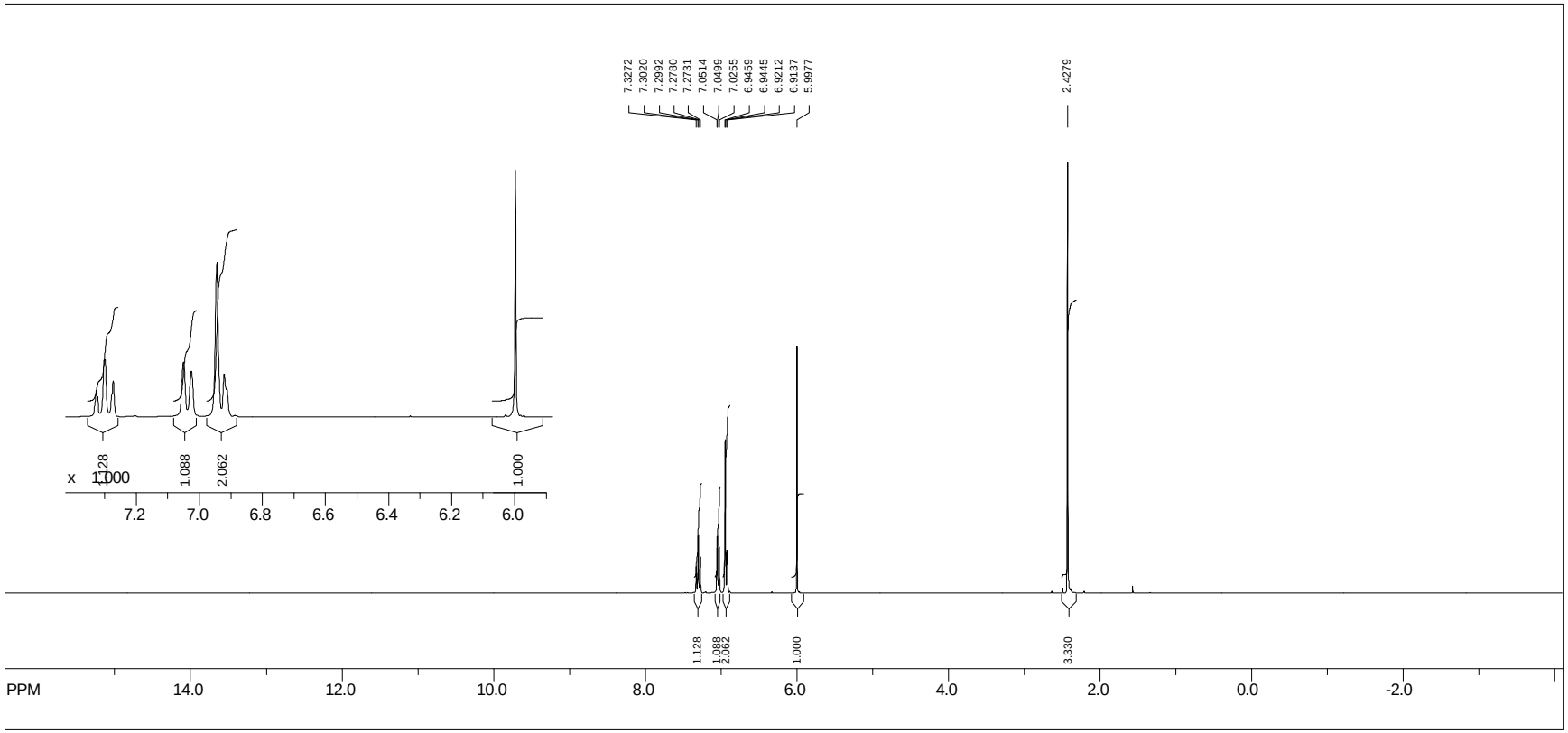

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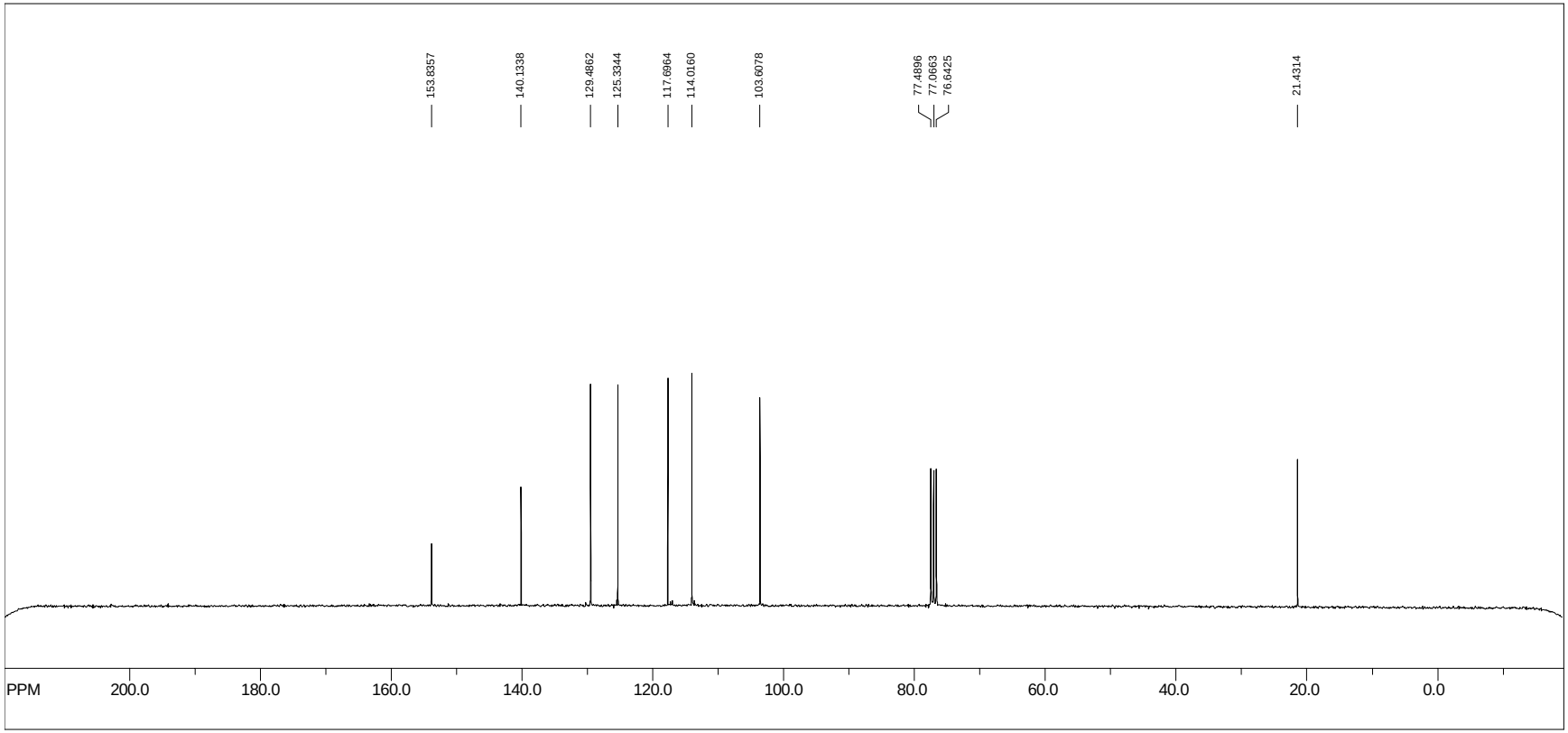

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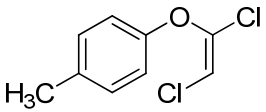
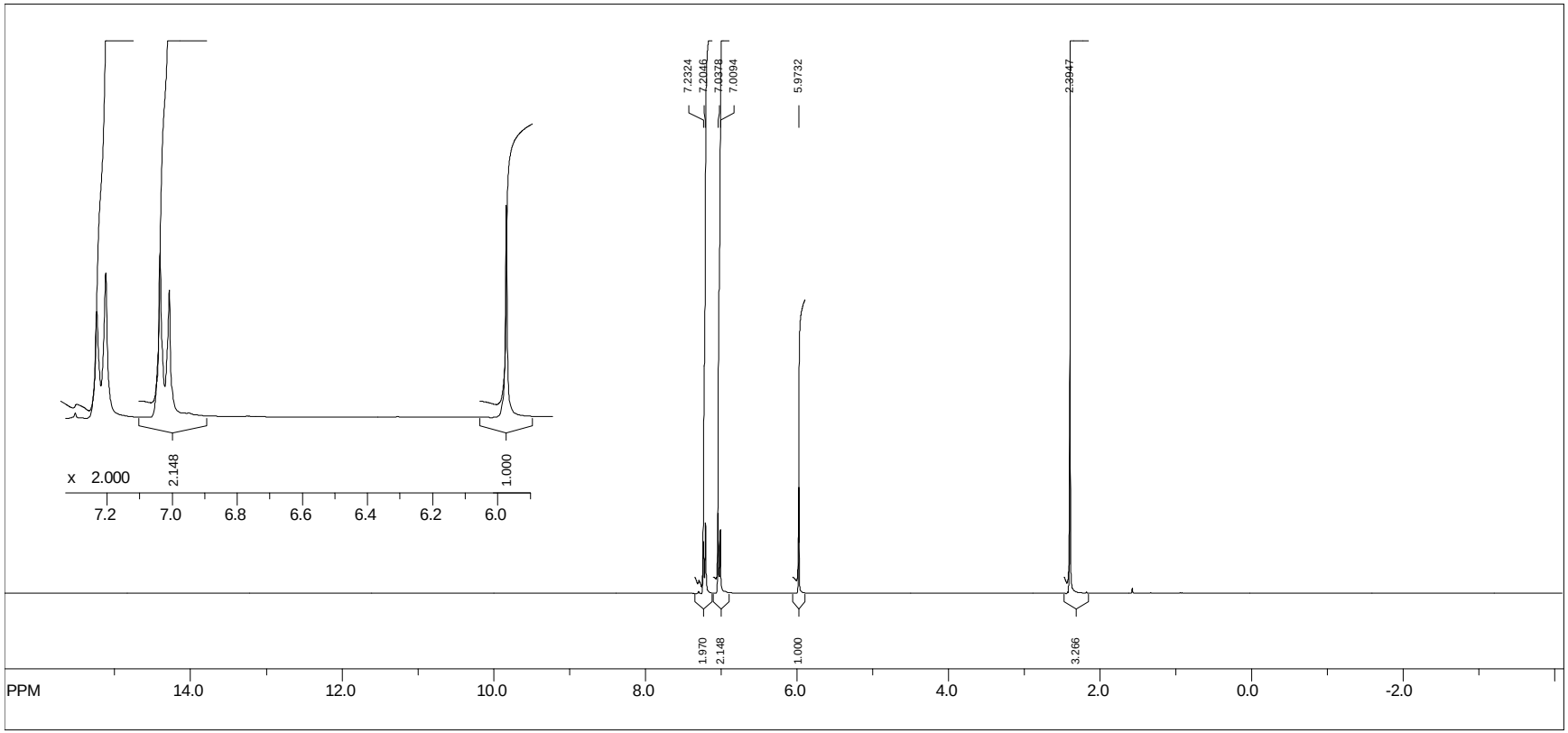
(*E*)-1-(1,2-Dichlorovinyloxy)-4-methylbenzene (113)



SpinWorks 2.5: p-Cresol addition to TCE



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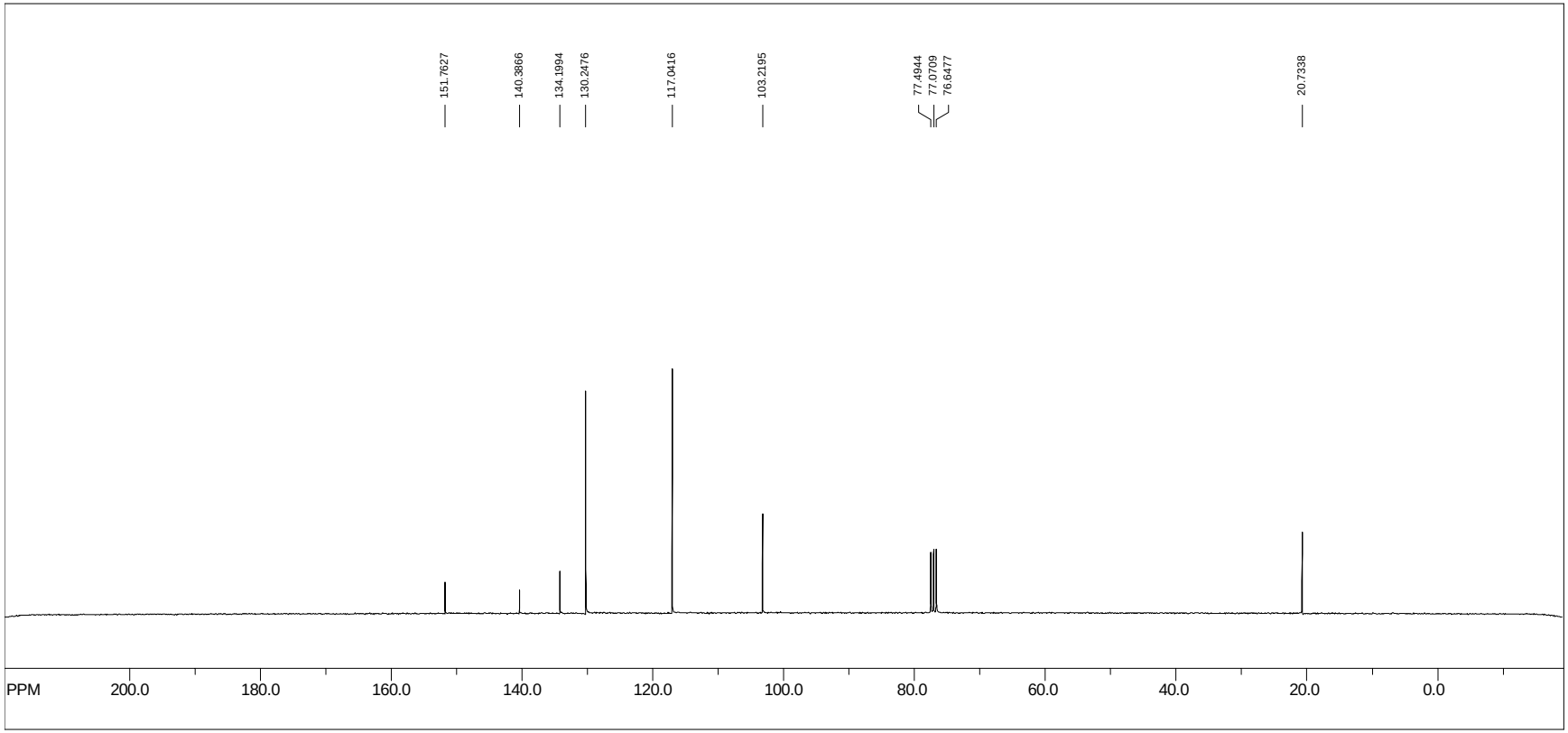

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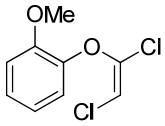
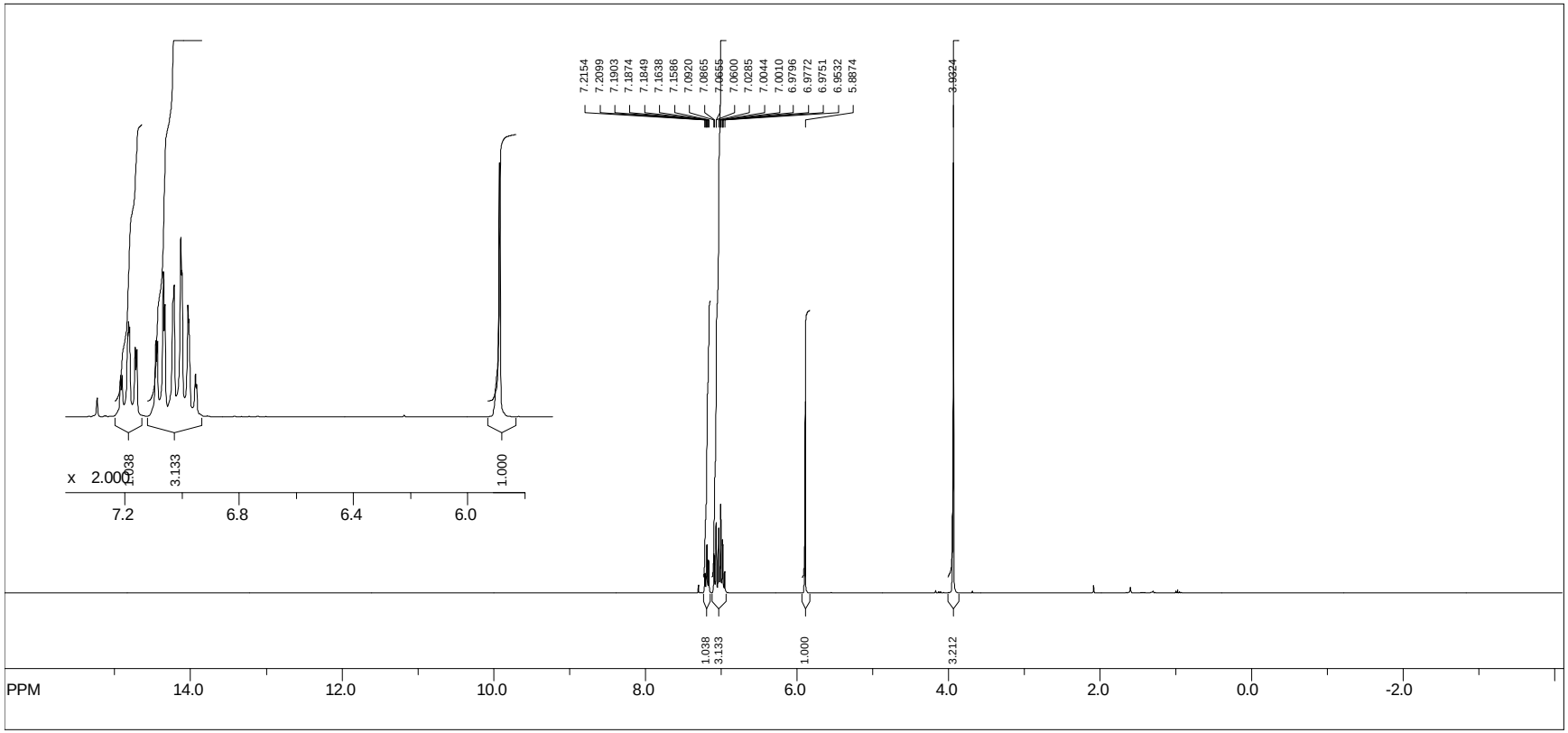
(*E*)-1-(1,2-Dichlorovinyloxy)-2-methoxybenzene (115)



SpinWorks 2.5: Guaiacol addition to TCE



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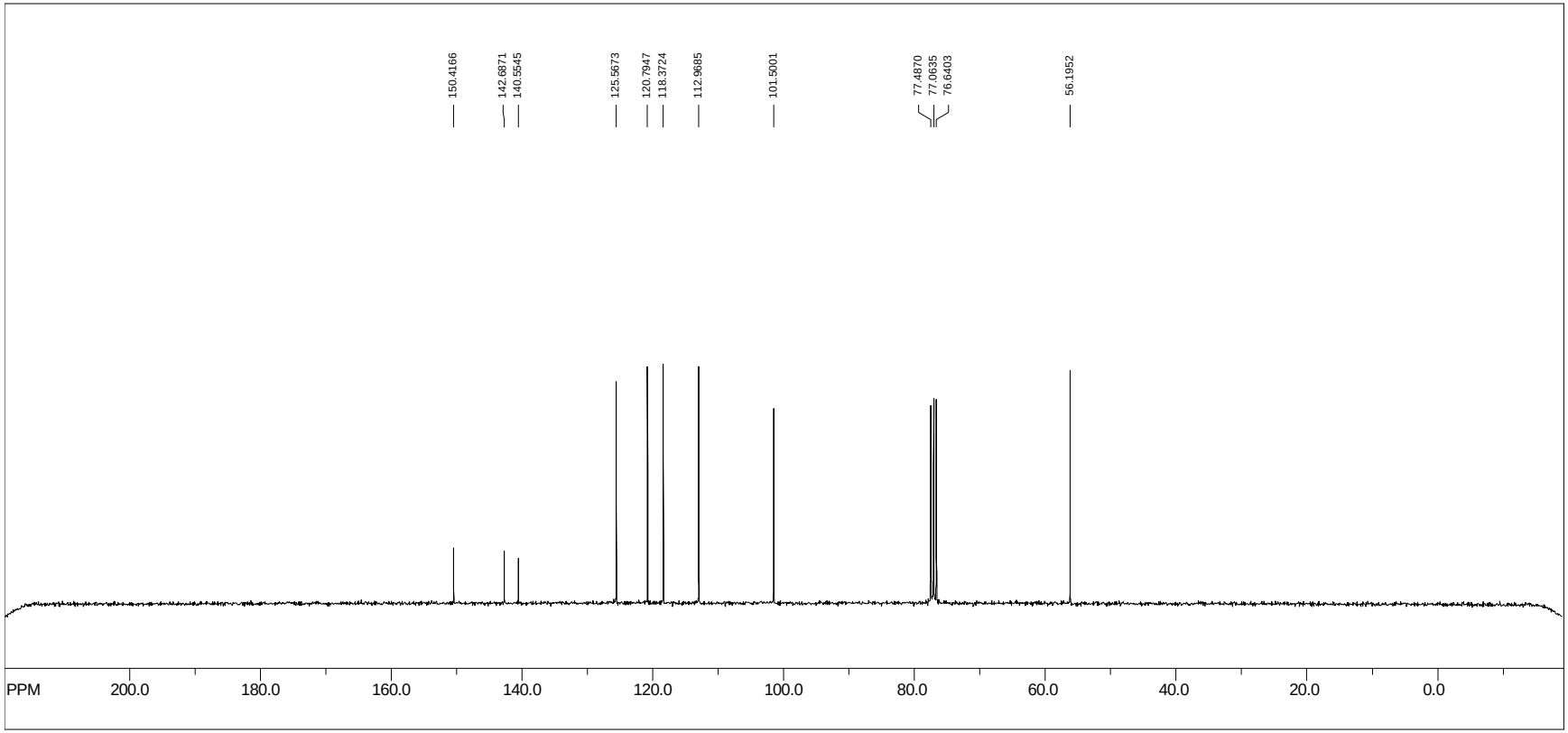

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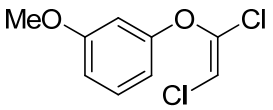
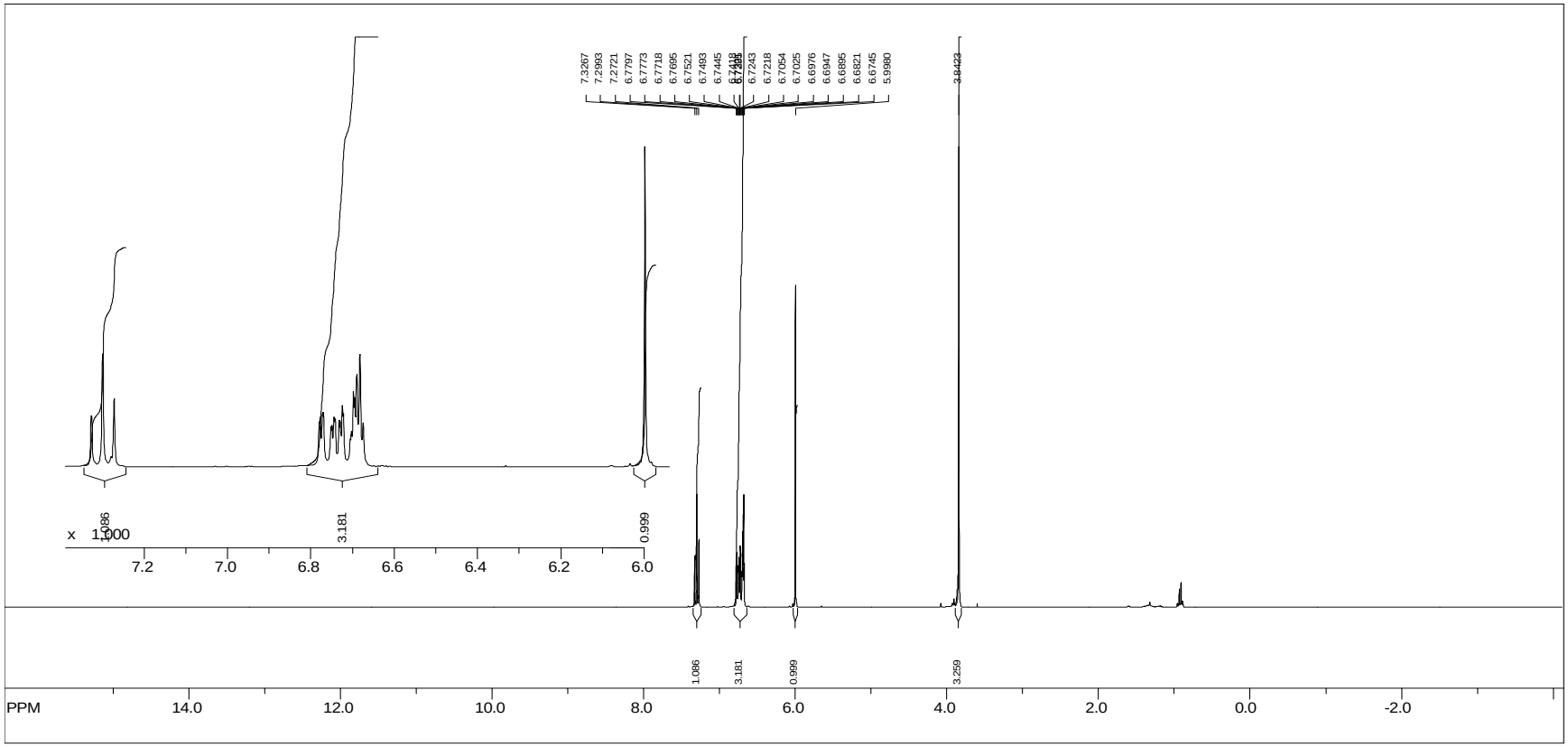
(*E*)-1-(1,2-Dichlorovinyloxy)-3-methoxybenzene (117)



SpinWorks 2.5: addition of m-methoxyphenol to TCE



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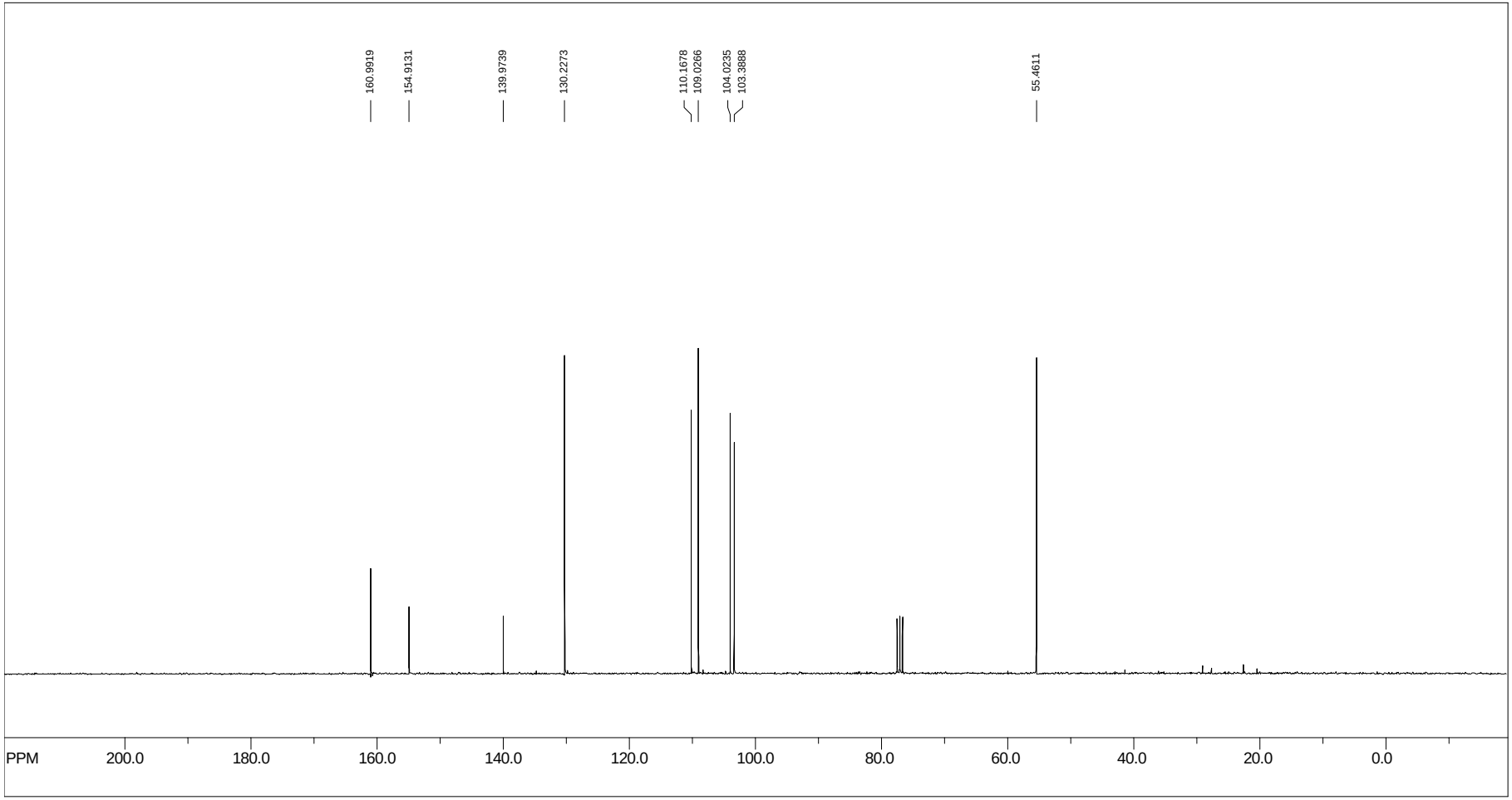
SpinWorks 2.5: addition of m-methoxyphenol to TCE



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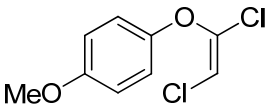
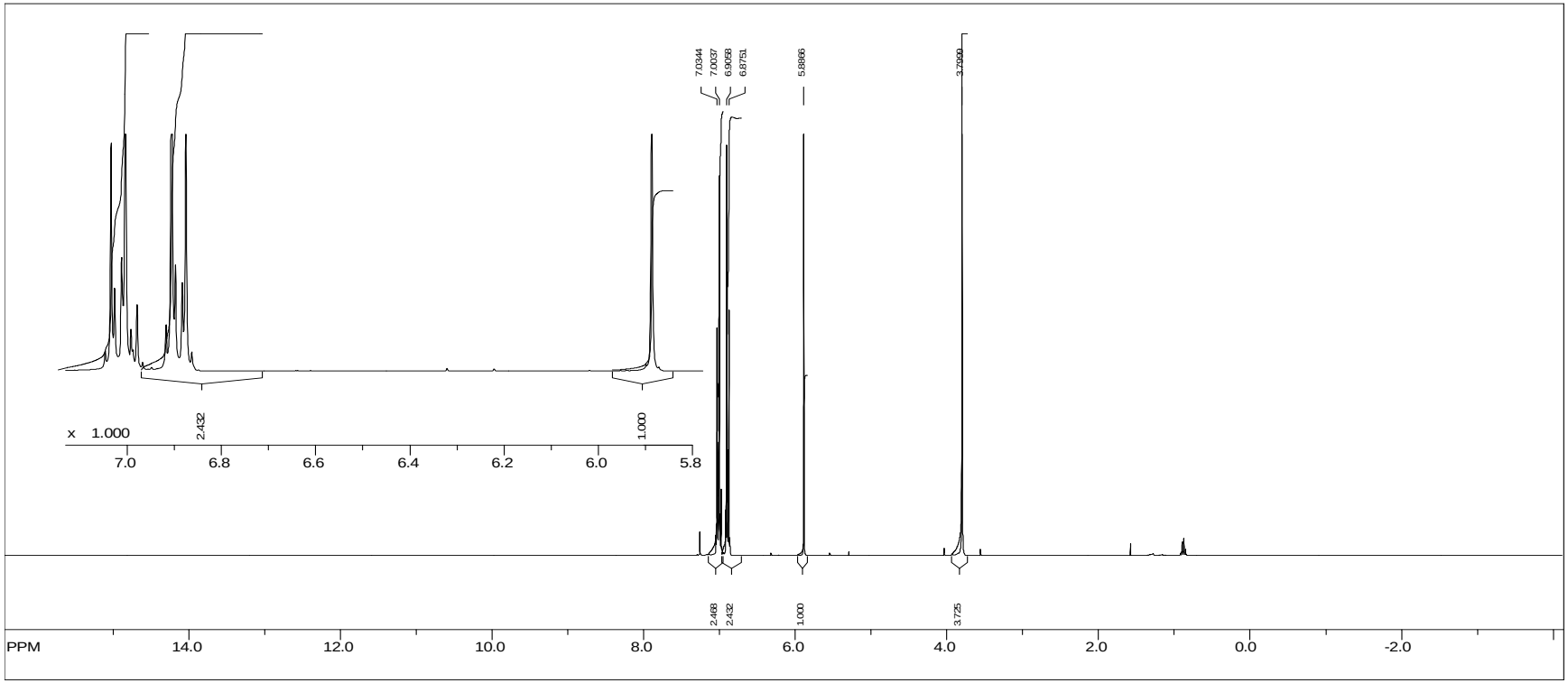
(E)-1-(1,2-Dichlorovinyloxy)-4-methoxybenzene (110)



SpinWorks 2.5: p-MeO-Ph-OK addition to TCE



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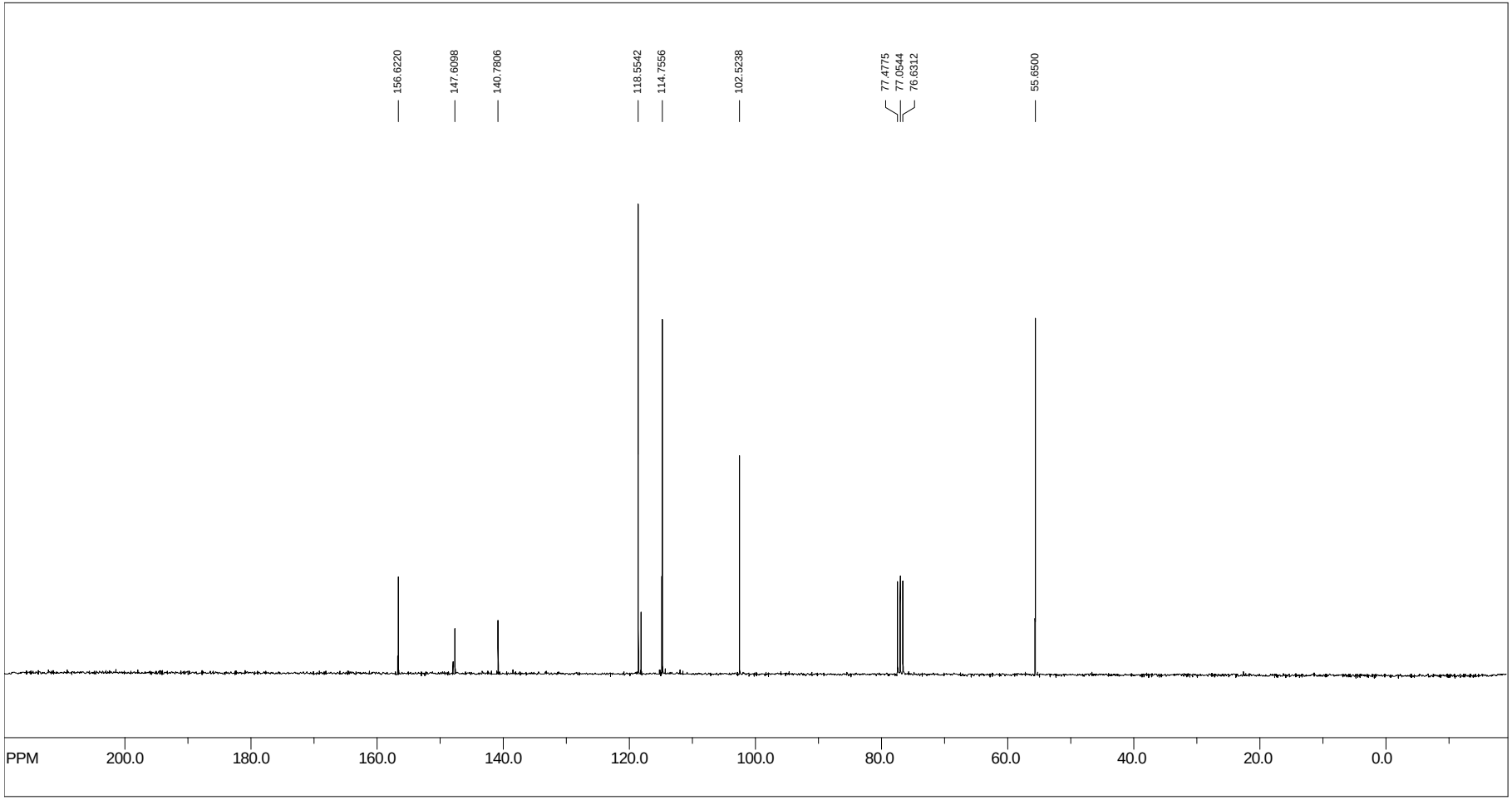

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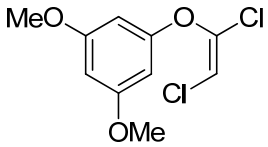
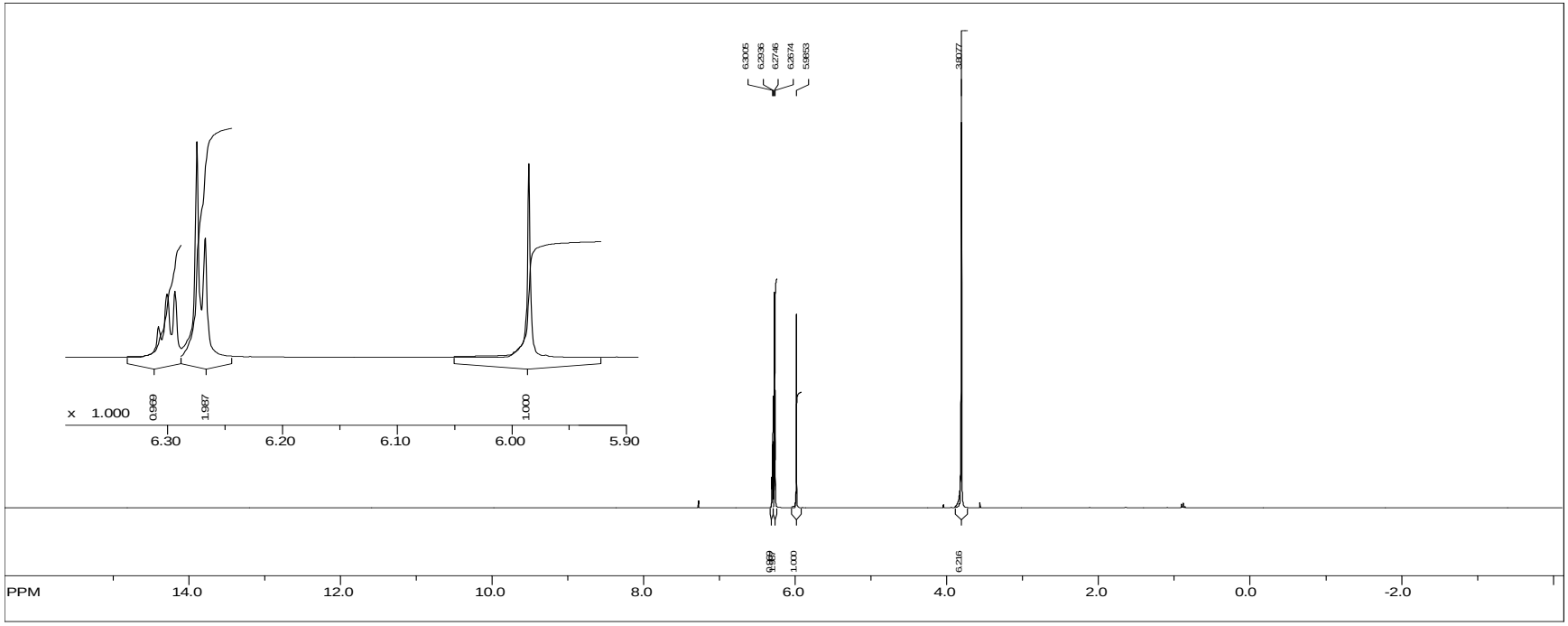
LB: 0.300 GB: 0.0000

(E)-1-(1,2-Dichlorovinyloxy)-3,5-dimethoxybenzene (112**)**



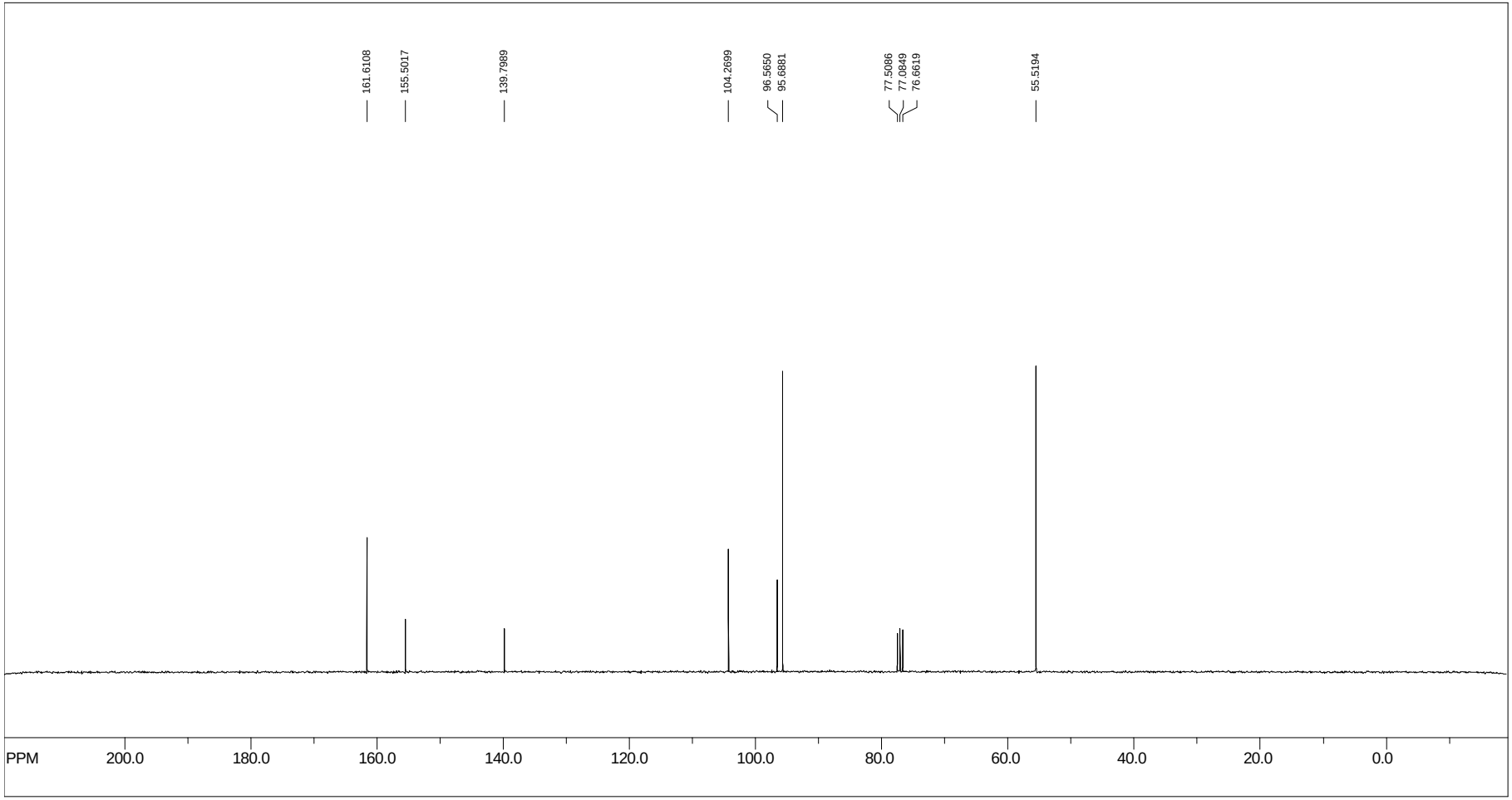
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



file: Z:\Laina\lmgix\lmgix_97a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

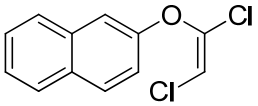
SpinWorks 2.5: C13CPD128 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



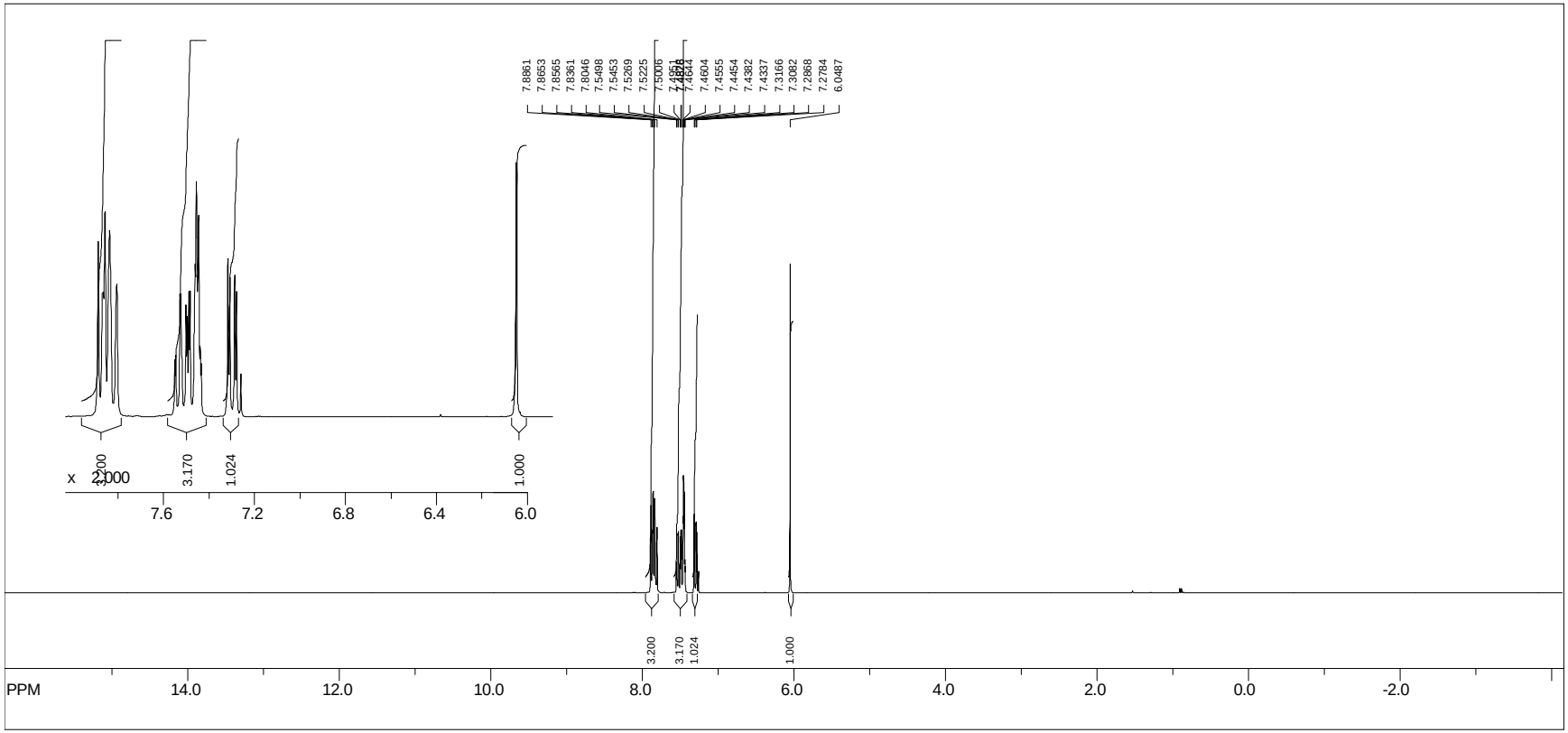
file: C:\Users\Laina\Documents\WORK\NMR\lmgix\lmgix_97a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 128

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(E)-2-(1,2-Dichlorovinyloxy)naphthalene (114**)**



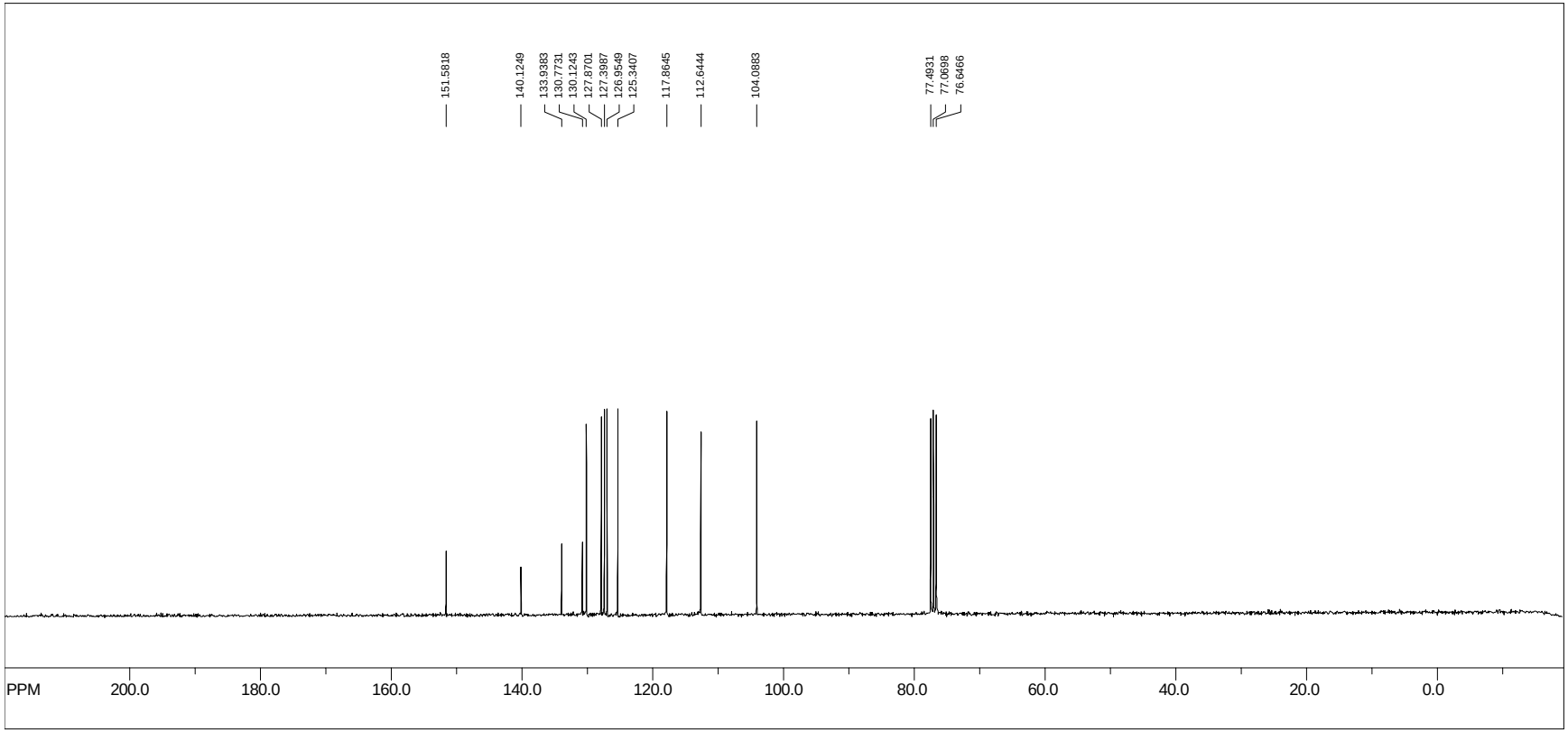
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



file: Z:\Laina\lmgxiv\lmgxiv_80a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

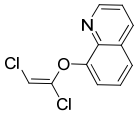
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



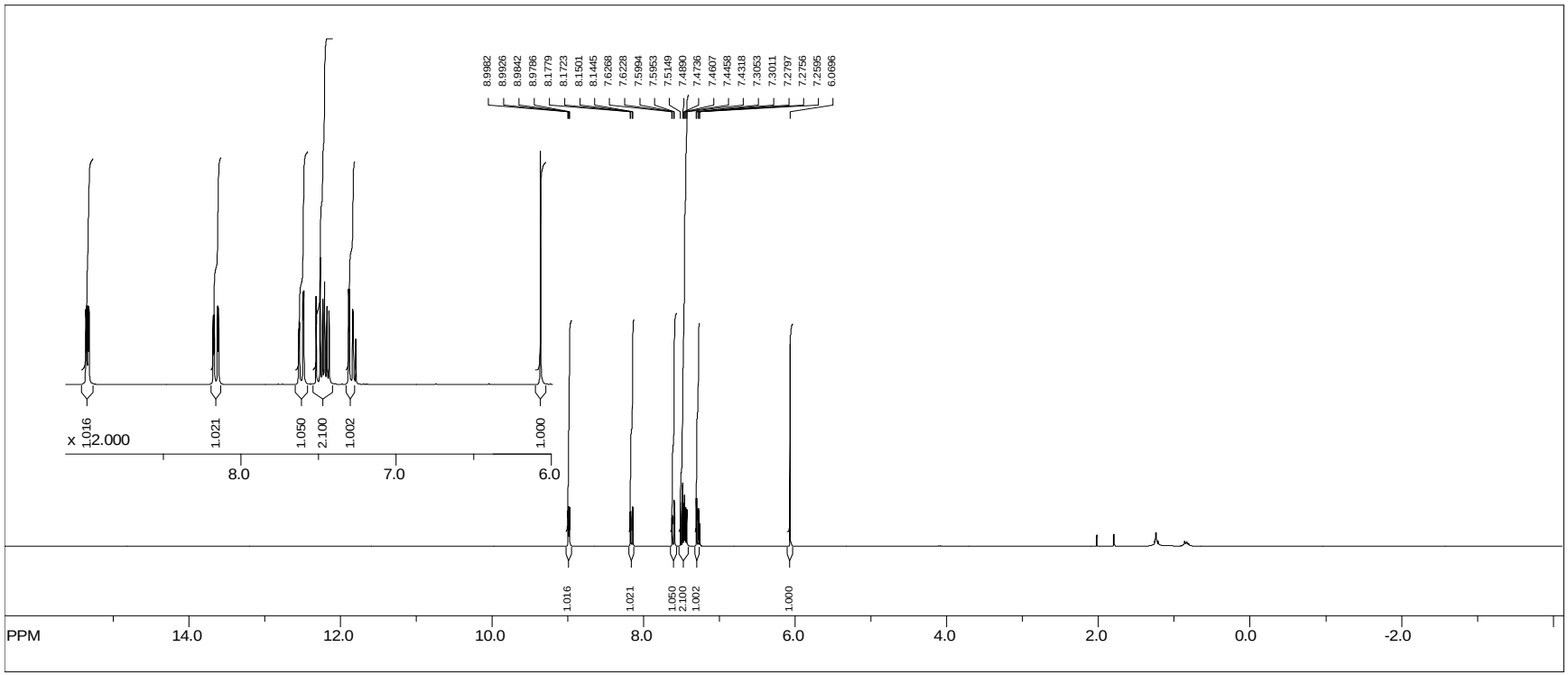
file: Z:\Laina\lmgxiv\lmgxiv_80a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(E)-8-(1,2-Dichlorovinyloxy)quinoline (116**)**



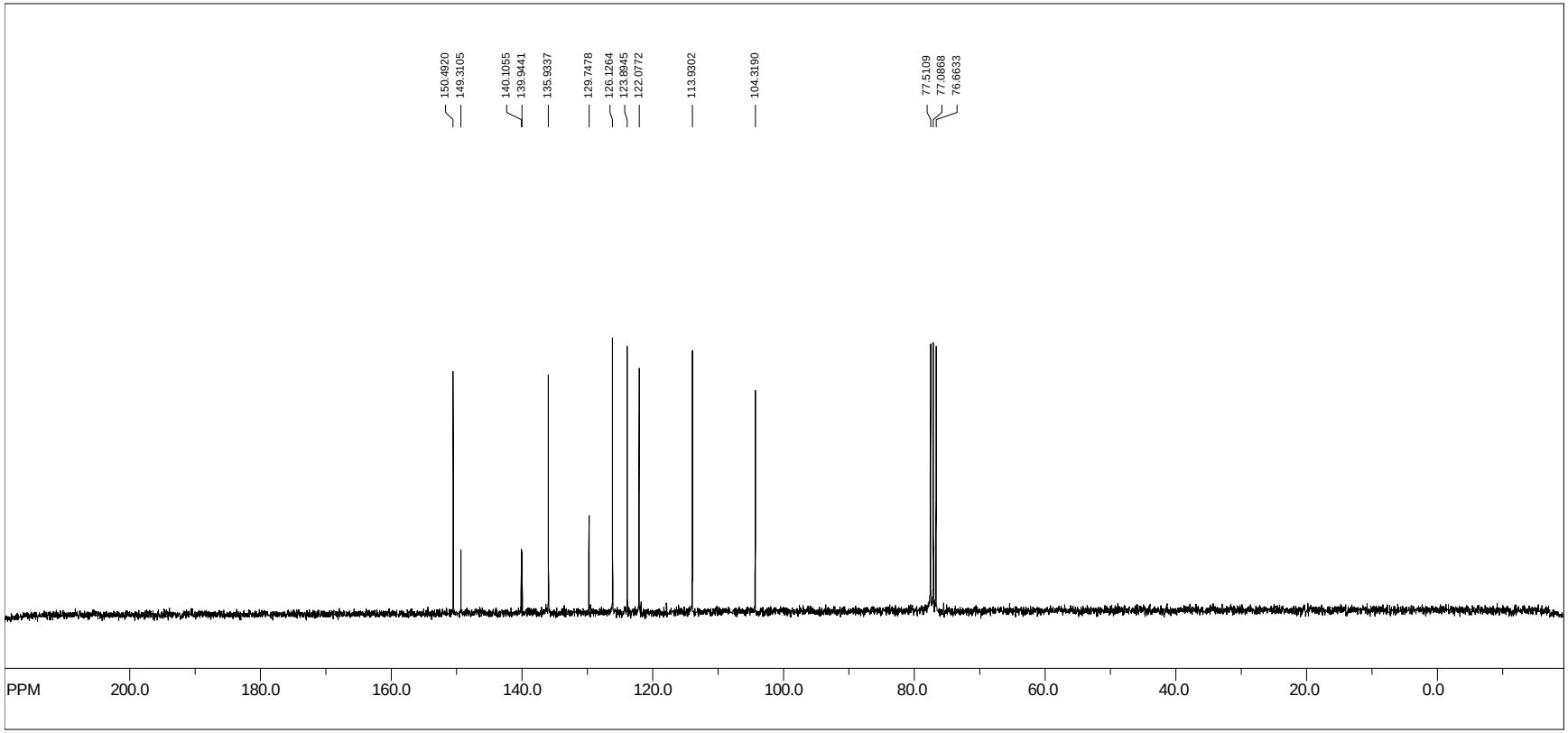
SpinWorks 2.5: (1,2-dichlorovinylether) 8-hydroxyquinoline



file: Z:\Laina\lmgvi\lmgvi_92a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

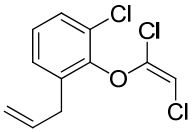
SpinWorks 2.5: addition of 8-hydroxyquinoline to TCE



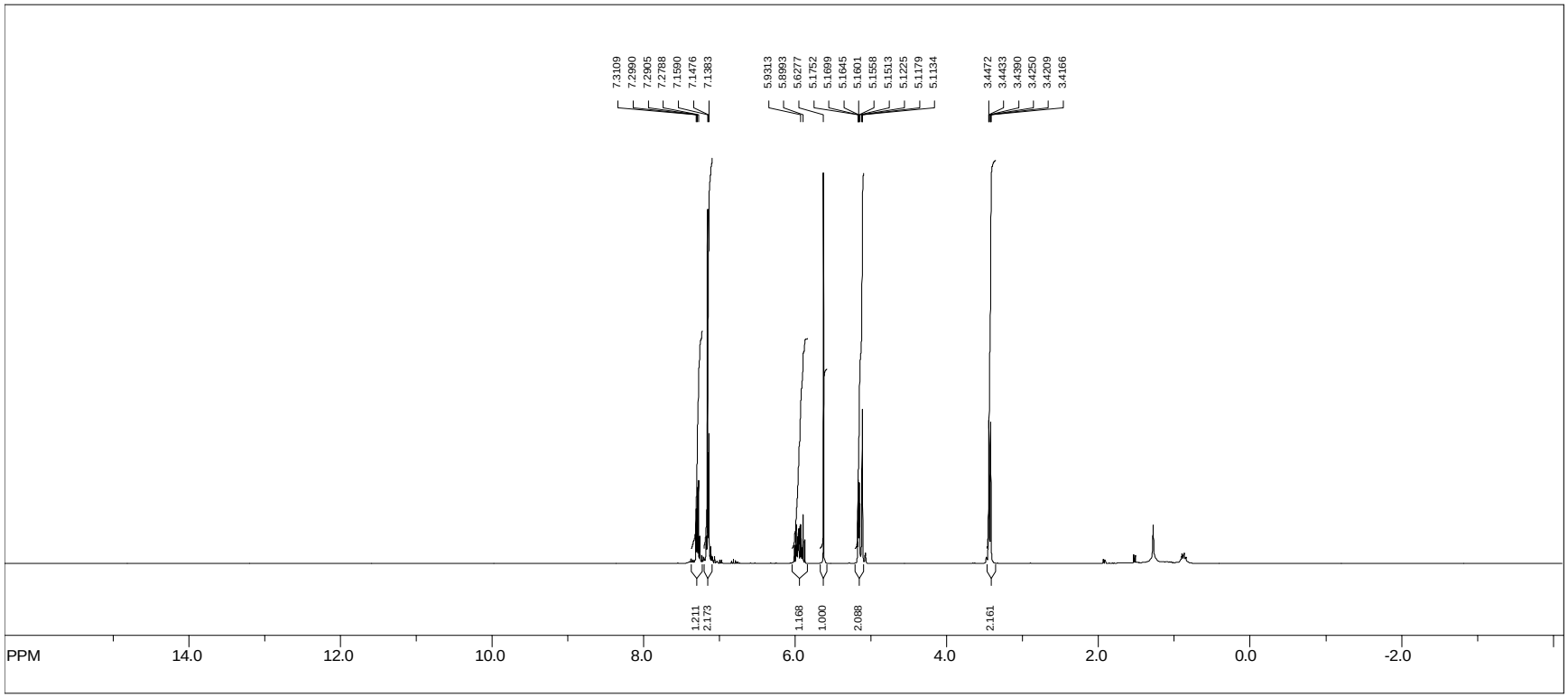
file: Z:\Laina\lmgix\lmgix_25a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 222

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

((E)-1-allyl-3-chloro-2-(1,2-Dichlorovinyloxy)benzene (119)



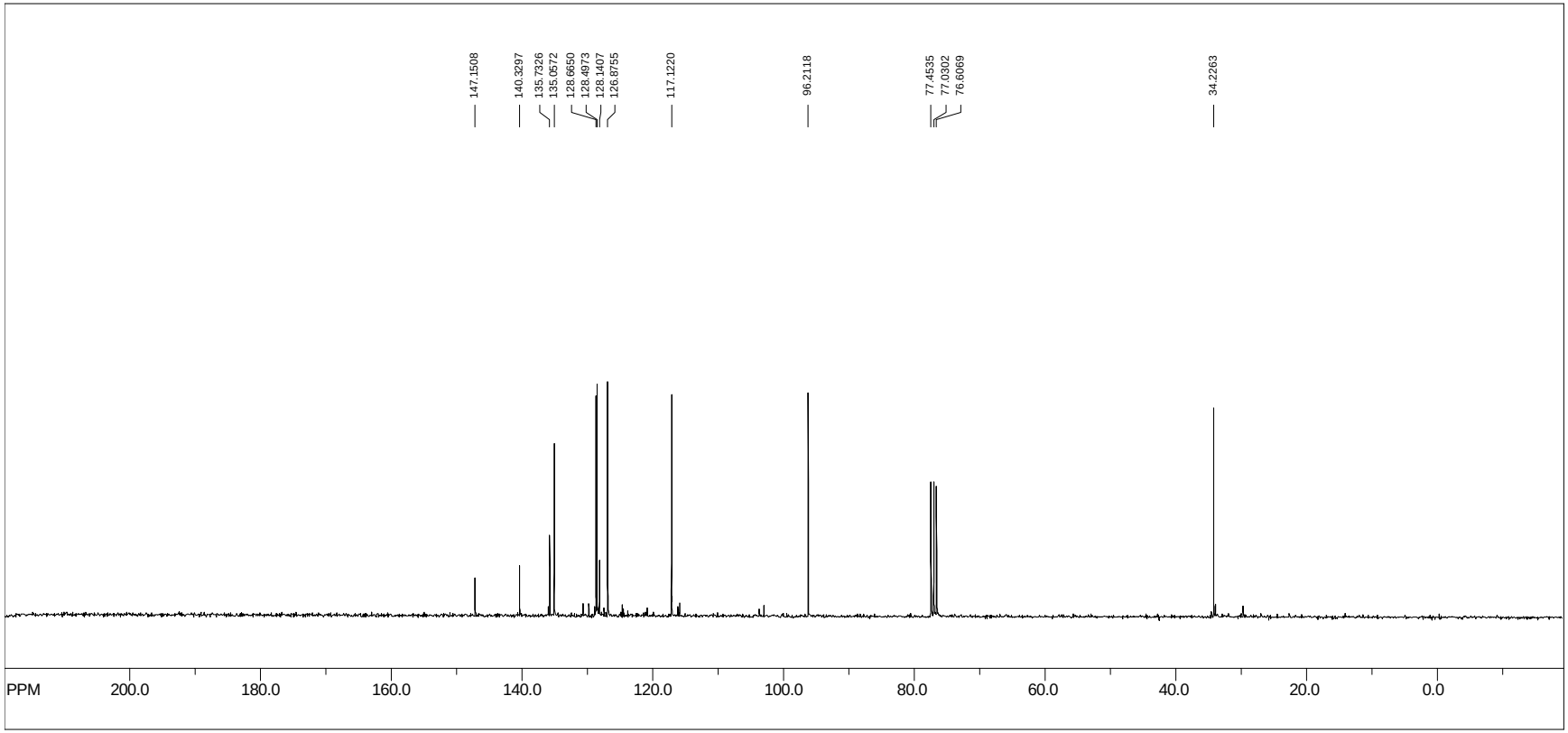
SpinWorks 2.5: 2-allyl-6-chlorophenol addition to trichloroethylene



file: Z:\Laina\lmgvii\lmgvii_66A\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

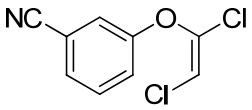
SpinWorks 2.5: 2-allyl-6-chlorophenol addition to trichloroethylene



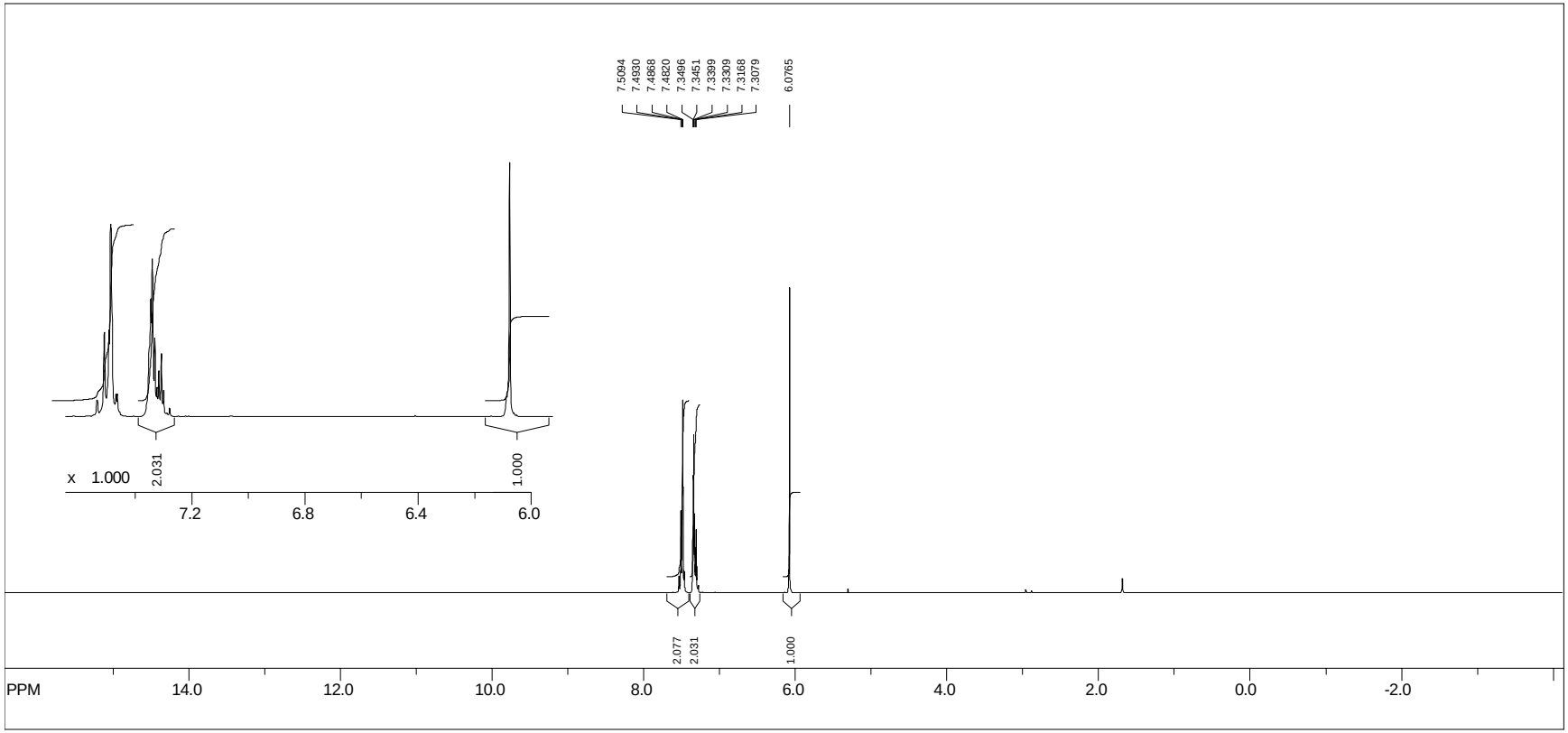
file: Z:\Laina\lmgvii\lmgvii_66A\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(E)-3-(1,2-dichlorovinyloxy)benzonitrile (122**)**



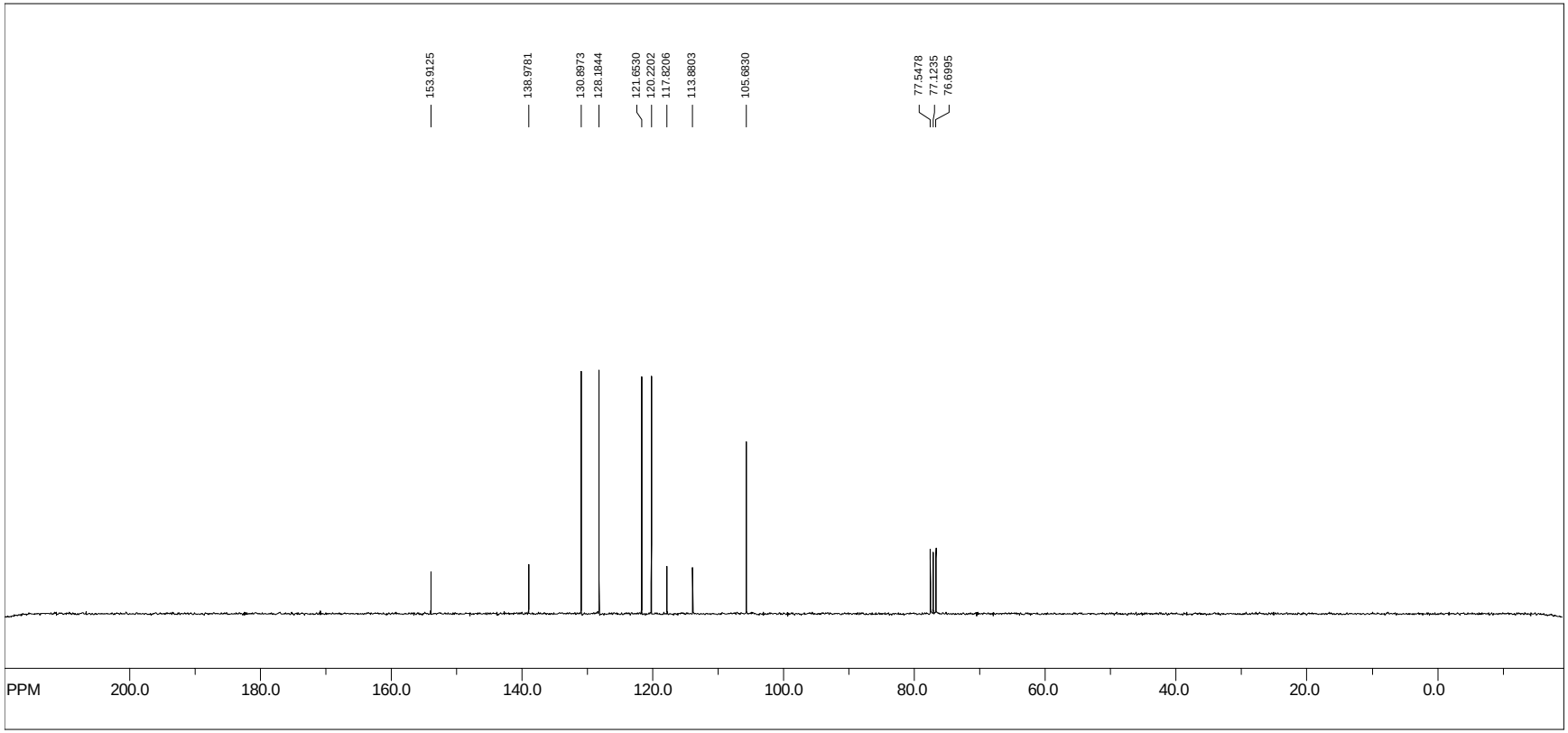
SpinWorks 2.5: m-cyanophenol addition to TCE



file: Z:\Laina\lmgxi\lmgxi_92a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

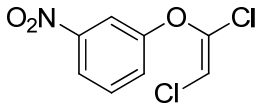
SpinWorks 2.5: m-cyanophenol addition to TCE



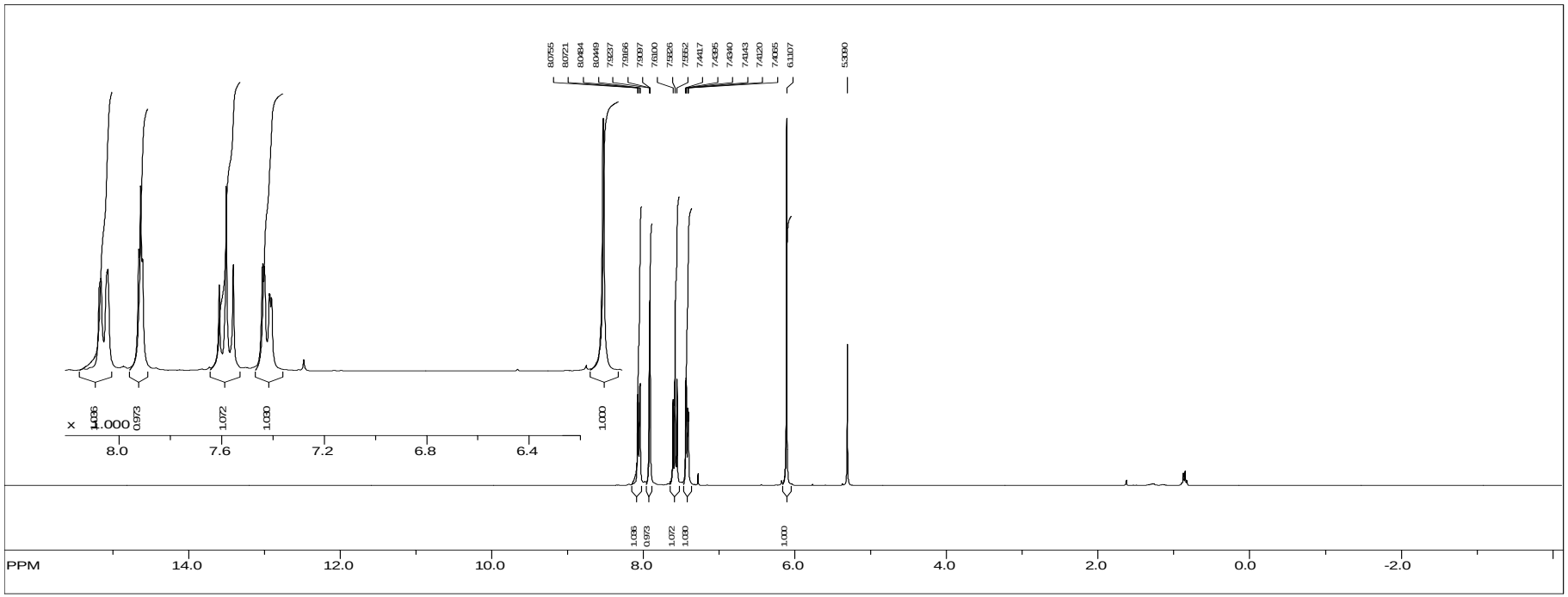
file: Z:\Laina\lmgxi\lmgxi_92a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(E)-1-(1,2-Dichlorovinyloxy)-3-nitrobenzene (125**)**



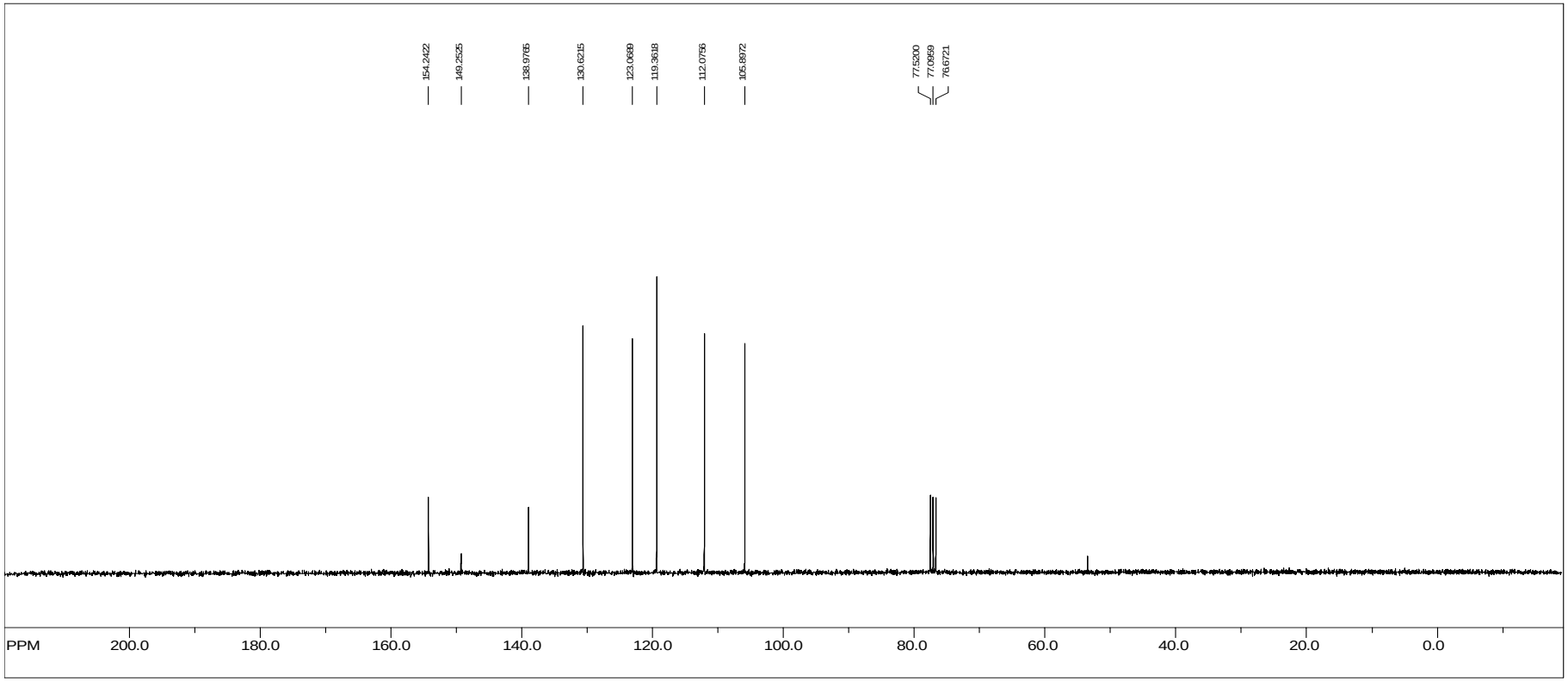
SpinWorks 2.5: addition of m-nitrophenol to TCE



file: Z:\Laina\lmgix\lmgix_26a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

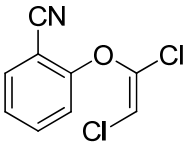
SpinWorks 2.5: addition of m-nitrophenol to TCE



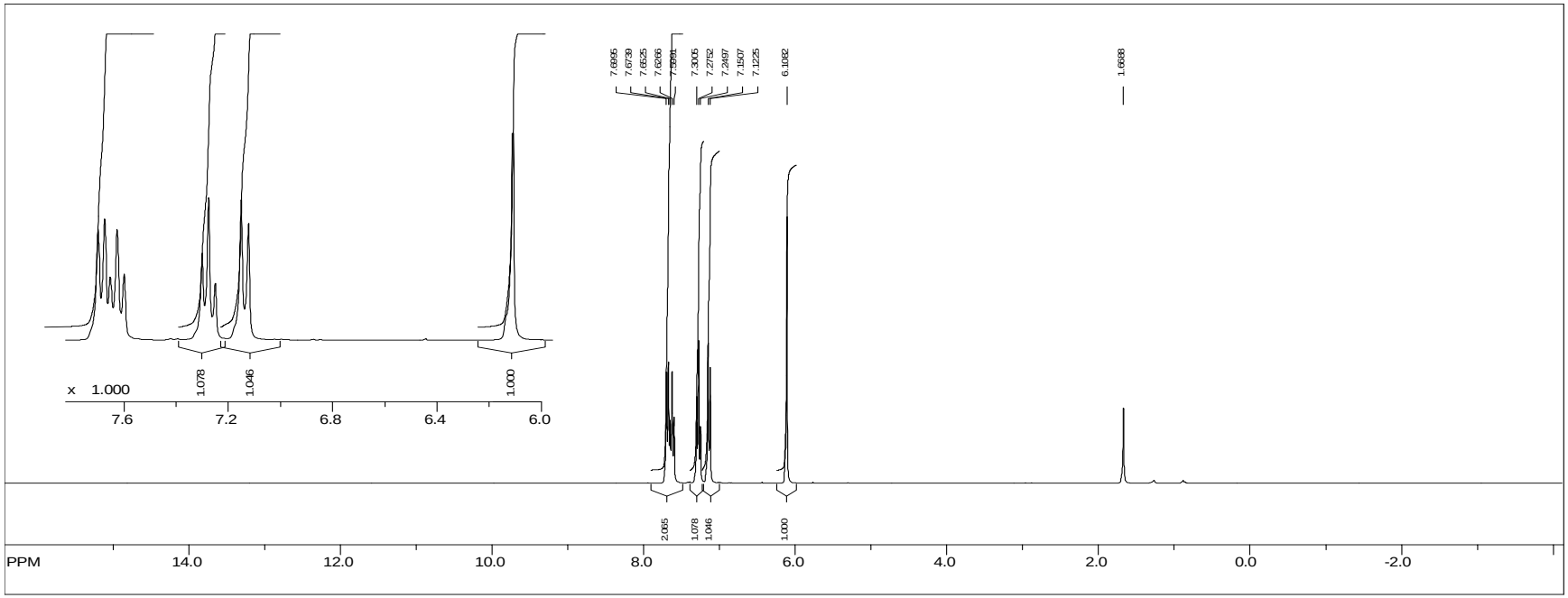
file: C:\Users\Laina\Documents\WORK\NMR\lmgix\lmgix_26a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 149

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-2-(1,2-dichlorovinyloxy)benzonitrile (128)



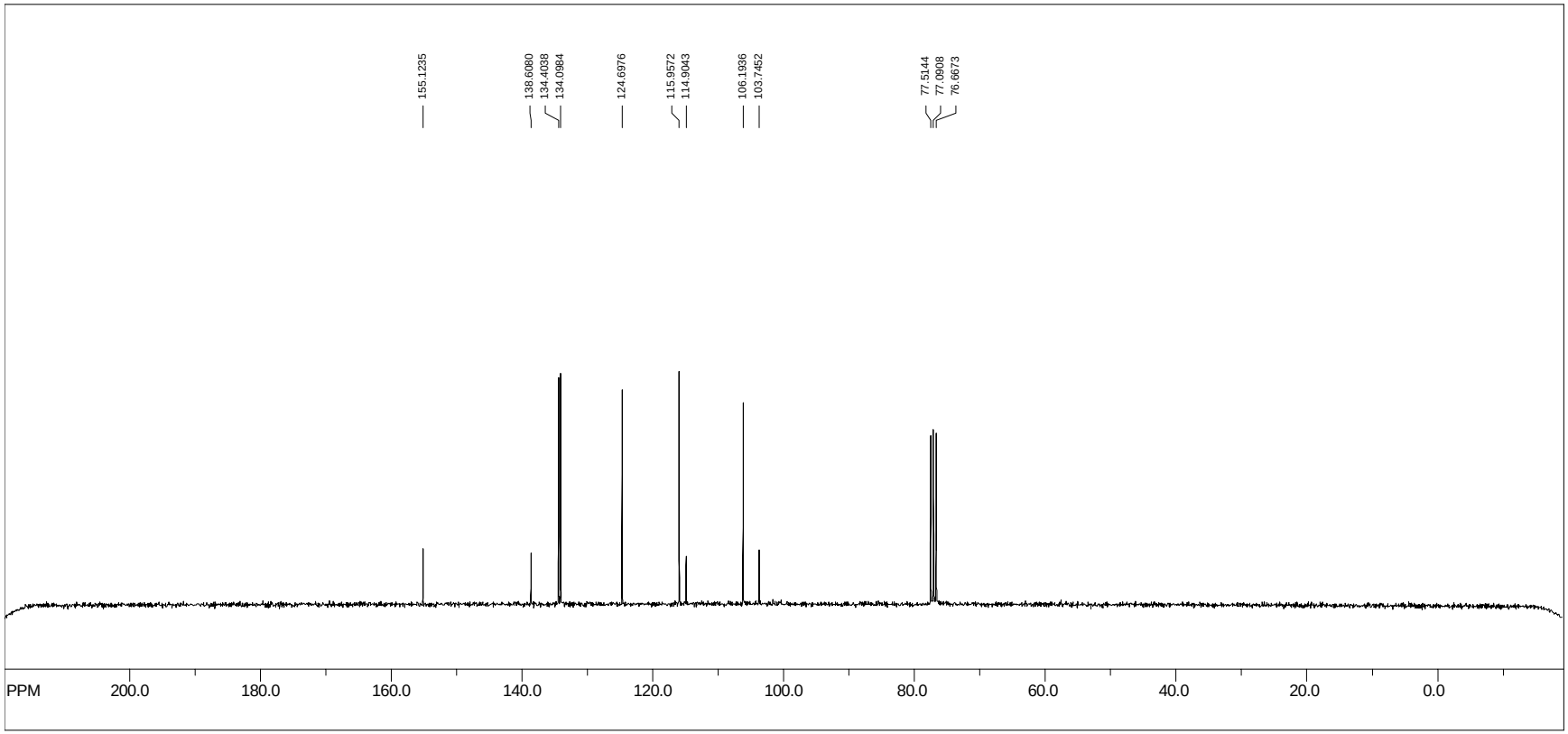
SpinWorks 2.5: o-cyanophenol addition to TCE



file: Z:\Laina\lmgxi\lmgxi_97a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

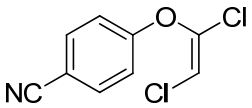
SpinWorks 2.5: o-cyanophenol addition to TCE



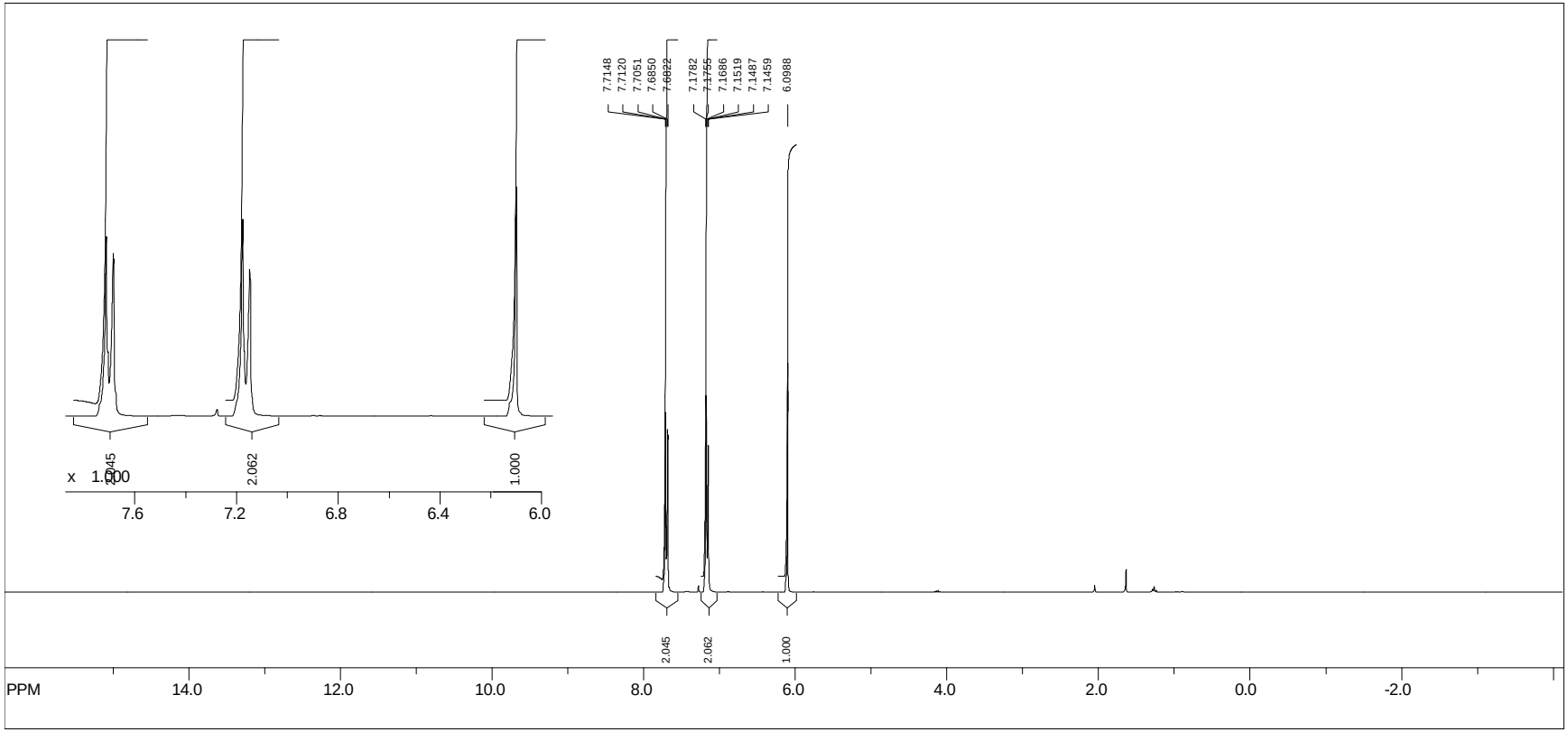
file: Z:\Laina\lmgxi\lmgxi_97a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 298

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-4-(1,2-dichlorovinyloxy)benzonitrile (129)



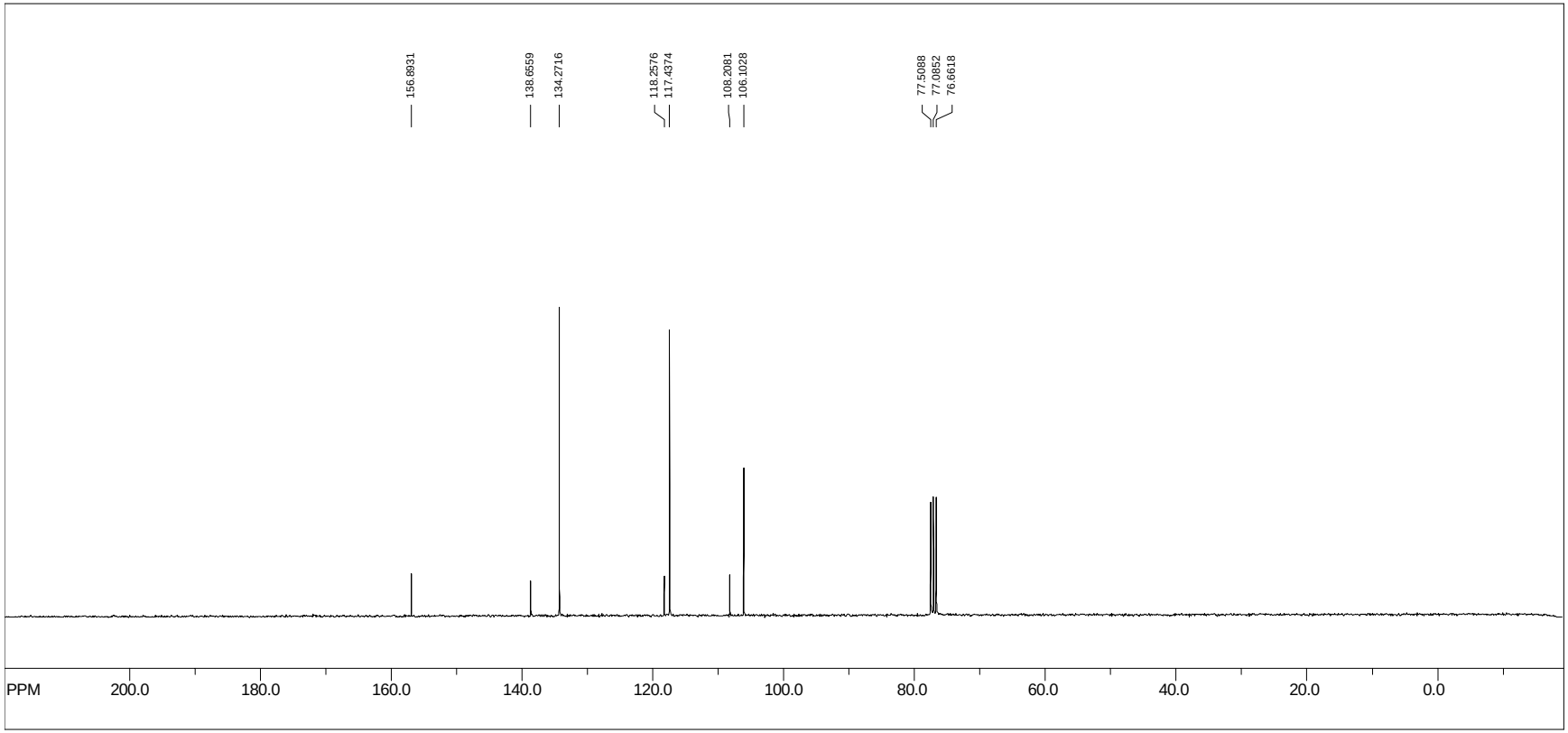
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



file: Z:\Laina\lmgxi\lmgxi_85a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

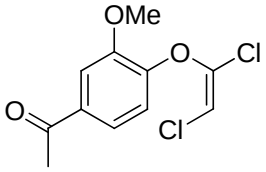
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



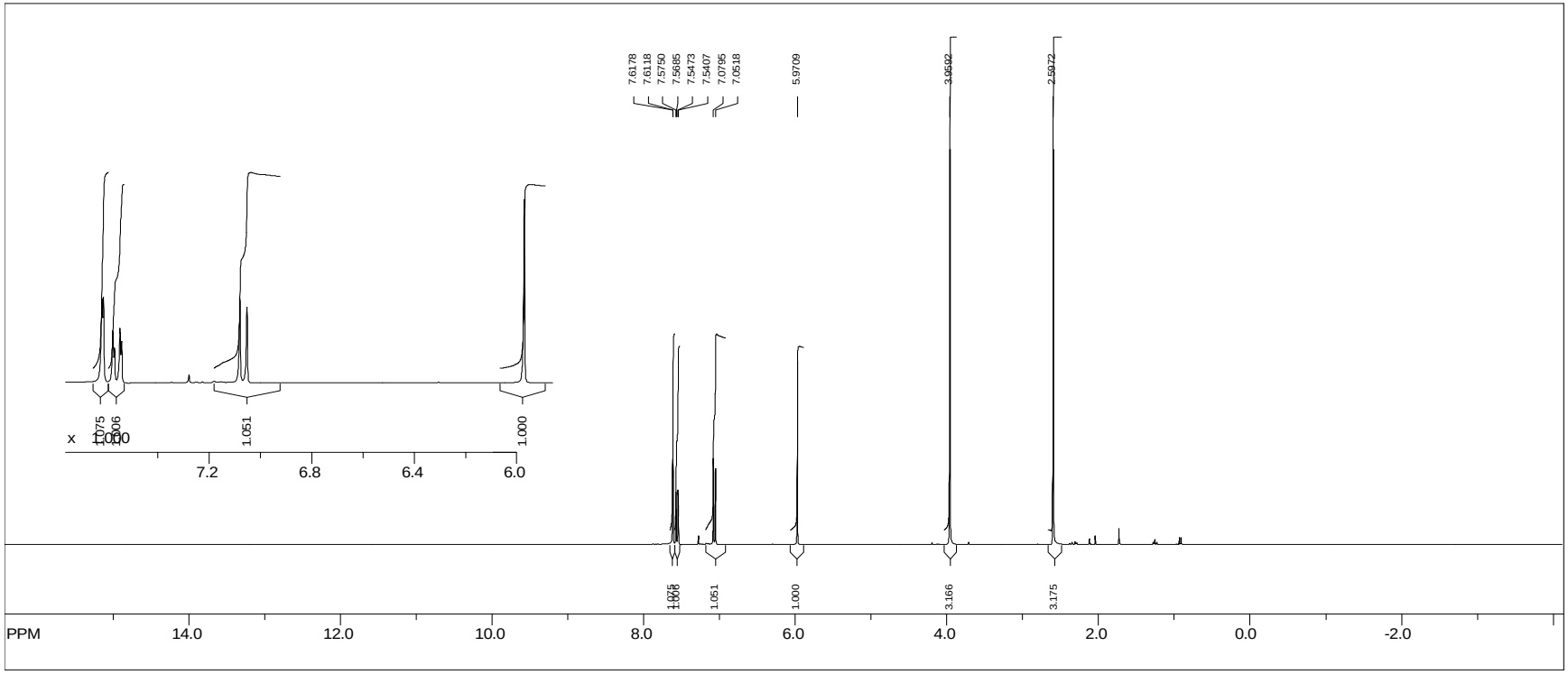
file: Z:\Laina\lmgxi\lmgxi_85a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-(4-(1,2-dichlorovinyloxy)-3-methoxyphenyl)ethanone (130)



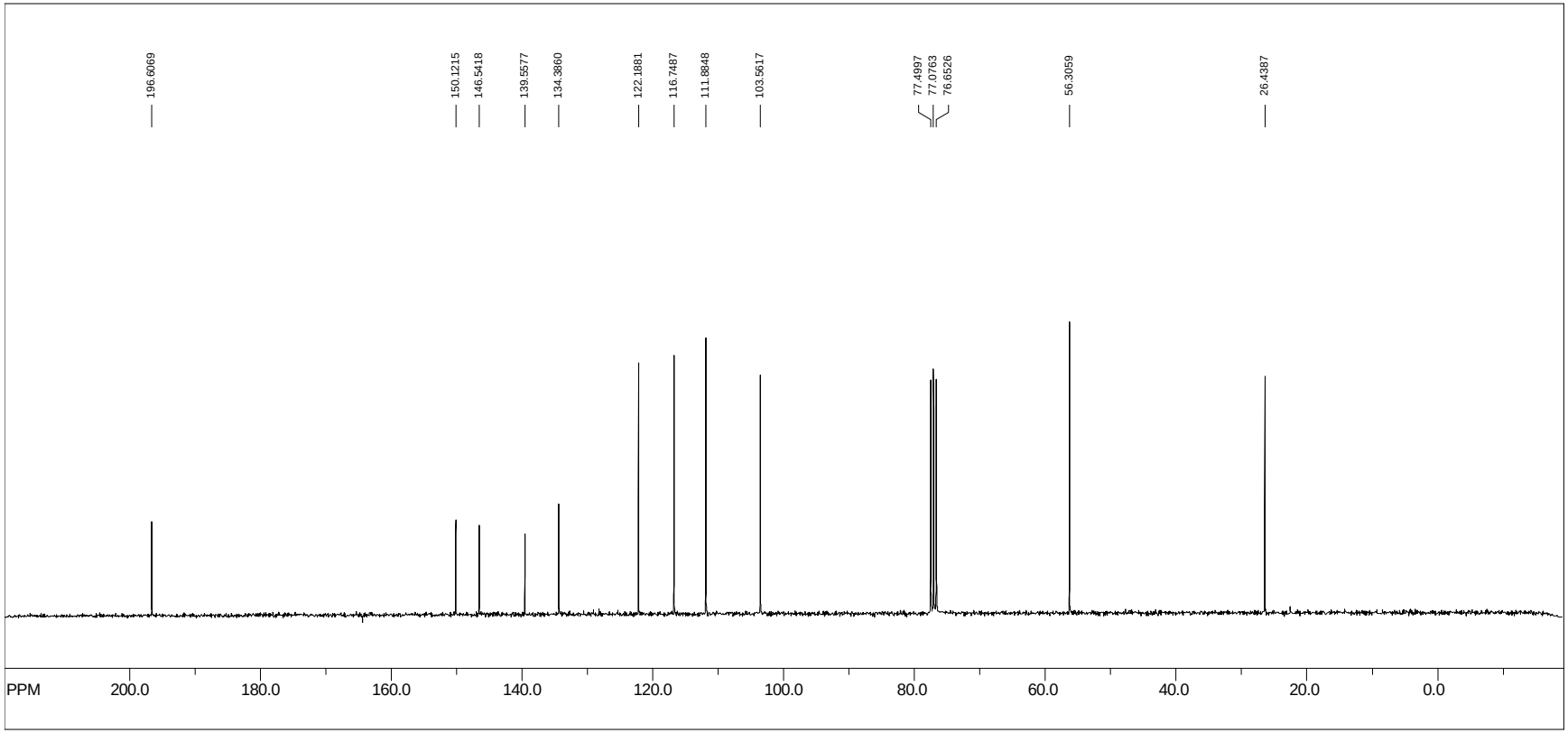
SpinWorks 2.5: addition of acetophenone deriv to TCE



file: Z:\Laina\lmgxi\lmgxi_77b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

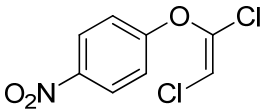
SpinWorks 2.5: addition of acetophenone deriv to TCE



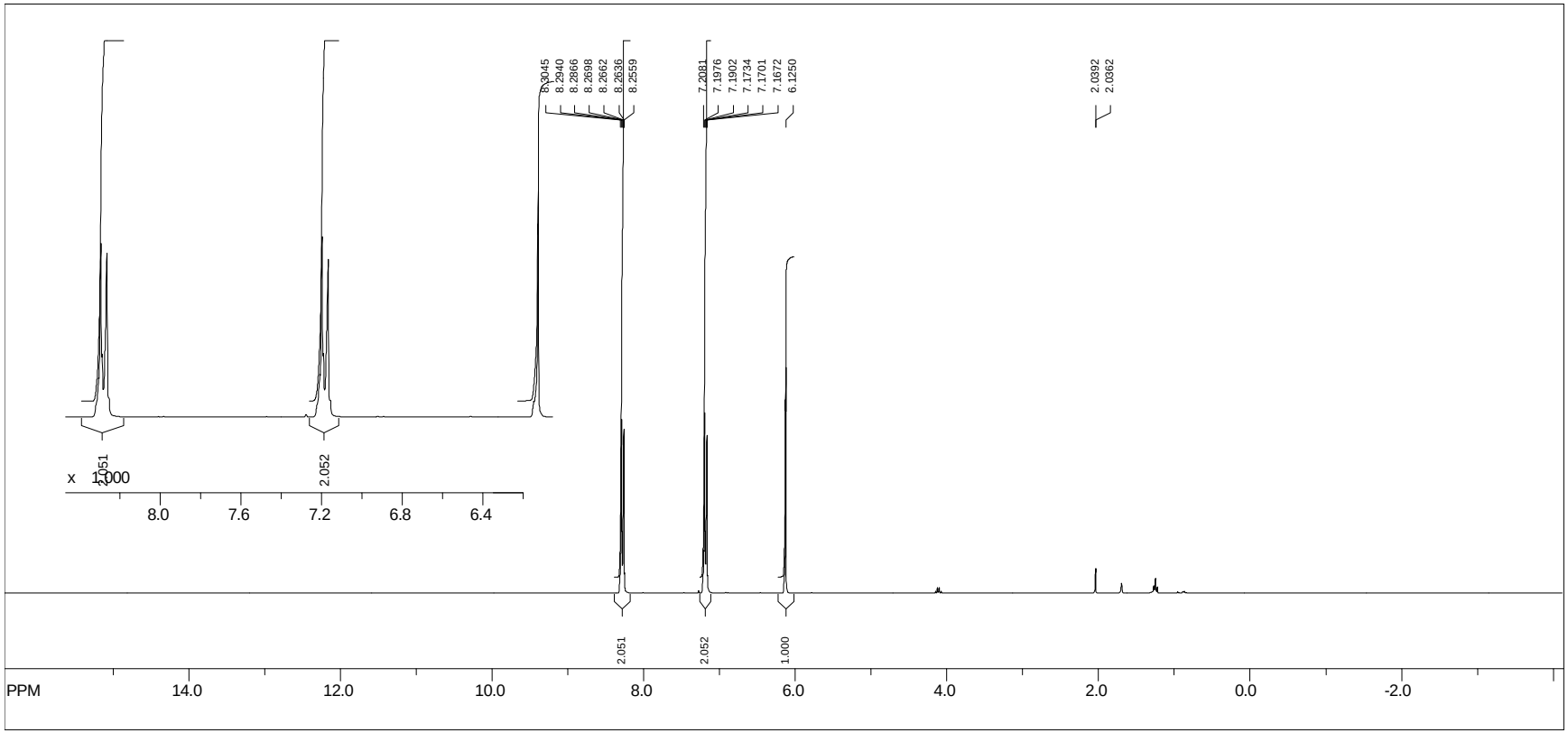
file: Z:\Laina\lmgxi\lmgxi_77b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-(1,2-dichlorovinyloxy)-4-nitrobenzene (131)



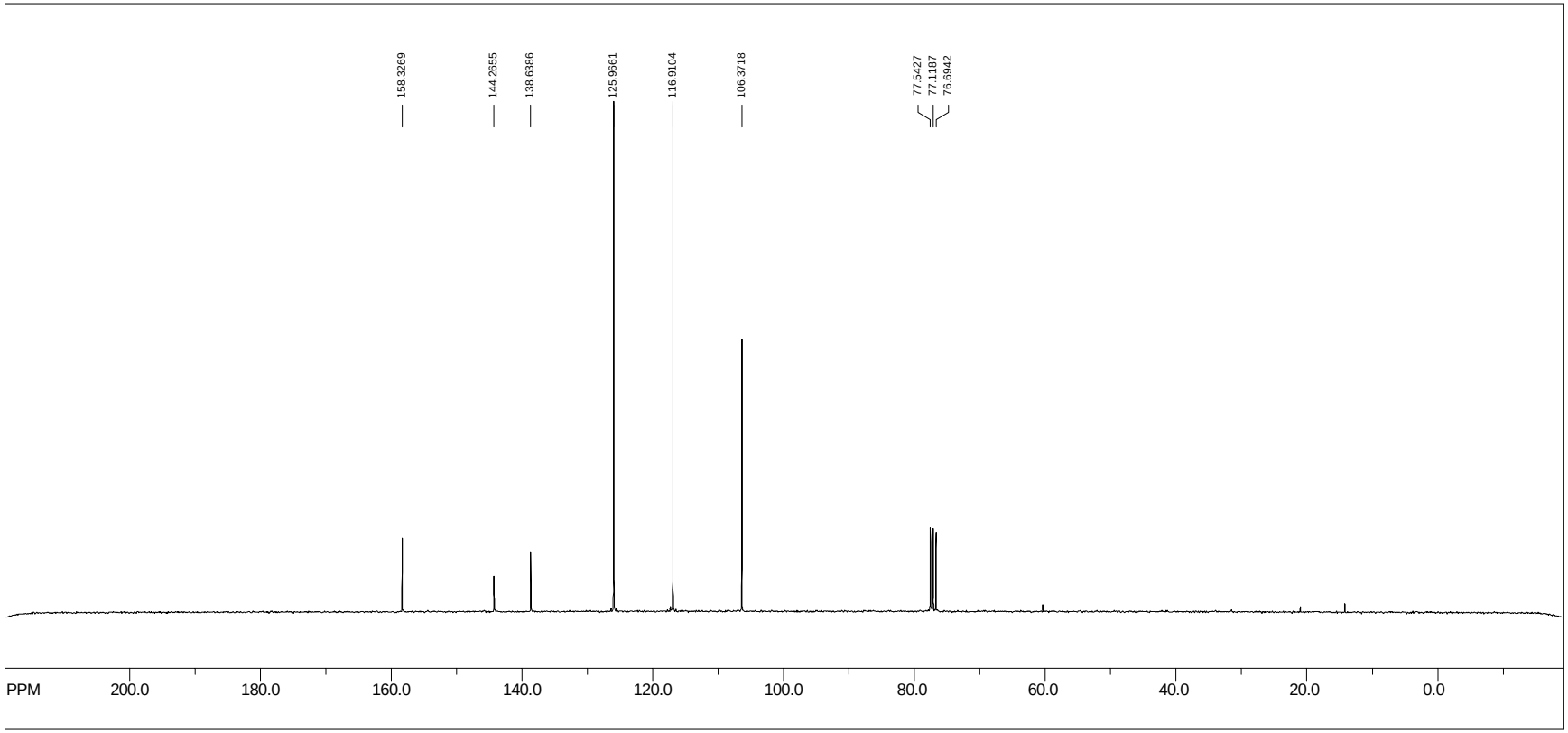
SpinWorks 2.5: p-nitrophenol addition to TCE



file: Z:\Laina\lmgxii\lmgxii_09a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

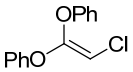
SpinWorks 2.5: p-nitrophenol addition to TCE



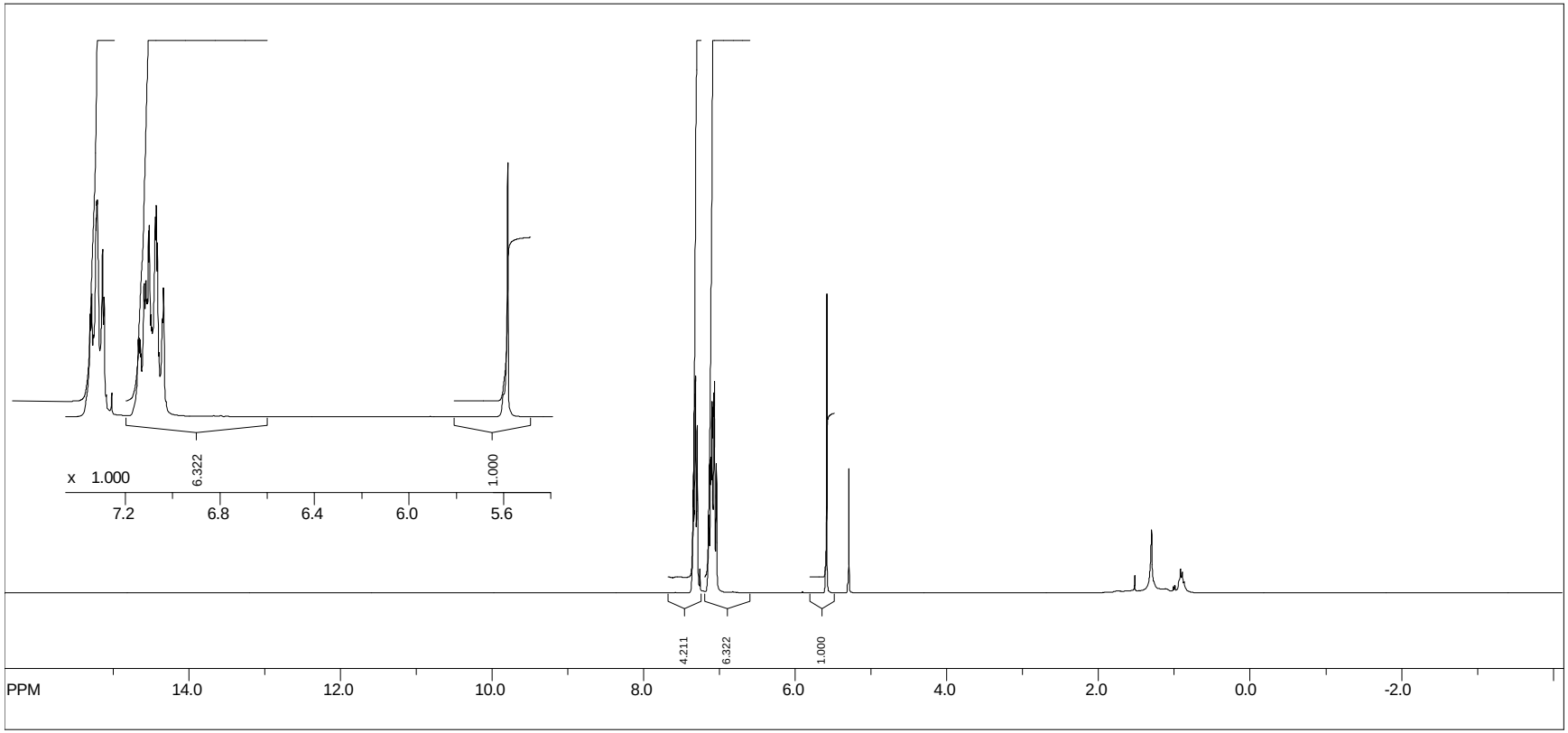
file: Z:\Laina\lmgxii\lmgxii_09a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 470

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-(2-chloro-1-phenoxyvinyloxy)benzene (132)



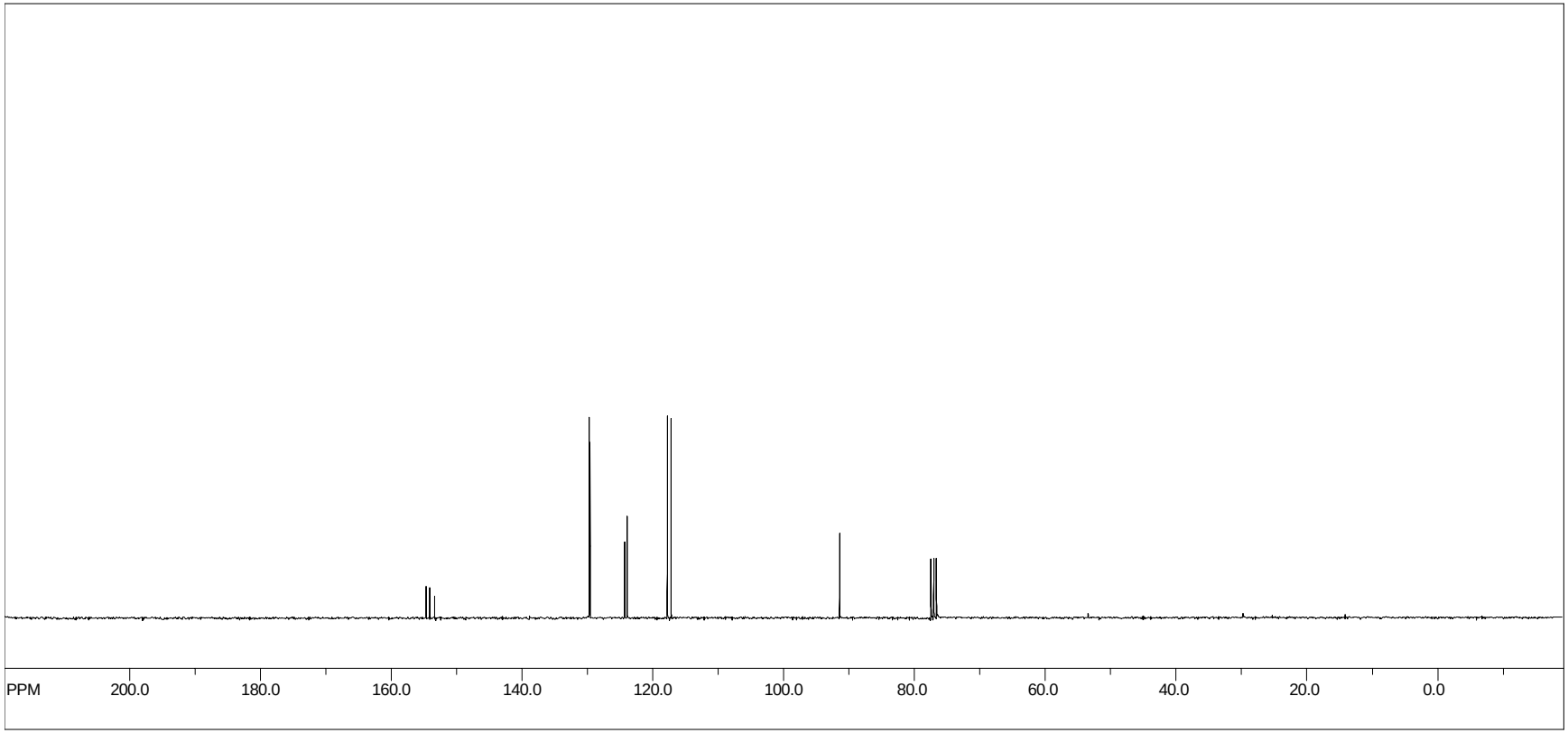
SpinWorks 2.5: after spe



file: Z:\Laina\lmgvii\lmgvii_25a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

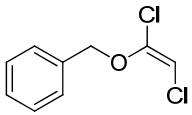
SpinWorks 2.5: after spe



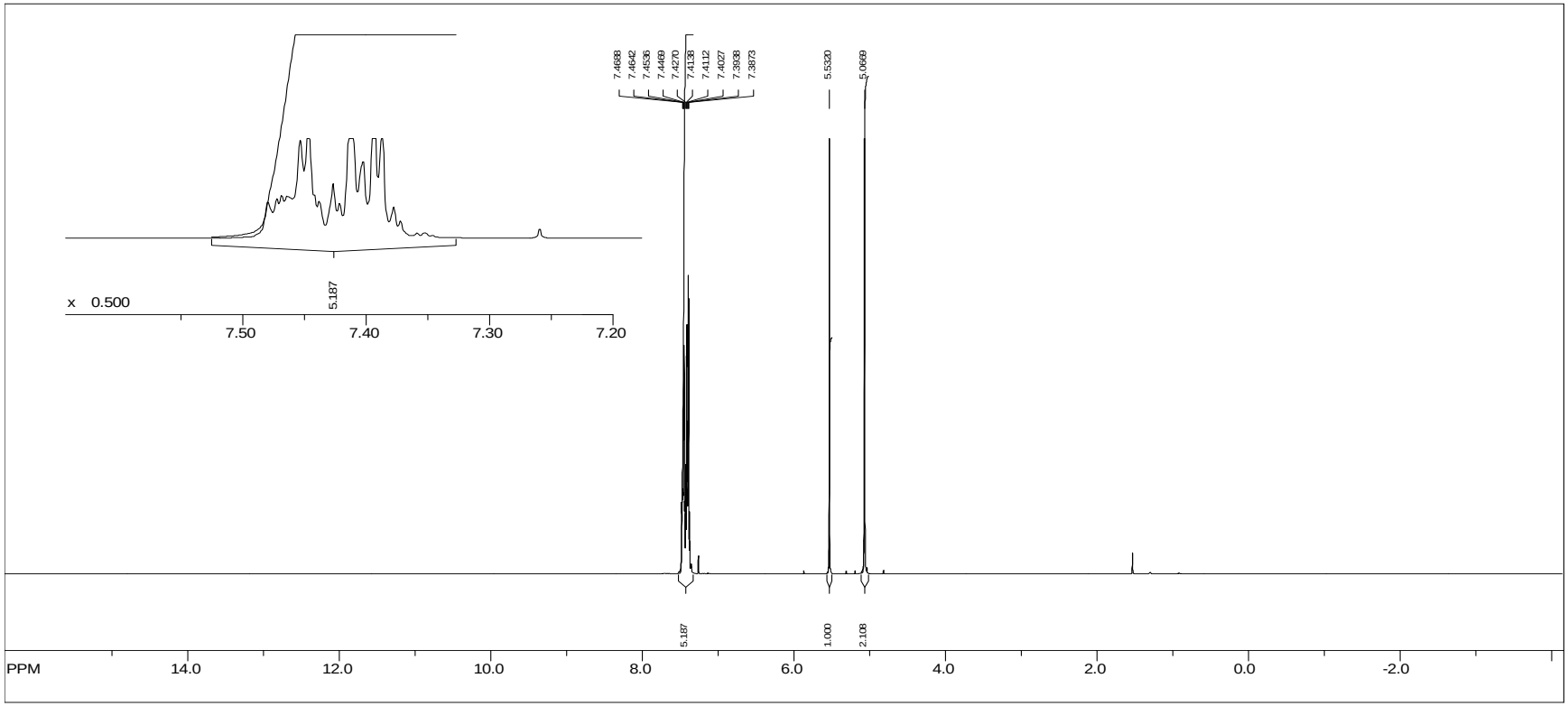
file: Z:\Laina\lmgvii\lmgvii_25a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 188

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-1-((1,2-dichlorovinyloxy)methyl)benzene (134)



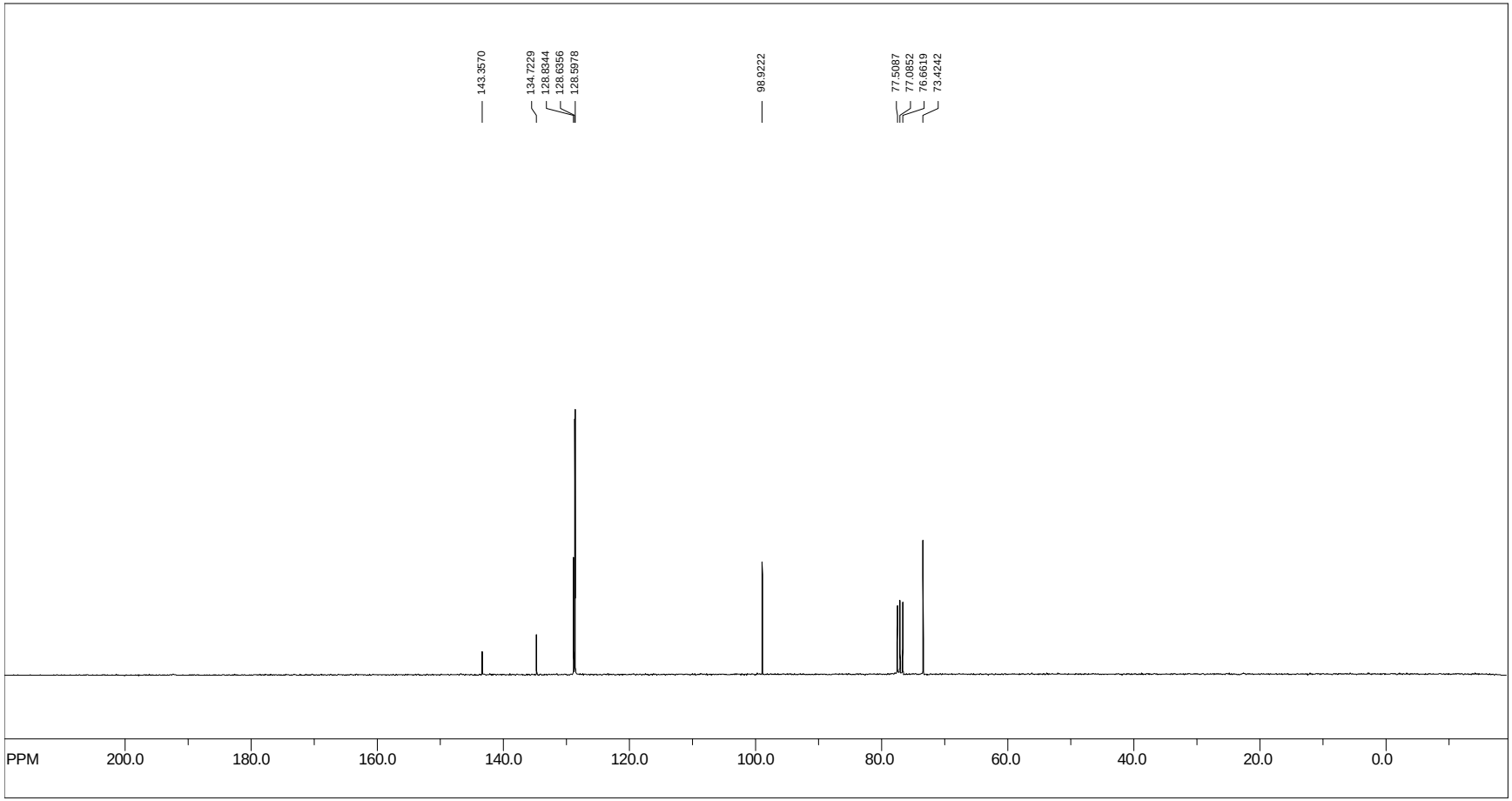
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgxl\lmgxl_87a\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

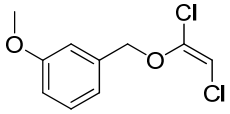
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



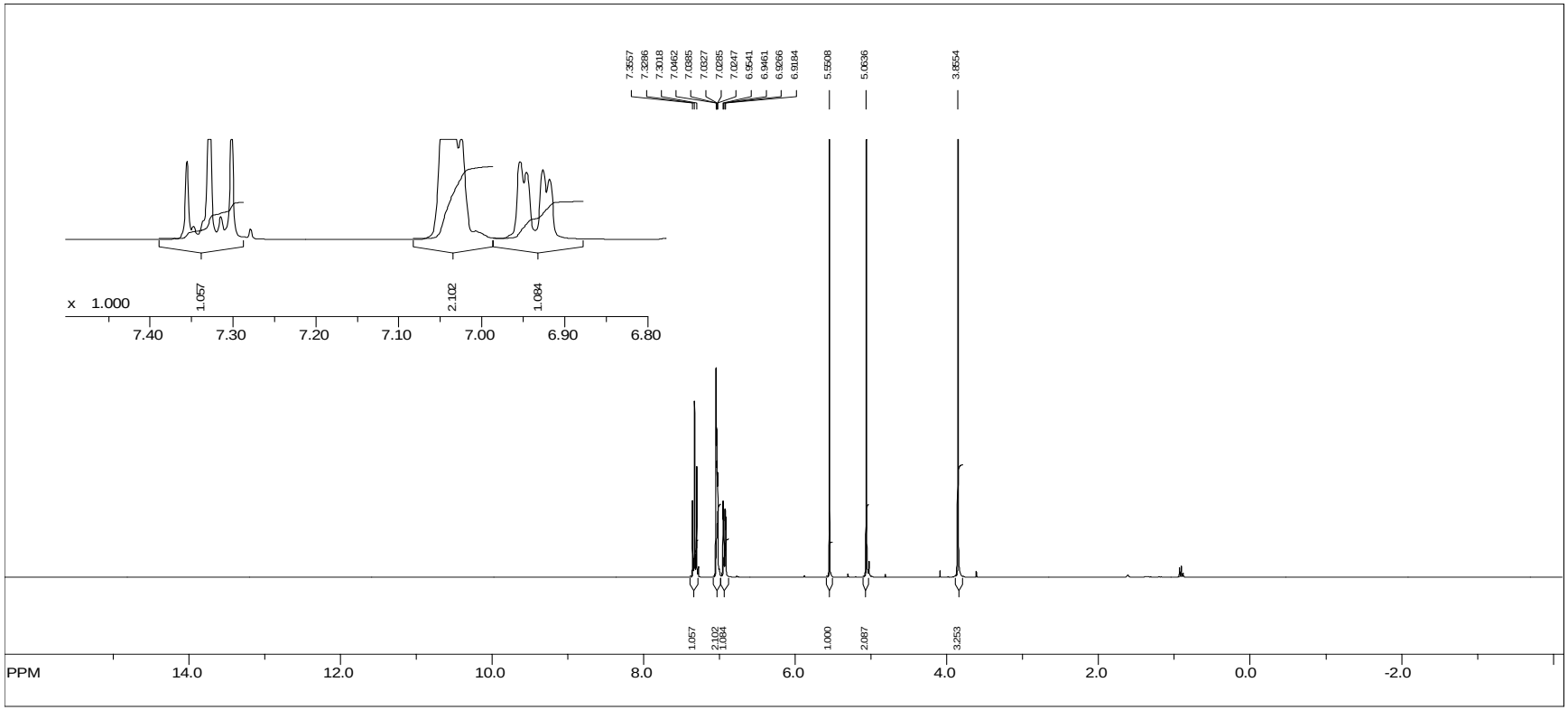
file: Z:\Laina\lmgxi\lmgxi_87a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 429

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-((1,2-dichlorovinyloxy)methyl)-3-methoxybenzene (136)



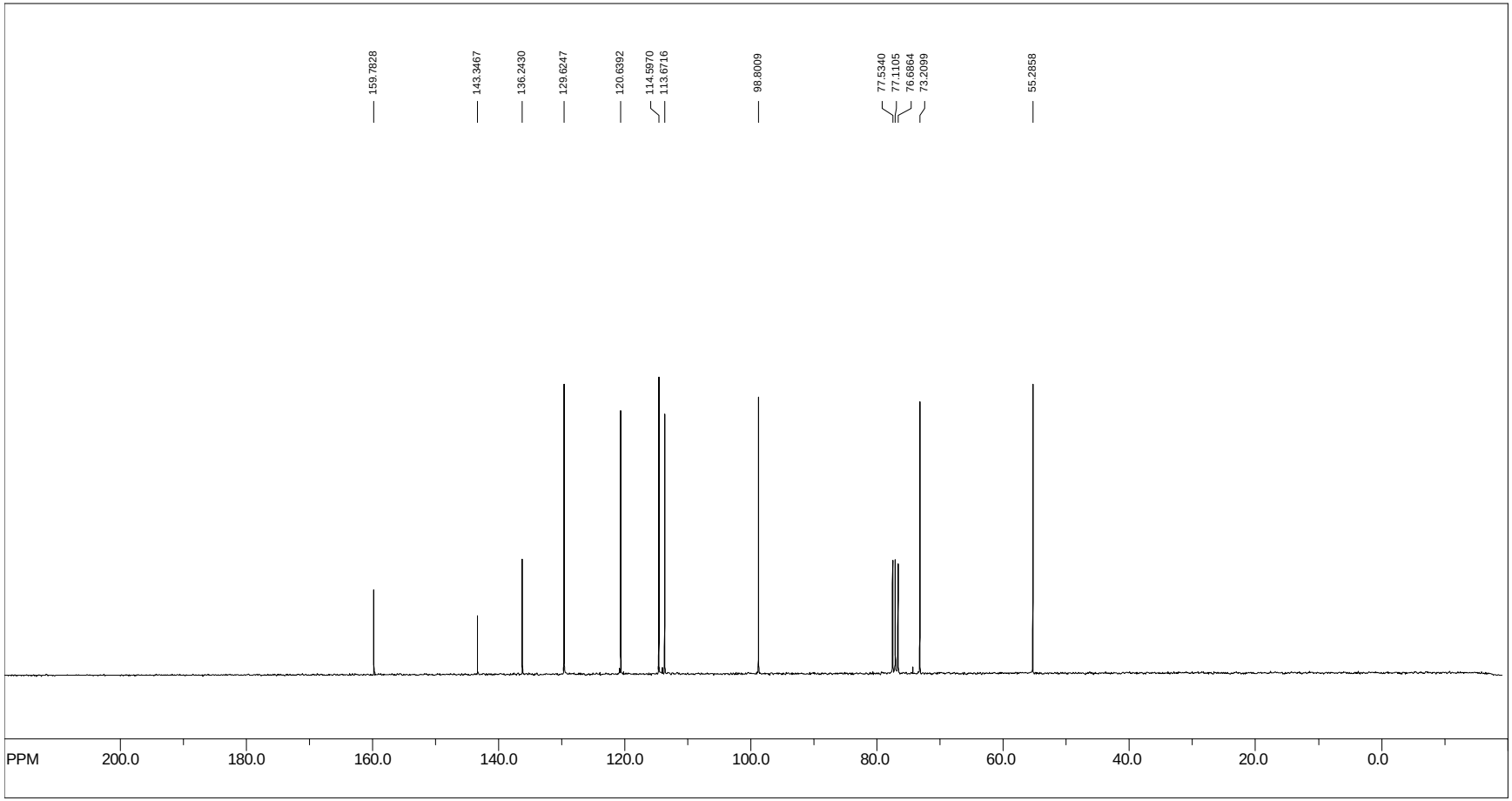
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgxi\lmgxi_70a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

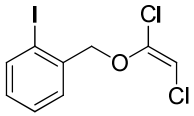
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



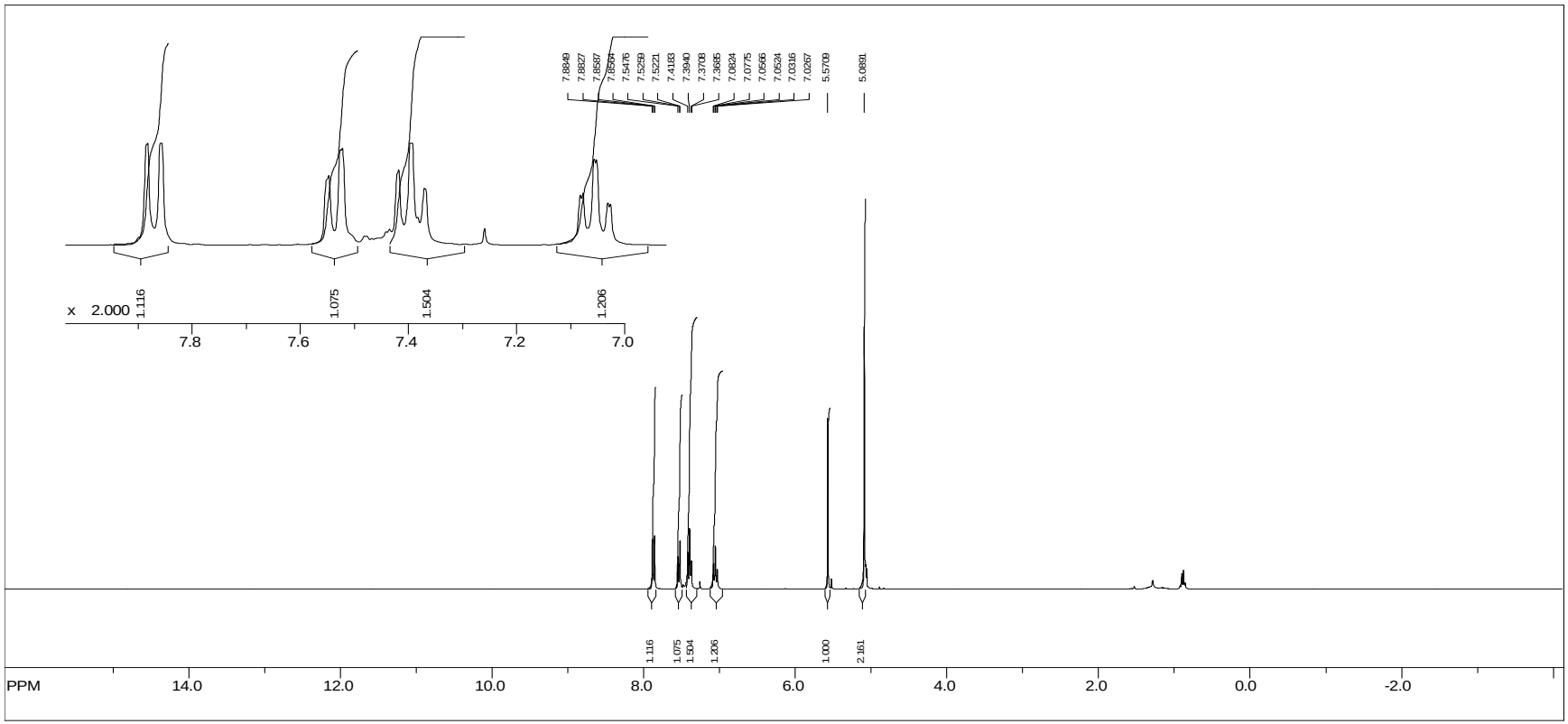
file: Z:\Laina\lmgxi\lmgxi_70a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-((1,2-dichlorovinyloxy)methyl)-2-iodobenzene (138)



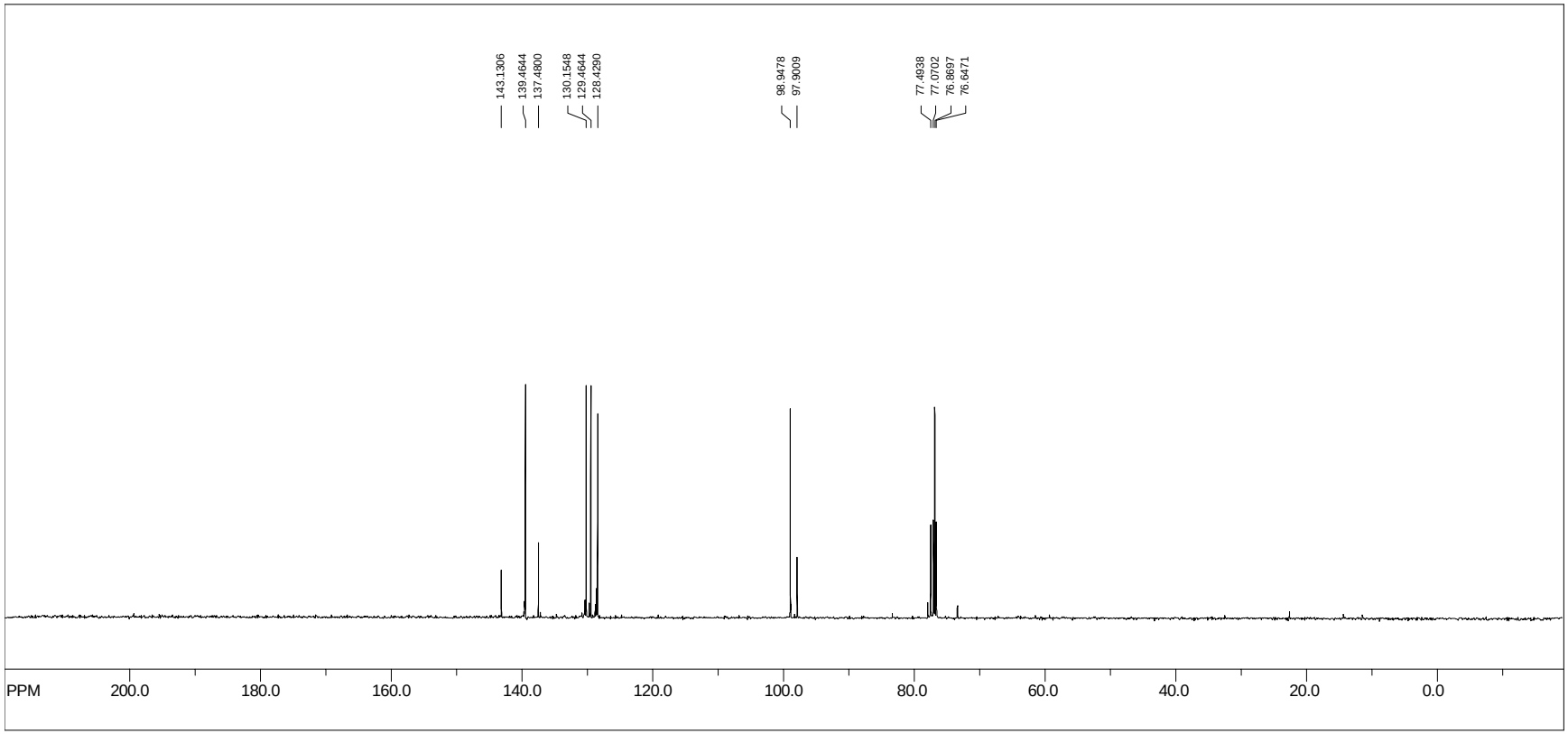
SpinWorks 2.5: addition of o-iodobenzyl alcohol



file: Z:\Laina\lmgvii\lmgvii_67B\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

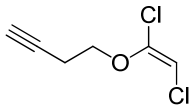
SpinWorks 2.5: addition of o-iodobenzyl alcohol



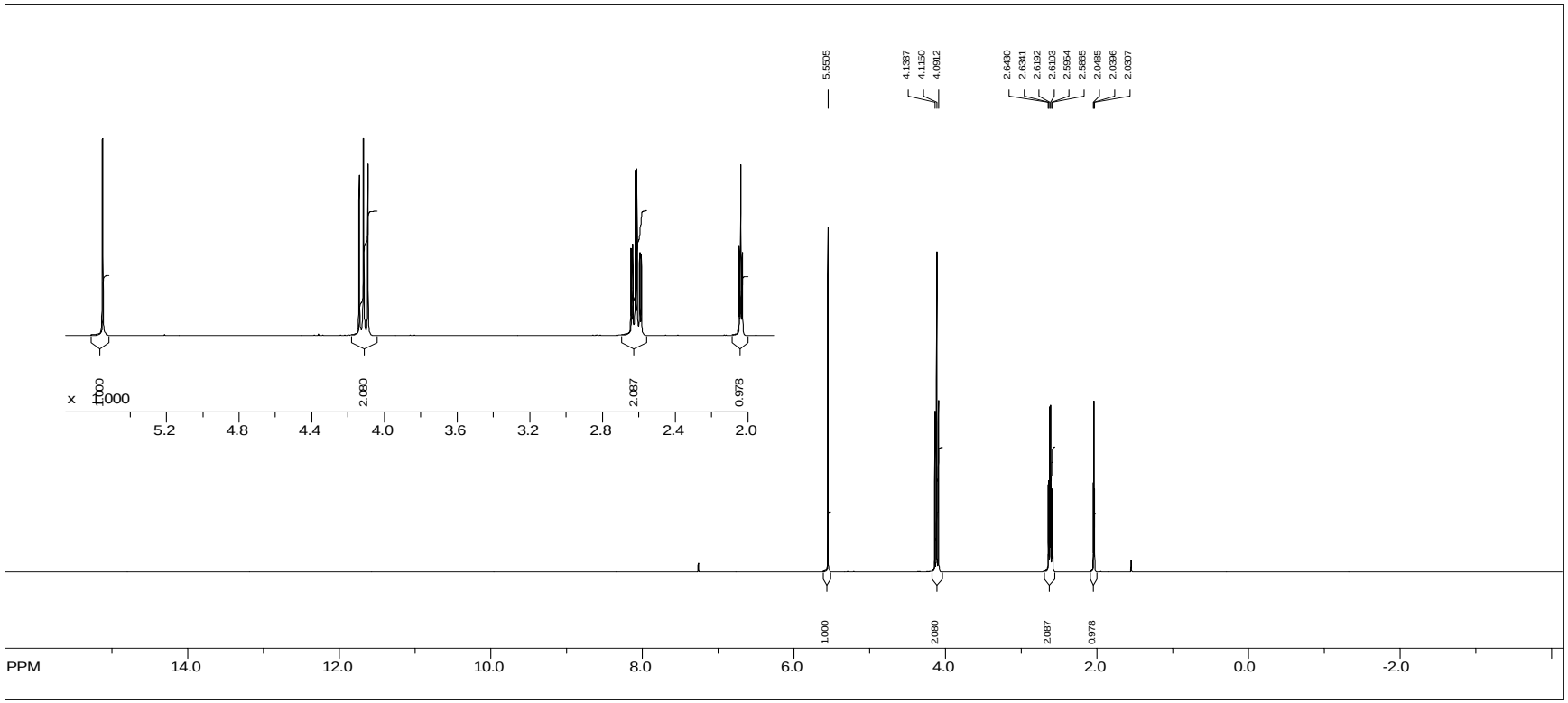
file: Z:\Laina\lmgvii\lmgvii_67B\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 228

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-4-(1,2-Dichlorovinyloxy)but-1-yne (140)



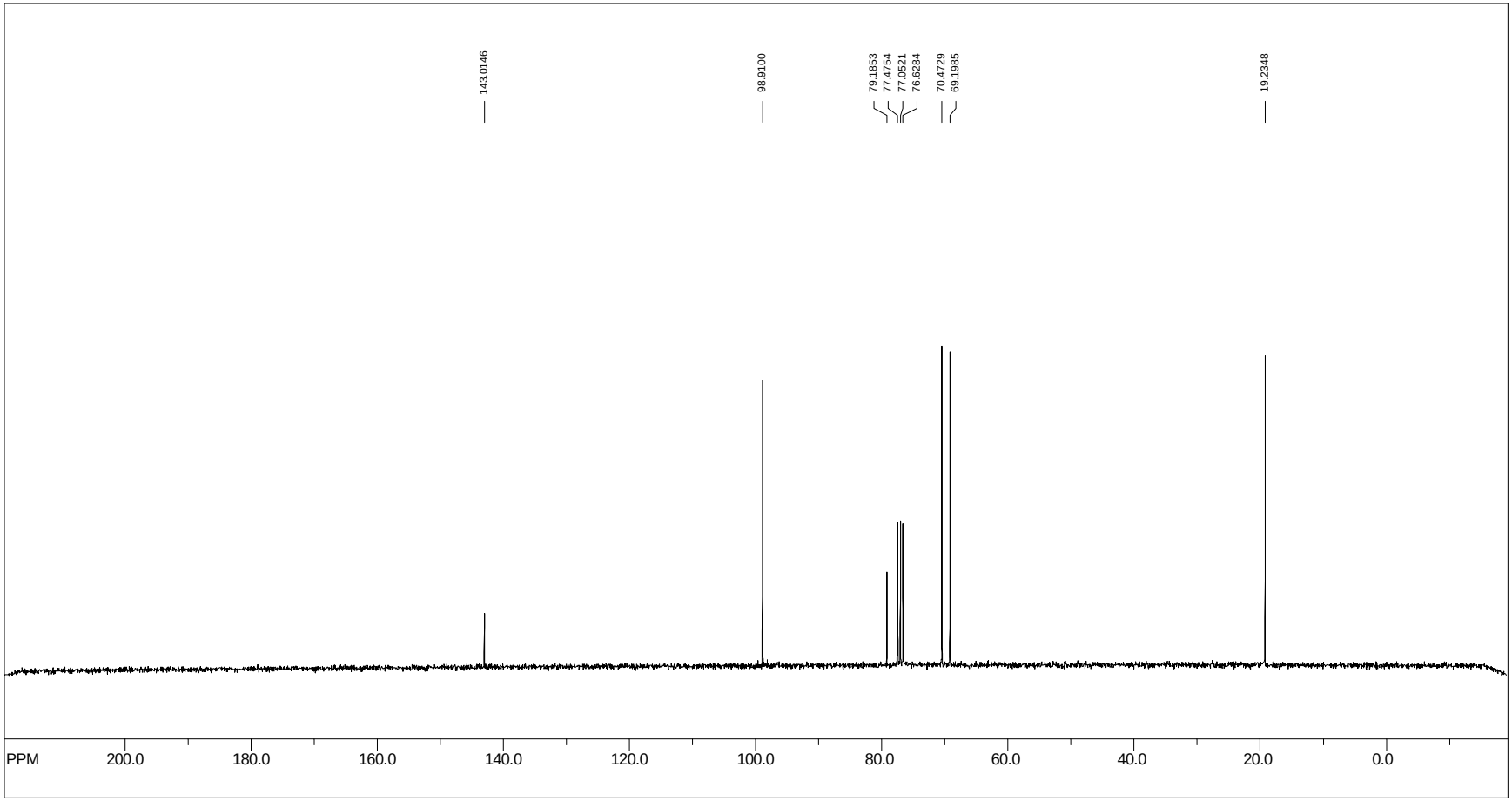
SpinWorks 2.5: fractions 6-9- from column



file: Z:\Laina\lmgx\lmgx_20a\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

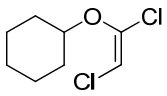
SpinWorks 2.5: fractions 6-9- from column



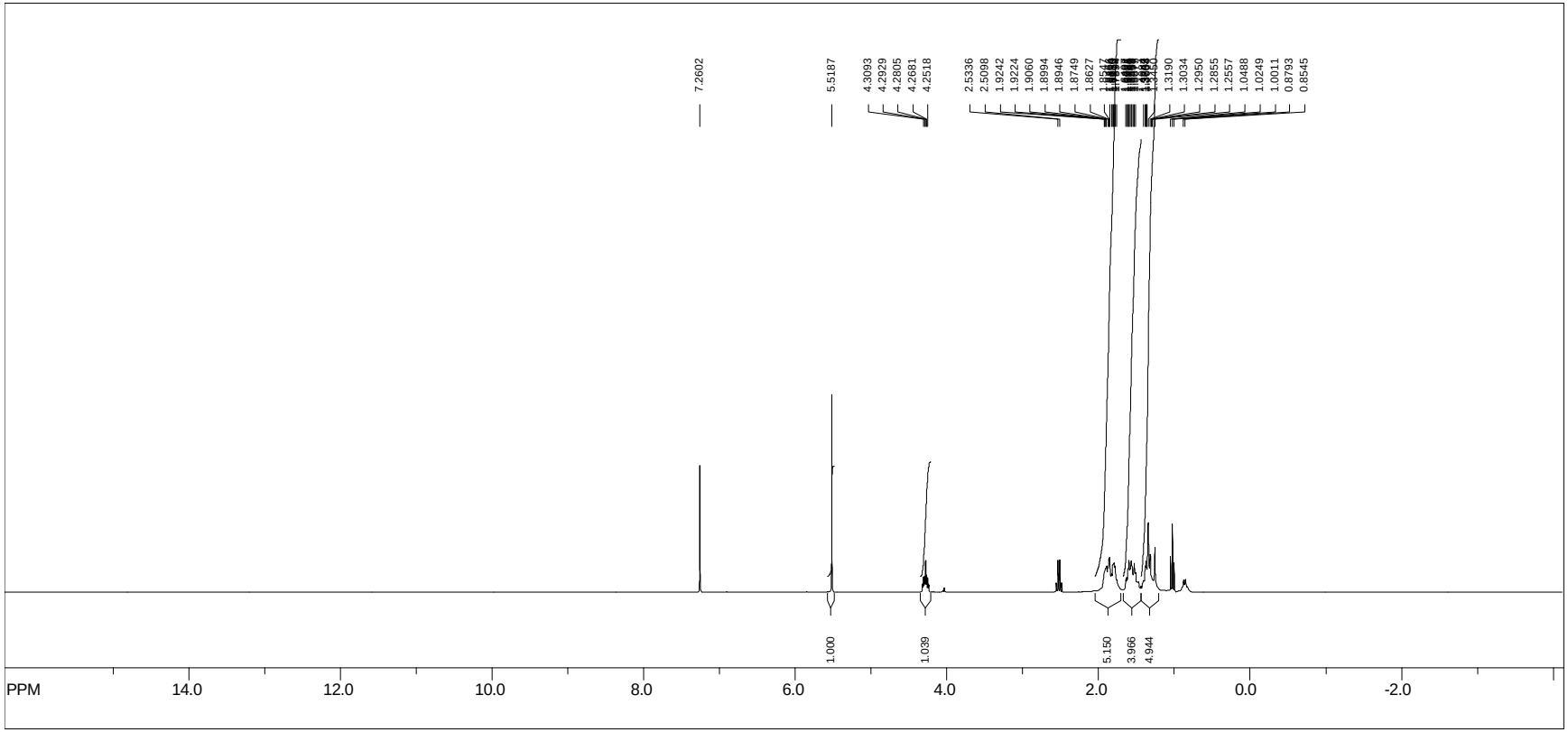
file: Z:\Laina\lmgx\lmgx_20a\4\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 128

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(E)-(1,2-Dichlorovinyloxy)cyclohexane (142**)**



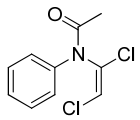
SpinWorks 2.5: dichlorocyclohexylenol ether, after SPE



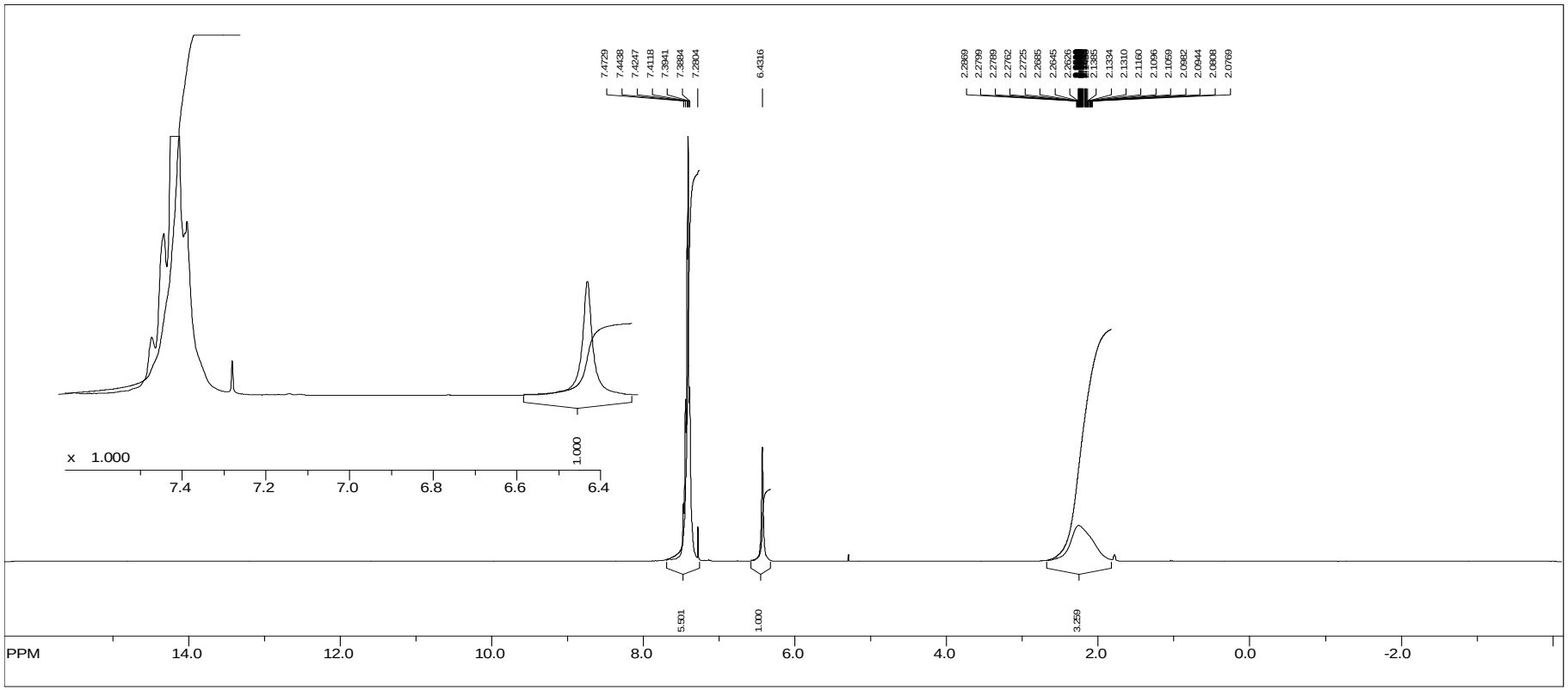
file: Z:\Laina\lmgvi\lmgvi_53a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-*N*-(1,2-dichlorovinyl)-*N*-phenylacetamide (149)



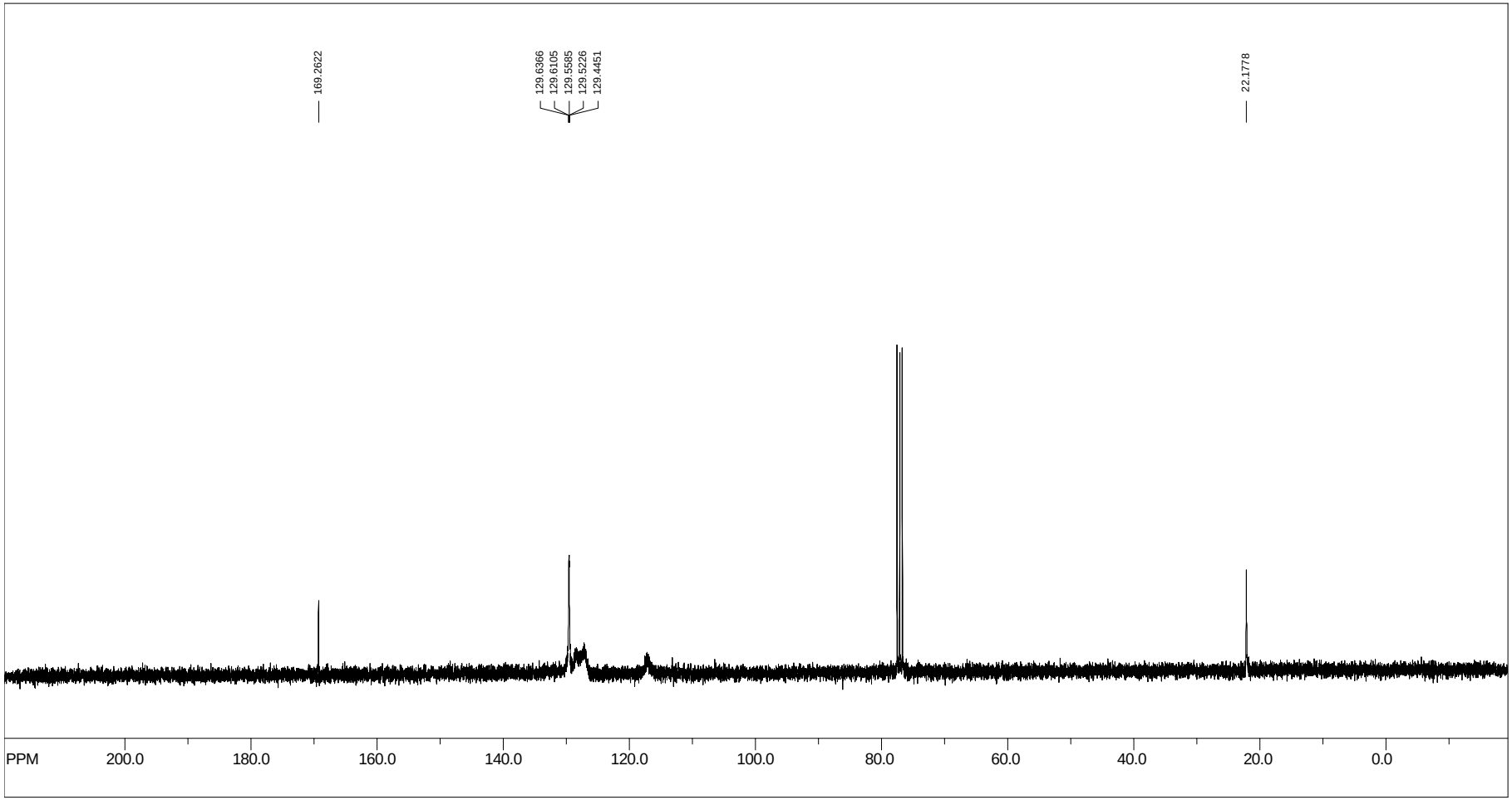
SpinWorks 2.5: enamine from acetanilide



file: Z:\Laina\lmgviii\lmgviii_96a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

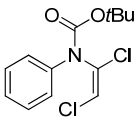
SpinWorks 2.5: enamine from acetanilide



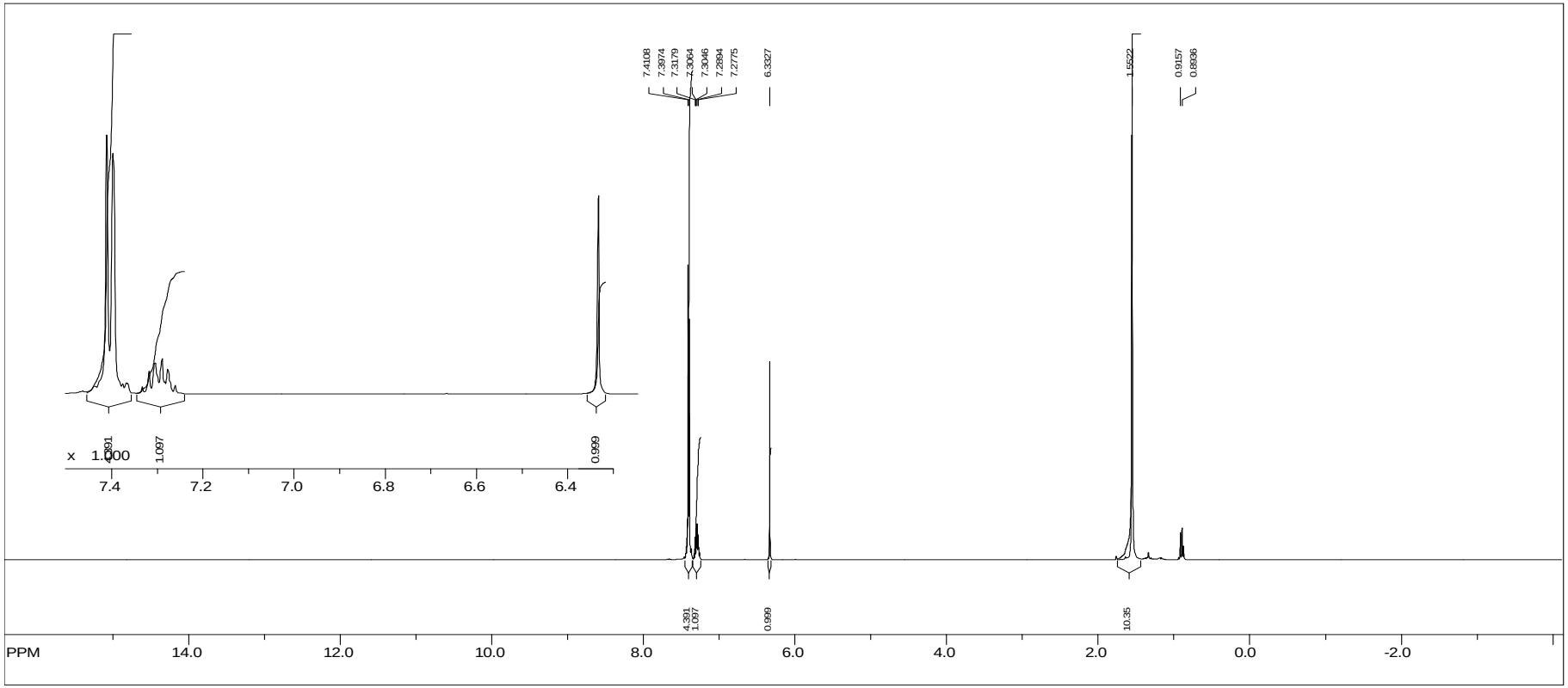
file: C:\Users\Laina\Documents\WORK\NMR\lmgviii\lmgviii_96a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-*tert*-Butyl (1,2-dichlorovinyl(phenyl)carbamate (150).



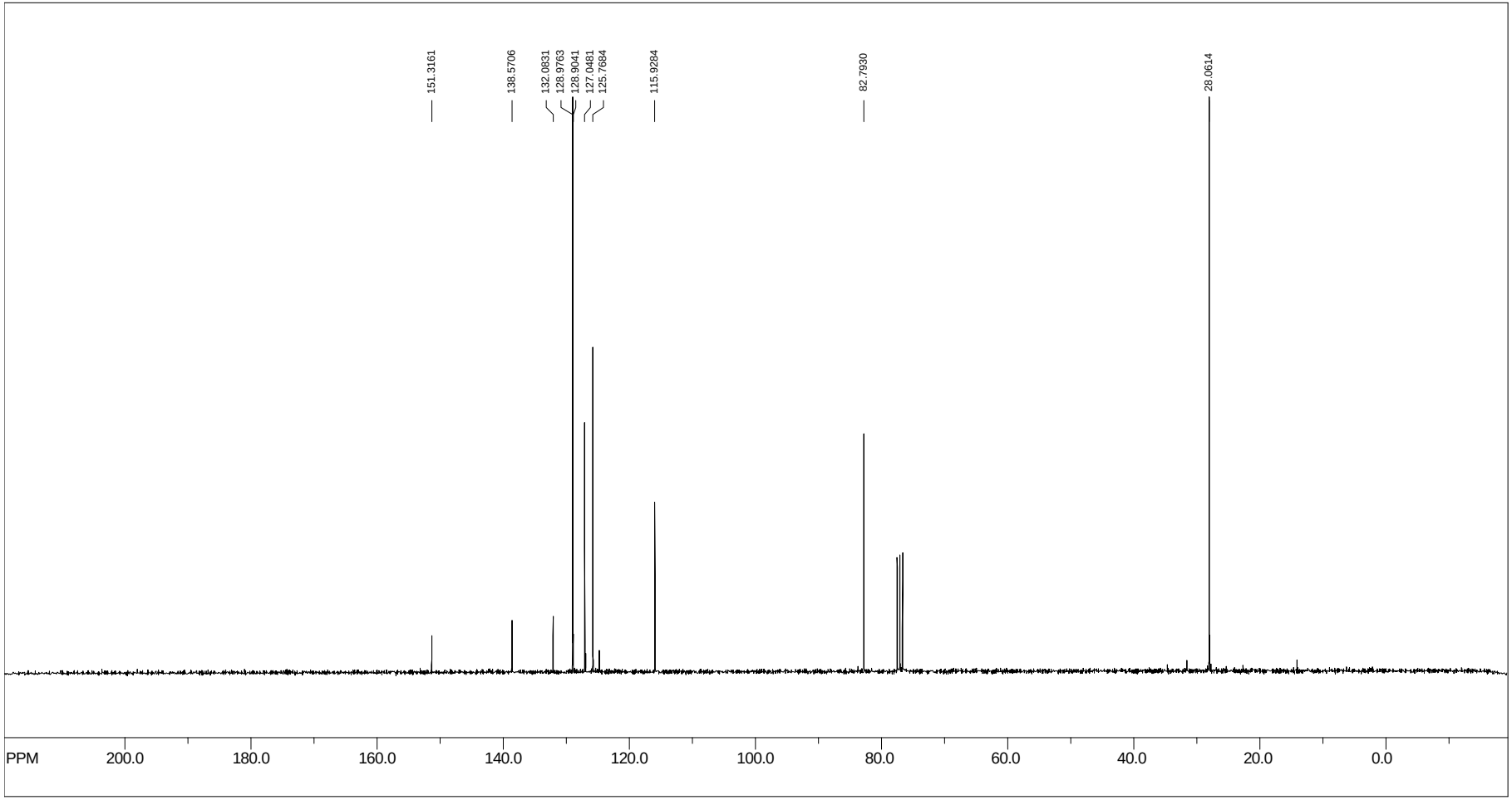
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



file: Z:\Laina\lmgx\lmgx_19c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

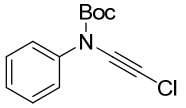
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



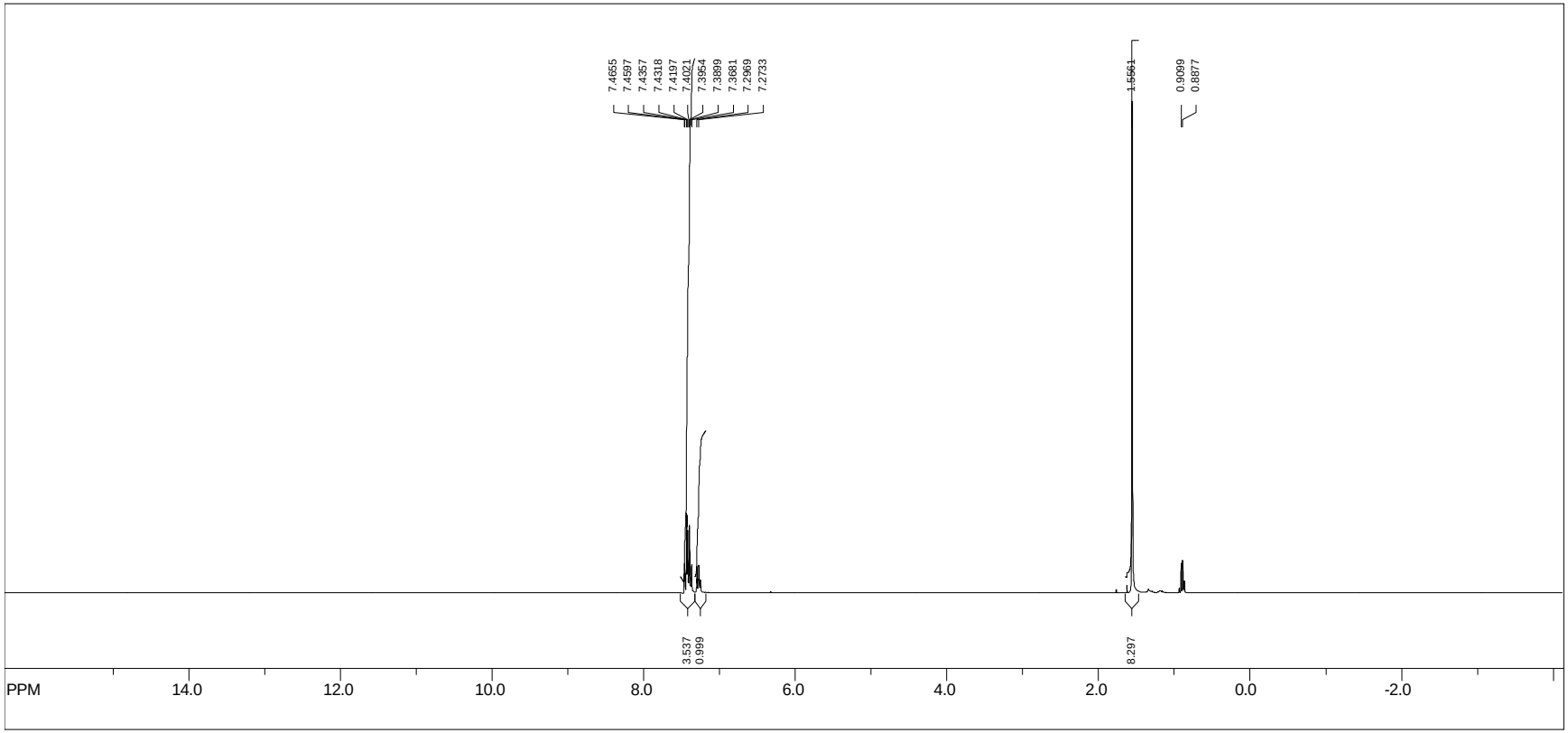
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_74a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 213

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

tert-Butyl 2-chloroethynyl(phenyl)carbamate (157)



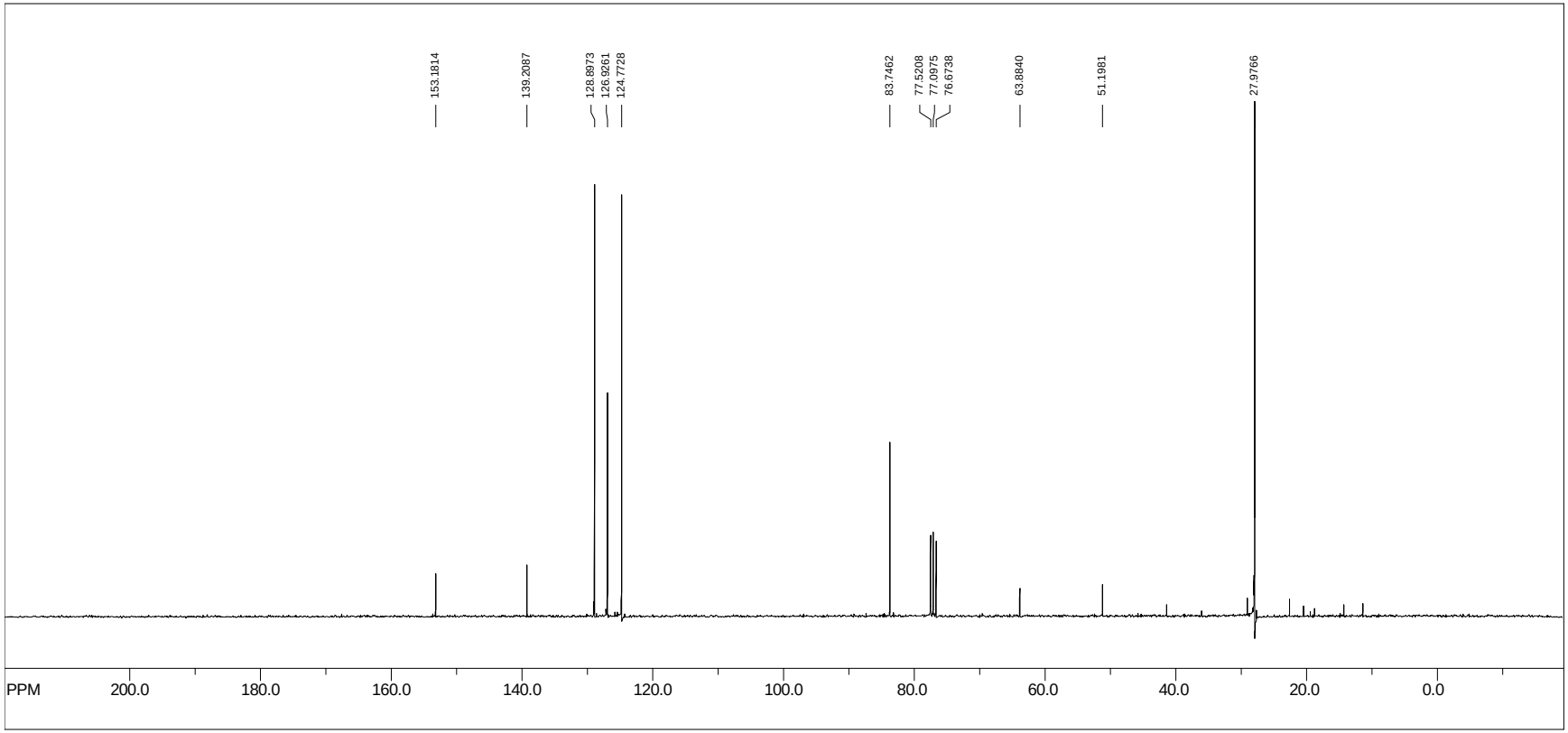
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgx\lmgx_19a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

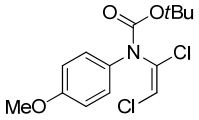
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



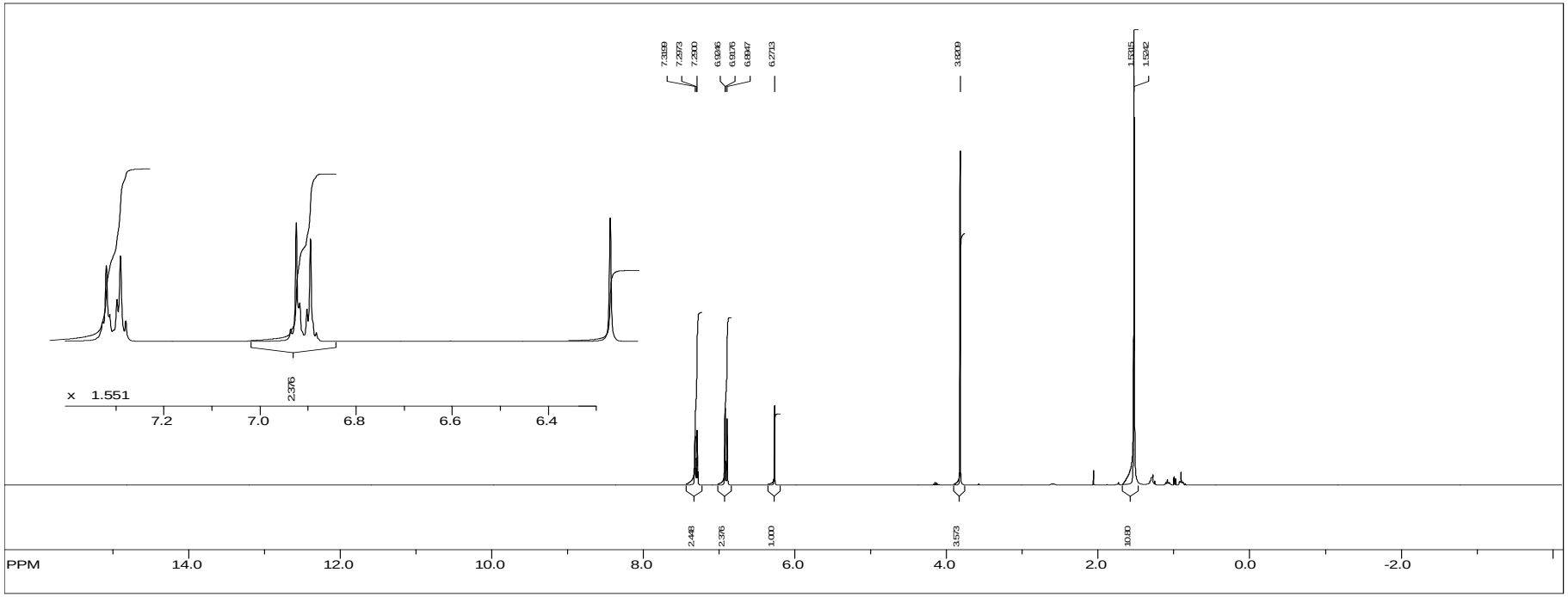
file: Z:\Laina\lmgx\lmgx_19a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 242

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

tert-Butyl 2-chloroethynyl(4-methoxyphenyl)carbamate (151)



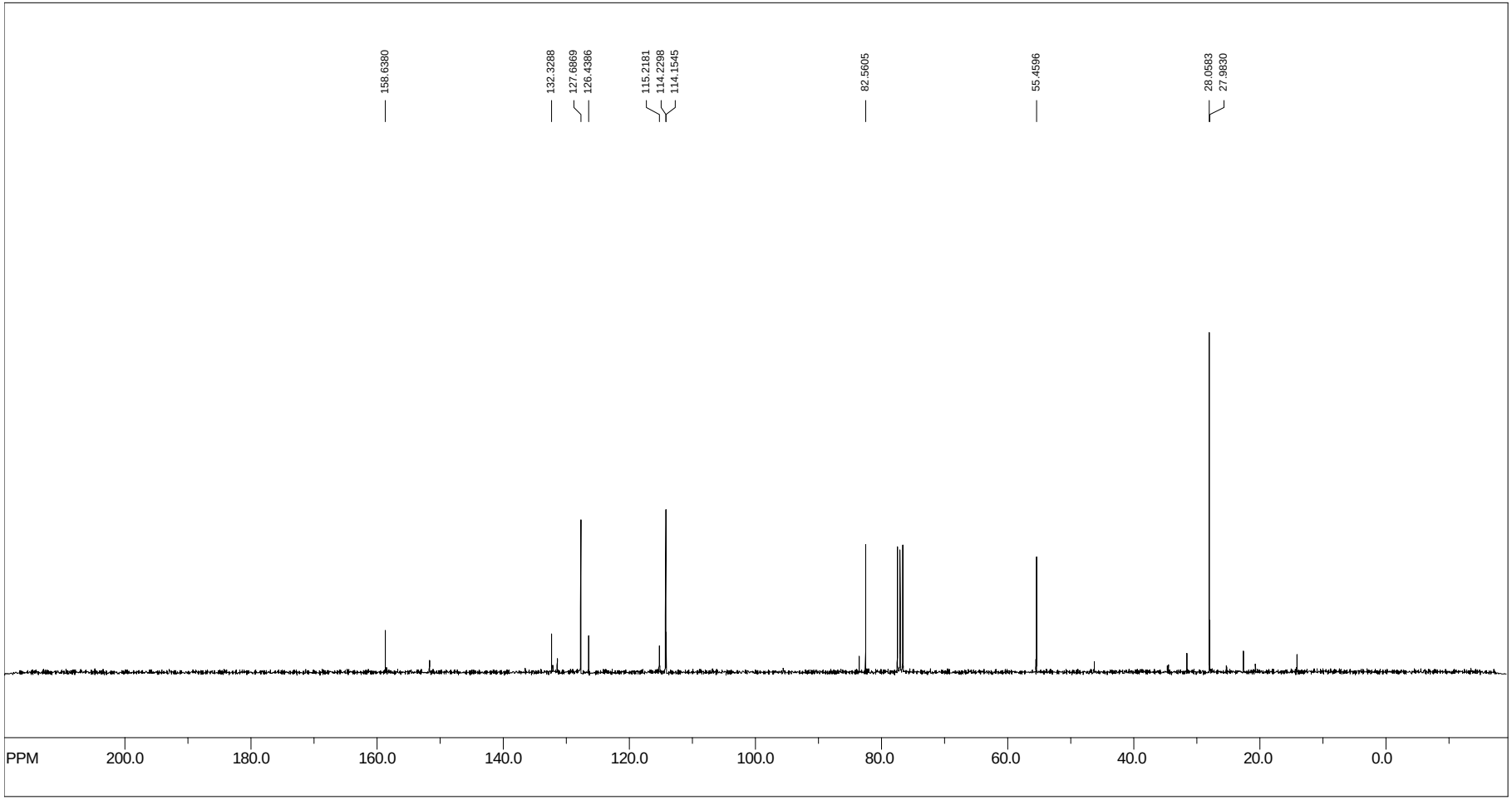
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgx\lmgx_75a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

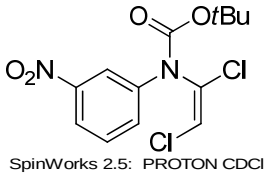
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



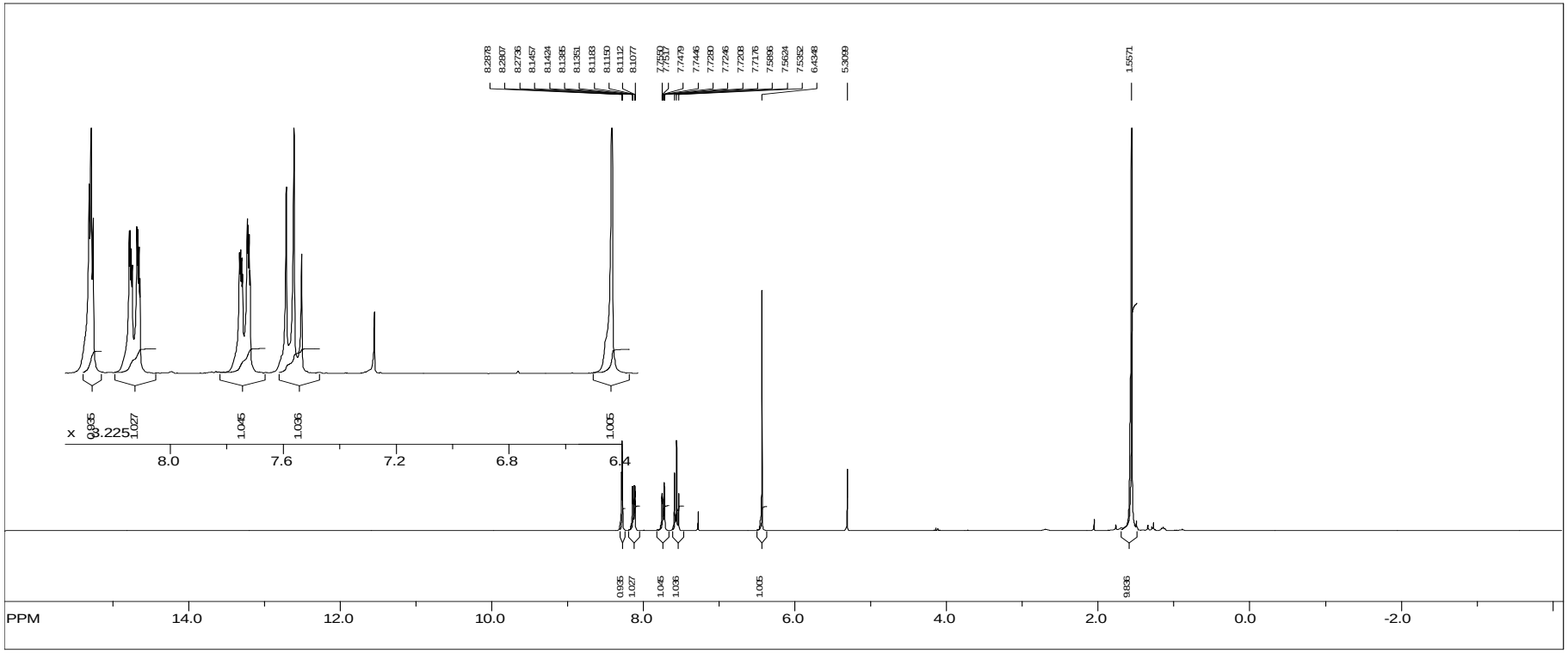
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_75a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

tert-Butyl 2-chloroethynyl(3-nitrophenyl)carbamate (152)



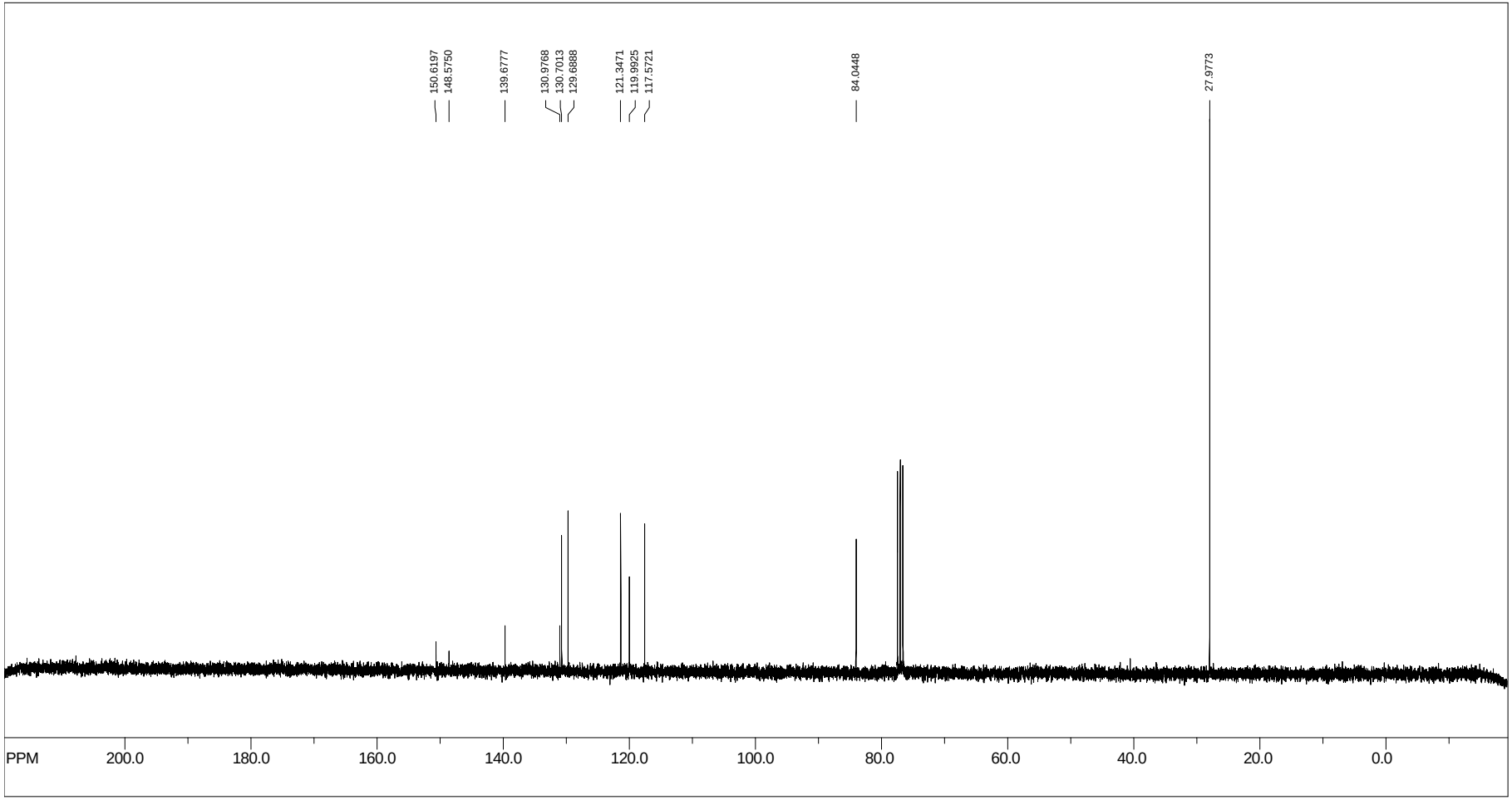
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



file: Z:\Laina\lmgx\lmgx_89a\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

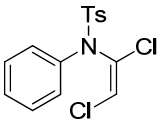
SpinWorks 2.5: C13CPD128 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



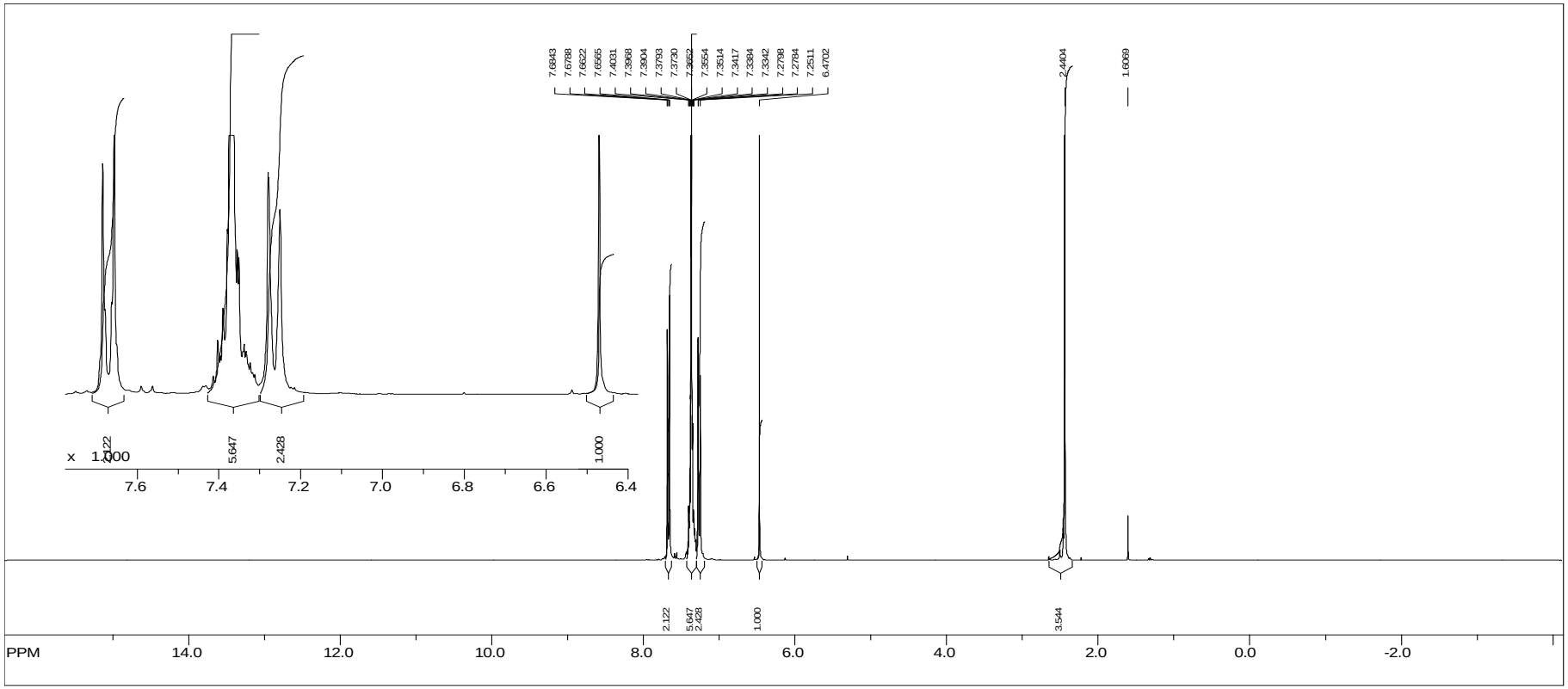
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_89a\4\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 90

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000

(*E*)-(*N*-1,2-dichlorovinyl)-4-methyl-*N*-phenylbenzenesulfonamide (153)



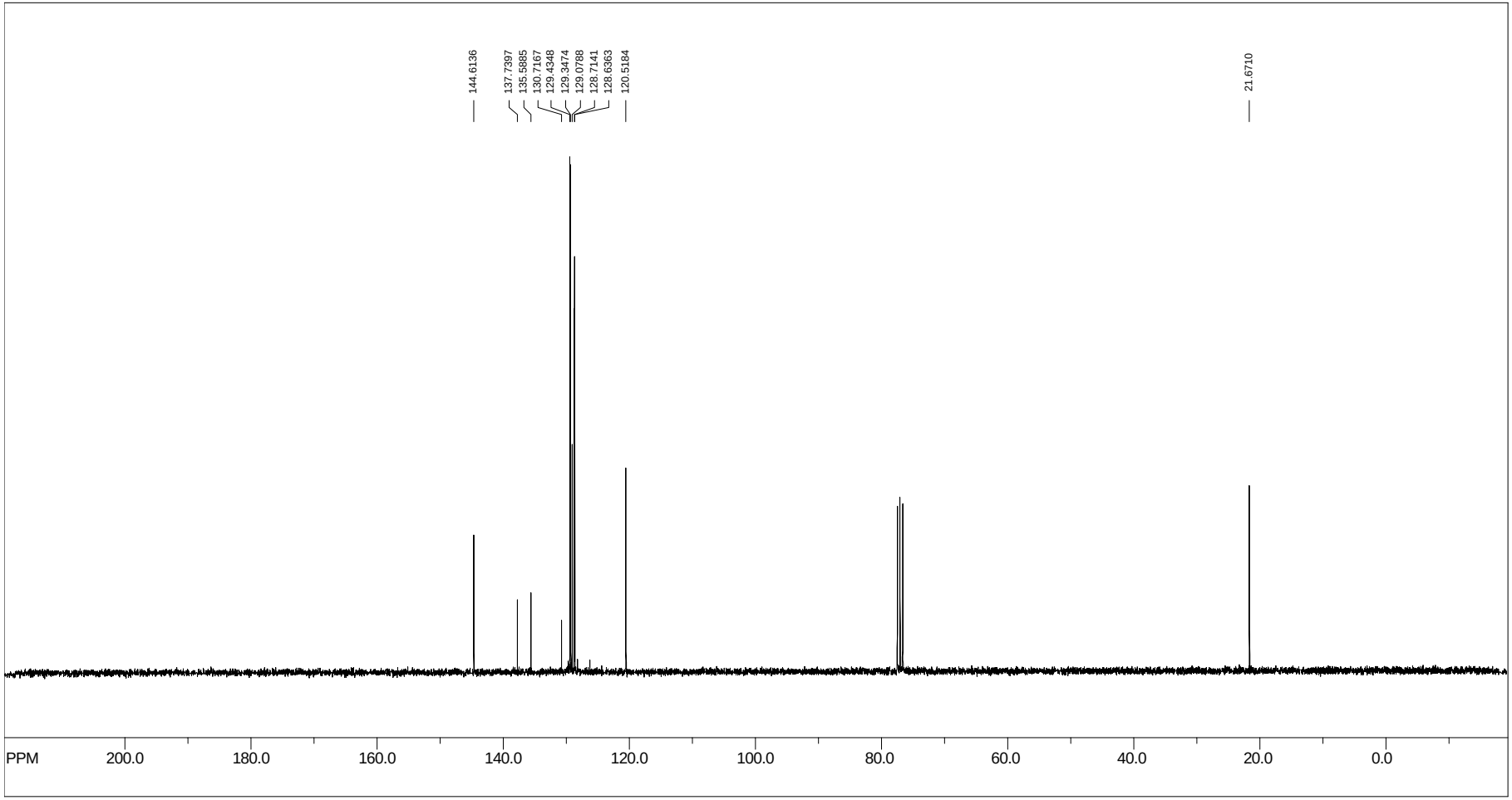
SpinWorks 2.5: N-Ts-Aniline dichloroenamine



file: Z:\Laina\lmgix\lmgix_49a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

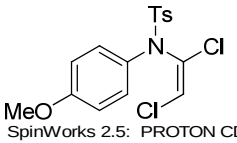
SpinWorks 2.5: N-Ts-Aniline dichloroenamine



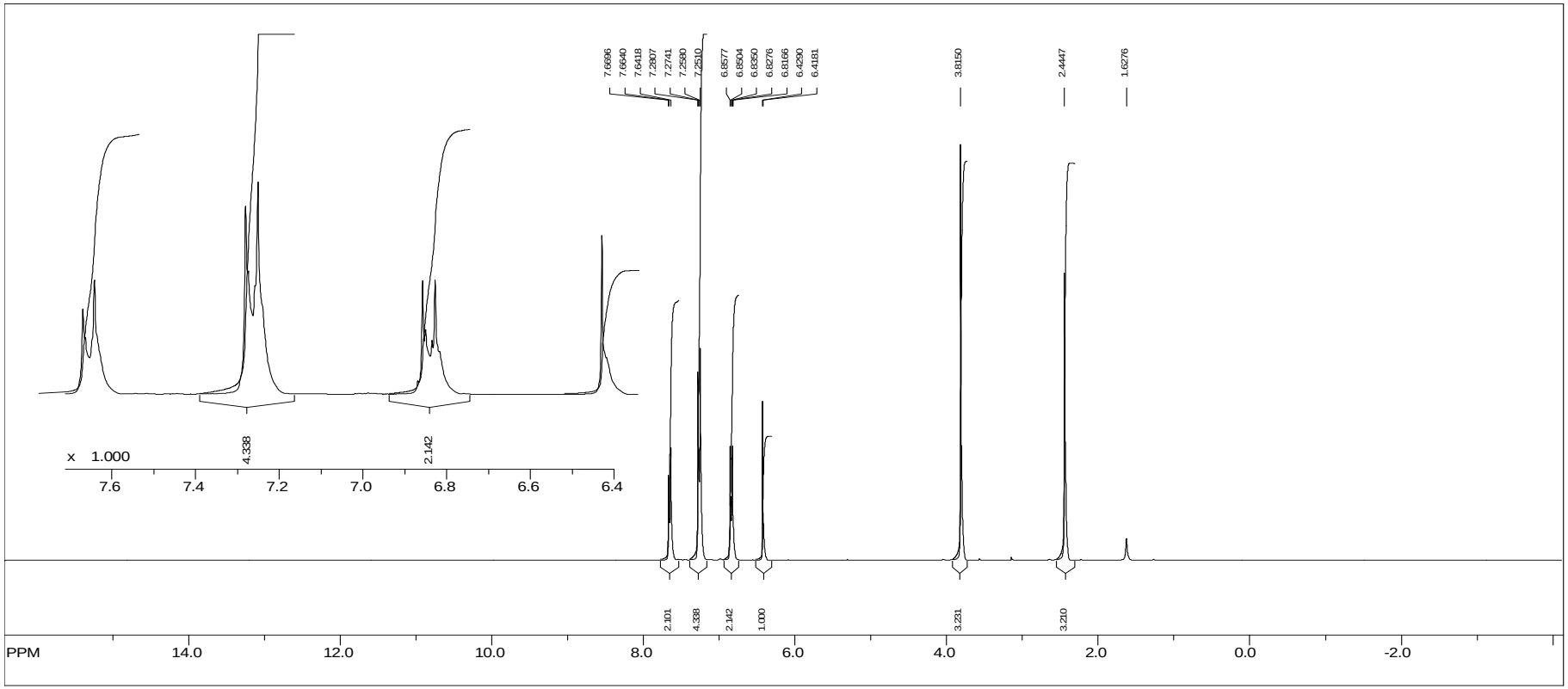
file: C:\Users\Laina\Documents\WORK\NMR\lmgix\lmgix_49a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-*N*-(1,2-dichlorovinyl) *N*-(4-methoxyphenyl)-4-methyl-benzenesulfonamide (154)



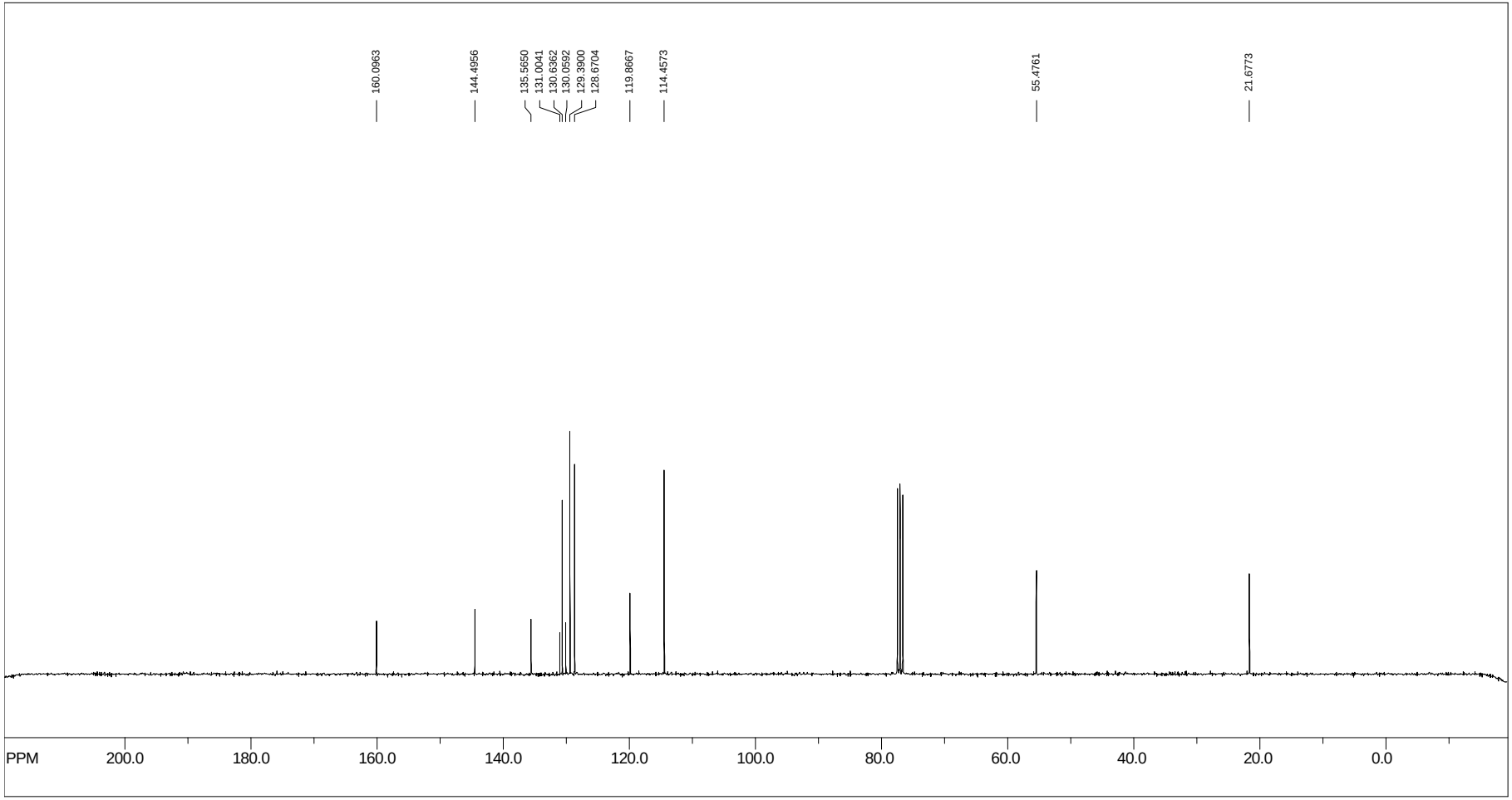
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgx\lmgx_98\lmgx_98a\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

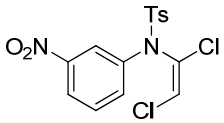
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



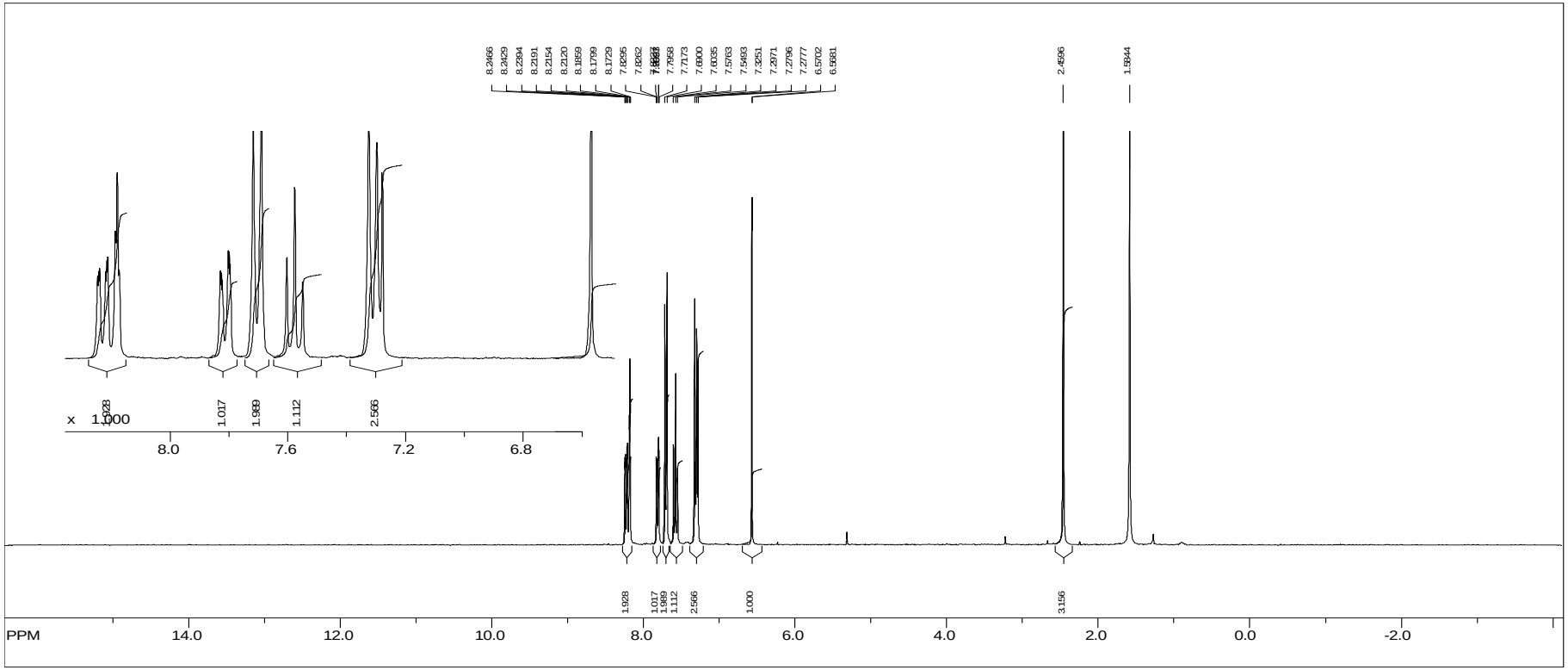
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_98a\lmgx_98a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-*N*-(1,2-dichlorovinyl) *N*-(3-nitrophenyl)-4-methyl-benzenesulfonamide (155)



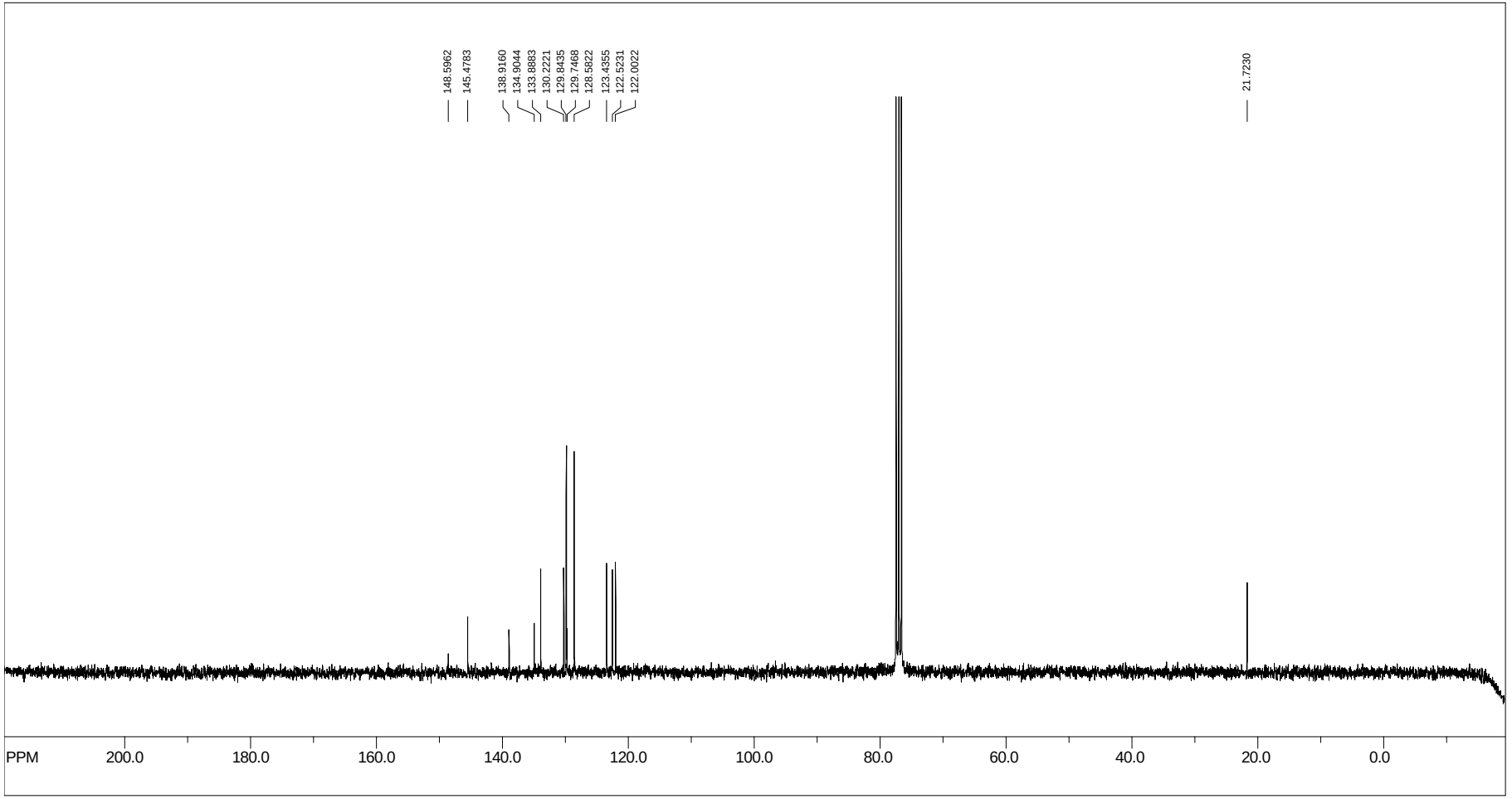
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



file: Z:\Laina\lmgxi\lmgxi_22a\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

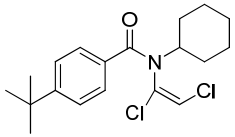
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



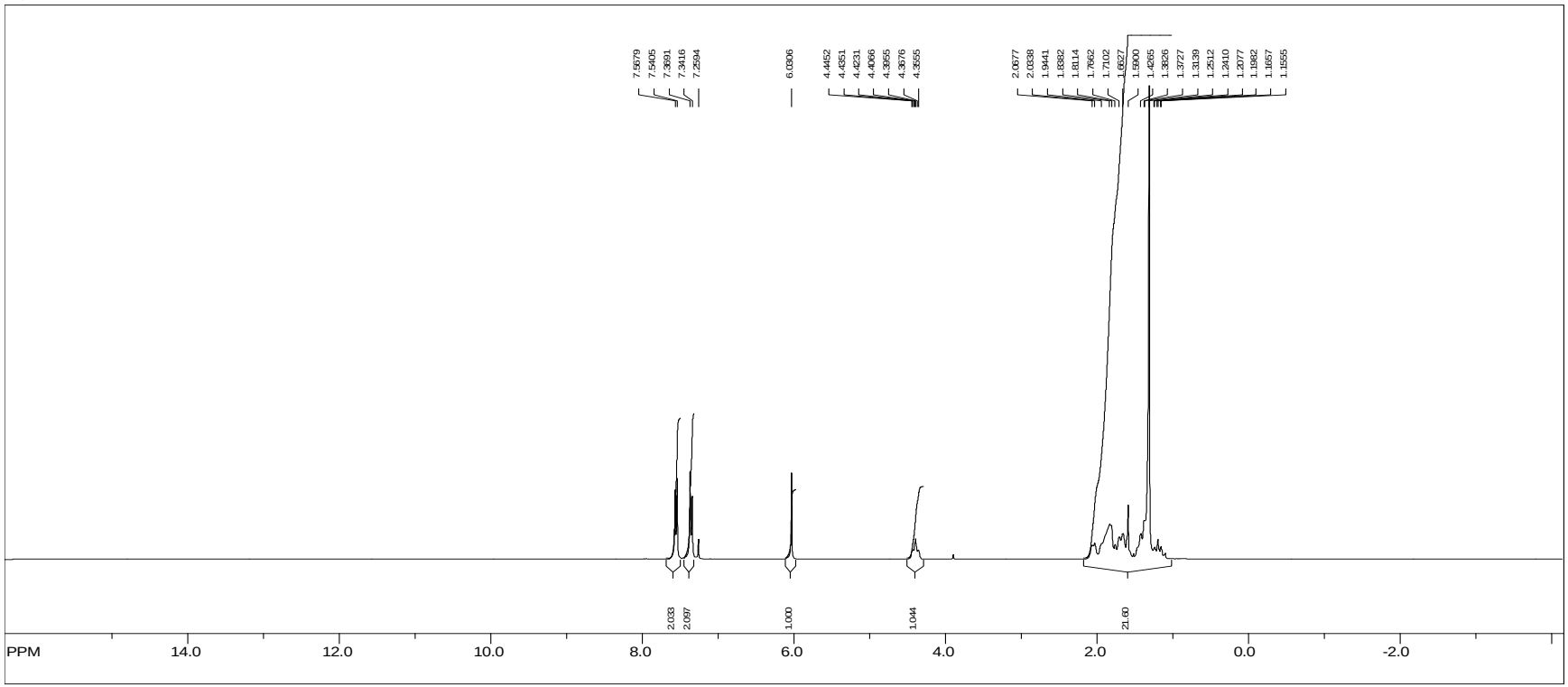
file: C:\Users\Laina\Documents\WORK\NMR\lmgxi\lmgxi_22a\lmgxi_22a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-4-*tert*-Butyl-*N*-cyclohexyl-*N*-(1,2-dichlorovinyl)-benzamide (156)



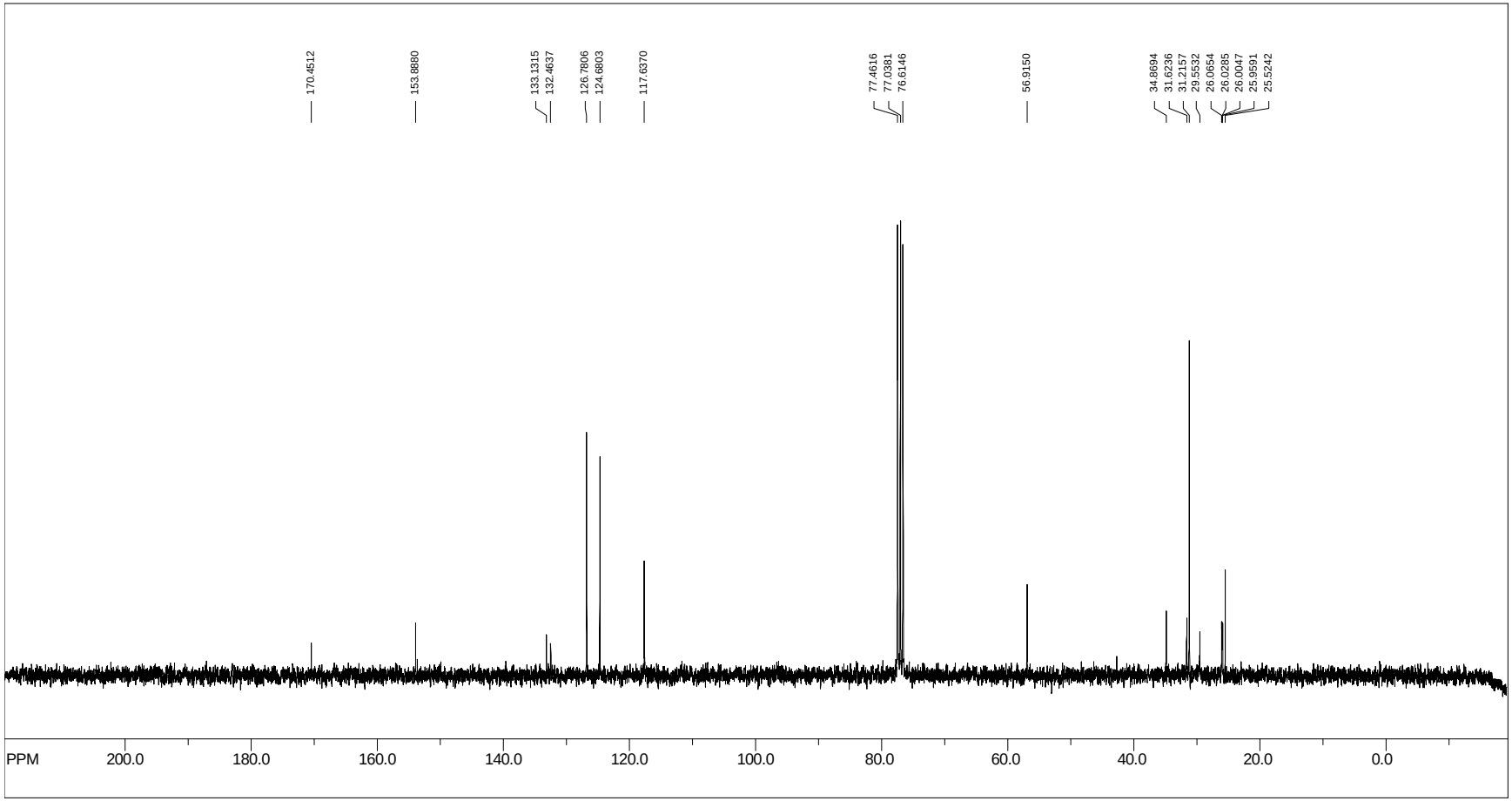
SpinWorks 2.5: dichloroenamine from benzamide derivative



file: Z:\Laina\lmgx\lmgx_96a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

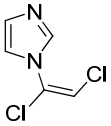
SpinWorks 2.5: dichloroenamine from benzamide derivative



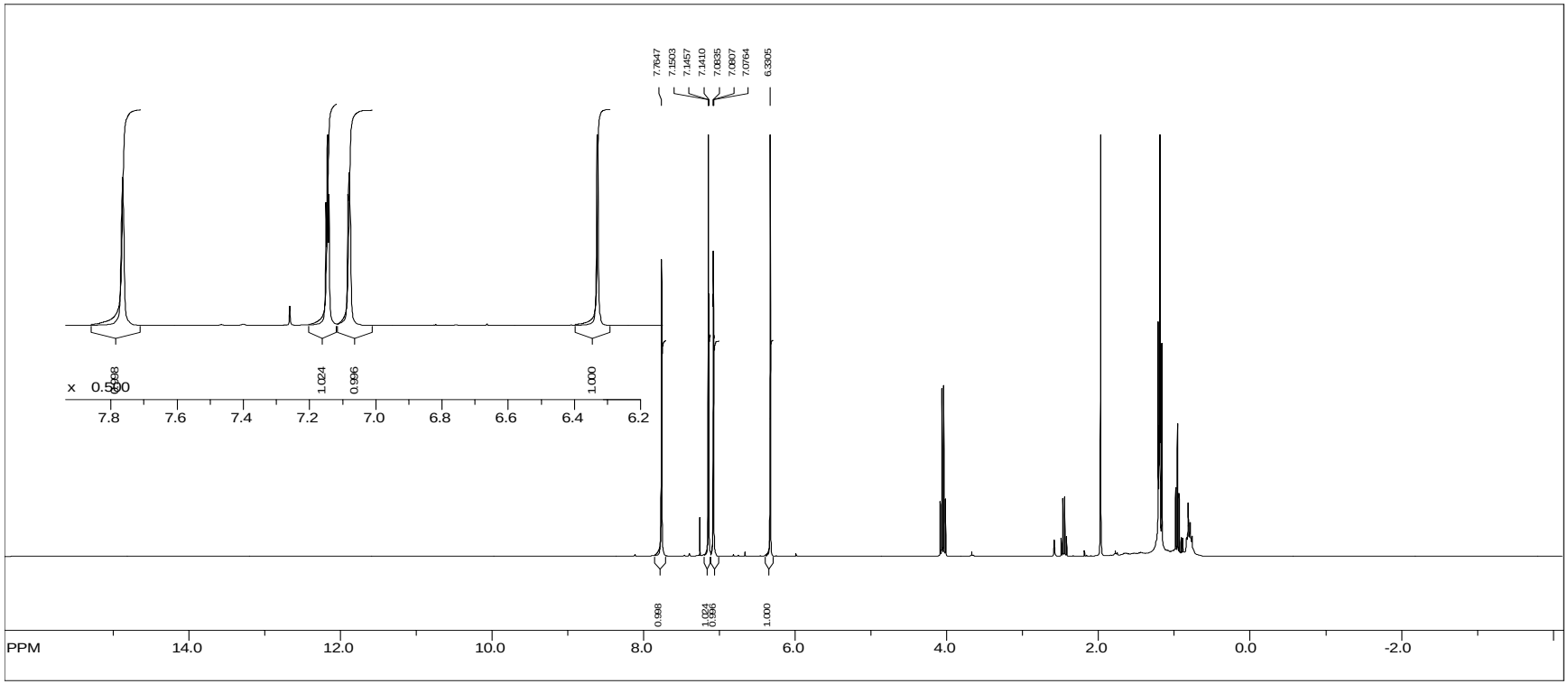
file: Z:\Laina\lmgx\lmgx_96a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 158

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-(1,2-Dichlorovinyl)-1*H*-imidazole (159)



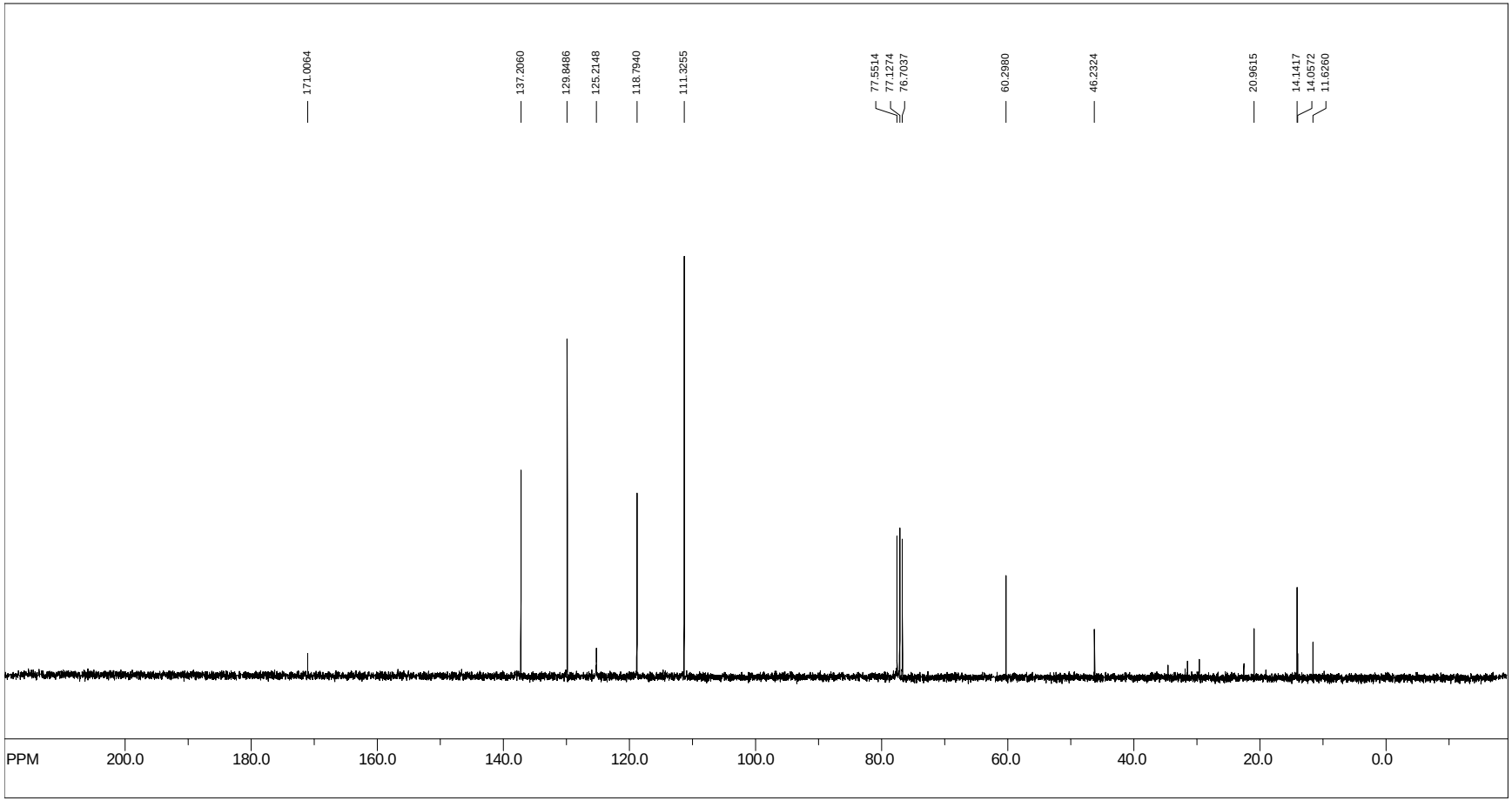
SpinWorks 2.5: imidazole derivative after SPE



file: Z:\Laina\lmgvi\lmgvi_07a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

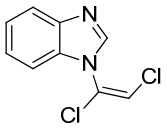
SpinWorks 2.5: imidazole derivative after SPE



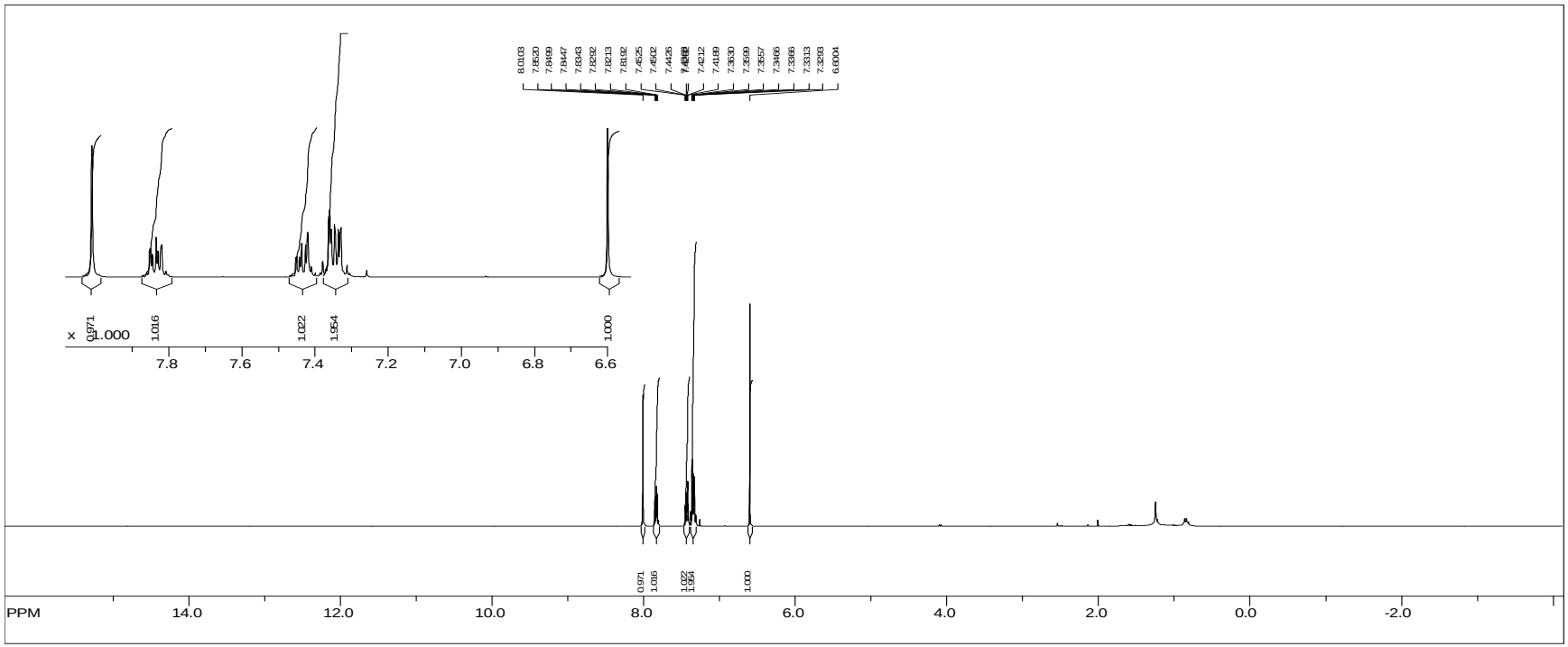
file: Z:\Laina\lmgvii\lmgvii_07a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 102

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-1-(1,2-Dichlorovinyl)-1*H*-benzo[*d*]imidazole (161)



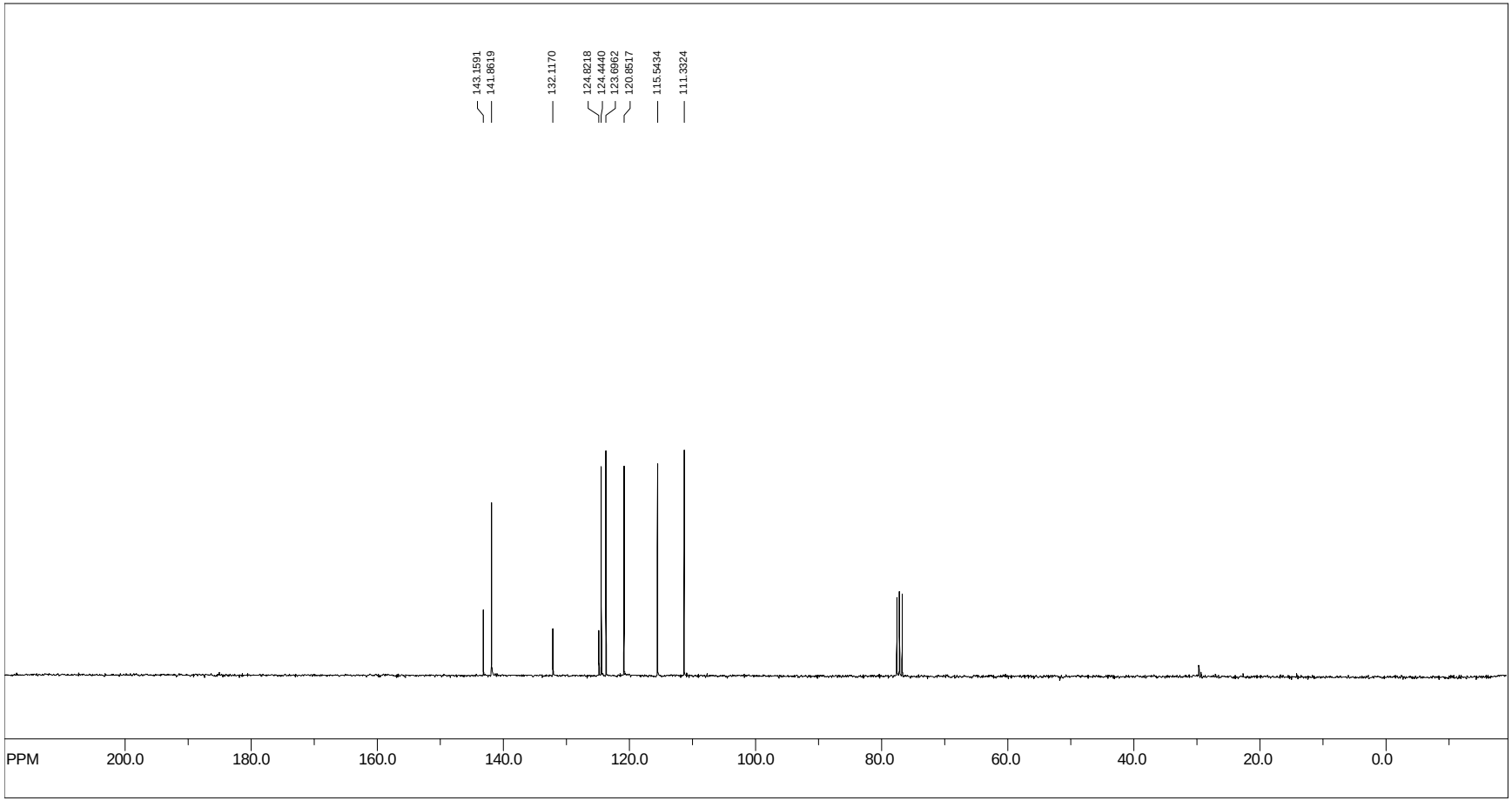
SpinWorks 2.5: benzimidazole derivative after SPE



file: Z:\Laina\lmgvii\lmgvii_08a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

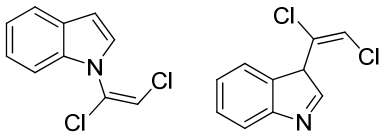
SpinWorks 2.5: benzimidazole derivative after SPE



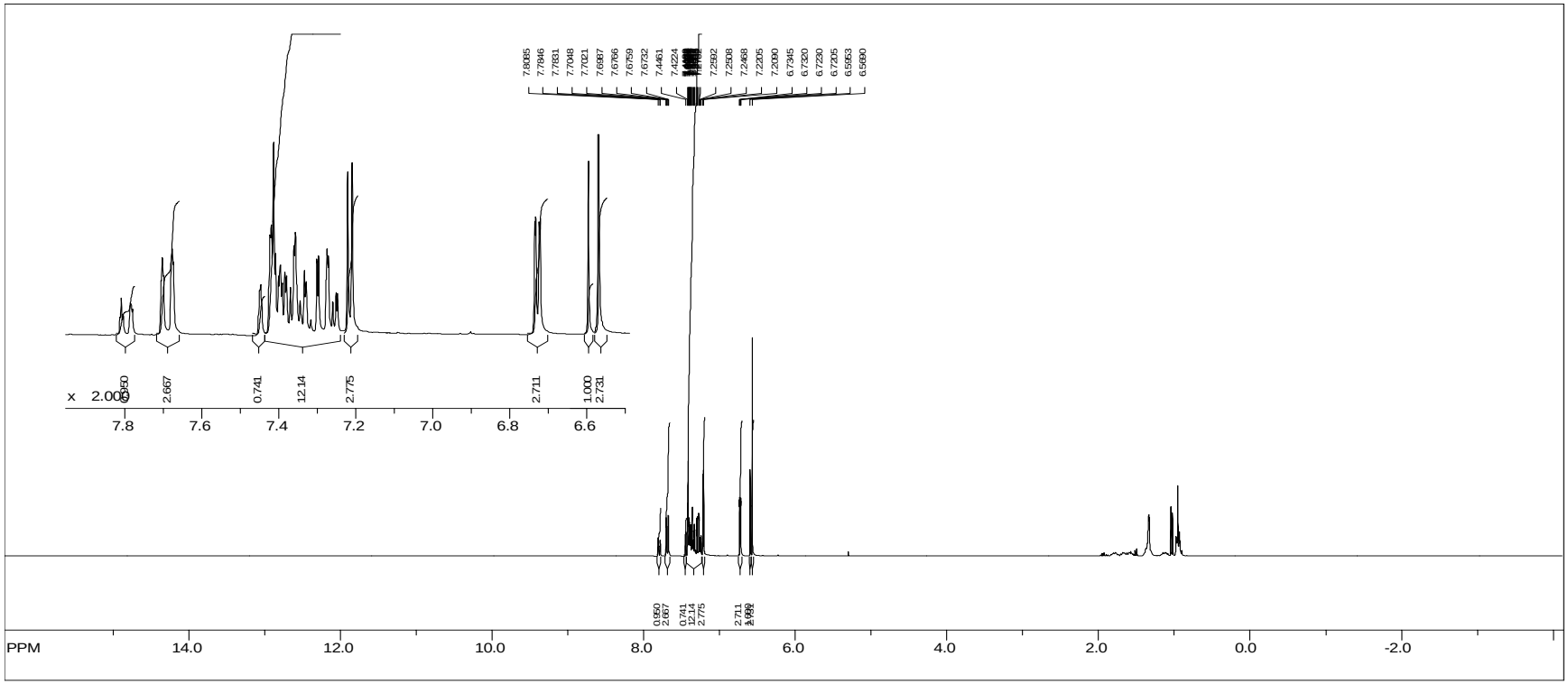
file: Z:\Laina\lmgvii\lmgvii_08a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 110

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-(1,2-Dichlorovinyl)-1*H*-indole (163) and (*E*)-3-(1,2-dichlorovinyl)-3*H*-indole (164)



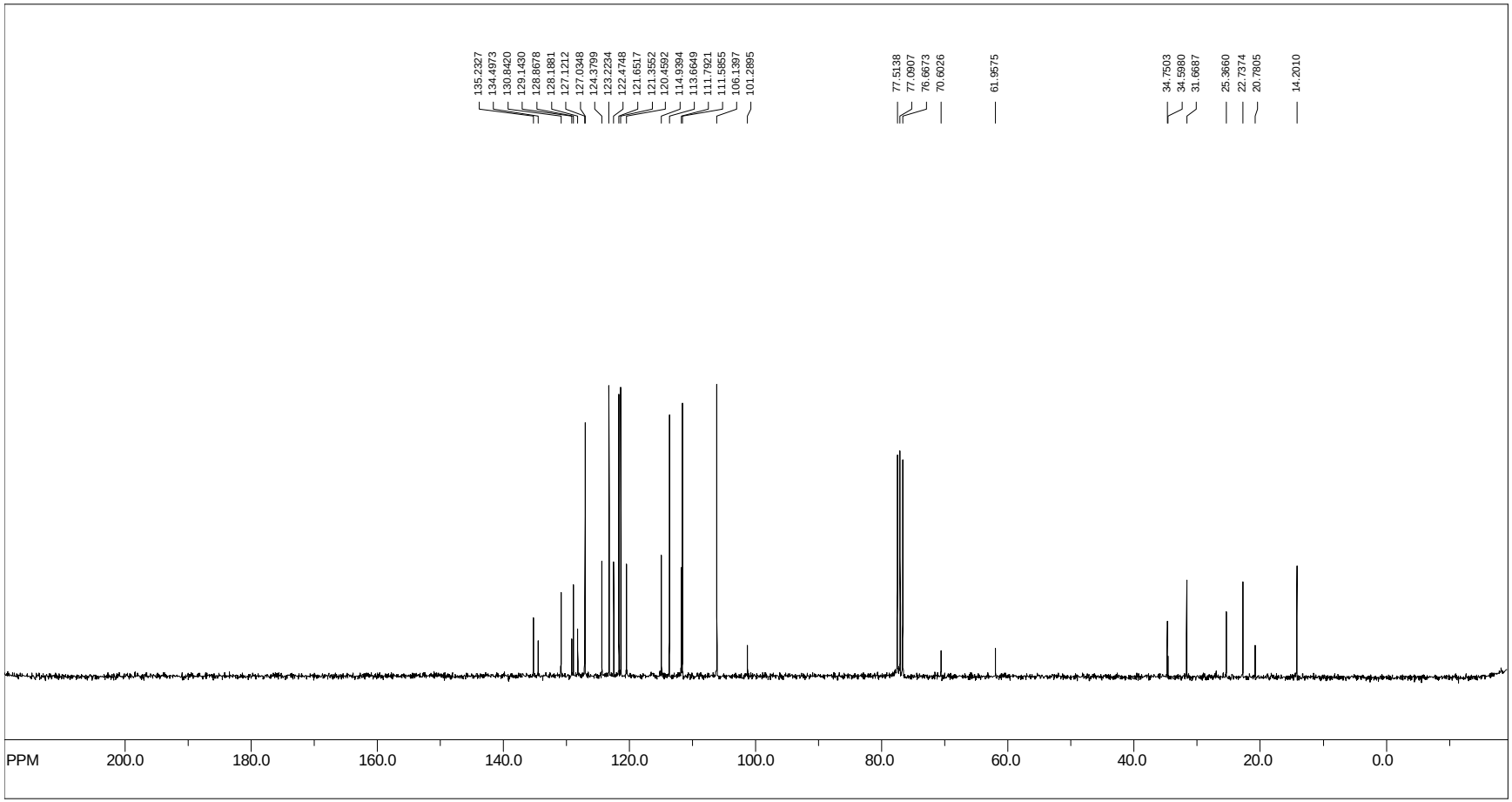
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 16



file: Z:\Laina\lmgvi\lmgvi_05b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

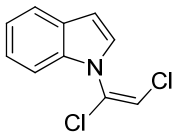
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 16



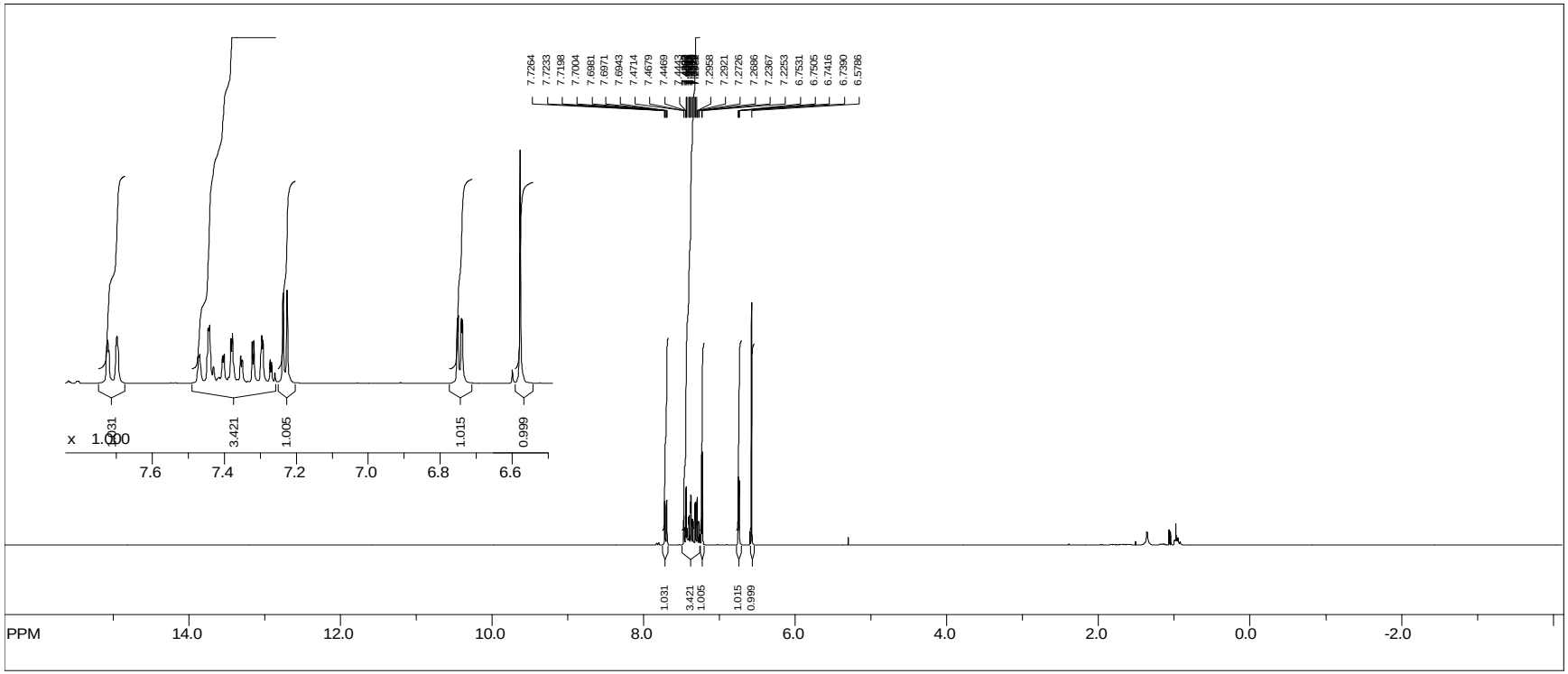
file: Z:\Laina\lmgvii\lmgvii_05b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(E)-1-(1,2-Dichlorovinyl)-1H-indole (163**)**



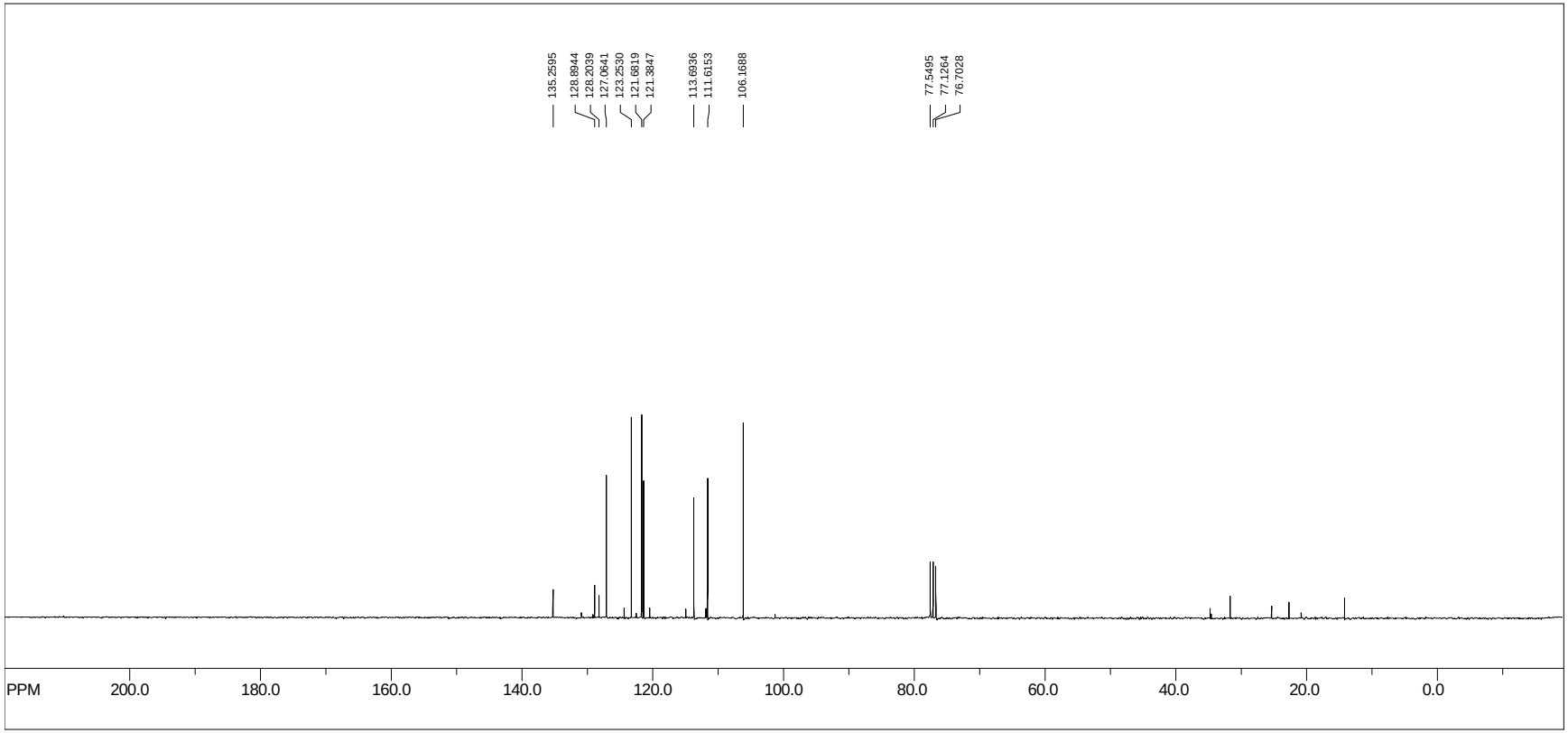
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 15



file: Z:\Laina\lmgvii\lmgvii_05a\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

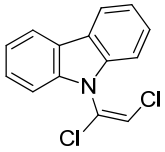
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 15



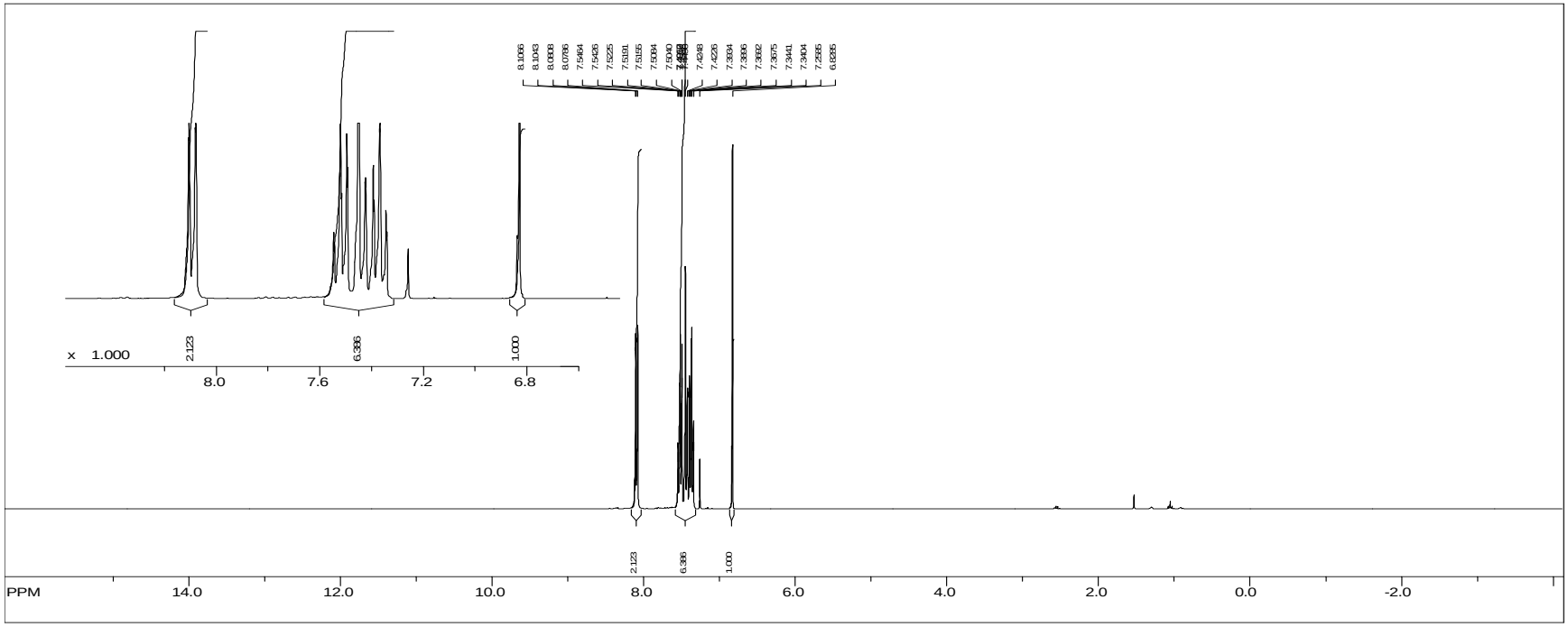
file: Z:\Laina\lmgvii\lmgvii_05a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-9-(1,2-Dichlorovinyl)-9*H*-carbazole (166)



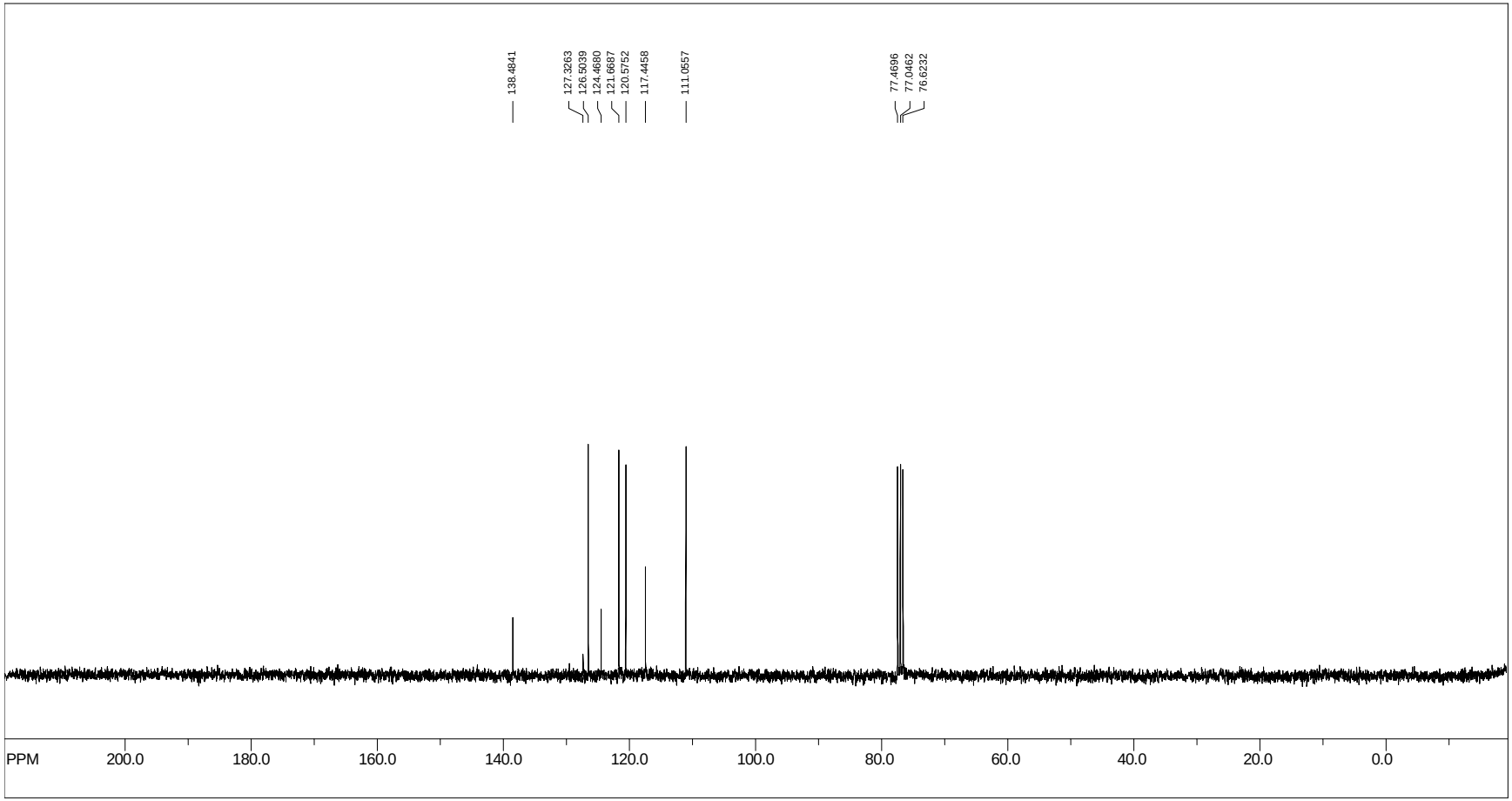
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



file: Z:\Laina\lmgvi\lmgvi_06cf\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

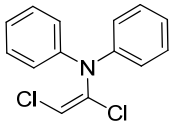
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



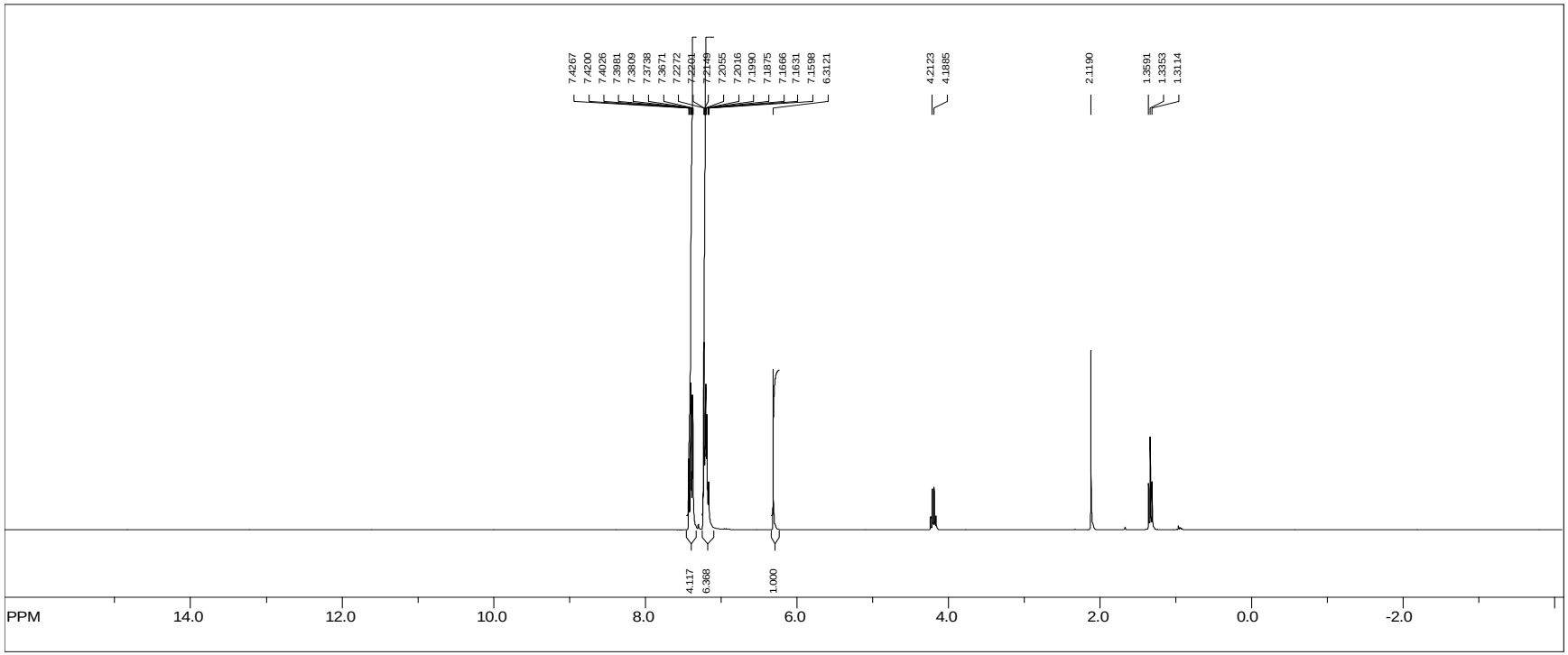
file: Z:\Laina\lmgvii\lmgvii_06d\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 53

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-*N*-(1,2-Dichlorovinyl)-*N*-phenylbenzenamine (168)



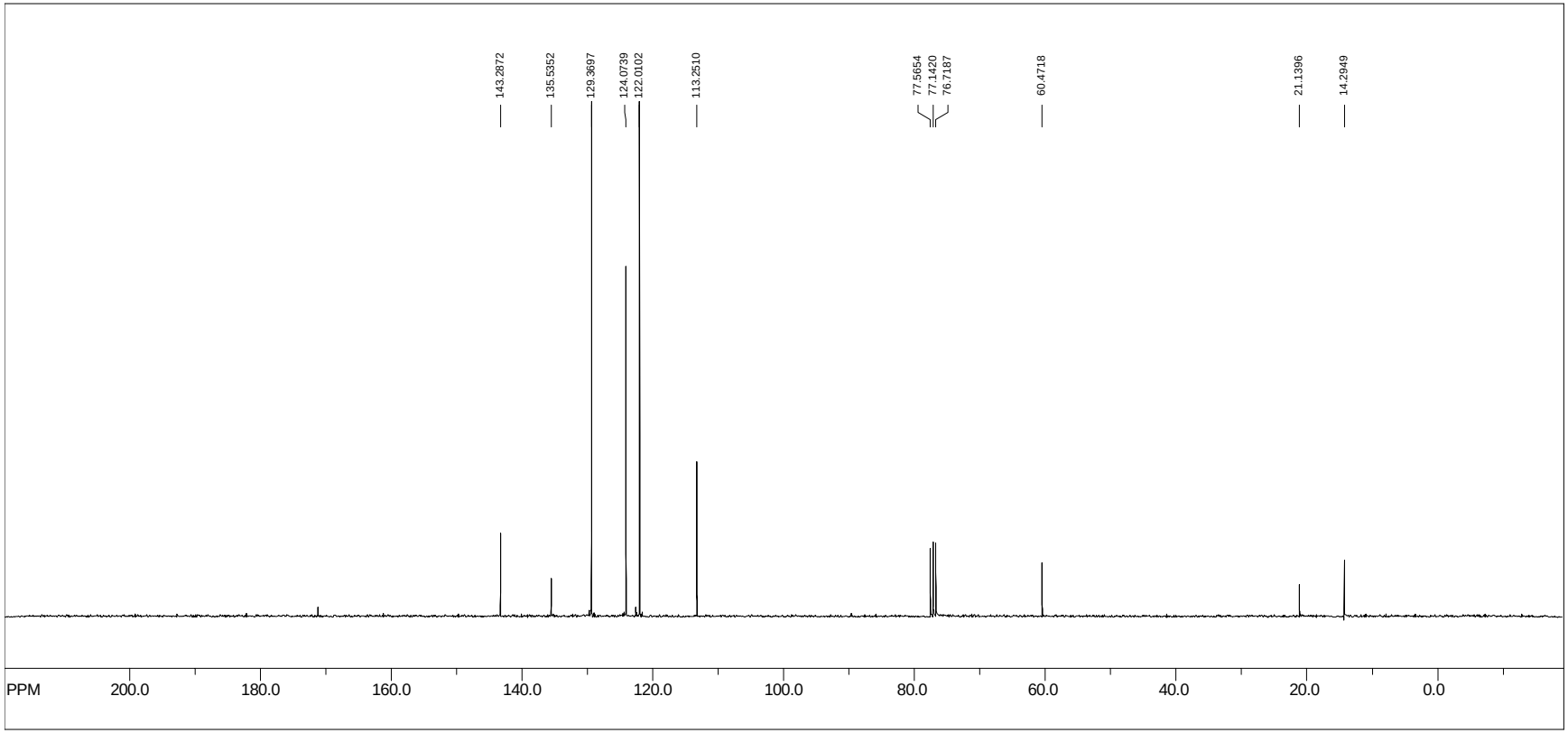
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxiii\lmgxiii_29b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

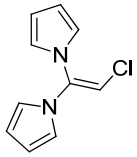
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



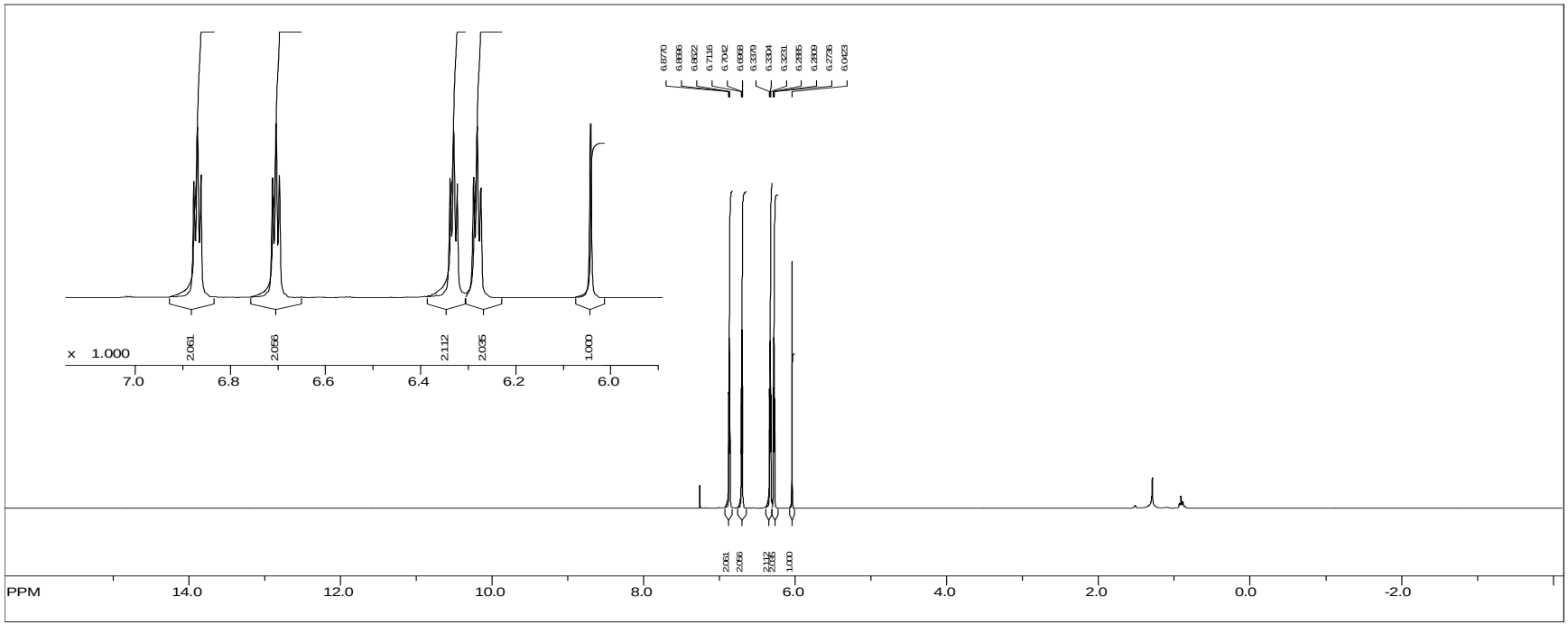
file: Z:\Laina\lmgxiii\lmgxiii_29b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 263

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

1-(2-Chloro-1-(1*H*-pyrrol-1-yl)vinyl)-1*H*pyrrole (170)



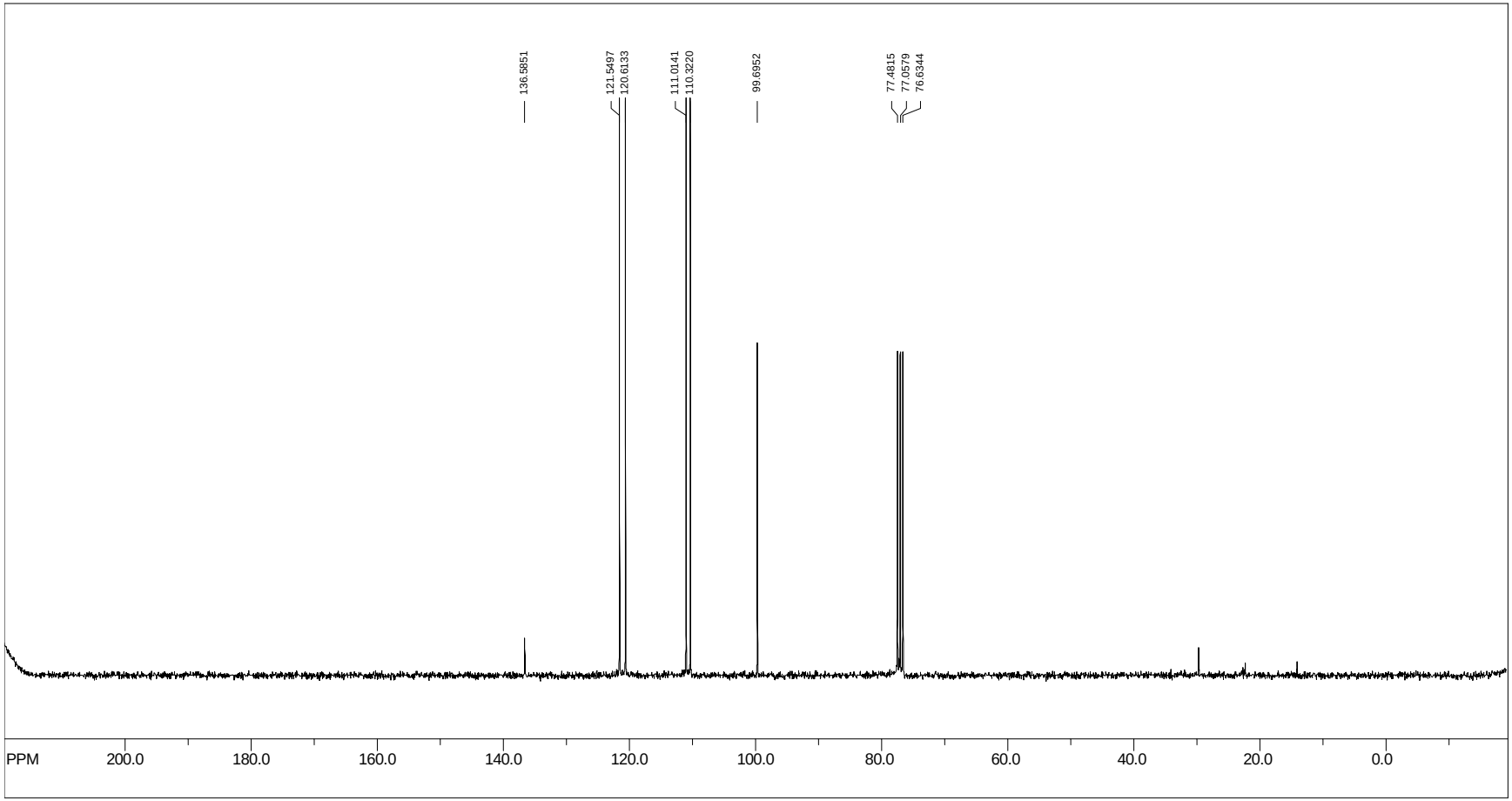
SpinWorks 2.5: dichloropyrrole enamine



file: Z:\Laina\lmgvl\lmgvl_85c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1

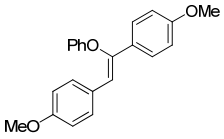


file: Z:\Laina\lmgvi\lmgvi_85c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

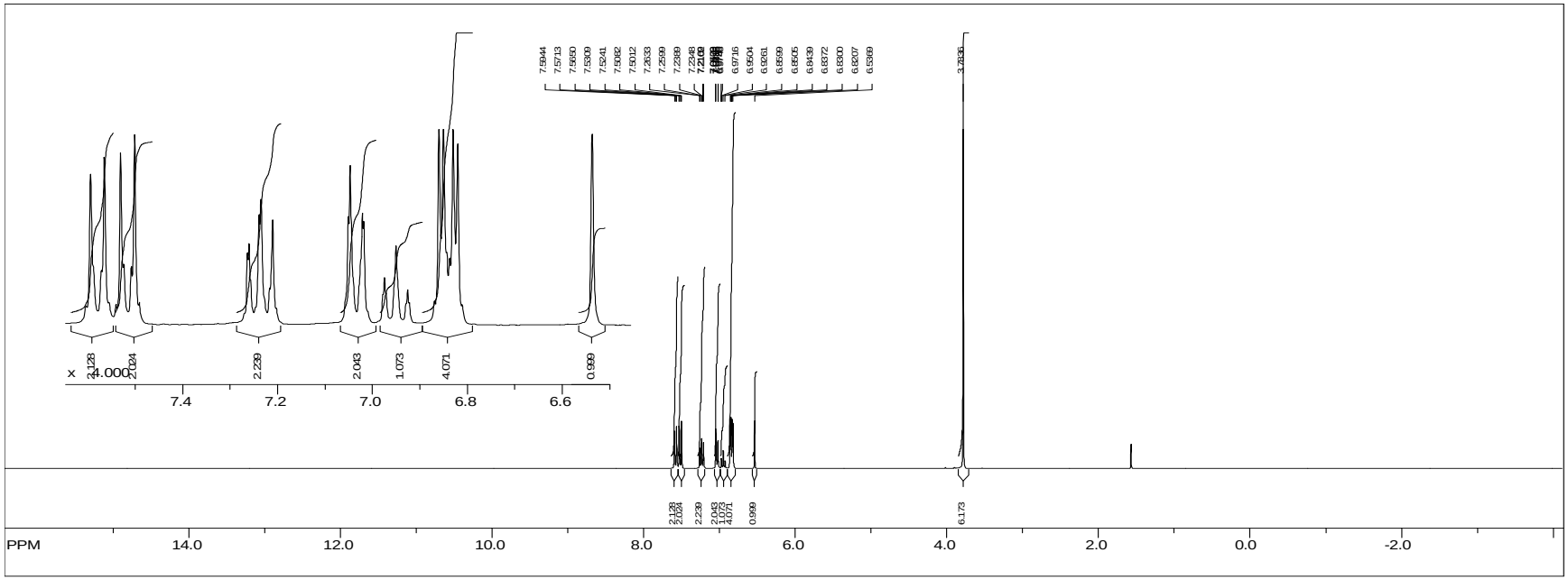
freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

6.2: Section 2.3 – Site Selective Cross-Coupling

(Z)-1,2-bis(4-methoxyphenyl)-1-phenoxyethene (175)



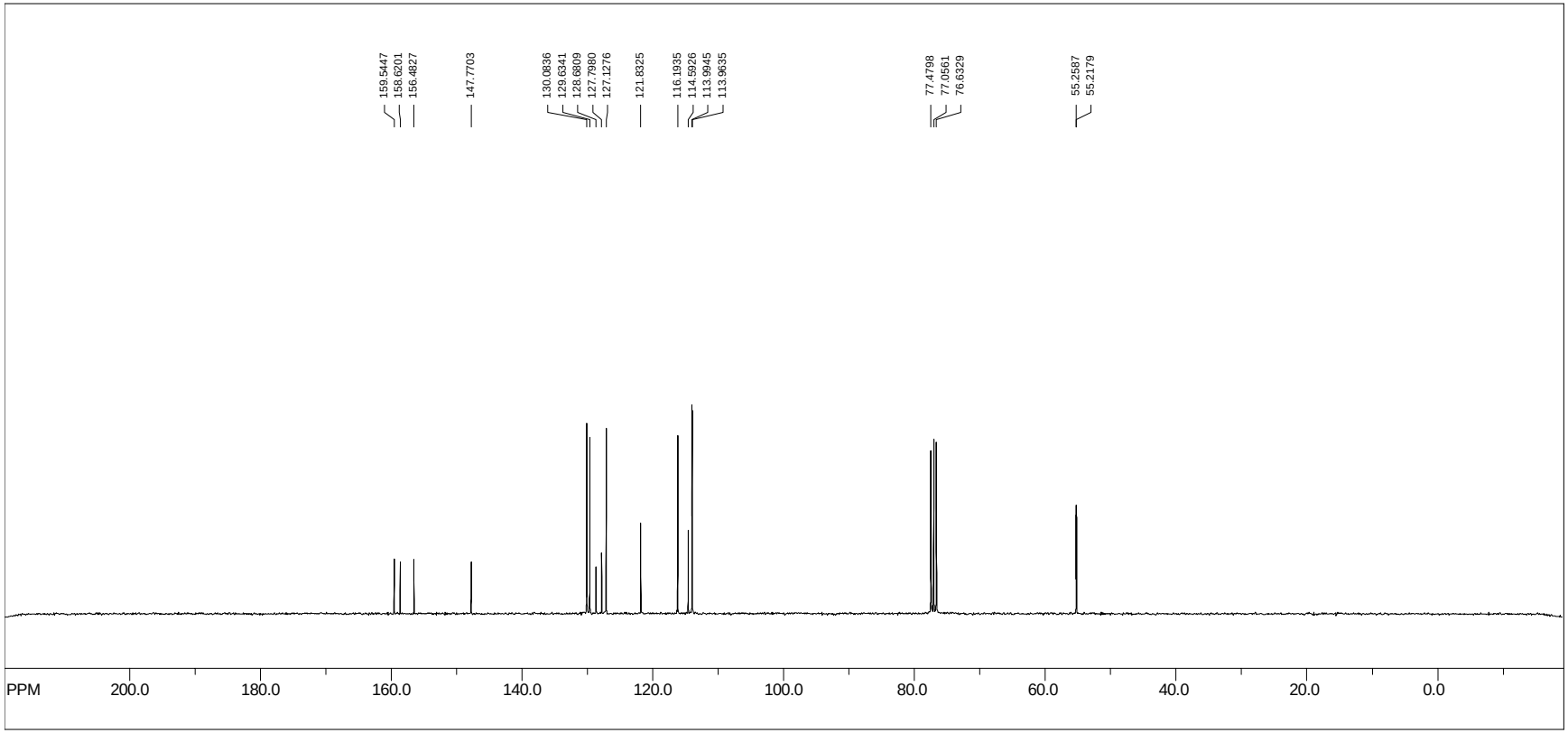
SpinWorks 2.5: fractions 8-10 from column



file: Z:\Laina\lmgvi\lmgvi_26c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

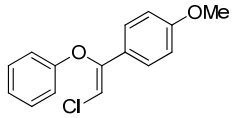
SpinWorks 2.5: fractions 8-10 from column



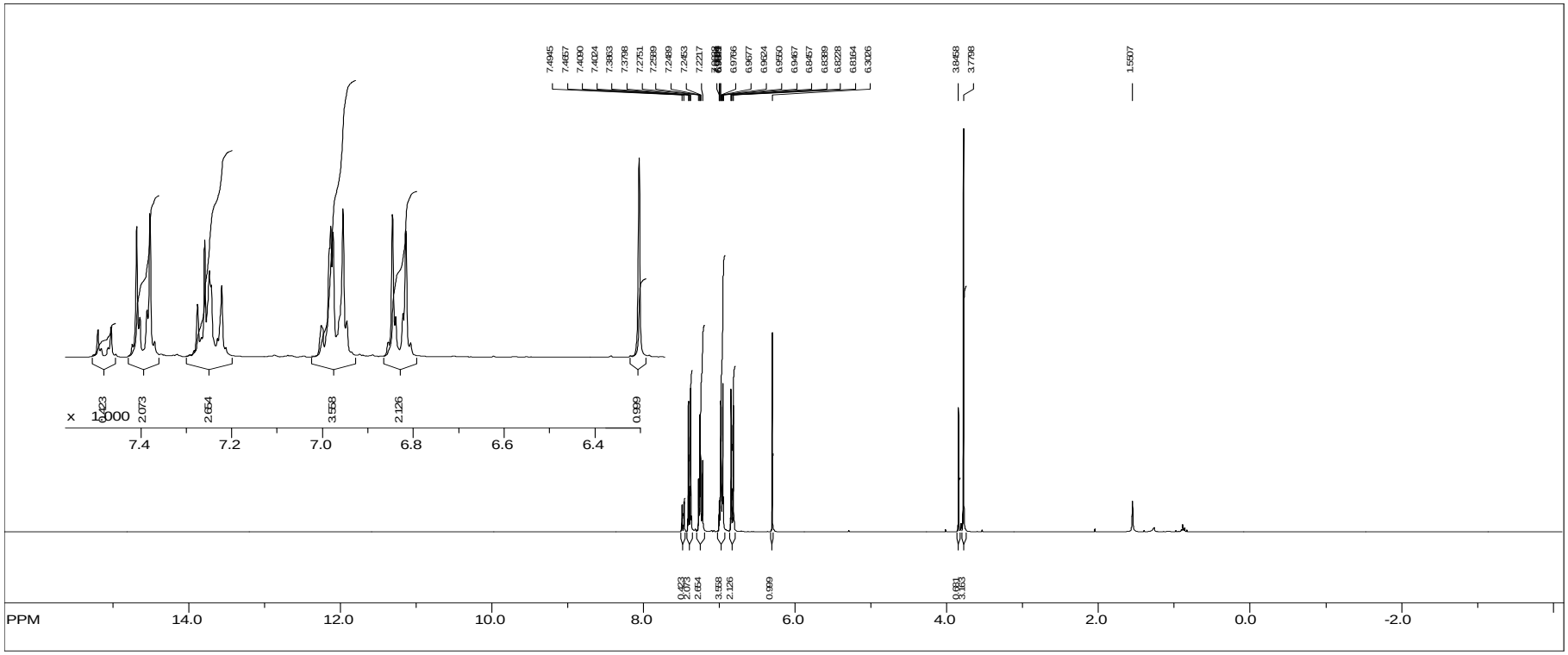
file: Z:\Laina\lmgvi\lmgvi_26c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(2-Chloro-1-(4-methoxyphenyl)vinyloxy)benzene (173)



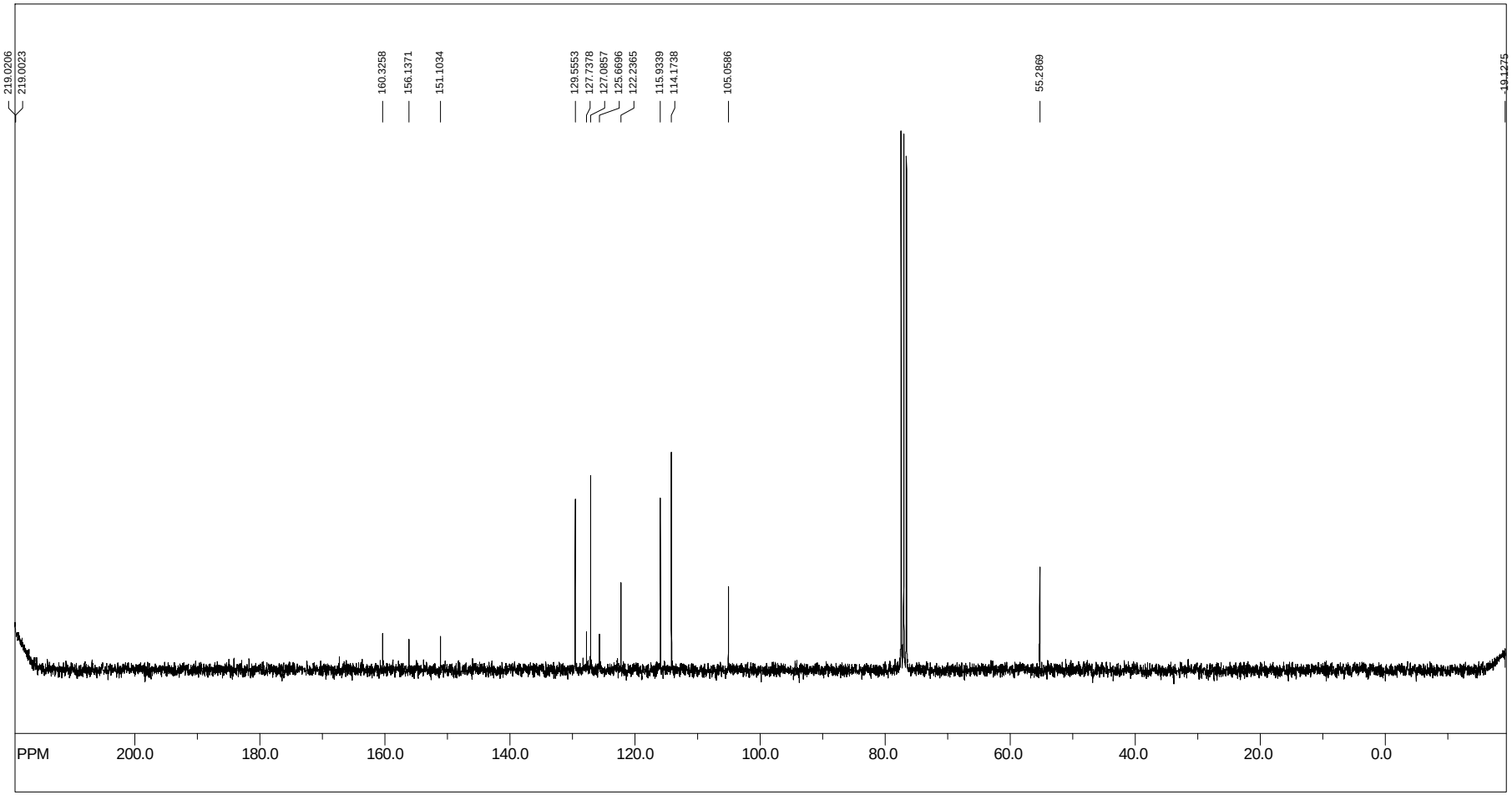
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgvi\lmgvi_09\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

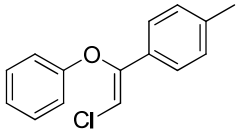
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



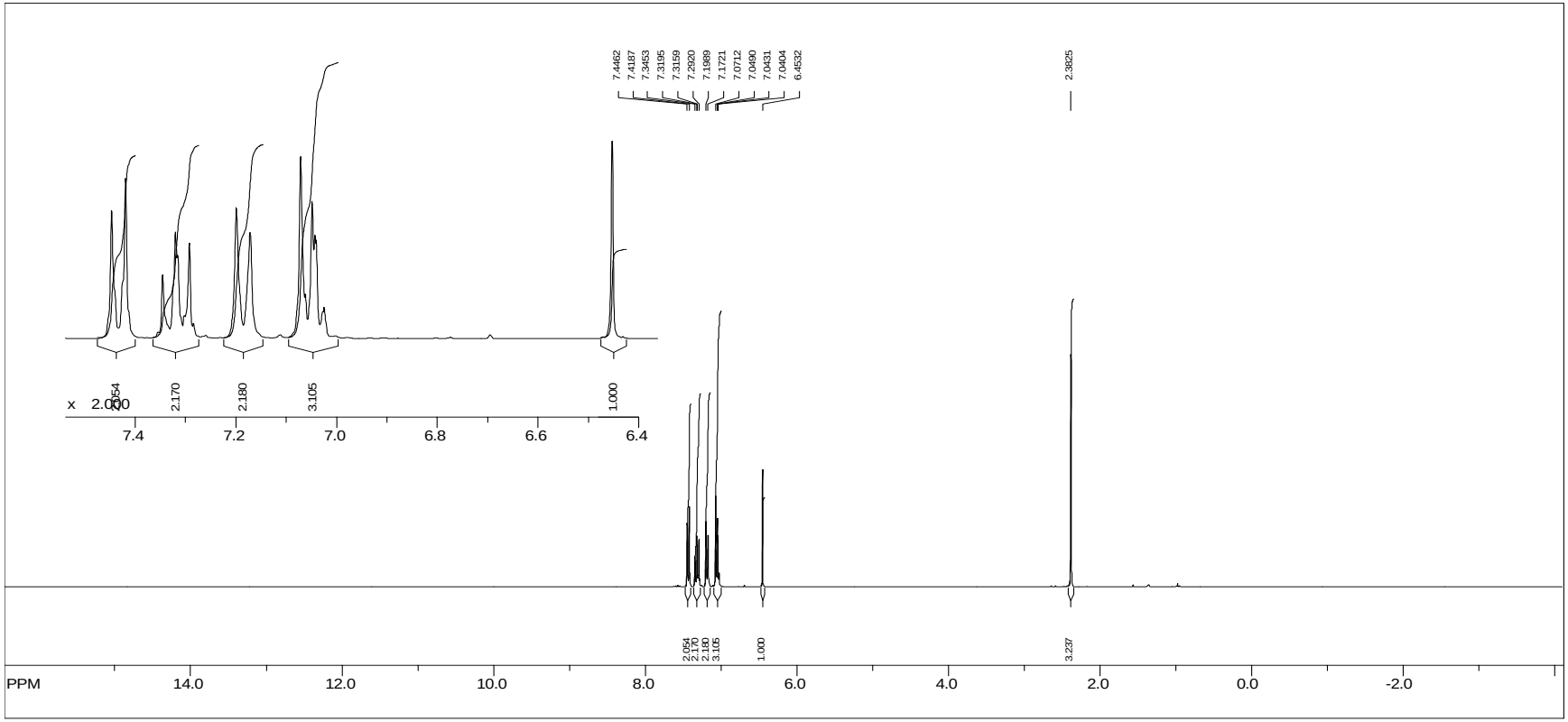
file: C:\Users\Laina\Documents\WORK\NMR\lmgvii\lmgvii_09\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-1-(2-Chloro-1-(4-methylphenyl)vinyloxy)benzene (193)



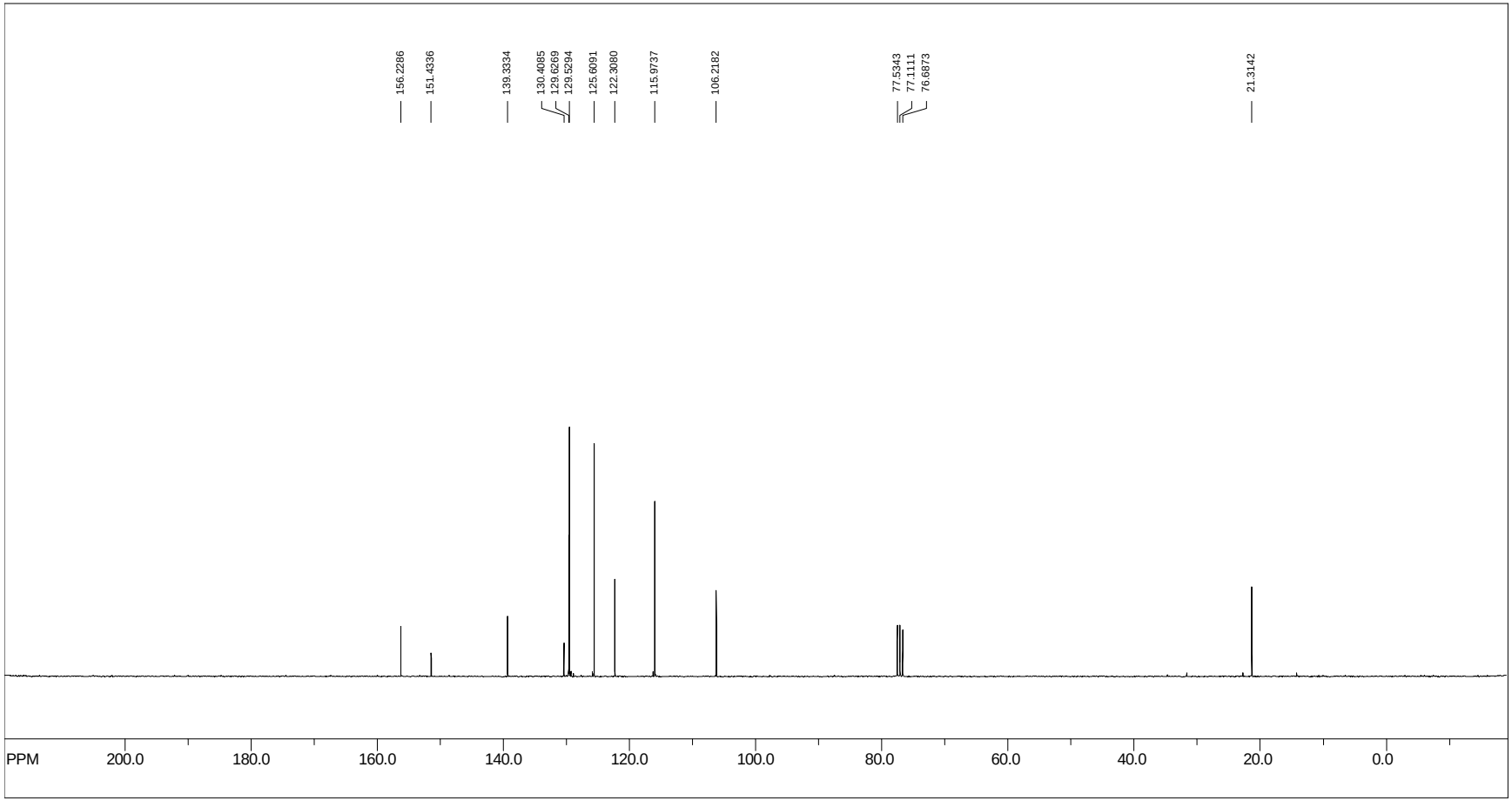
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



file: Z:\Laina\lmgxiv\lmgxiv_28b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 12

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

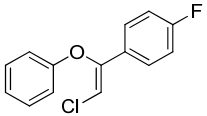
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



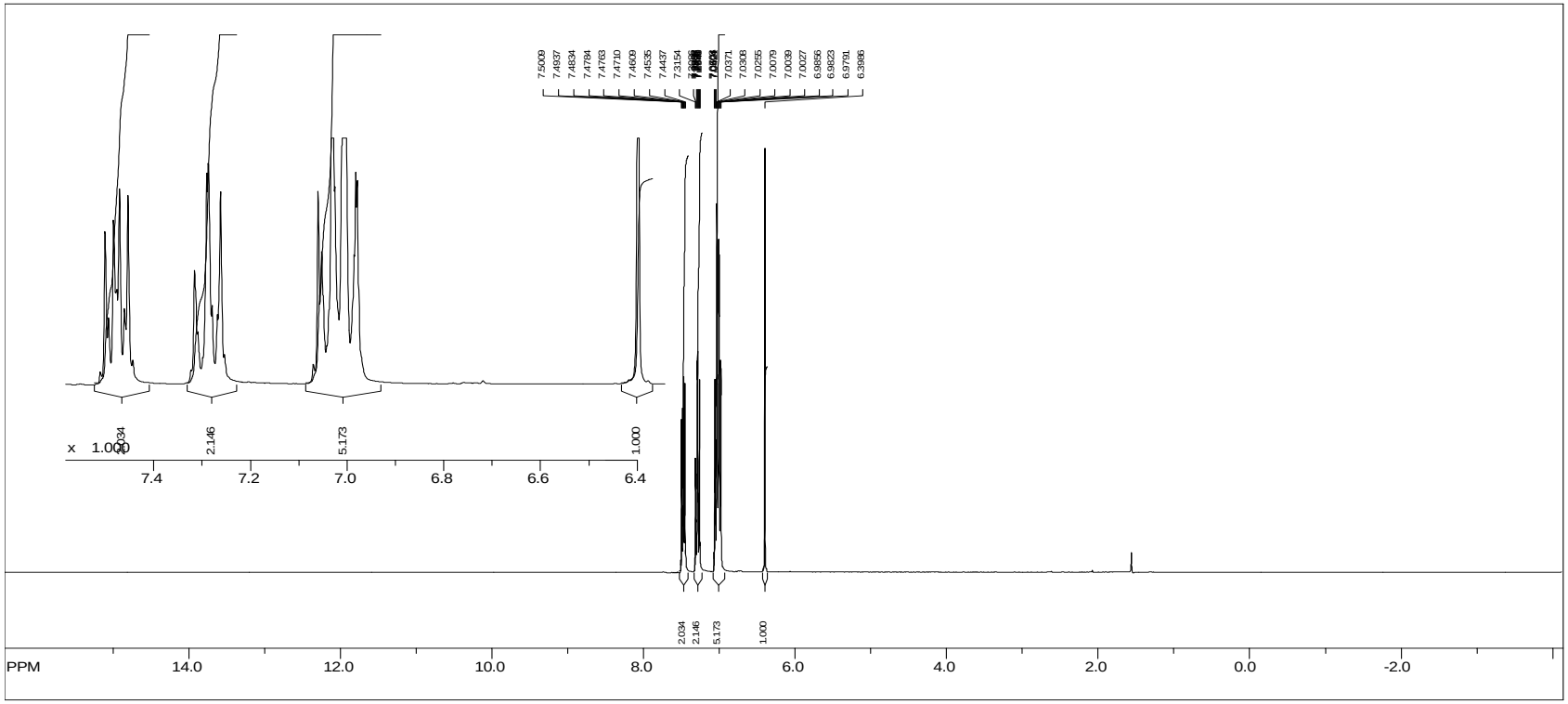
file: Z:\Laina\lmgxiv\lmgxiv_28b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 441

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(Z)-1-(2-Chloro-1-(4-fluorophenyl)vinyloxy)benzene (194**)**



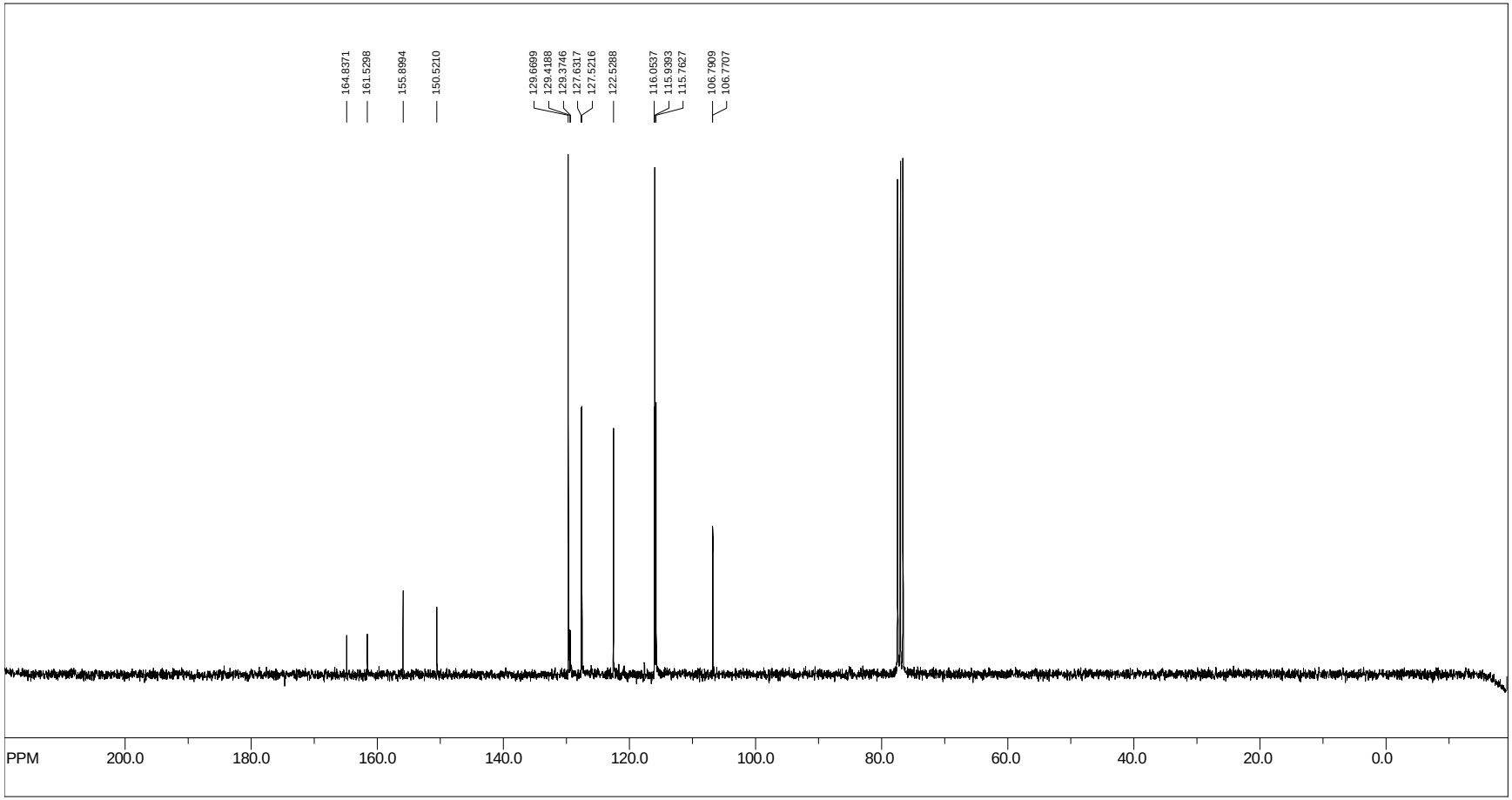
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgx\lmgx_12a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

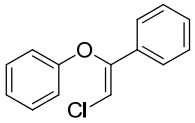
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



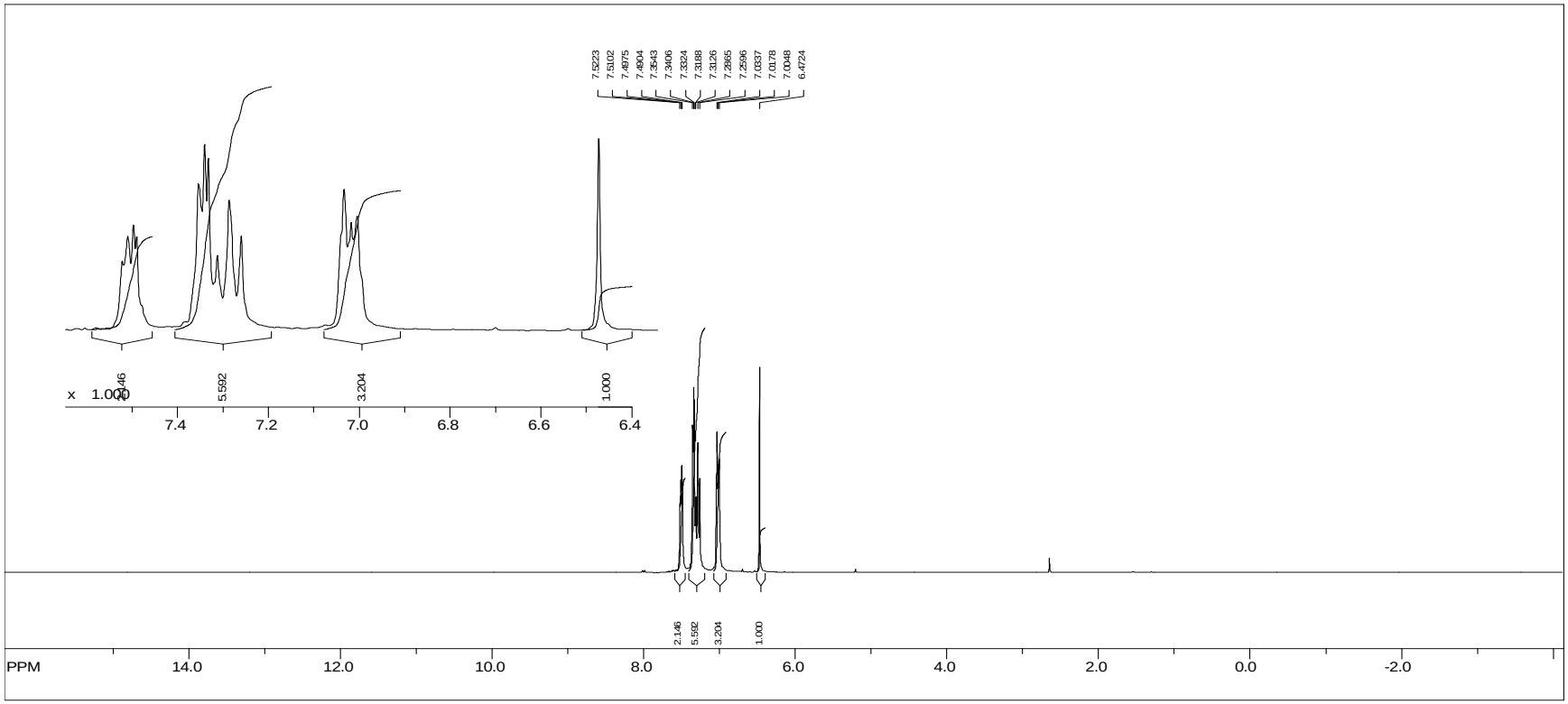
file: Z:\Laina\lmgx\lmgx_71a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(2-Chloro-1-phenoxyvinyl)benzene (195)



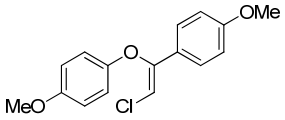
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



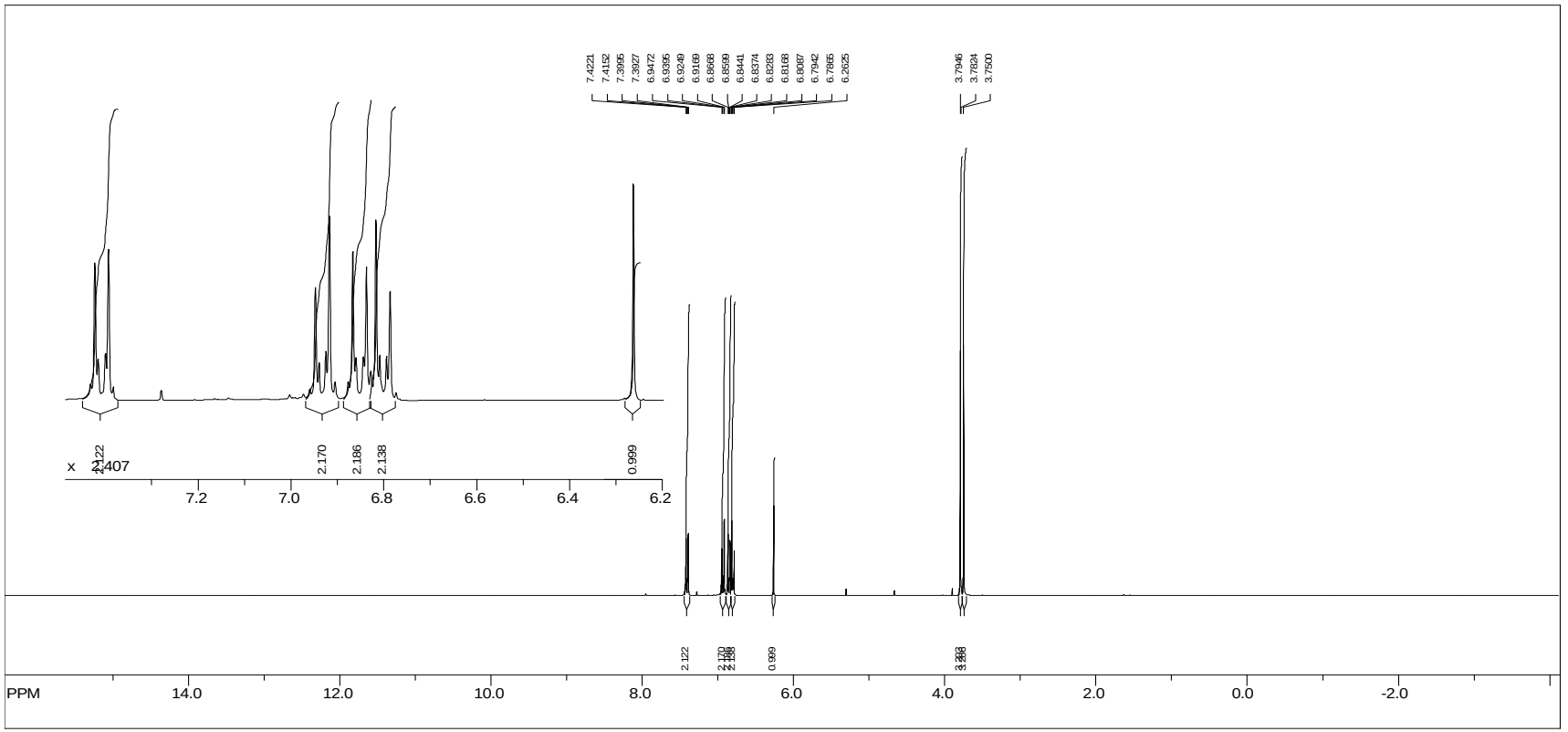
file: Z:\Laina\lmgix\lmgix_51b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(2-Chloro-1-(4-methoxyphenoxy)vinyl)-4-methoxybenzene (196)



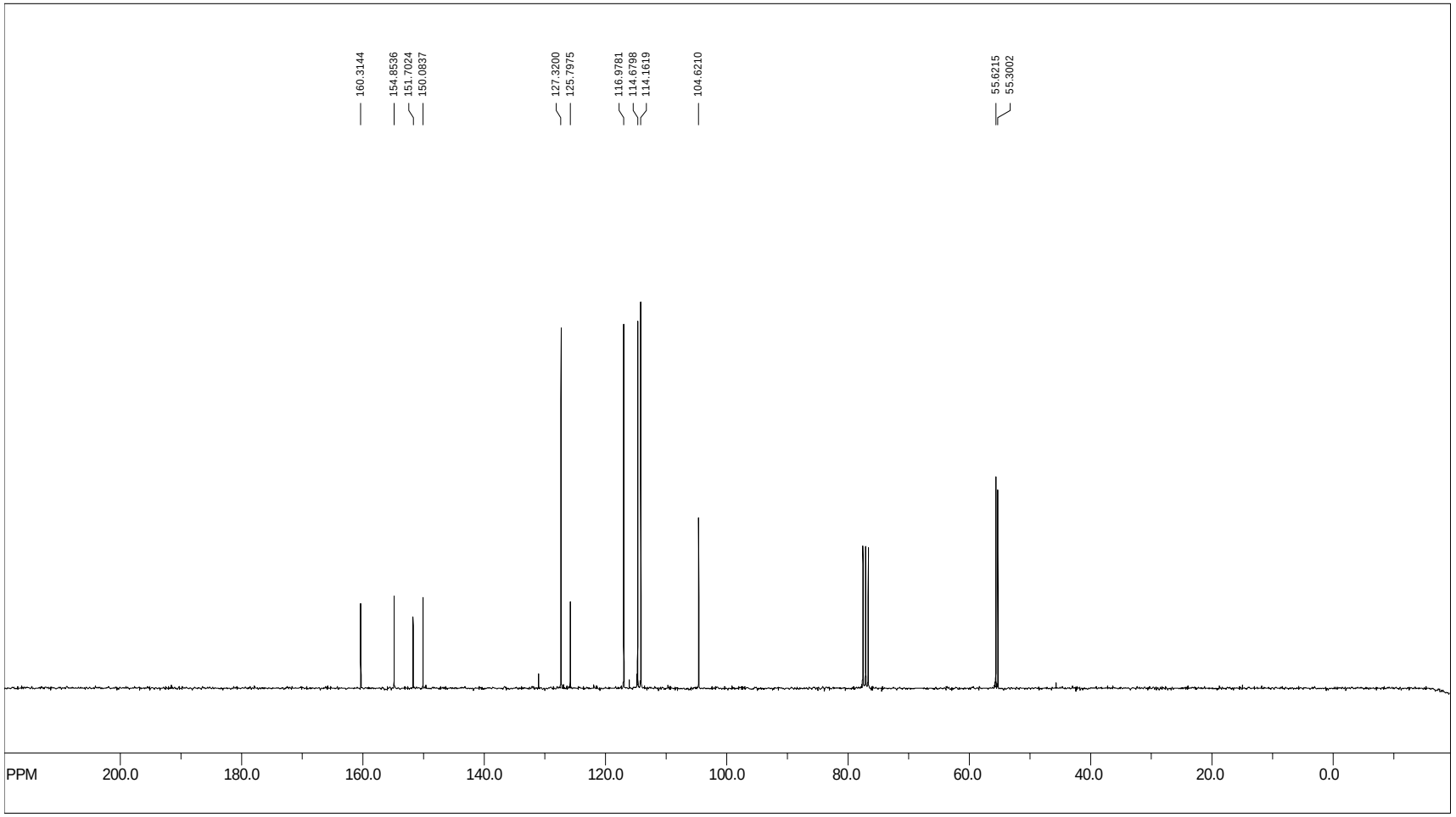
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgx\lmgx_84b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

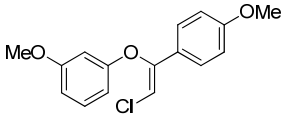
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



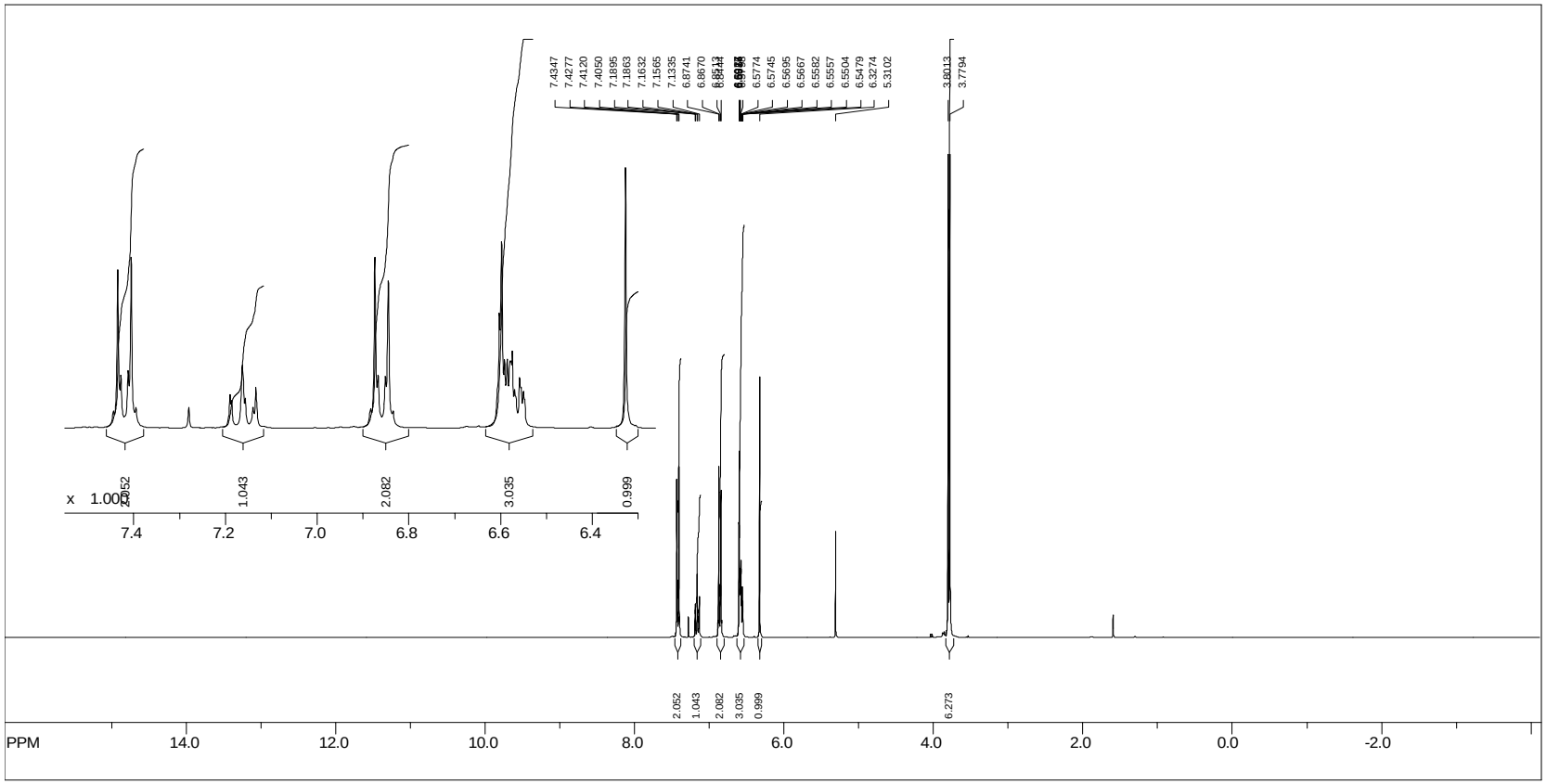
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_84b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(2-Chloro-1-(3-methoxyphenoxy)vinyl)-4-methoxybenzene (197)



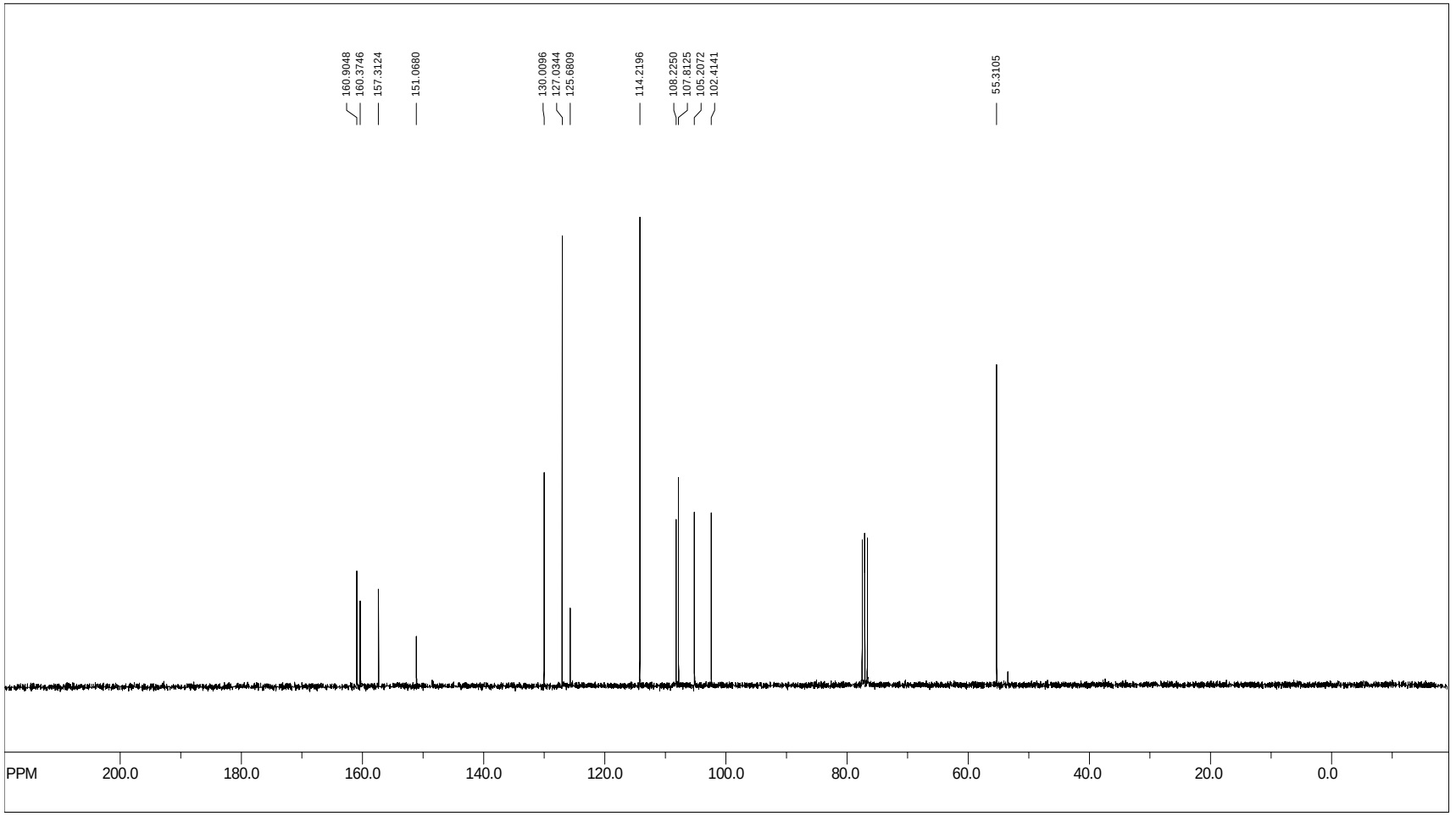
SpinWorks 2.5: suzuki between m-methoxy and p-methoxy



file: Z:\Laina\lmgix\lmgix_36a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

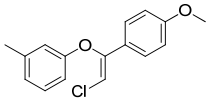
SpinWorks 2.5: suzuki between m-methoxy and p-methoxy



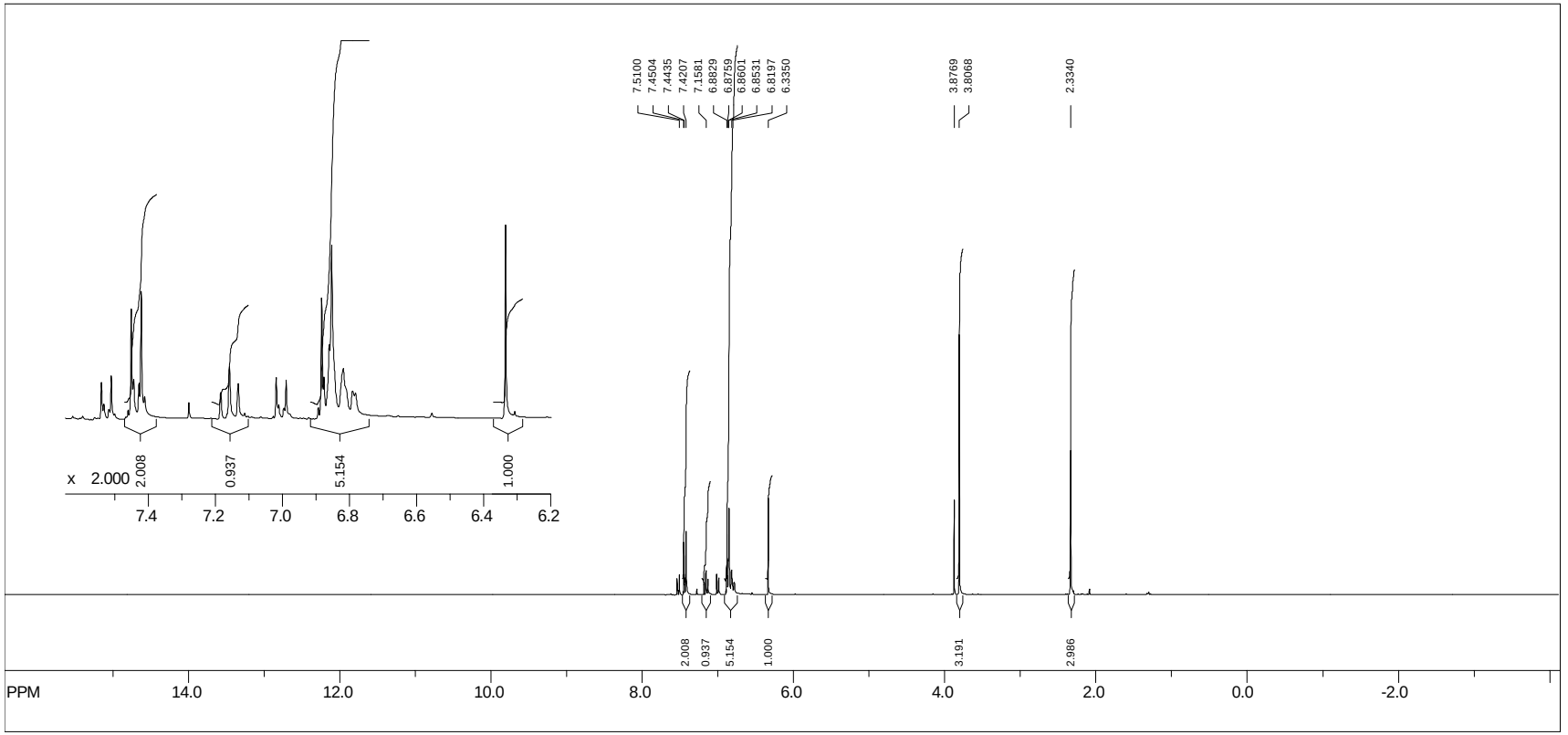
file: C:\Users\Laina\Documents\WORK\NMR\lmgix\lmgix_36a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(2-Chloro-1-(3-methylphenoxy)vinyl)-4-methoxybenzene (198)



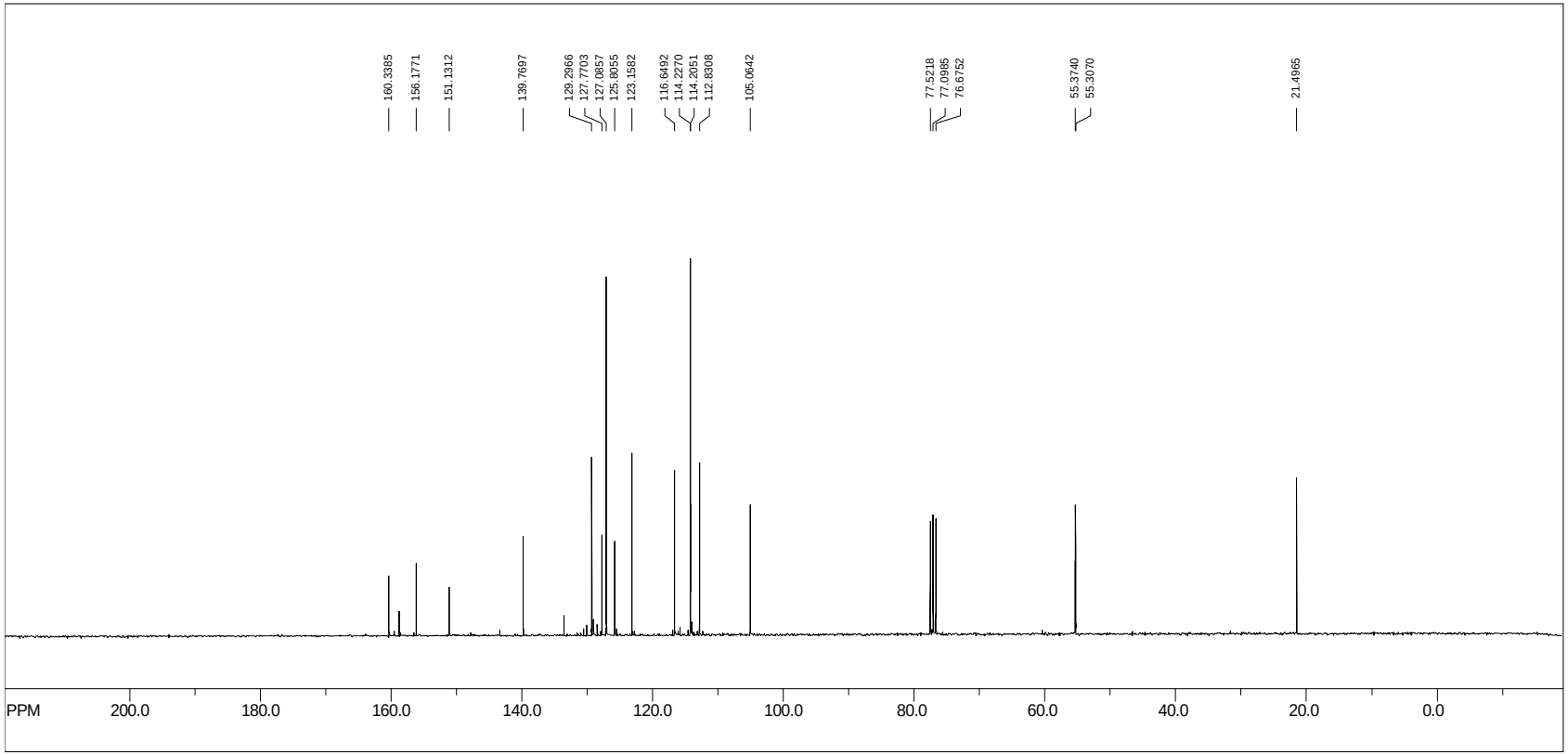
SpinWorks 2.5: rt suzuki between m-cresol derived enamine and pmethoxyphenyl boronic acid



file: Z:\Laina\lmgix\lmgix_82b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

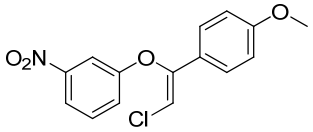
SpinWorks 2.5: rt suzuki between m-cresol derived enamine and pmethoxyphenyl boronic acid



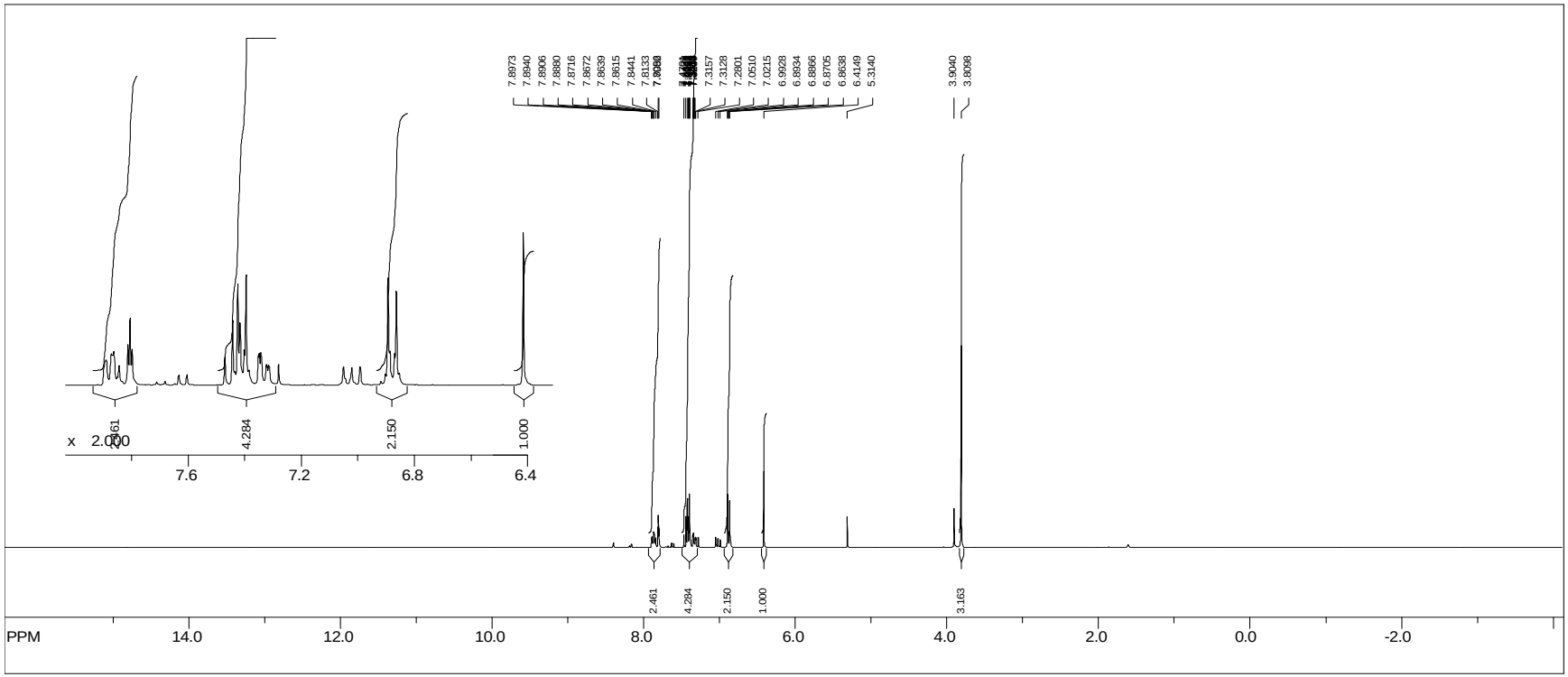
file: Z:\Laina\lmgix\lmgix_82b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 639

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*Z*)-1-(2-Chloro-1-(3-nitrophenoxy)vinyl)-4-methoxybenzene (199)



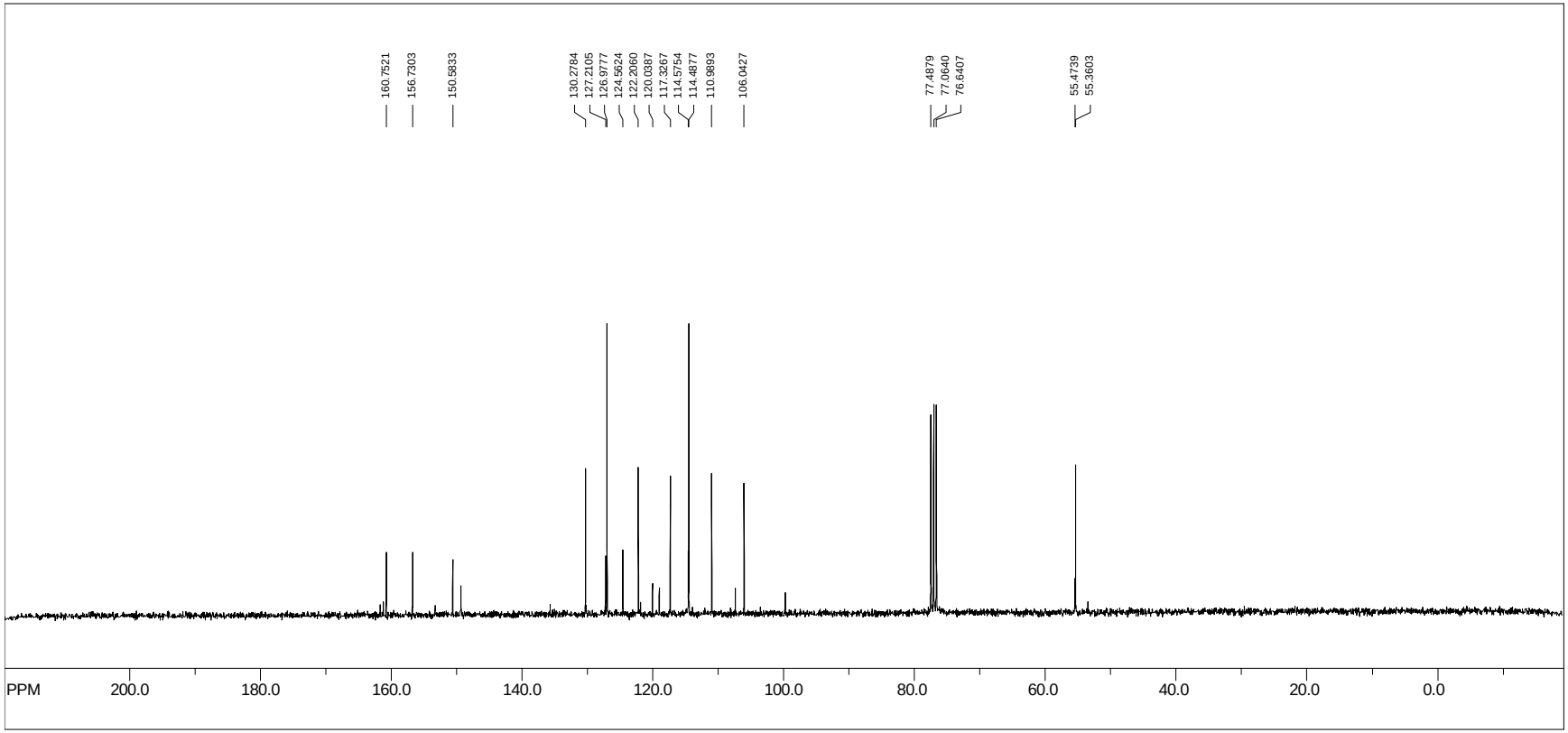
SpinWorks 2.5: suzuki between m-nitro and p-methoxy



file: Z:\Laina\lmgix\lmgix_38a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

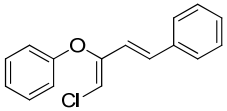
SpinWorks 2.5: suzuki between m-nitro and p-methoxy



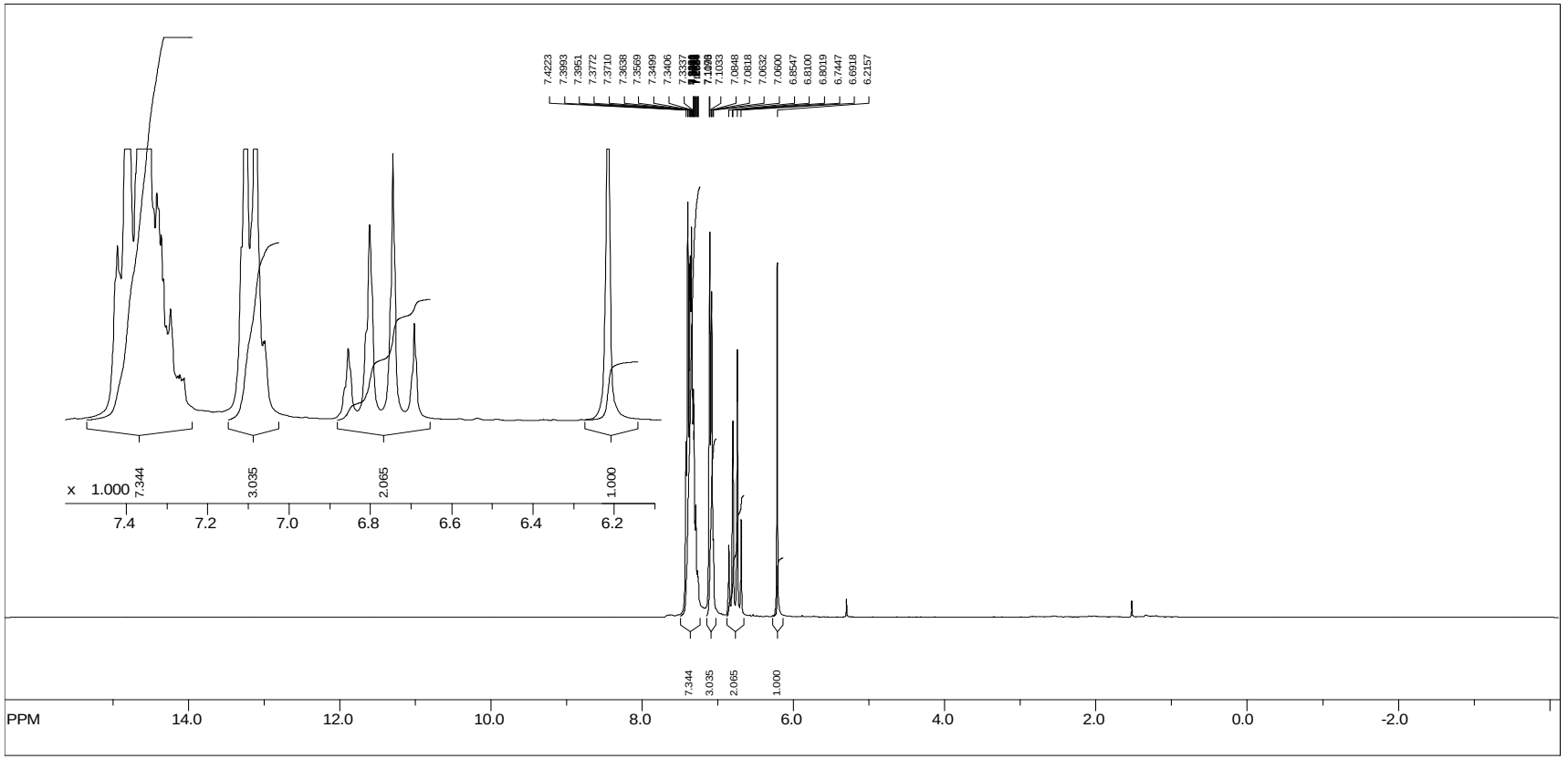
file: Z:\Laina\lmgix\lmgix_38a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-((1*E*,3*Z*)-4-Chloro-3-phenoxybuta-1,3-dienyl)benzene (200)



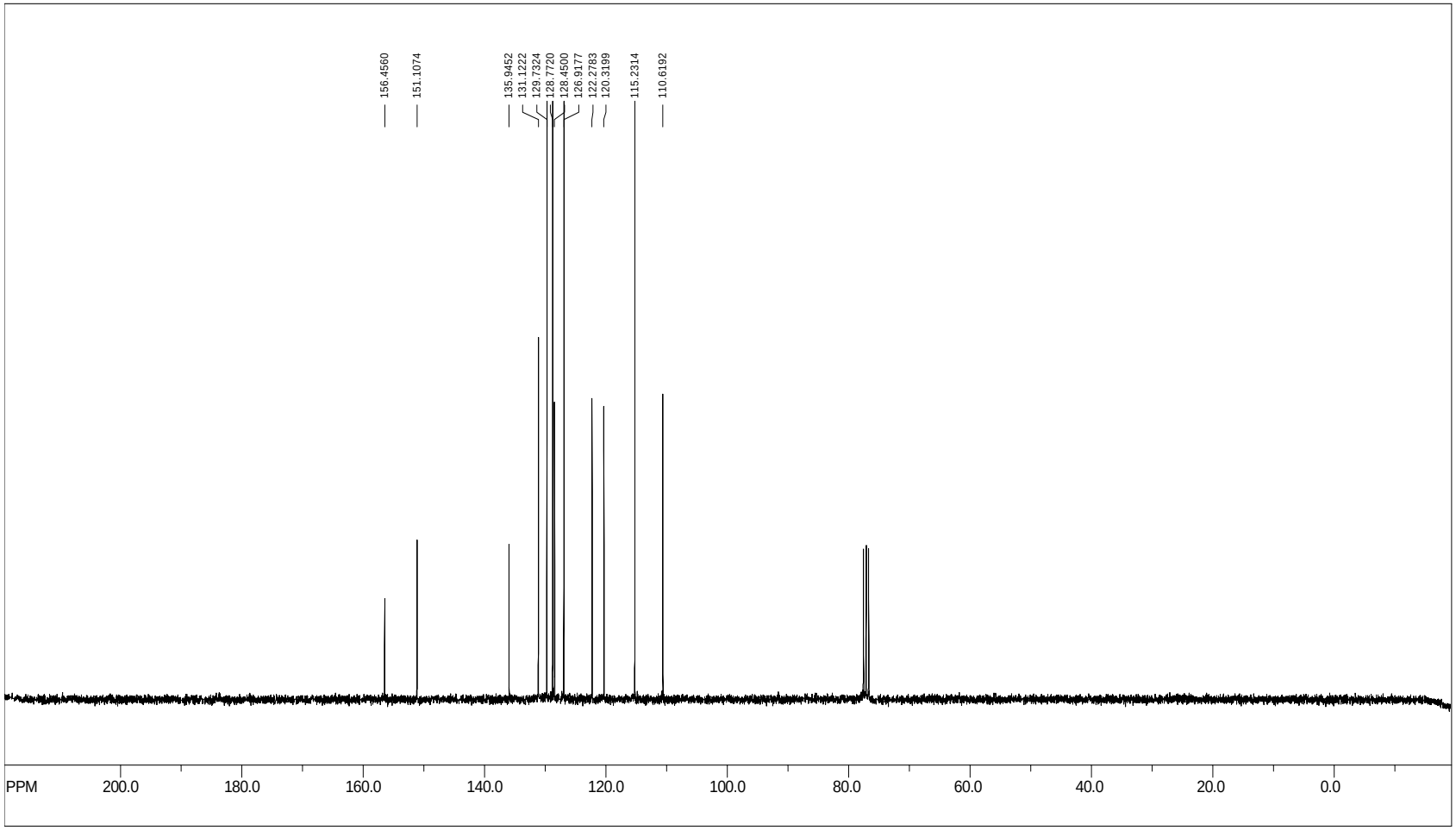
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgviii\lmgviii_51aii\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

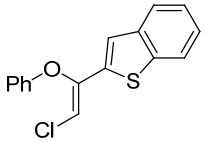
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



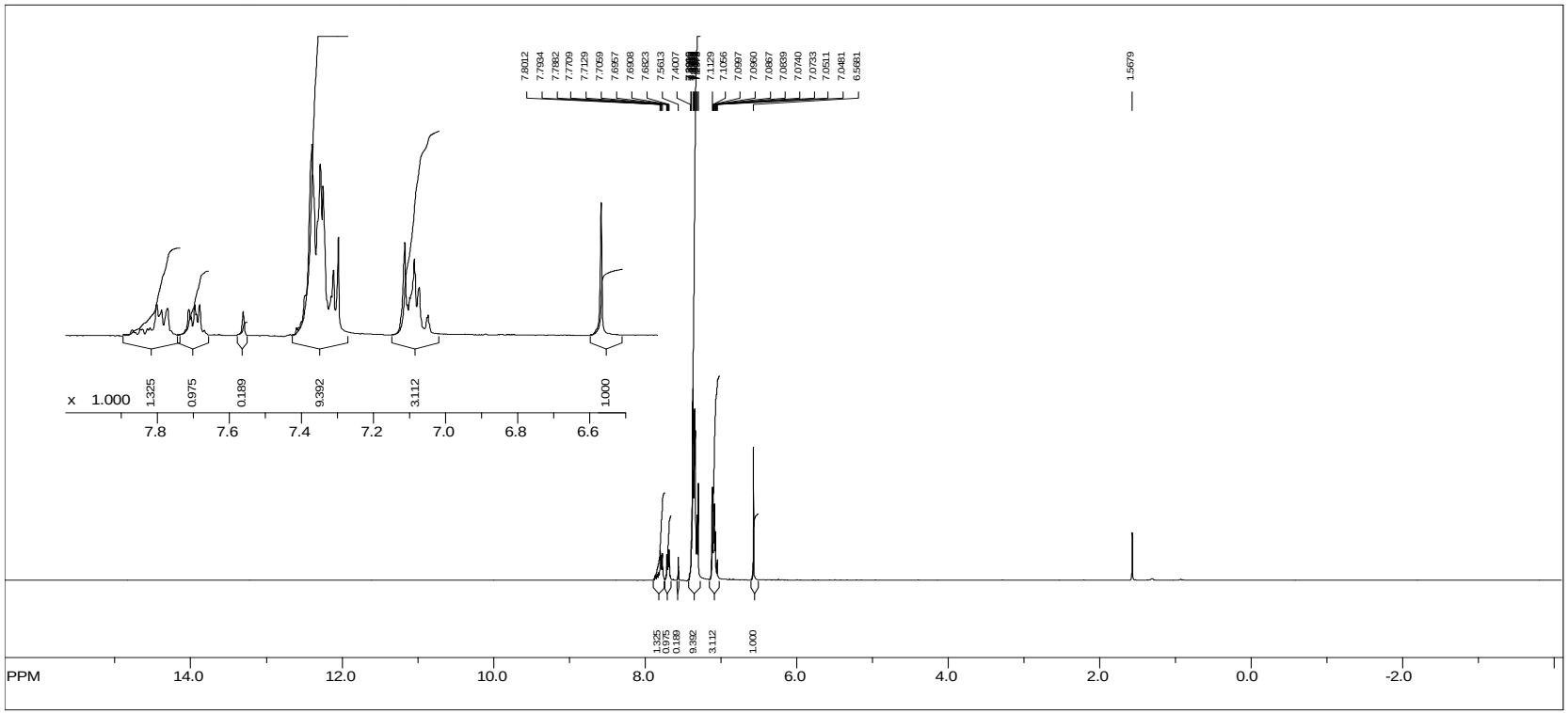
file: C:\Users\Laina\Documents\WORK\NMR\lmgviii\lmgviii_51aii\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-2-(2-Chloro-1-phenoxyvinyl)benzo[b]thiophene (201)



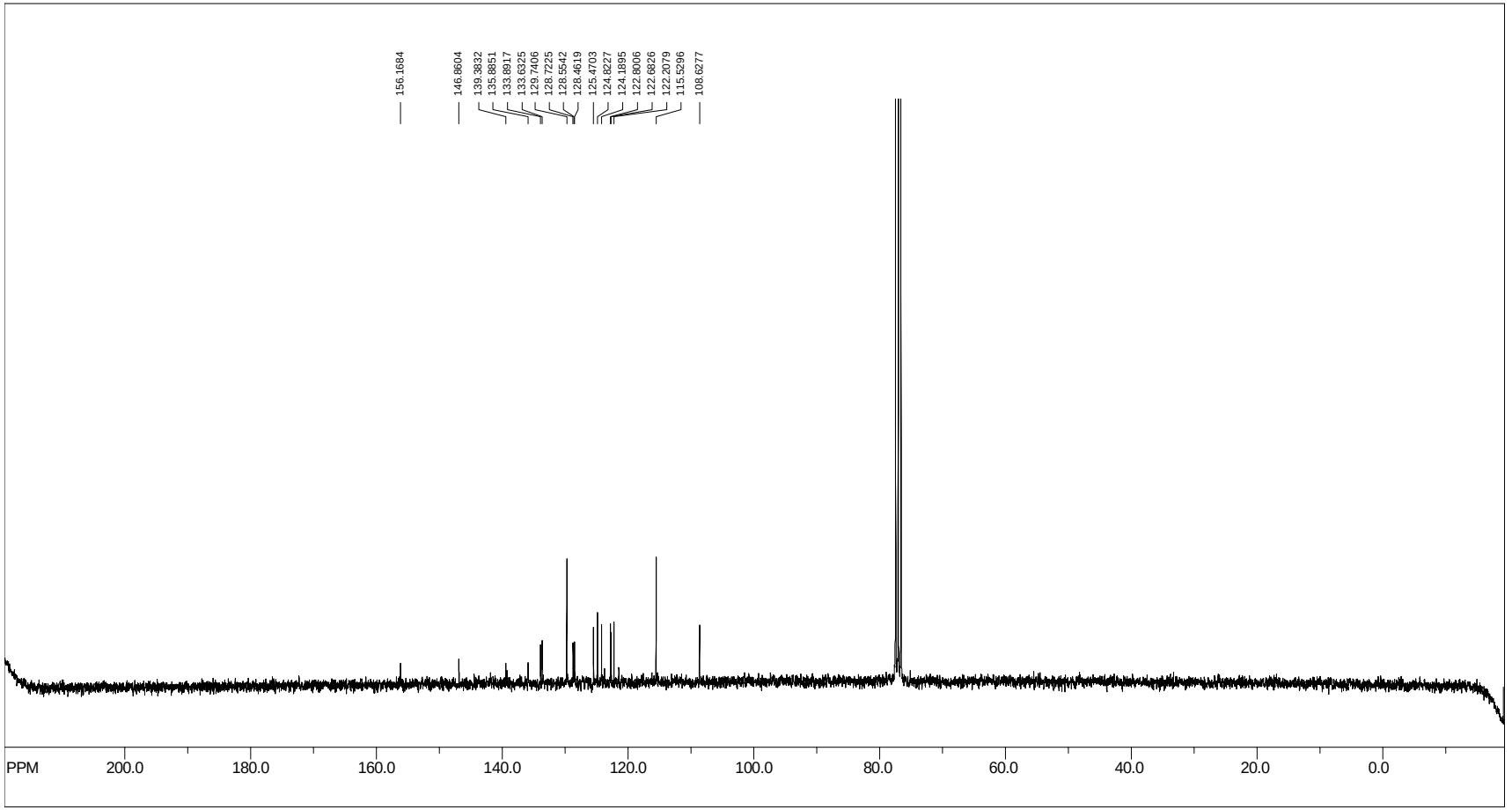
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxA\lmgxv_09b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

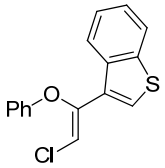
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



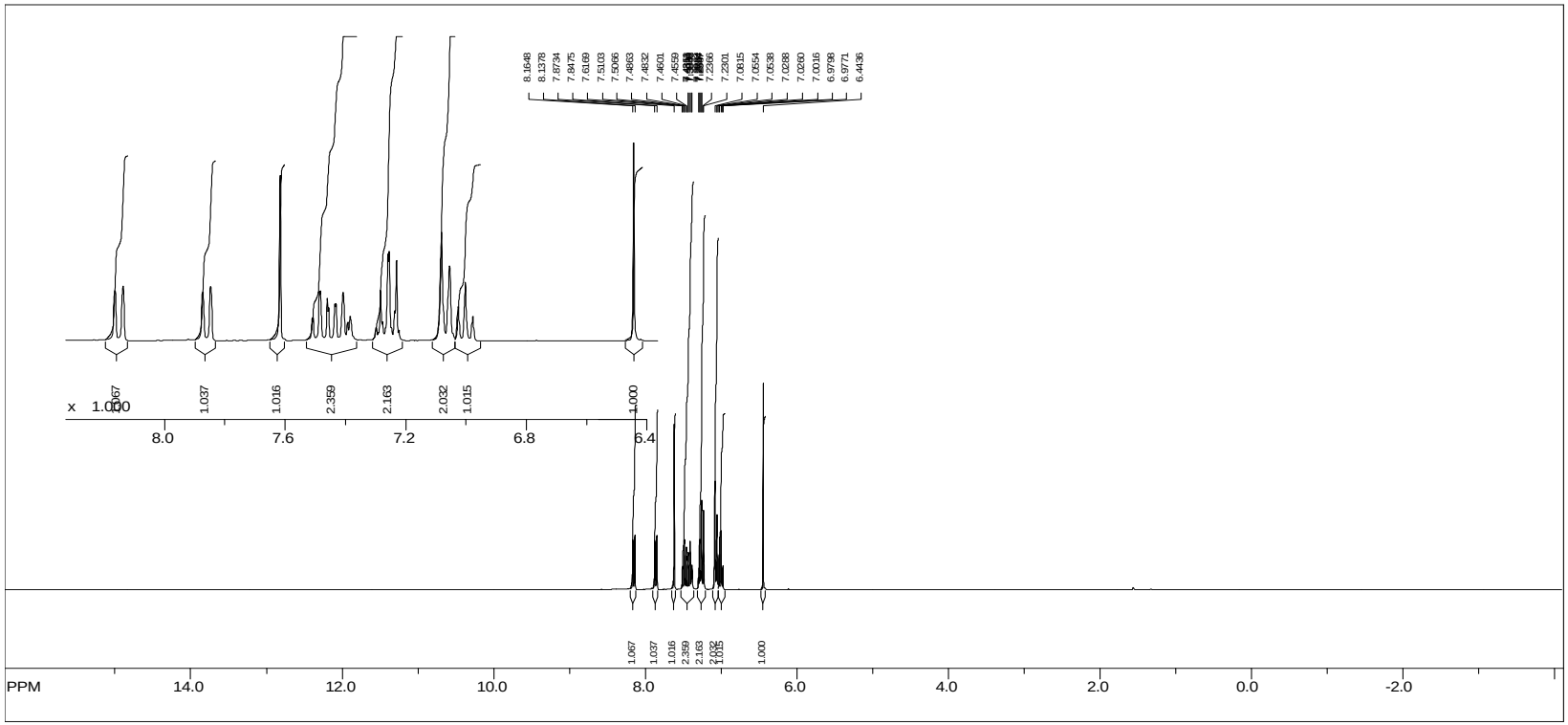
file: Z:\Laina\lmgxv\lmgxv_09b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 495

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-3-(2-Chloro-1-phenoxyvinyl)benzo[b]thiophene (202)



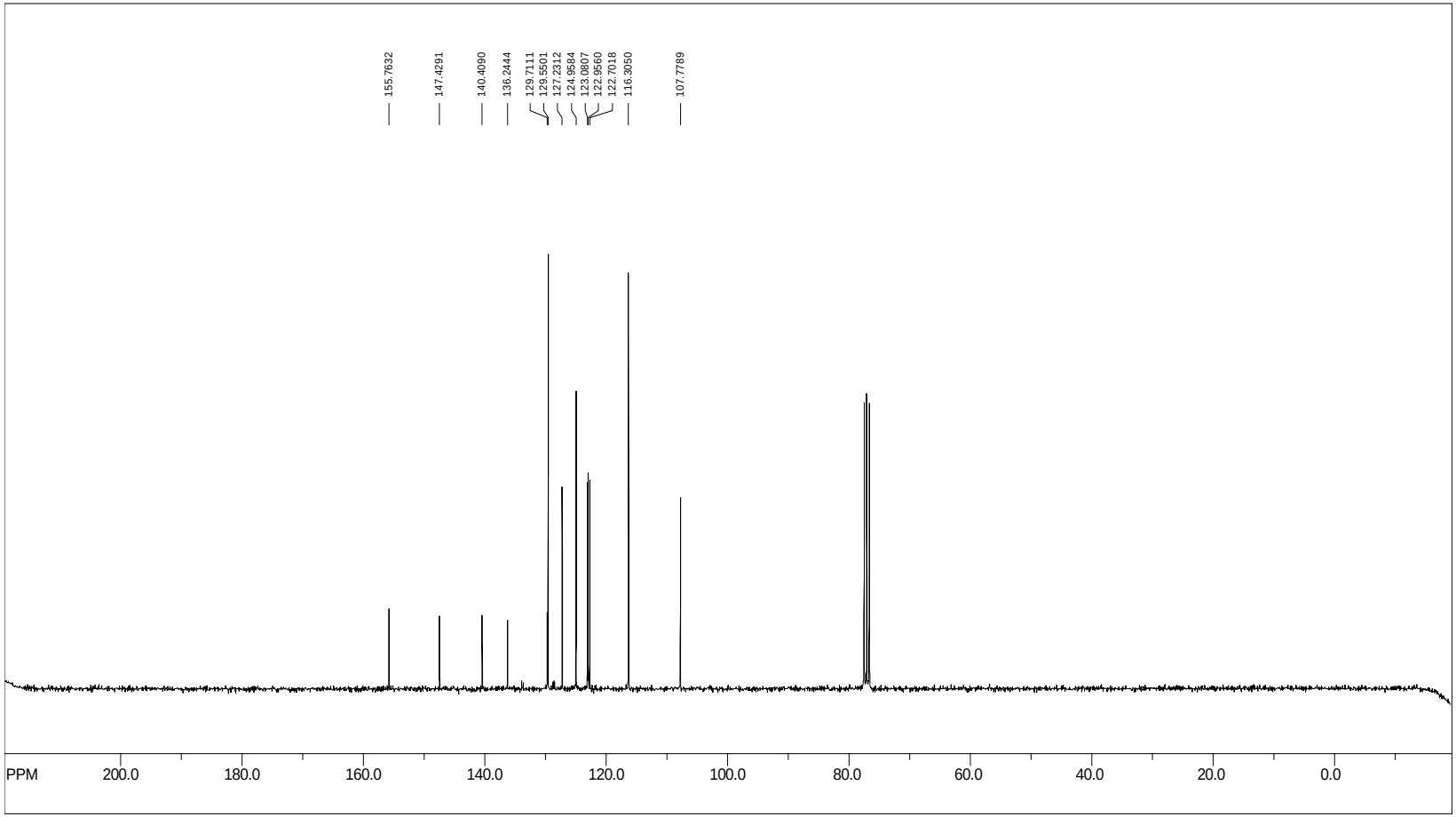
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgx\lmgxv_08c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

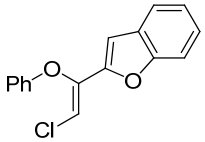
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



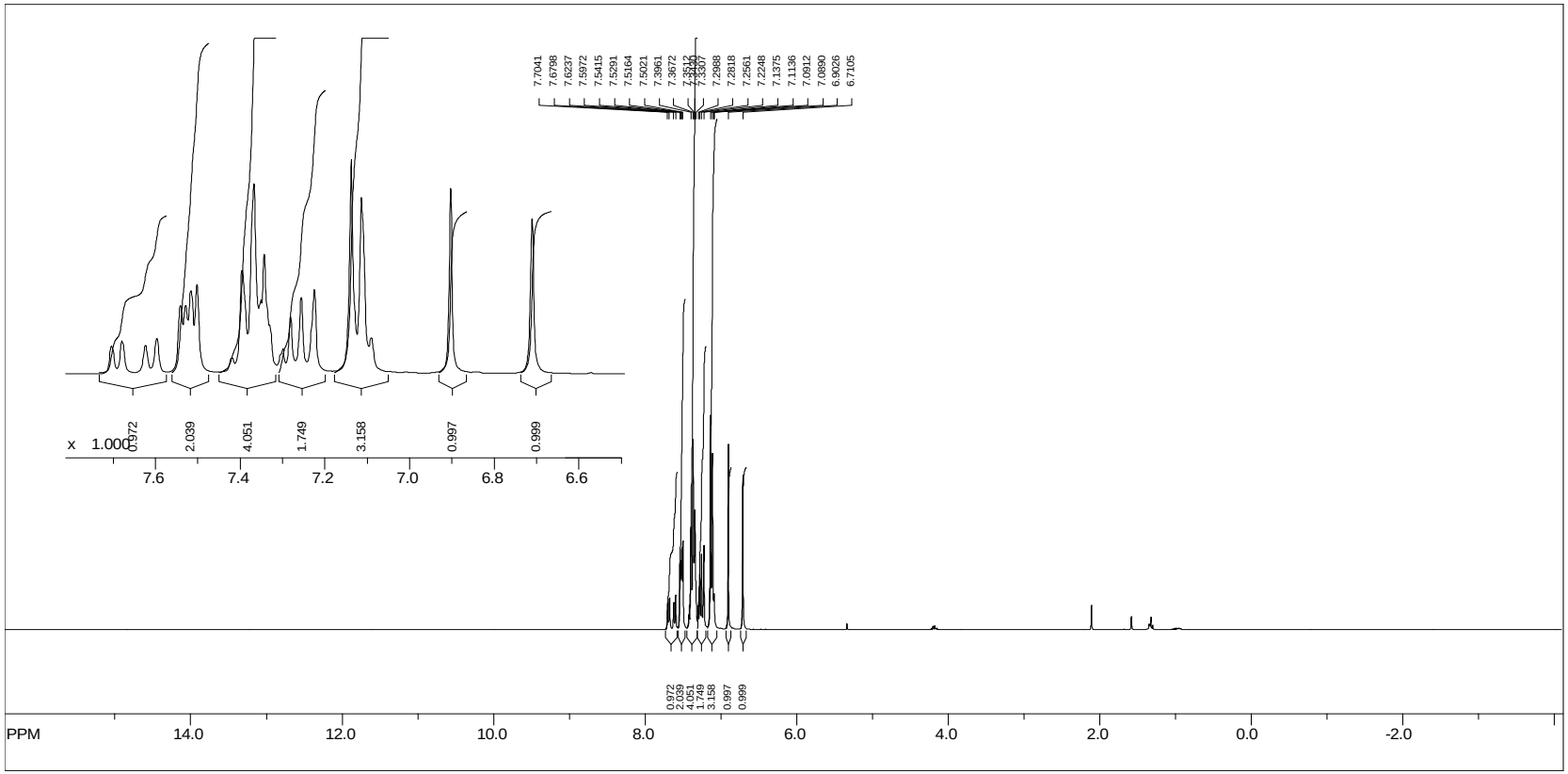
file: Z:\Laina\lmgx\lmgxv_08c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-2-(2-Chloro-1-phenoxyvinyl)benzofuran (203)



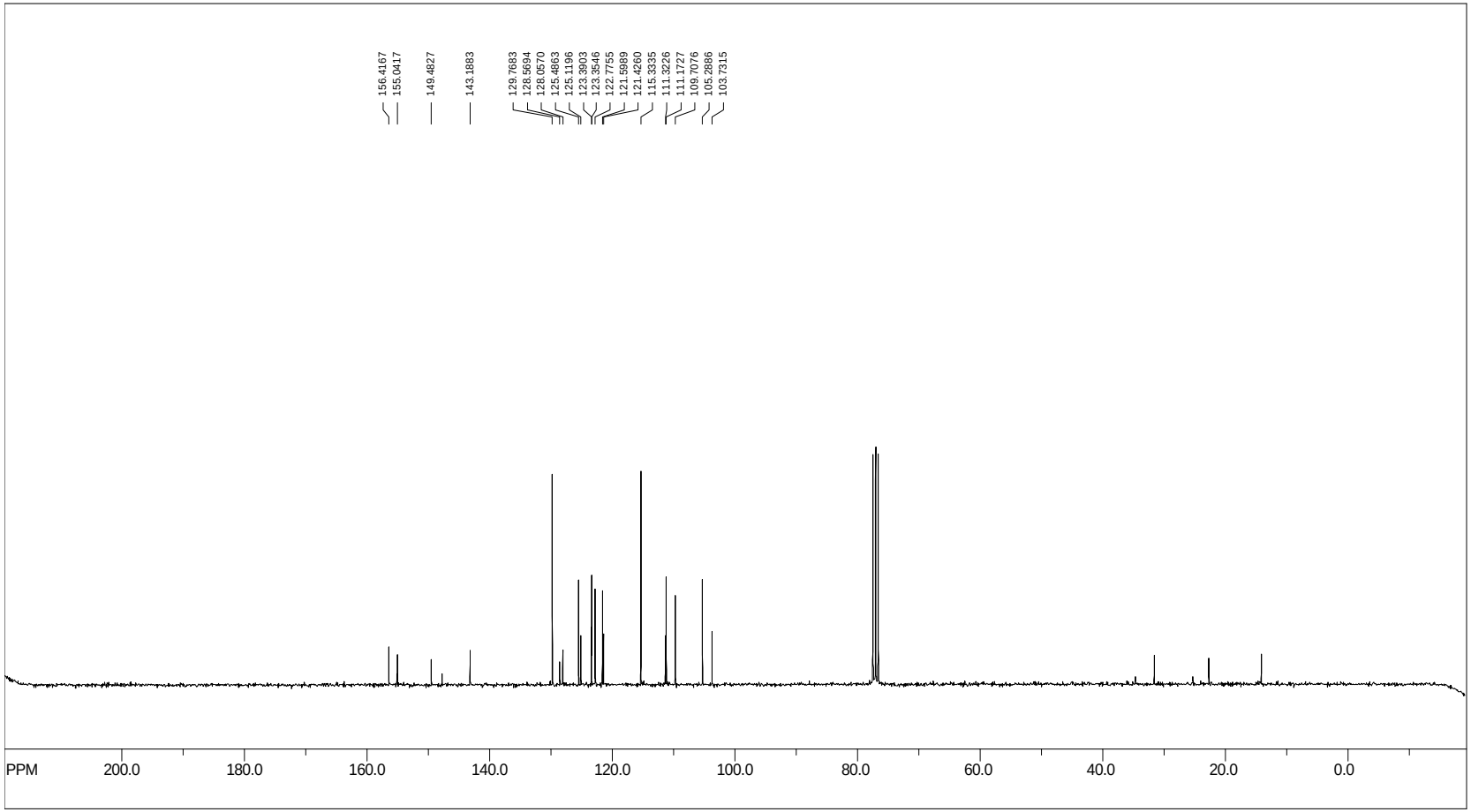
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgxiii\lmgxiii_55ai\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

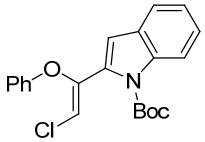
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



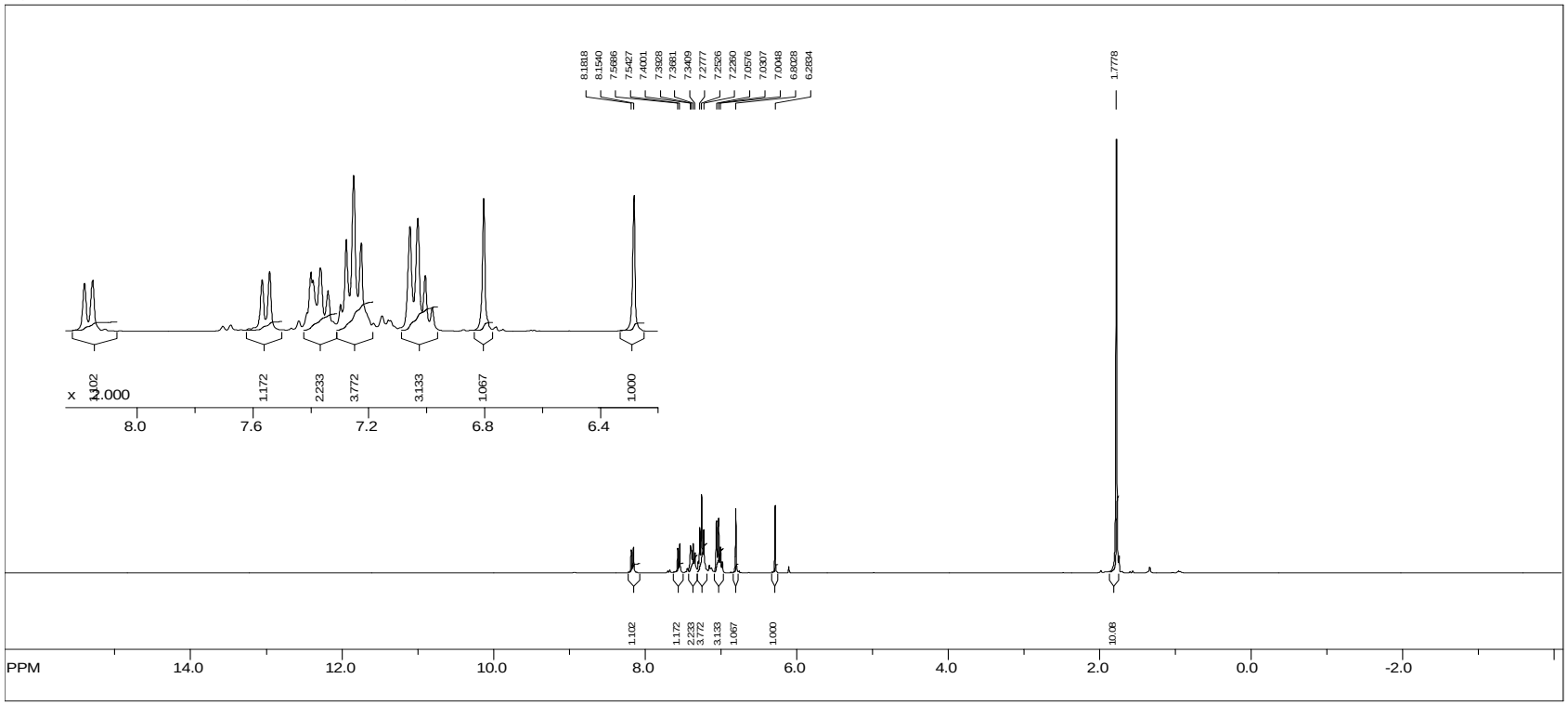
file: Z:\Laina\lmgxv\lmgxv_07b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-*tert*-Butyl 2-(2-chloro-1-phenyloxyvinyl)-1*H*-indole-1-carbonxylate (204)



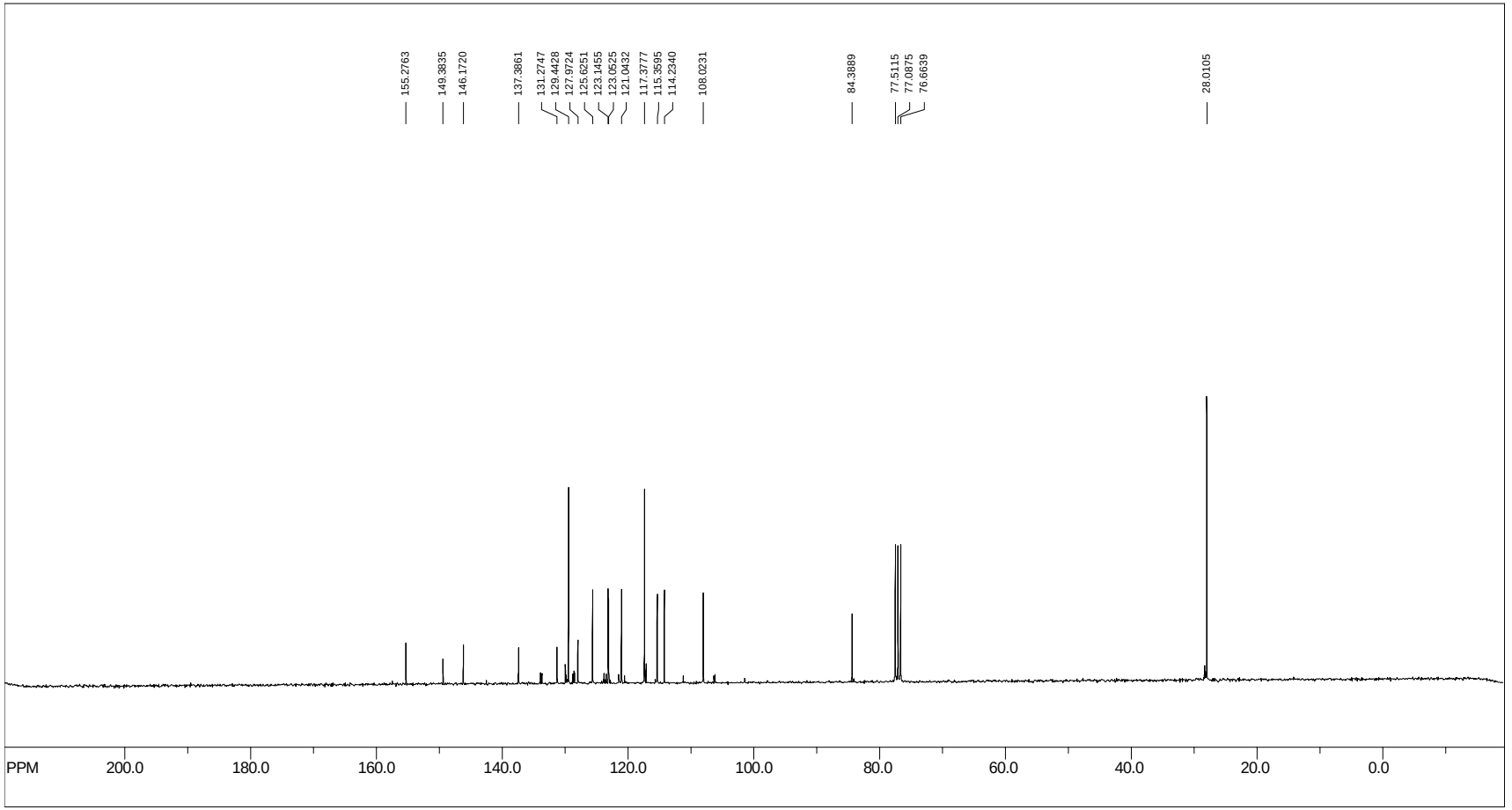
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgx\lmgxv_06b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

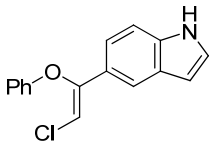
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



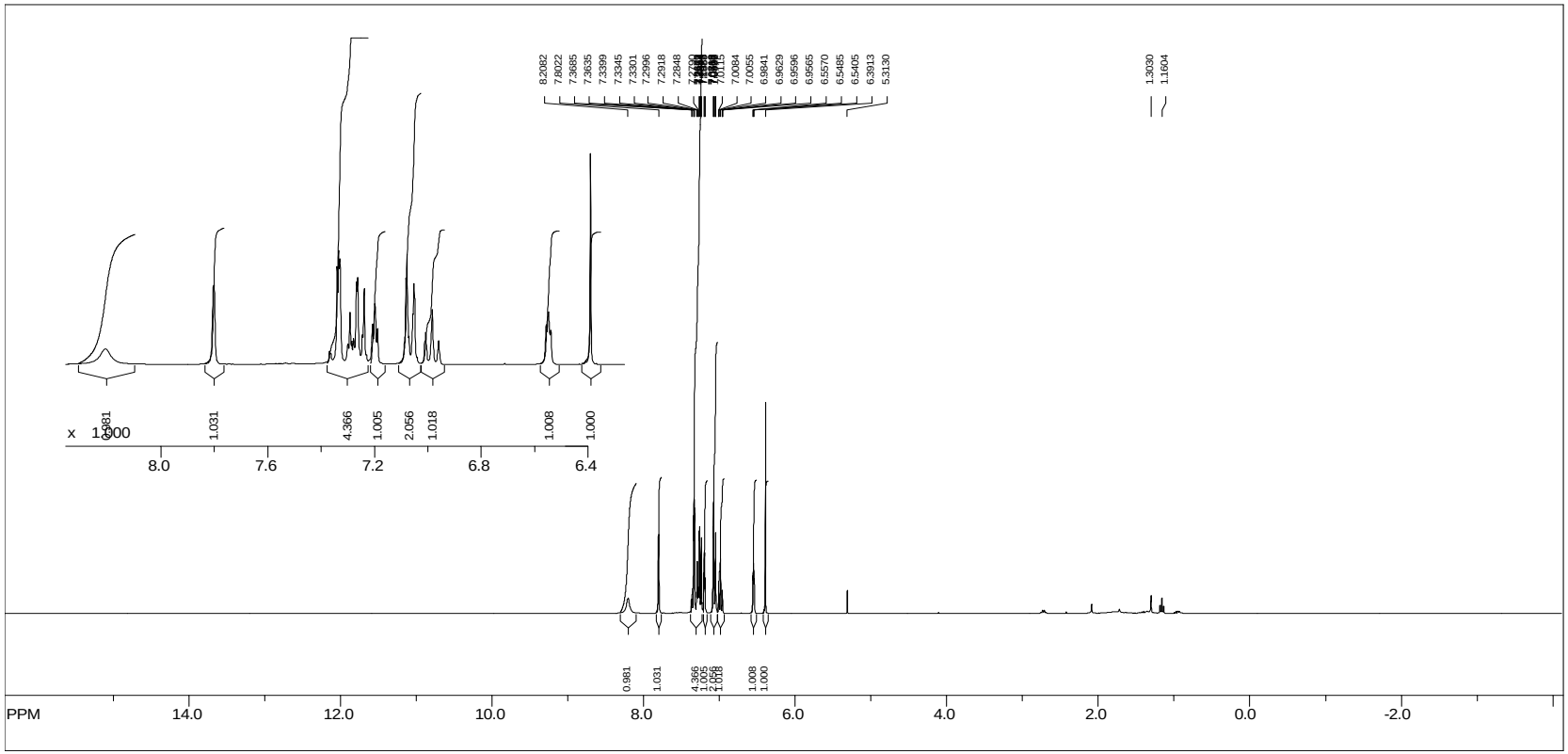
file: Z:\Laina\lmgxv\lmgxv_06b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-5-(2-Chloro-1-phenoxyvinyl)-1*H*-indole (205)



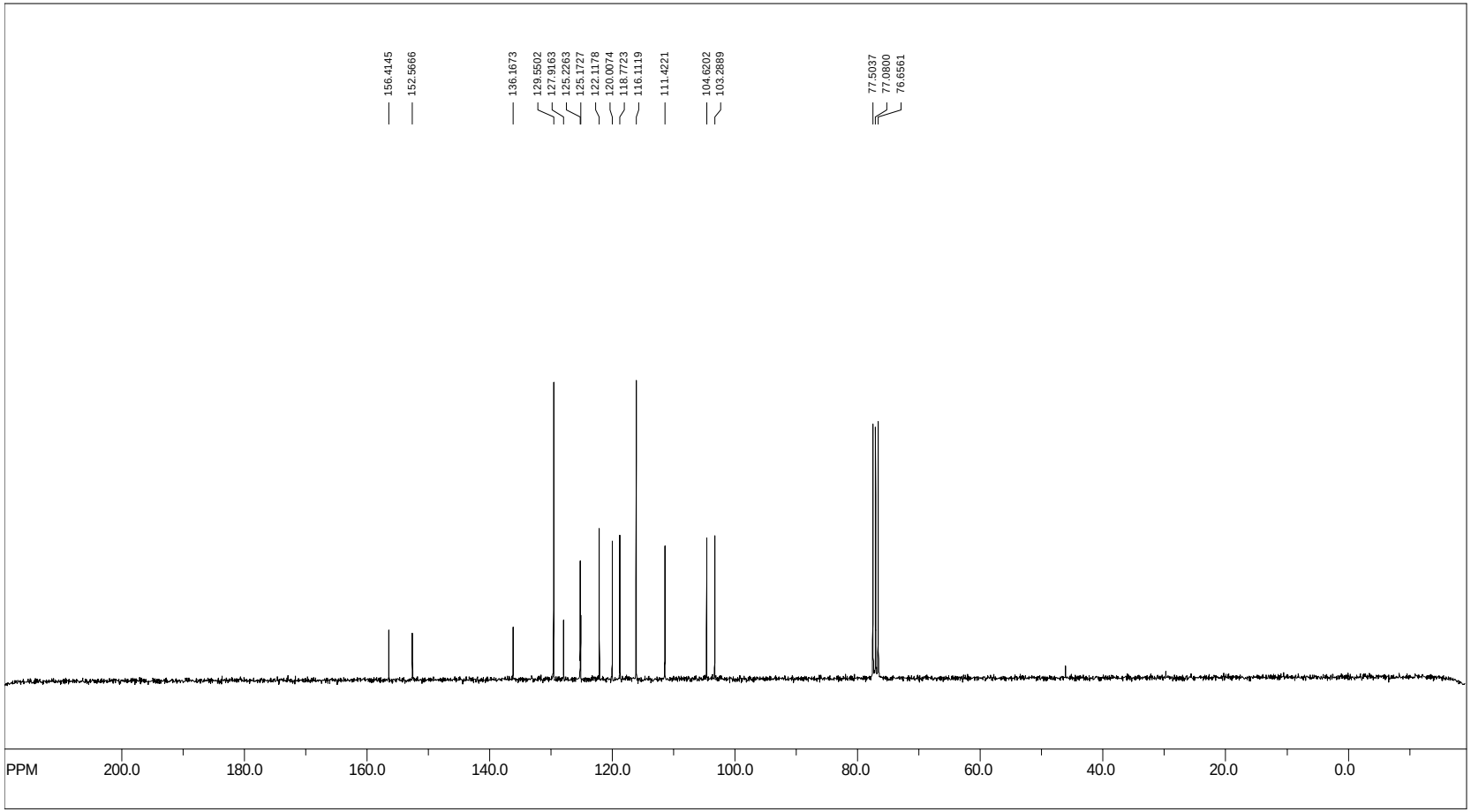
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgx\lmgx_83a\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

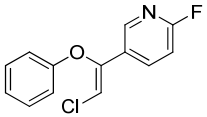
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



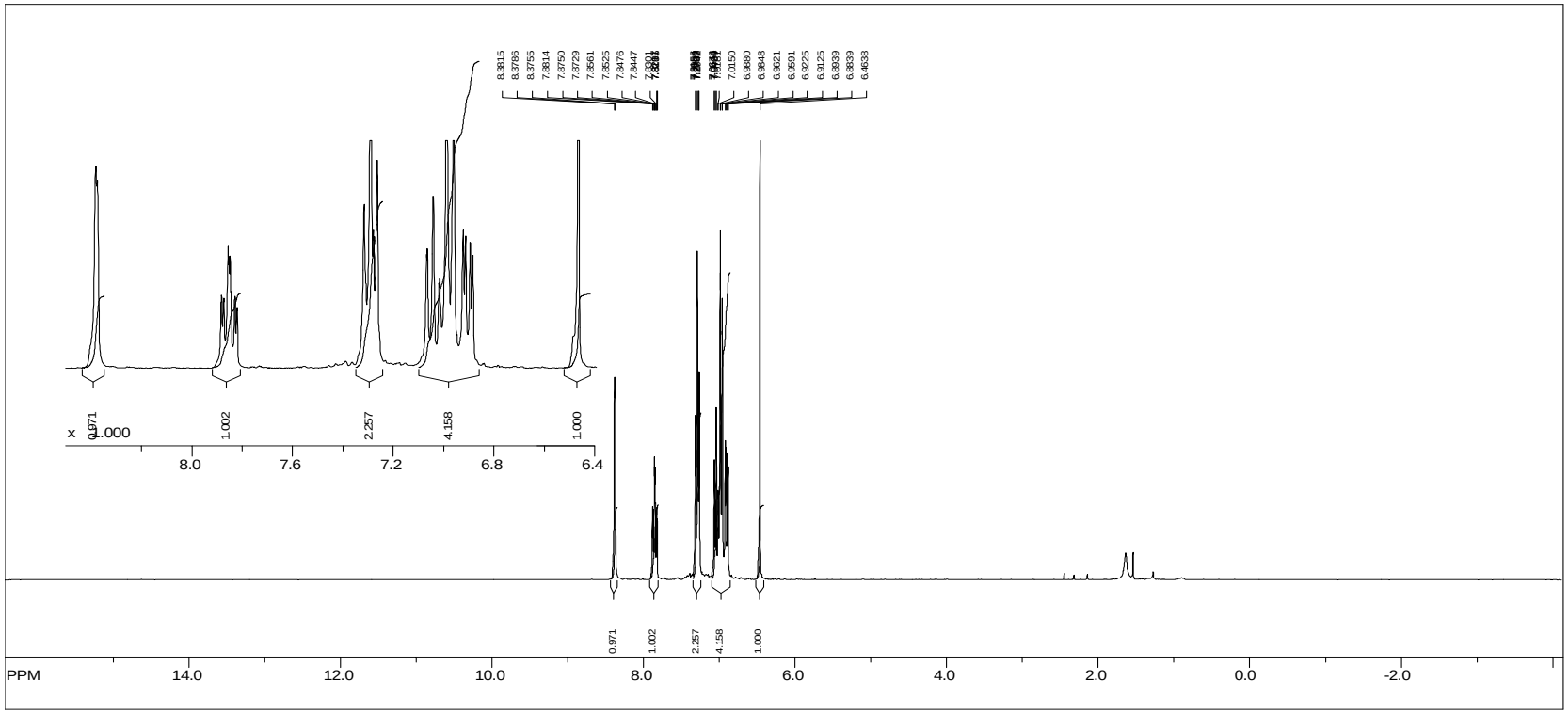
file: Z:\Laina\lmgx\lmgx_83a\4\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 459

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-5-(2-Chloro-1-phenoxyvinyl)-2-fluoropyridine (206)



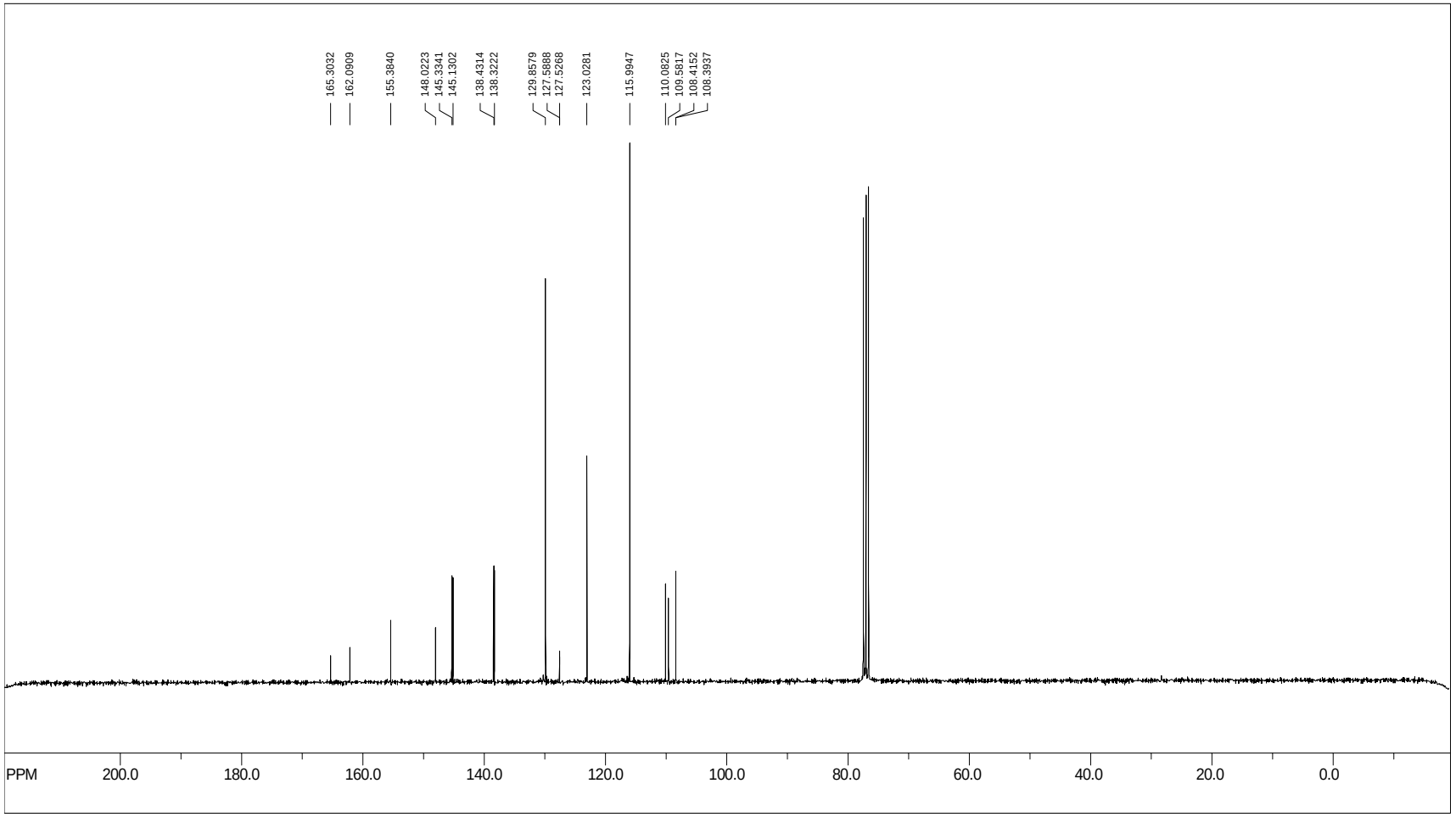
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 9



file: Z:\Laina\lmgx\lmgx_13d\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 8

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000

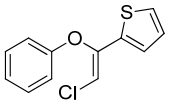
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 18



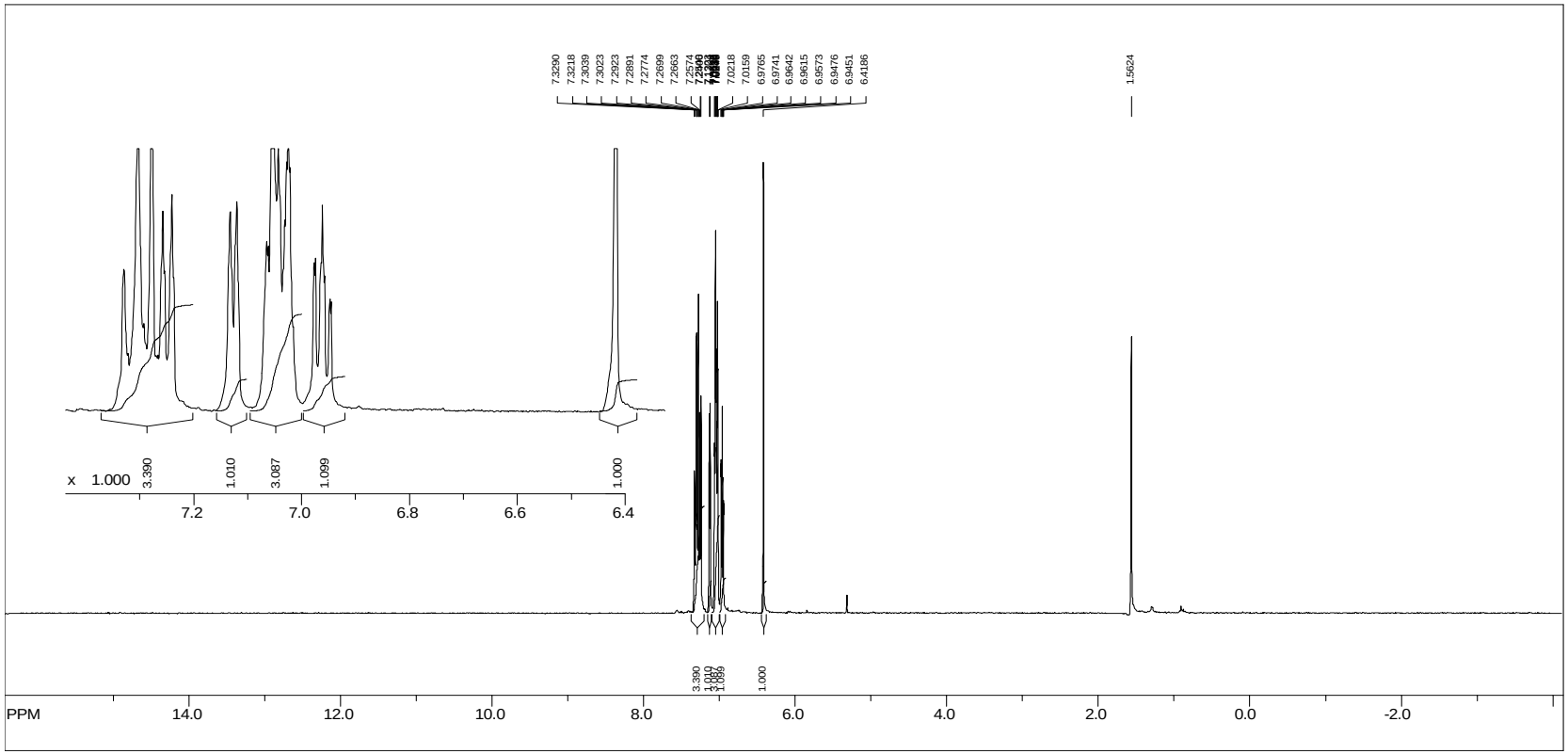
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_13cl\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4096

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-2-(2-Chloro-1-phenoxyvinyl)thiophene (207)



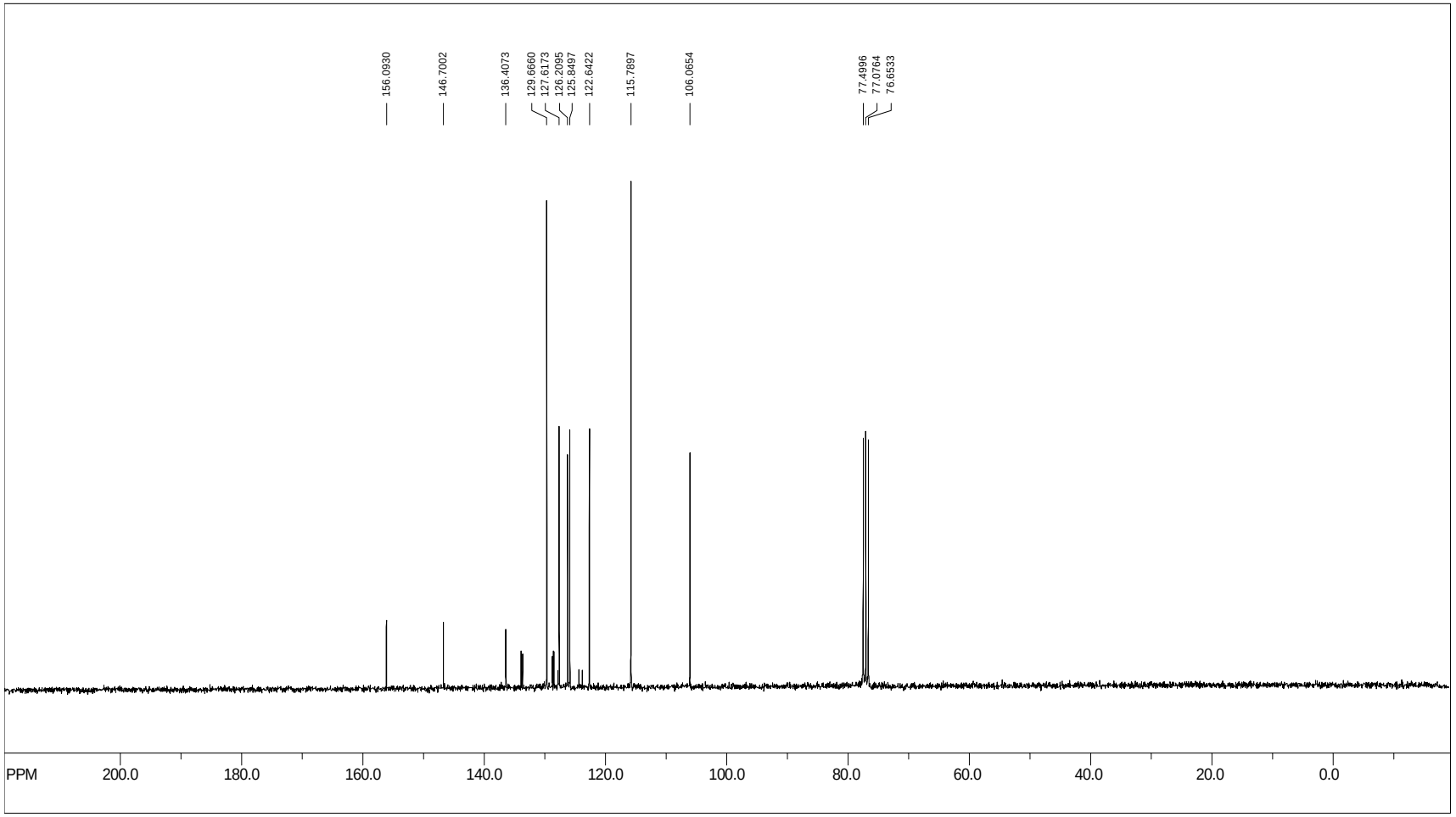
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



file: Z:\Laina\lmgx\lmgx_72b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

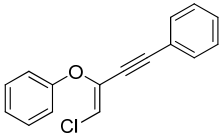
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



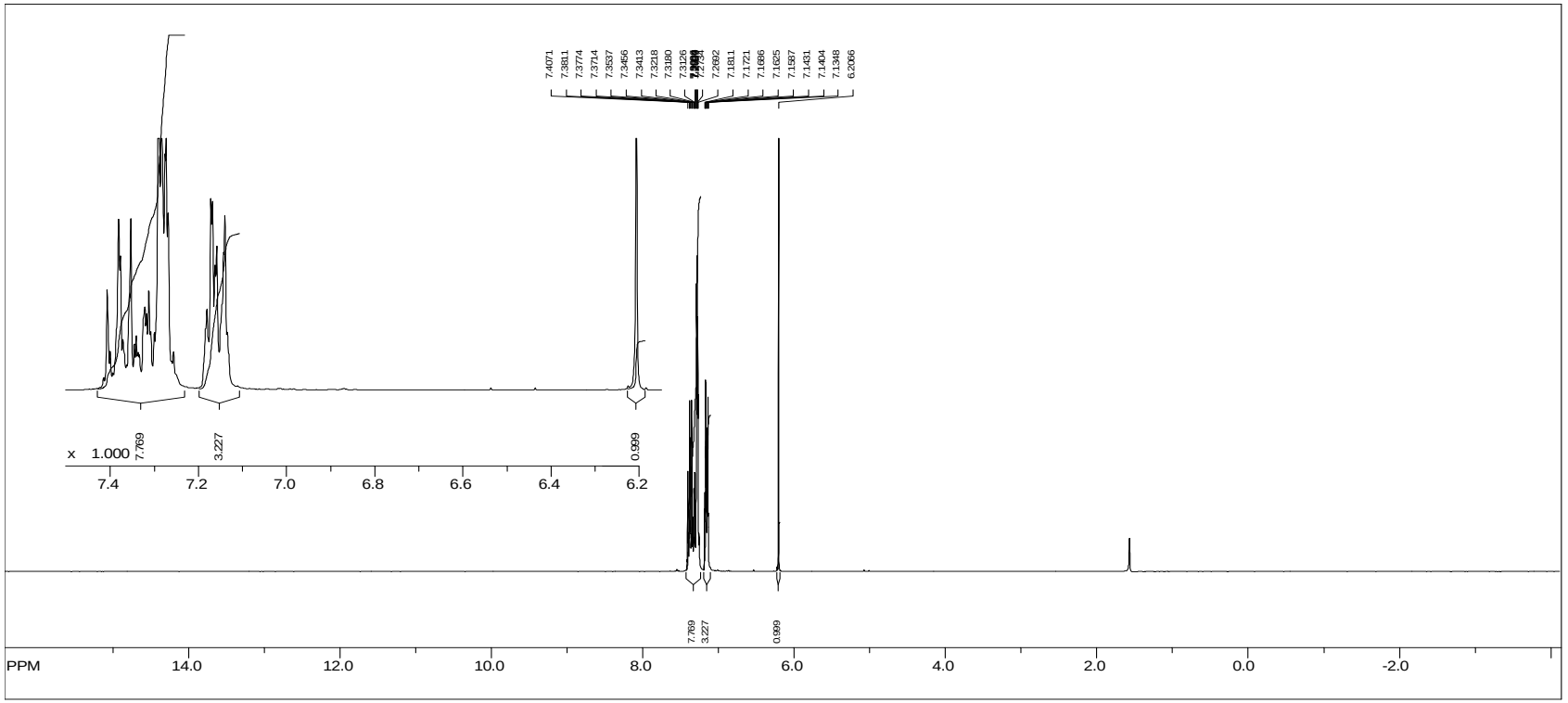
file: Z:\Laina\lmgix\lmgix_17ei\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 409

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(4-Chloro-3-phenoxybut-3-en-1-ynyl)benzene (214)



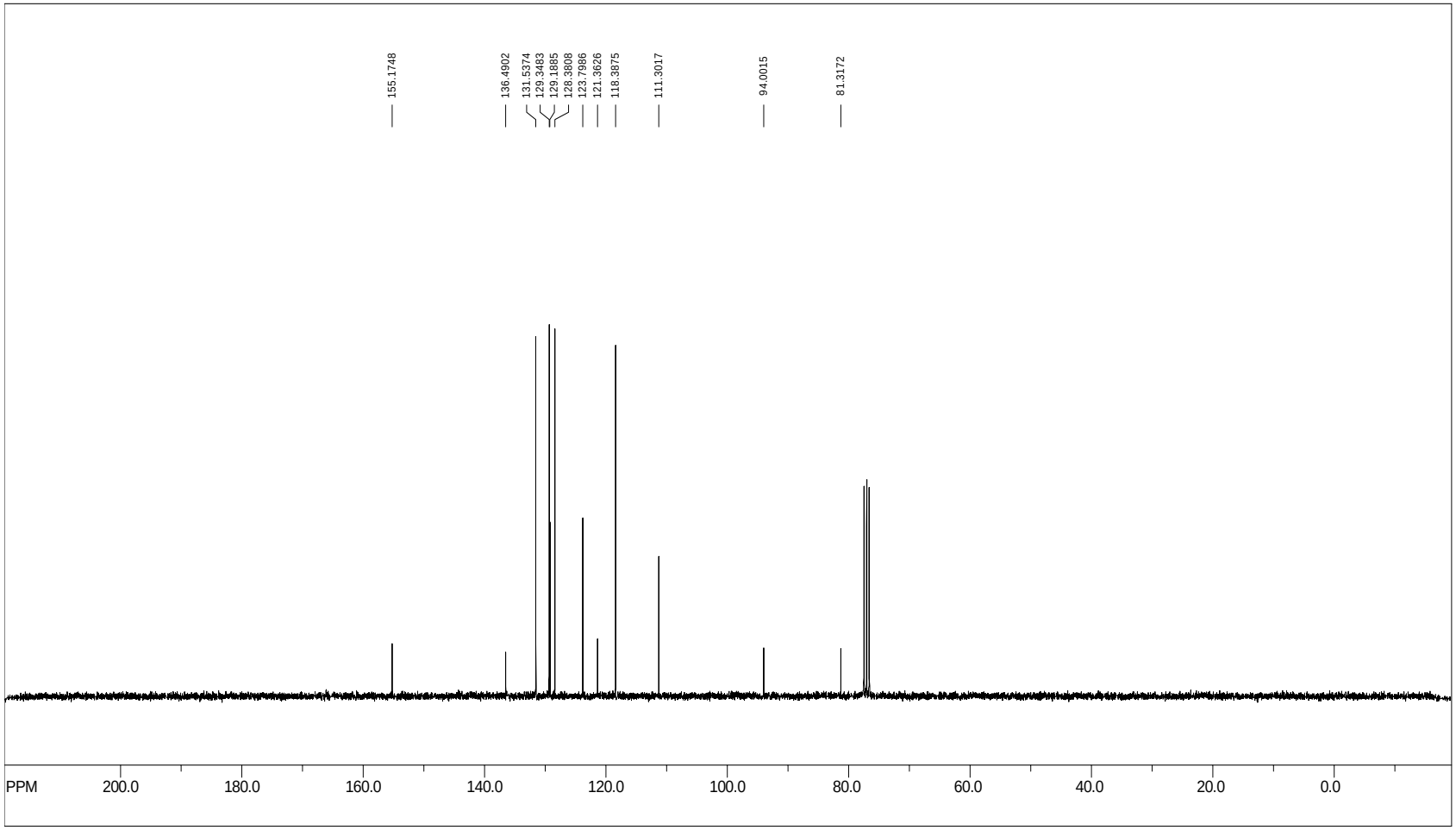
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgx\lmgx_54aii\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

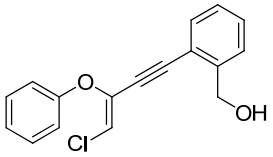
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



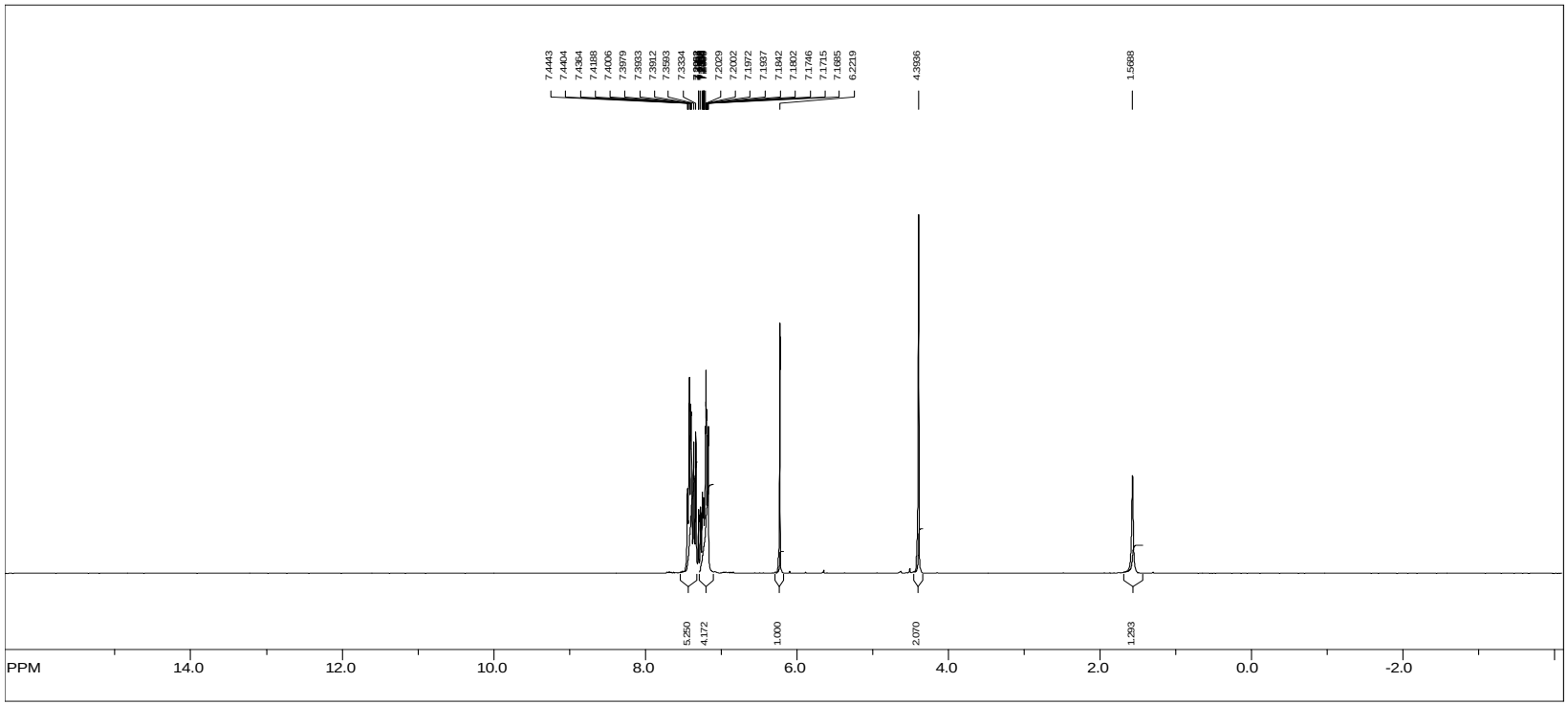
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_54aiii\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 389

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-(2-(4-Chloro-3-phenoxybut-3-en-1-ynyl)phenyl)methanol (215)



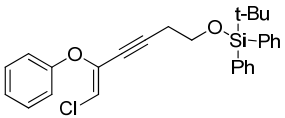
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



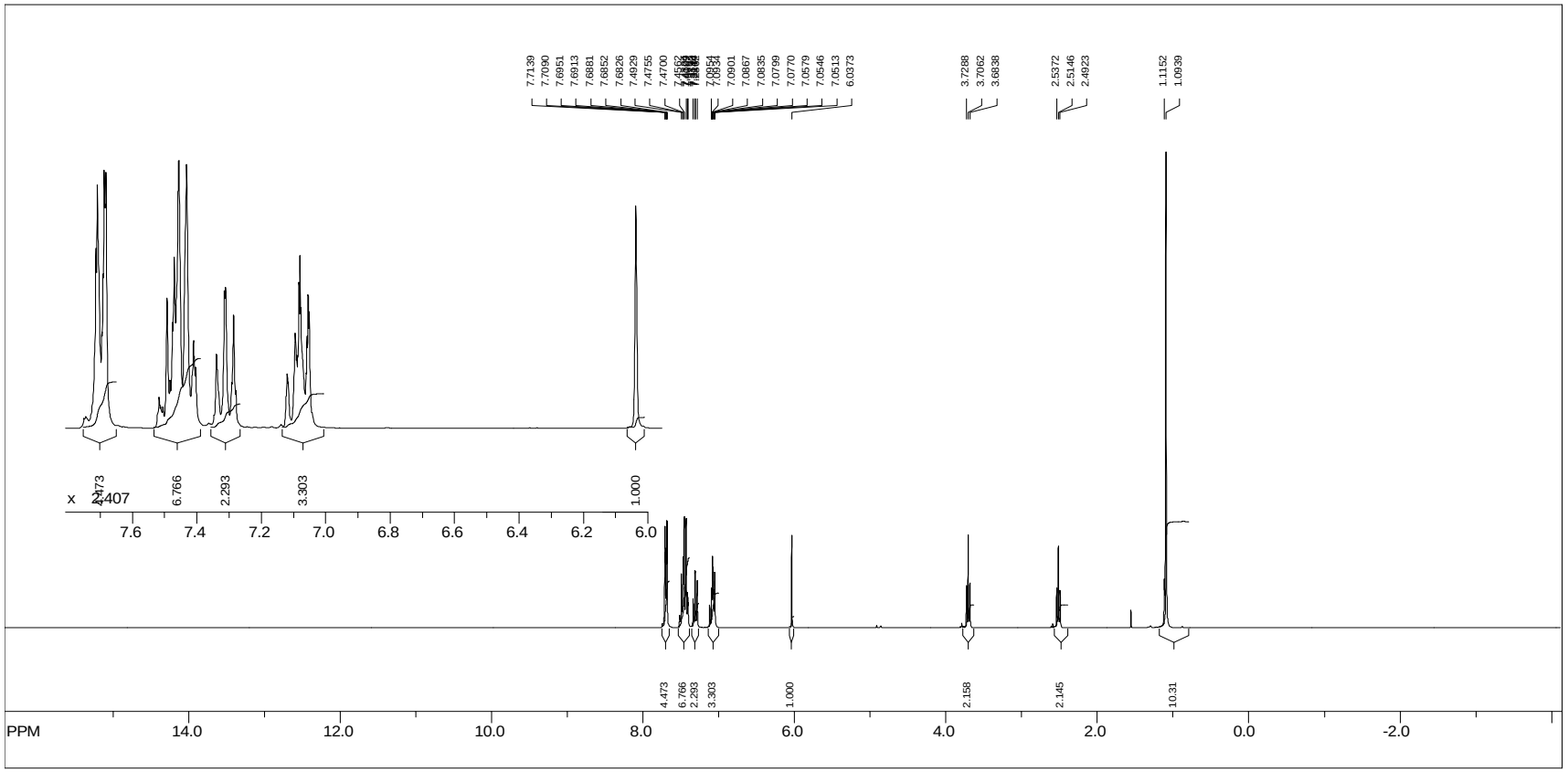
file: Z:\Laina\lmgxii\lmgxiii_25bi\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*Z*)-*tert*-Butyl(6-chloro-5-phenoxyhex-5-en-3-ynyloxy)diphenylsilane (216)



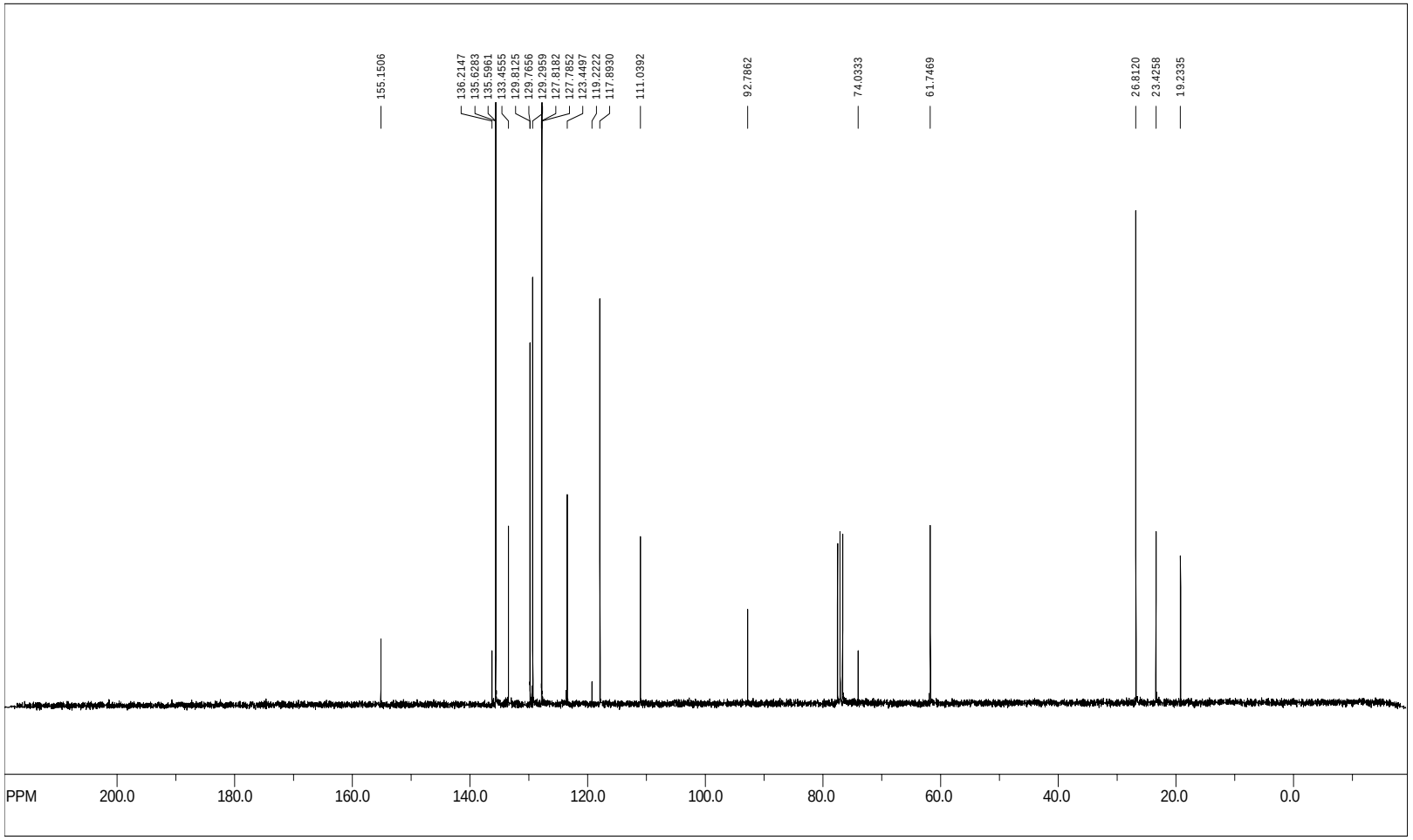
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



file: Z:\Laina\lmgx\lmgx_56ai\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

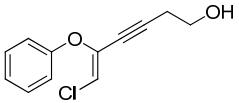
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



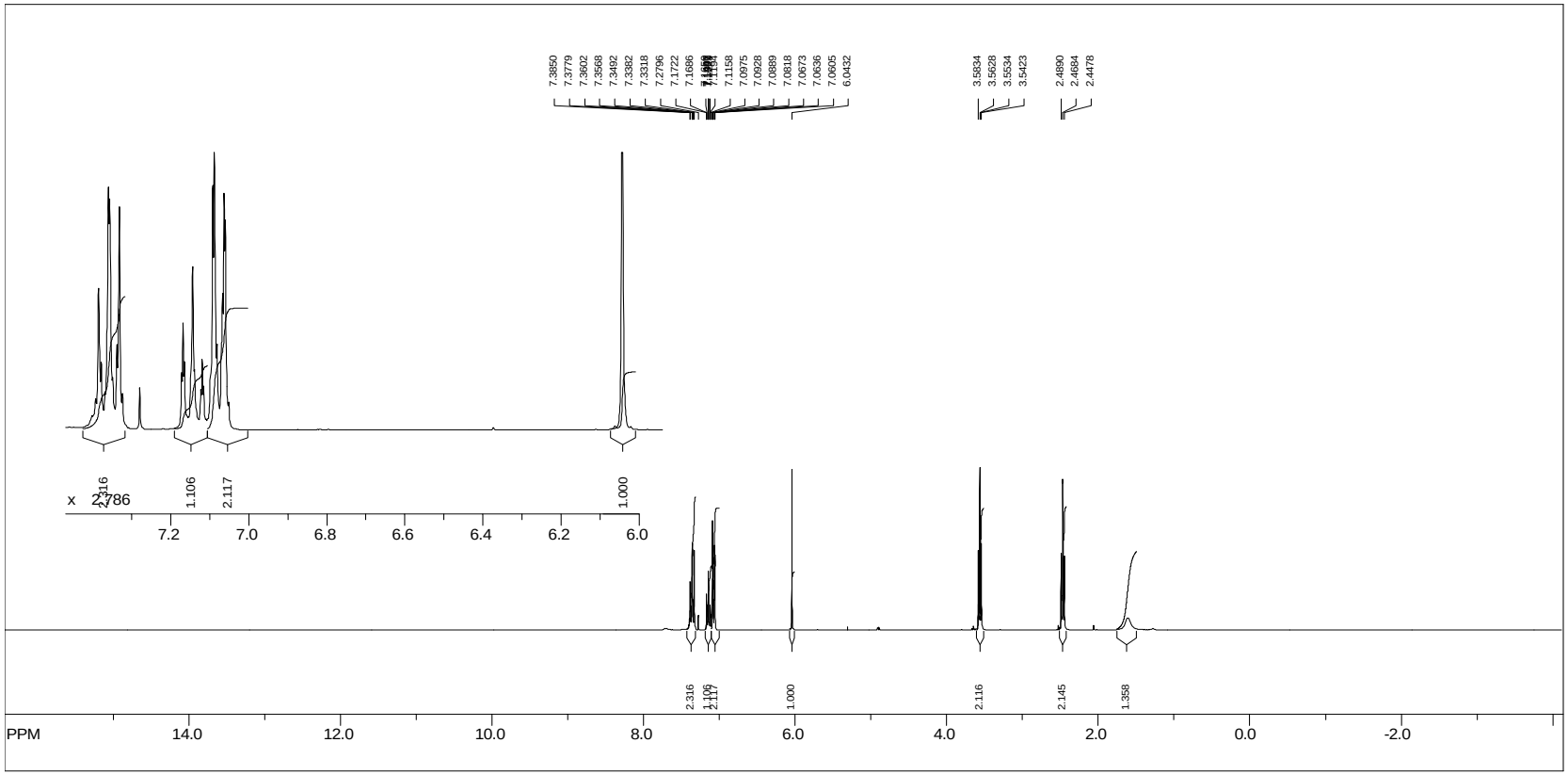
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_56ai\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-6-Chloro-5-Phenoxyhex-5-en-3-yn-1-ol (217)



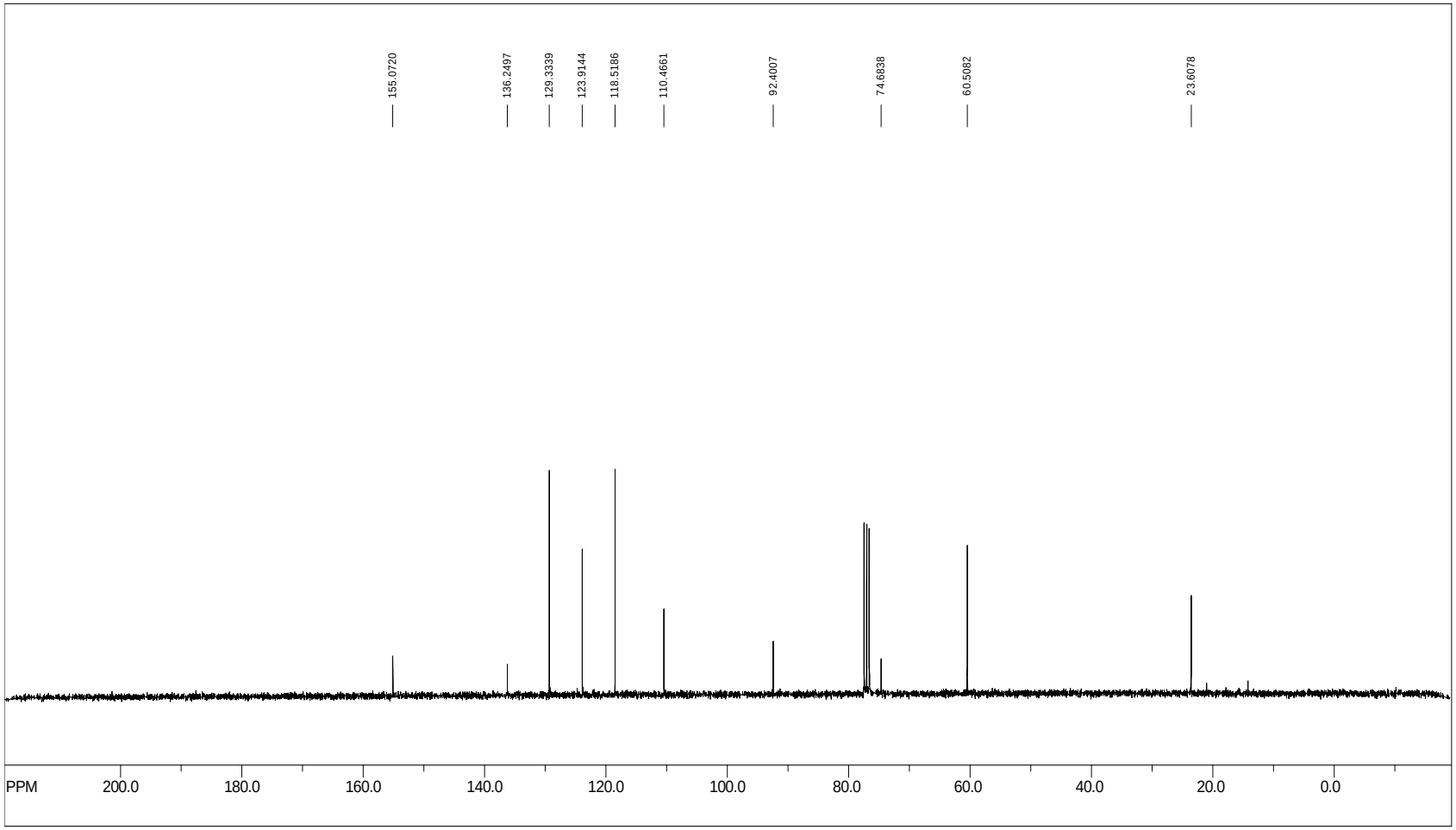
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgx\lmgx_55c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 6

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

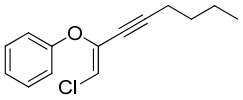
SpinWorks 2.5: sonogashira with 3-butyn-1-ol



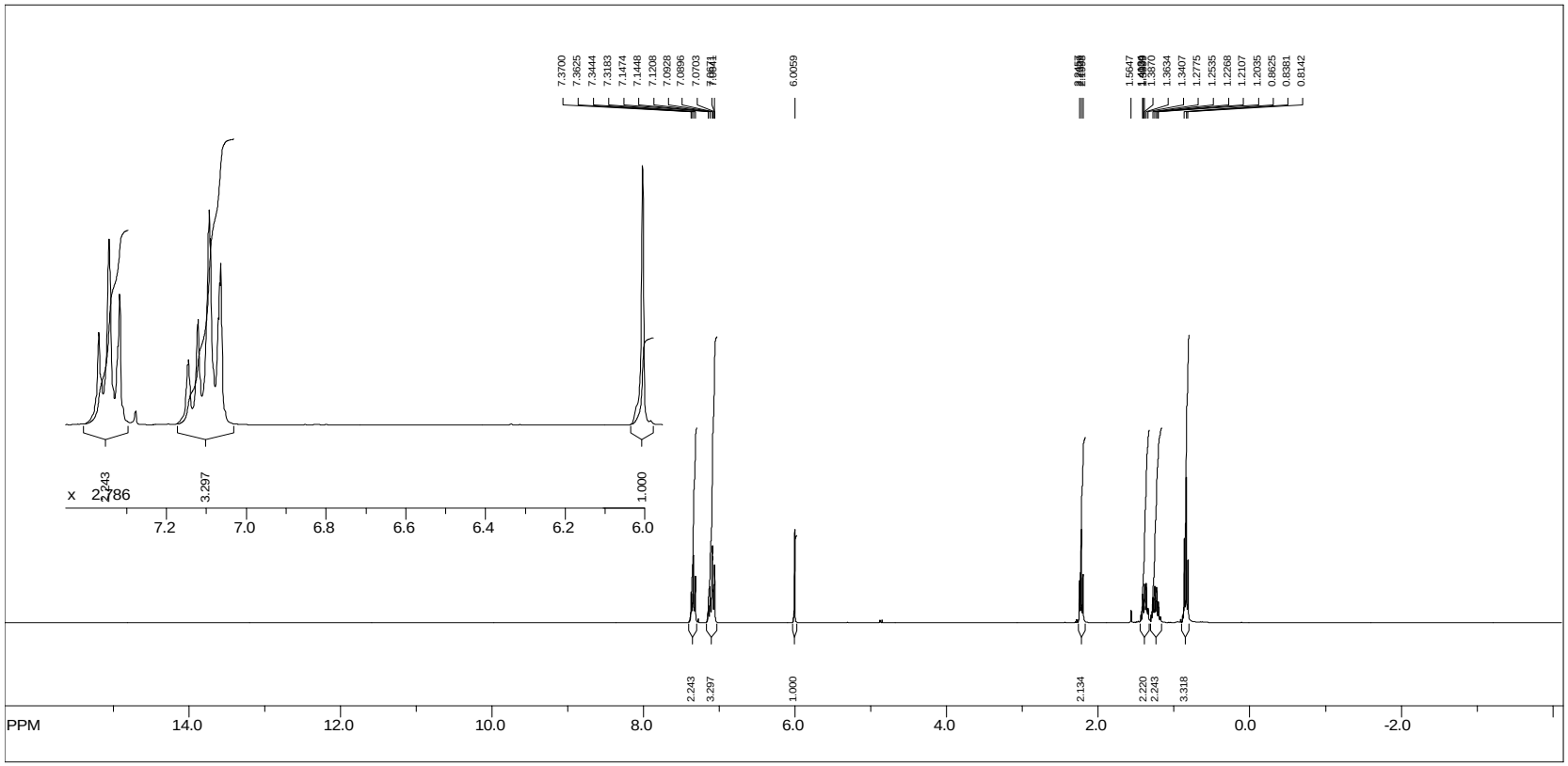
file: C:\Users\Laina\Documents\WORK\NMR\lmgix\lmgix_21a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 302

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*Z*)-1-(1-Chlorooct-1-en-3-yn-2-yloxy)benzene (218)



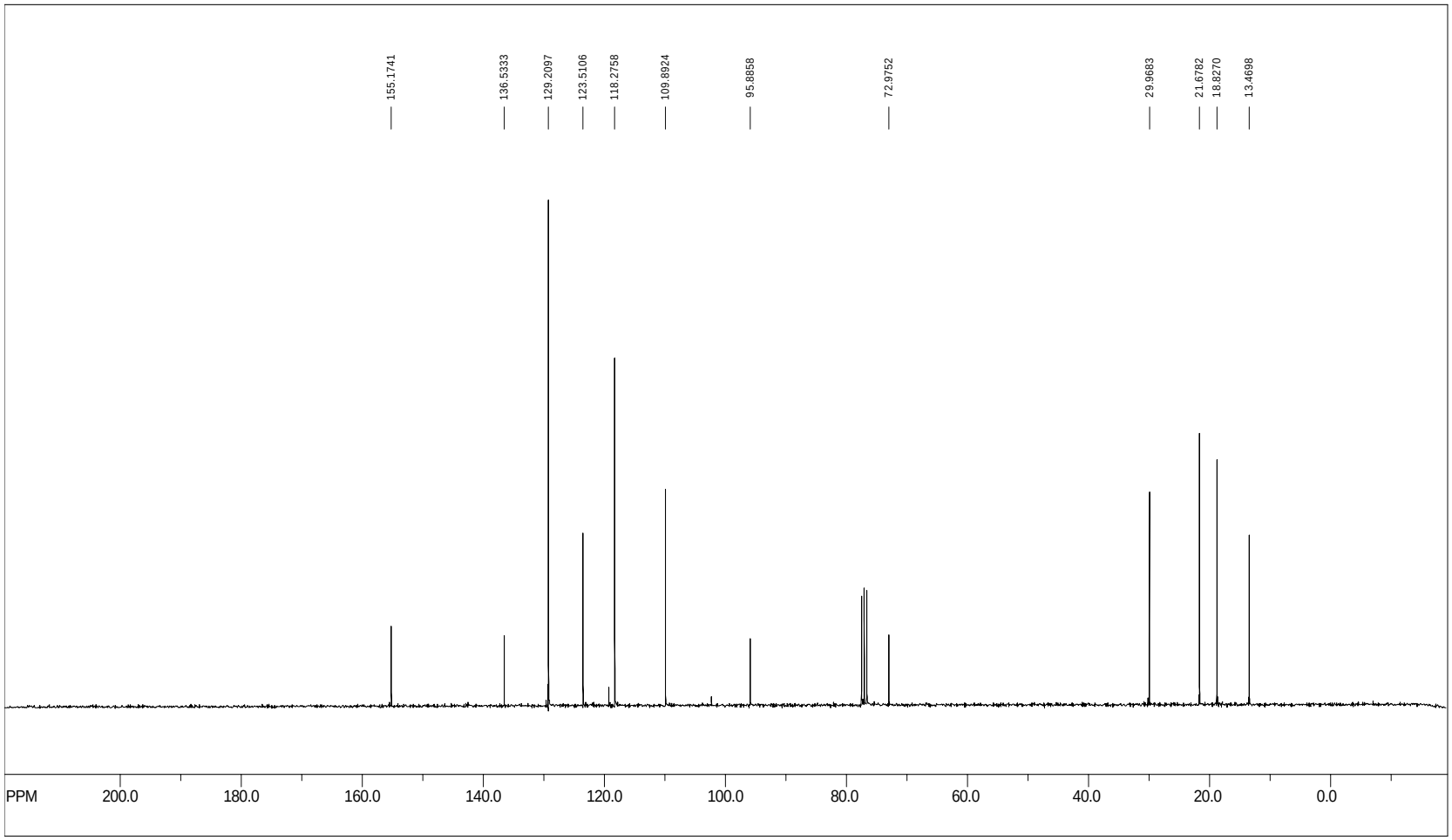
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



file: Z:\Laina\lmgx\lmgx_59bl\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

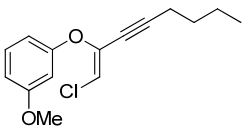
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



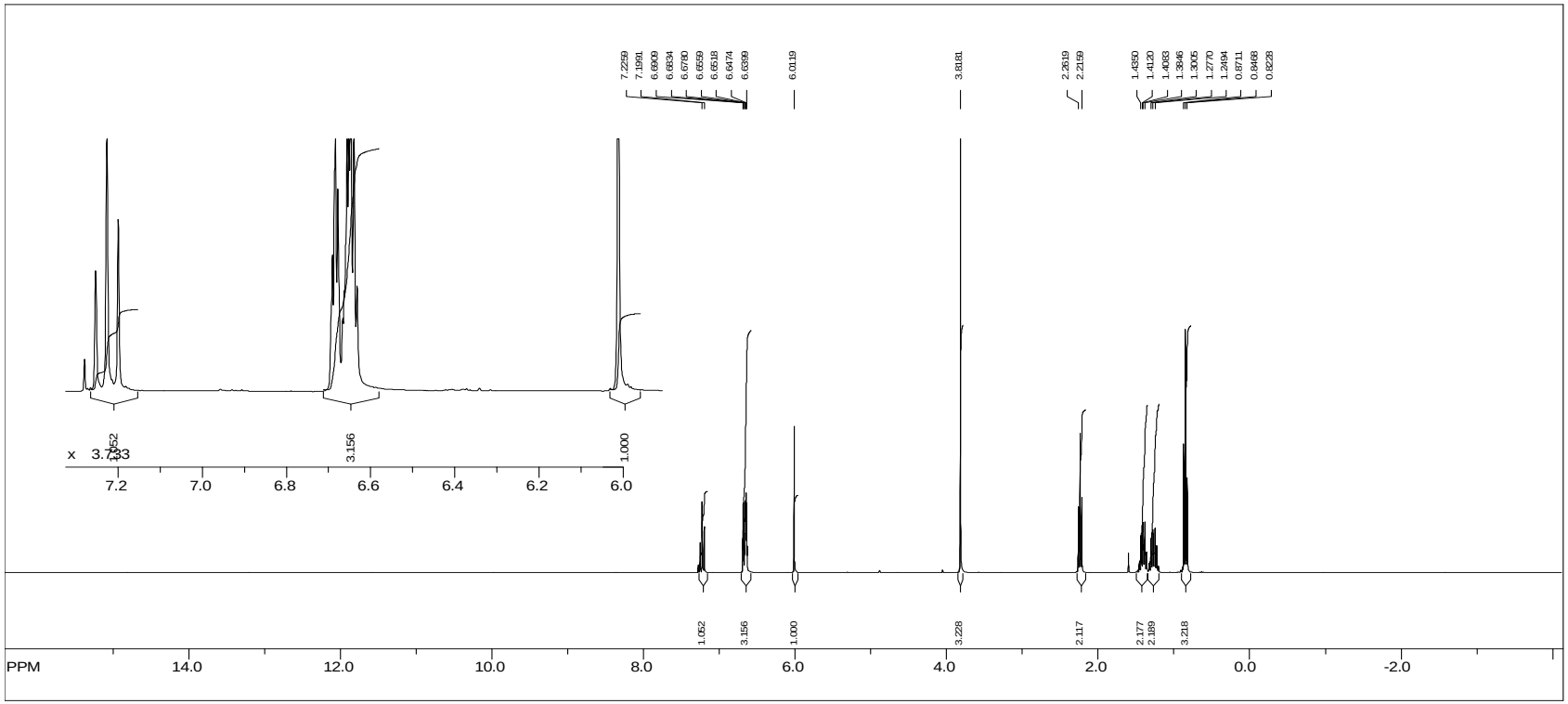
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_59b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 420

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(1-Chlorooct-1-en-2-yn-2-yloxy)-3-methoxybenzene (219)



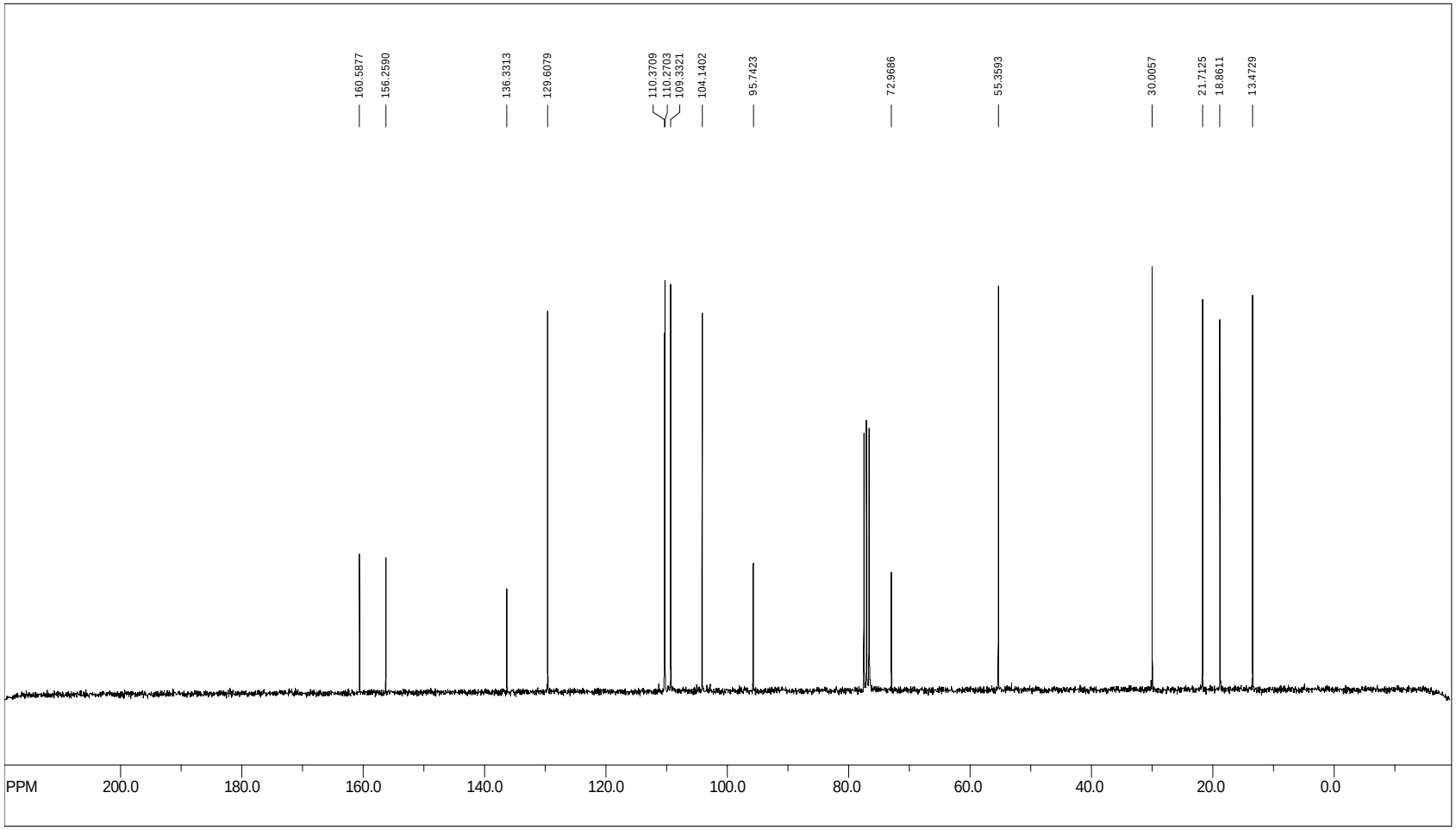
SpinWorks 2.5: f3+4



file: Z:\Laina\lmgx\lmgx_58a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

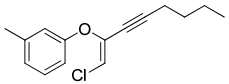
SpinWorks 2.5: f3+4



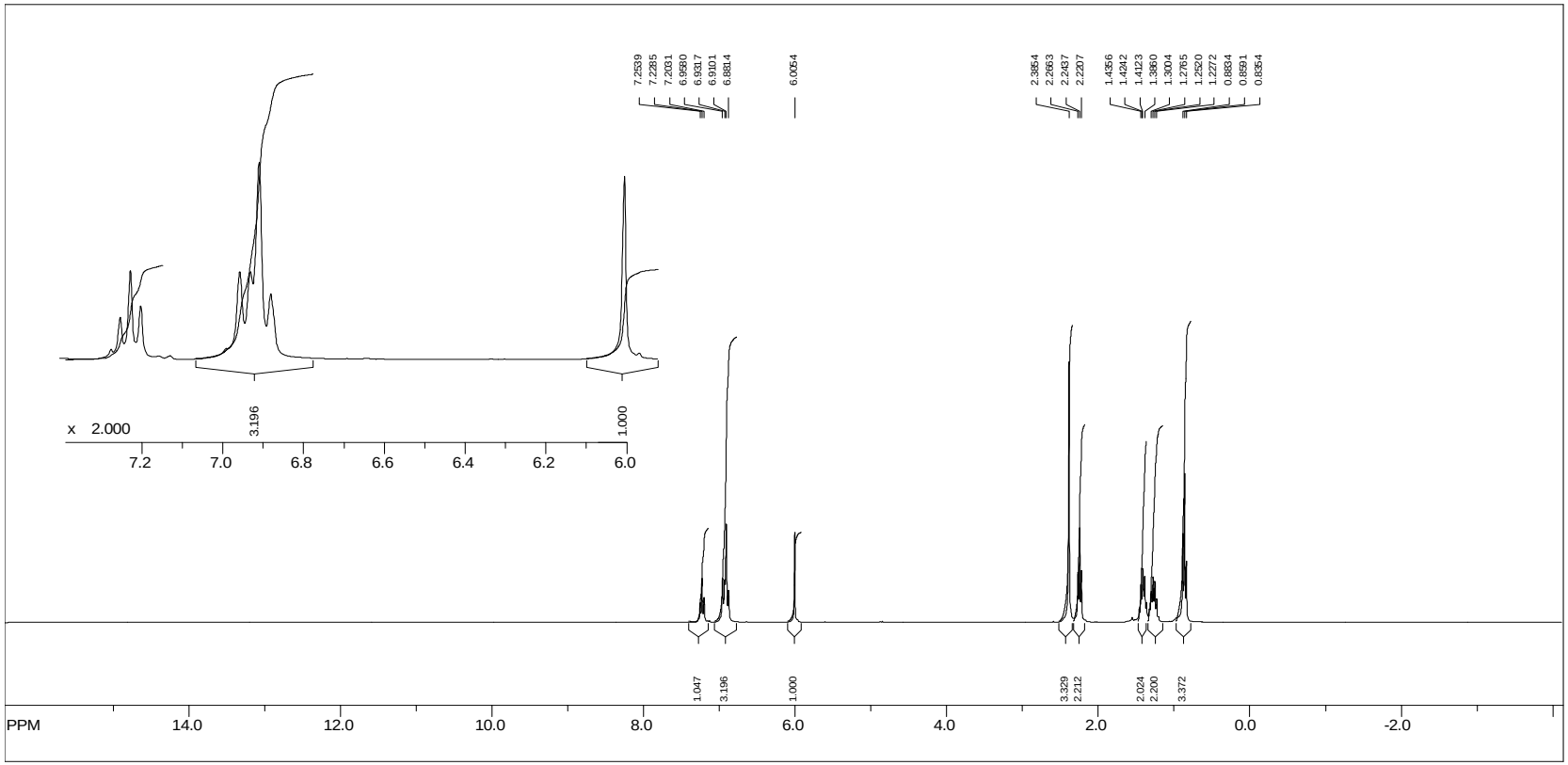
file: Z:\Laina\lmgx\lmgx_58a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 339

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(1-Chlorooct-1-en-2-yn-2-yloxy)-3-methylbenzene (220)



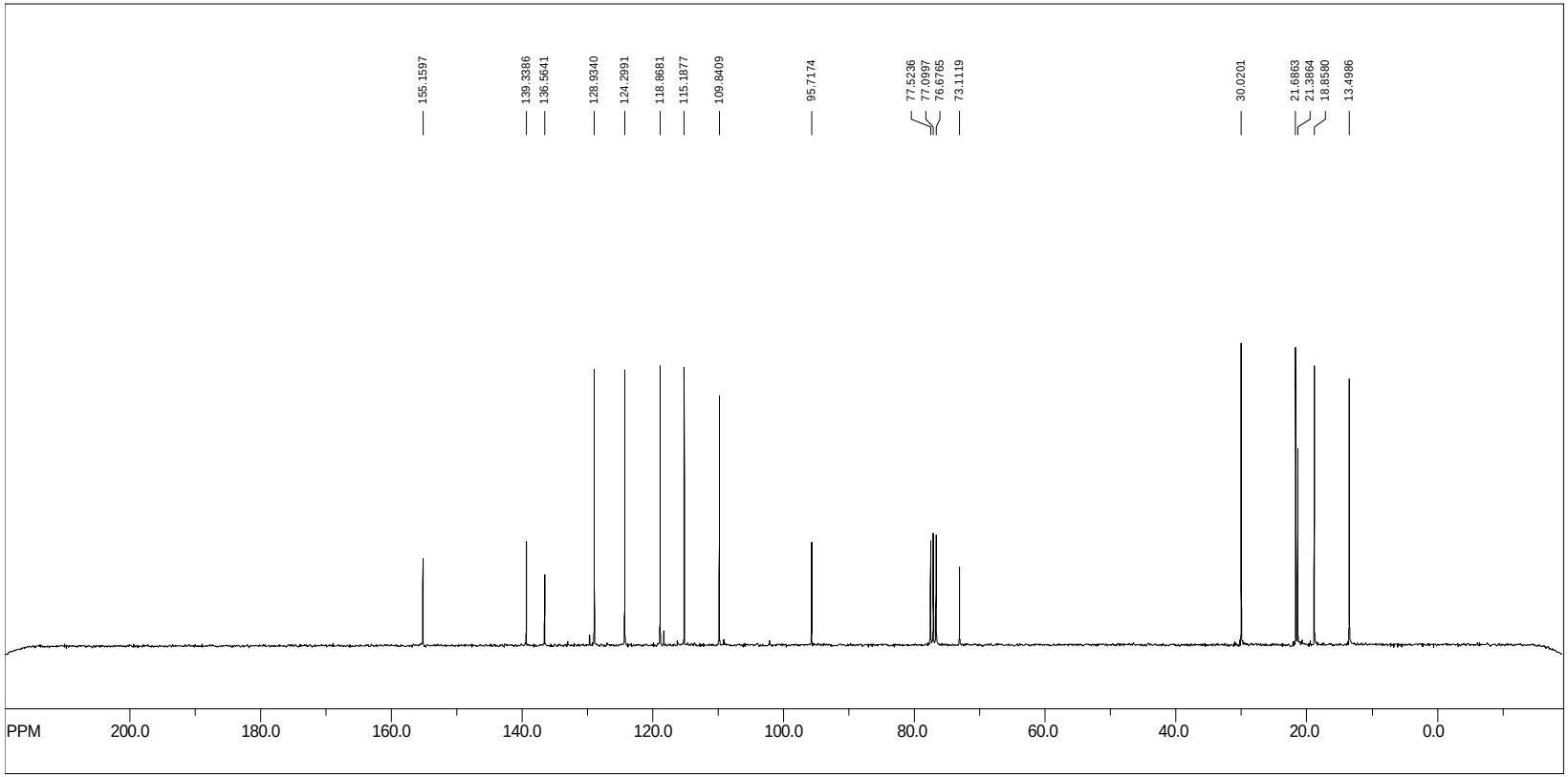
SpinWorks 2.5: rt sonogashira between m-cresol derived enamine and hexyne



file: Z:\Laina\lmgix\lmgix_83a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

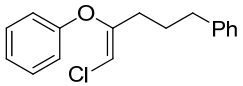
SpinWorks 2.5: rt sonogashira between m-cresol derived enamine and hexyne



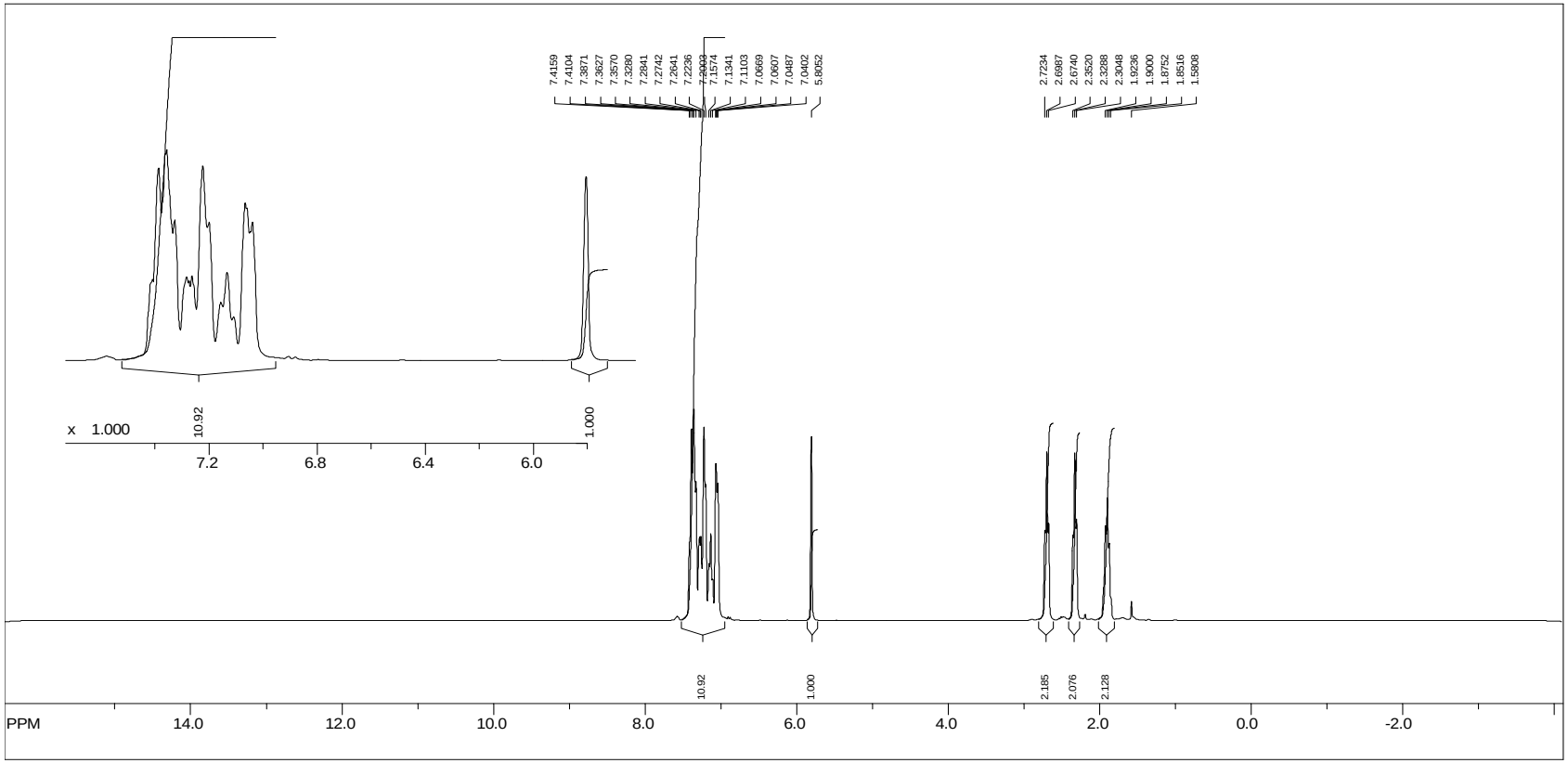
file: Z:\Laina\lmgix\lmgix_83a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-1-(5-Chloro-4-phenoxypent-4-enyl)benzene (221)



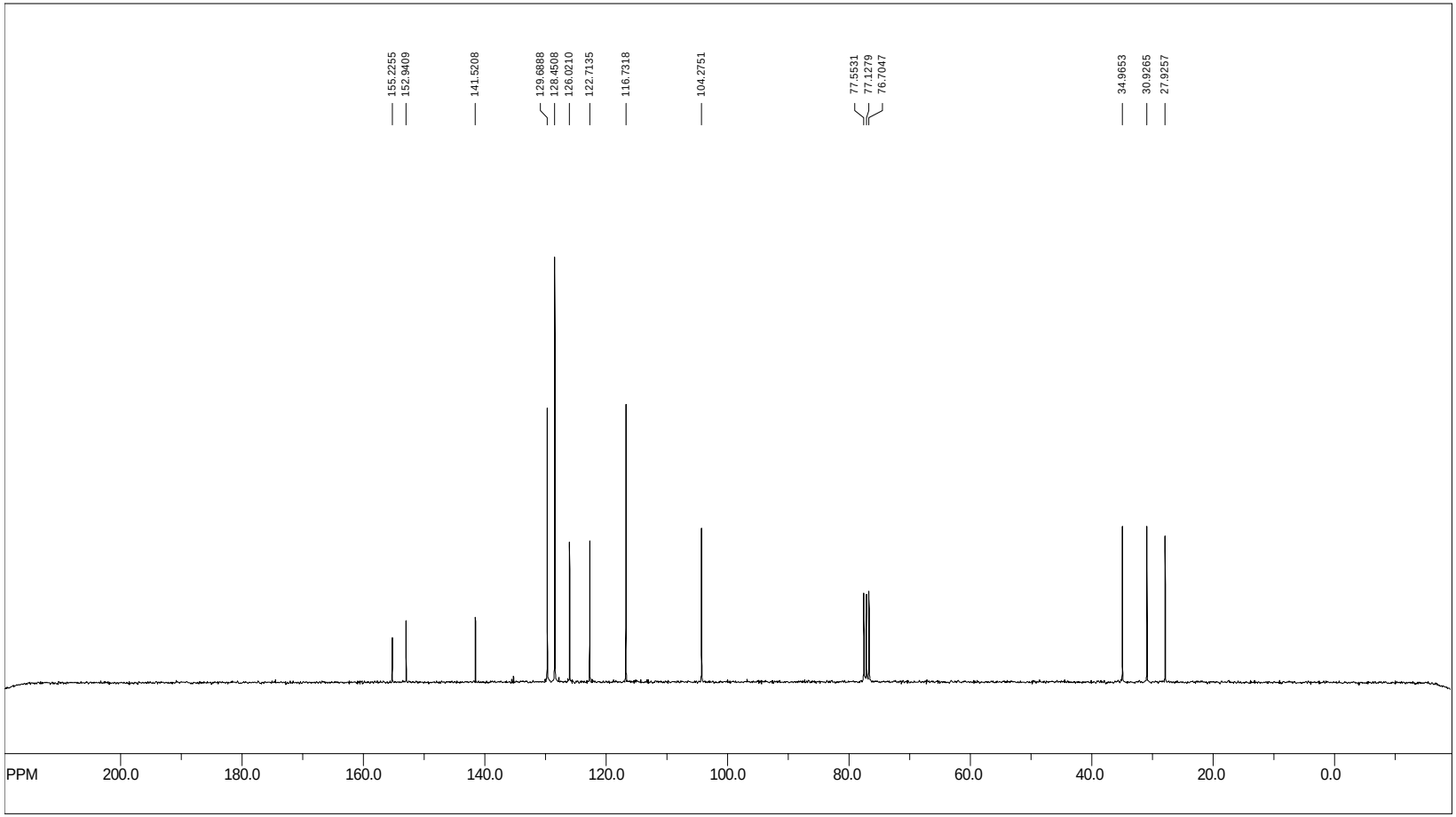
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxii\lmgxii_57a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

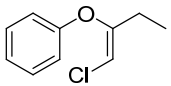
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



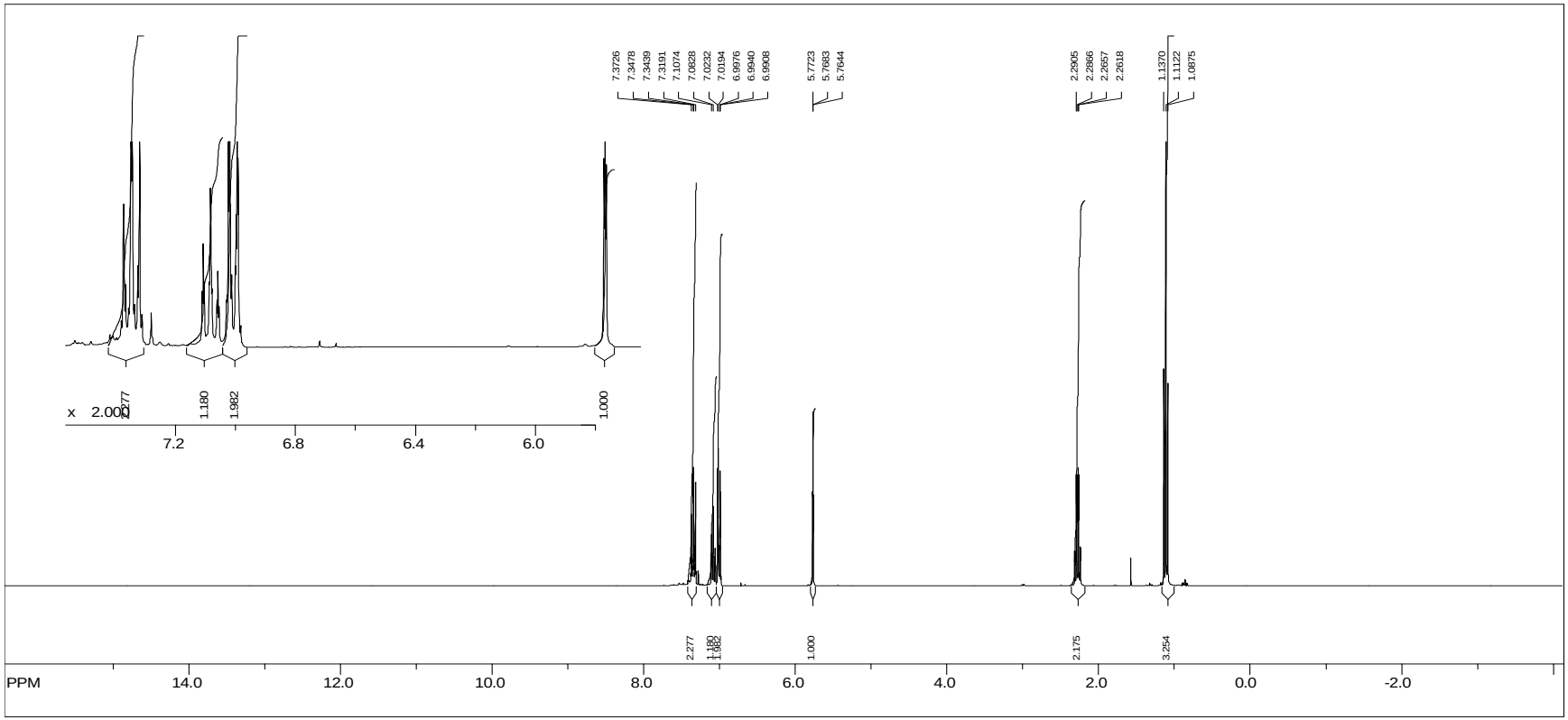
file: Z:\Laina\lmgxii\lmgxii_57a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-1-(1-Chlorobut-1-en-2-yloxy)benzene (222**)**



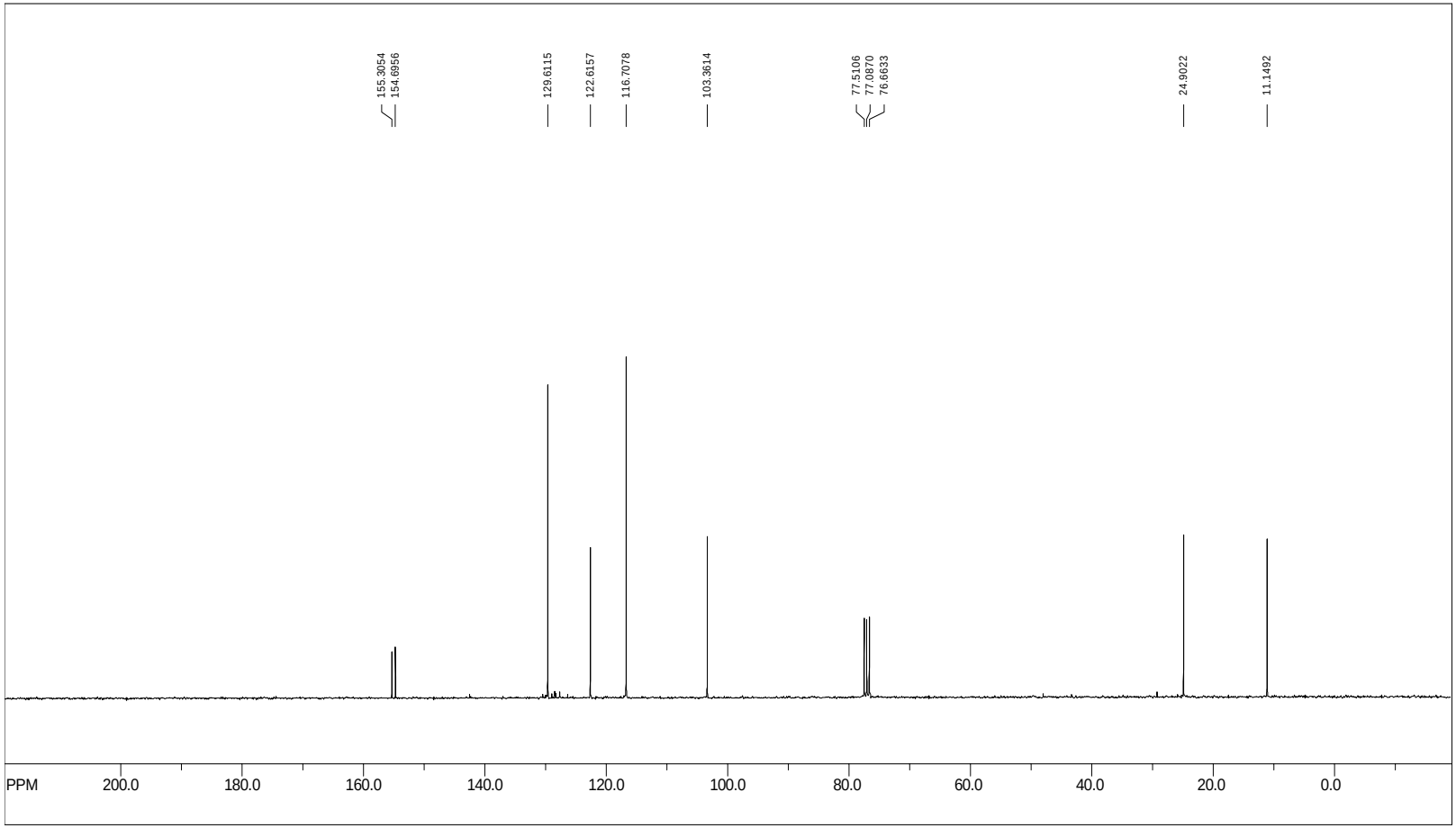
SpinWorks 2.5: (Z)-1-phenoxy-1-ethyl-2-chloroethene



file: Z:\Laina\lmgvii\lmgvii_84a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

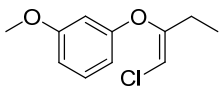
SpinWorks 2.5: (Z)-1-phenoxy-1-ethyl-2-chloroethene



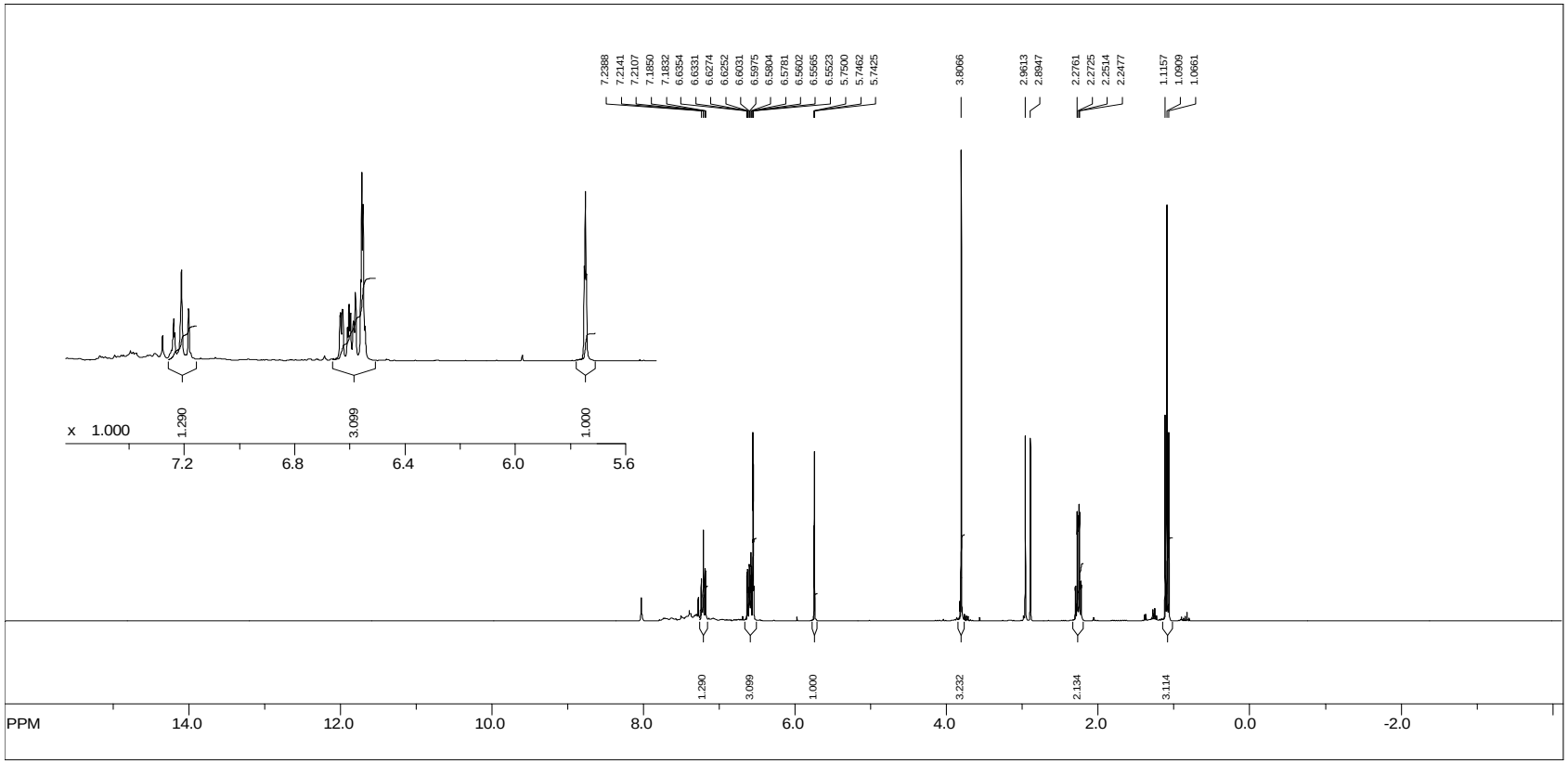
file: Z:\Laina\lmgvii\lmgvii_84a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 205

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-1-(1-Chlorobut-1-en-2-yloxy)-3-methoxybenzene (223)



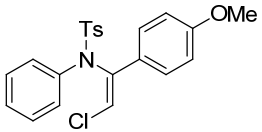
SpinWorks 2.5: negishi between diethylzinc and m-methoxyphenol derivative



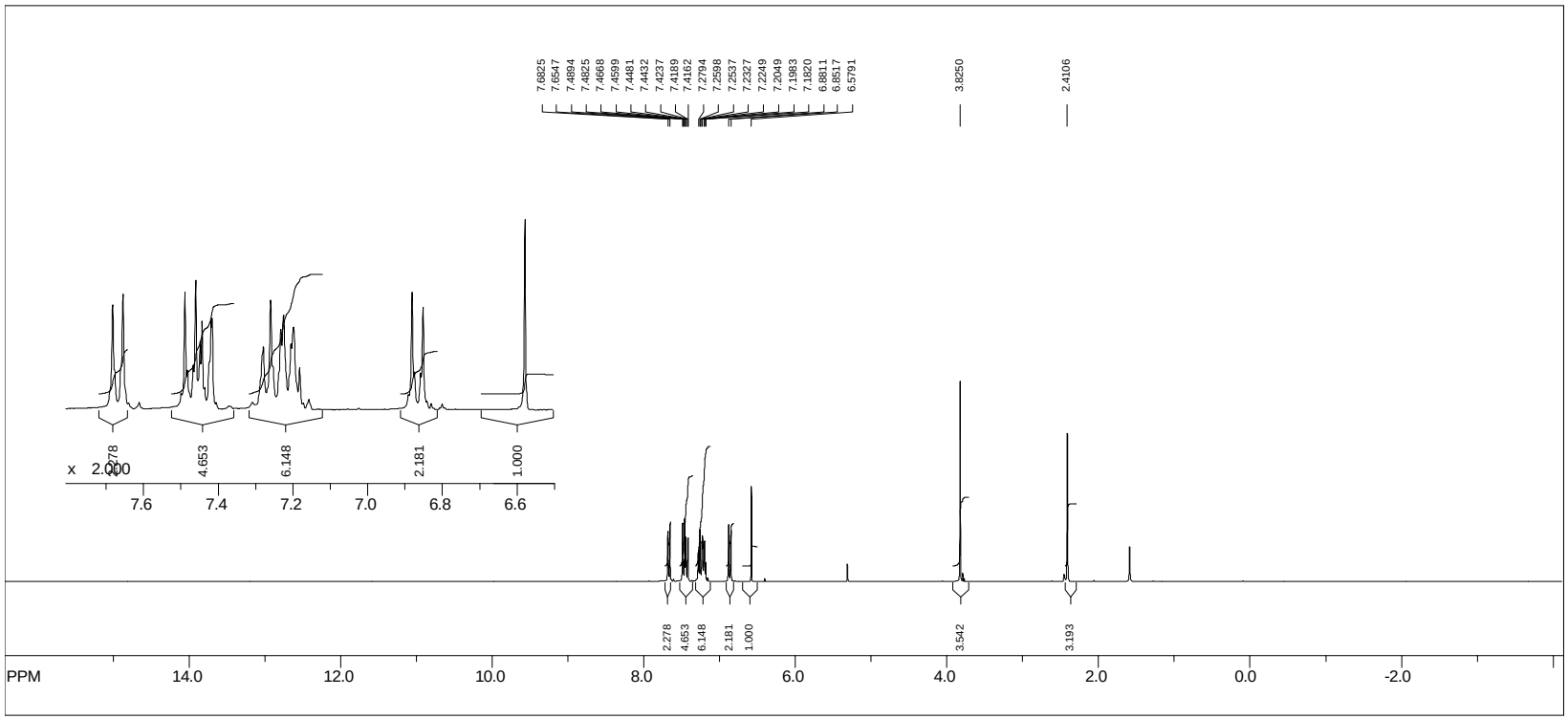
file: Z:\Laina\lmgx\lmgx_24\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(Z)-N-(2-Chloro-1-(4-methoxyphenyl)vinyl)-4-methyl-*N*-phenylbenzenesulfonamide (225)



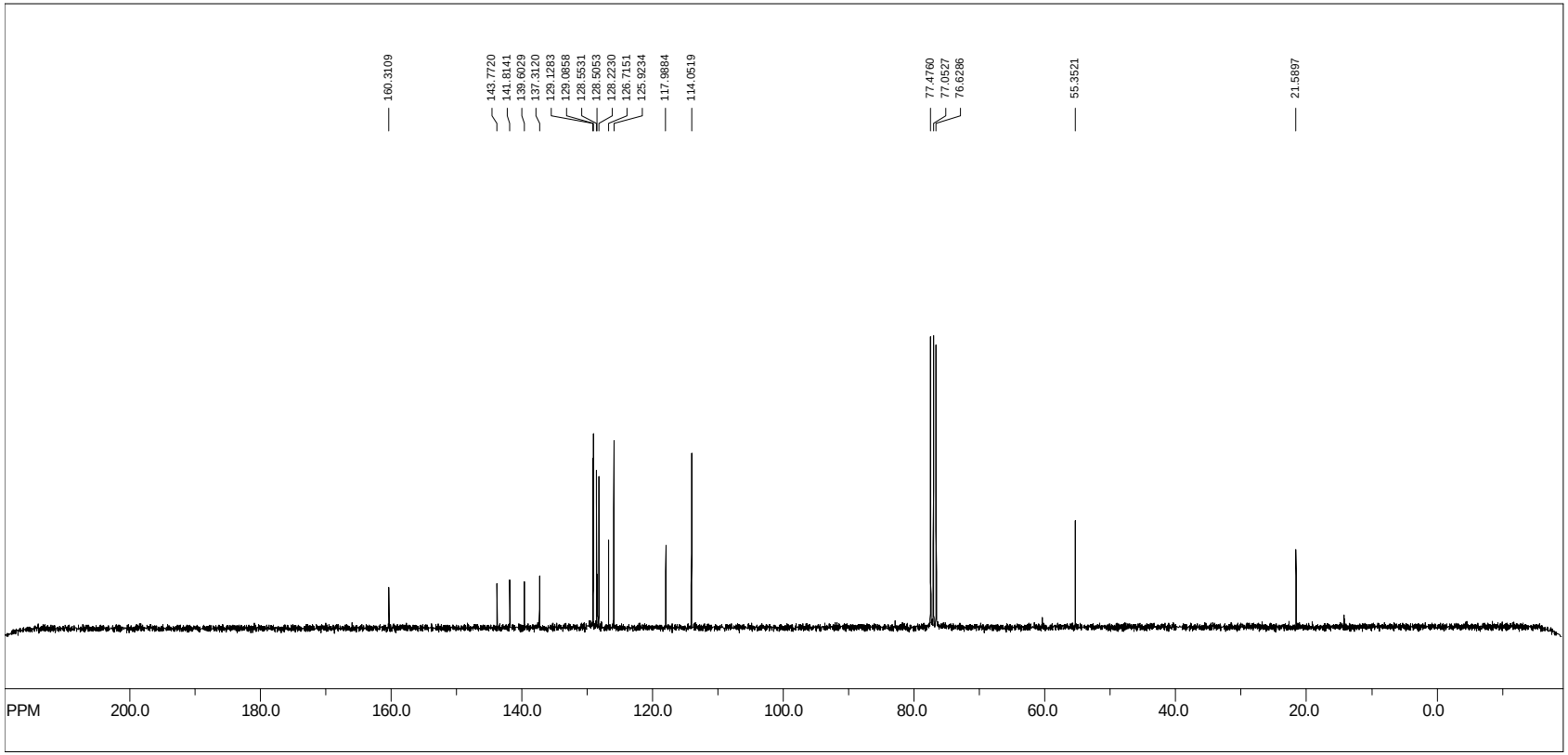
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



file: Z:\Laina\lmgxi\lmgxi_44e\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

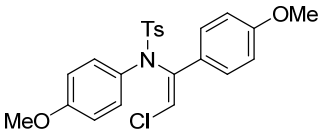
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



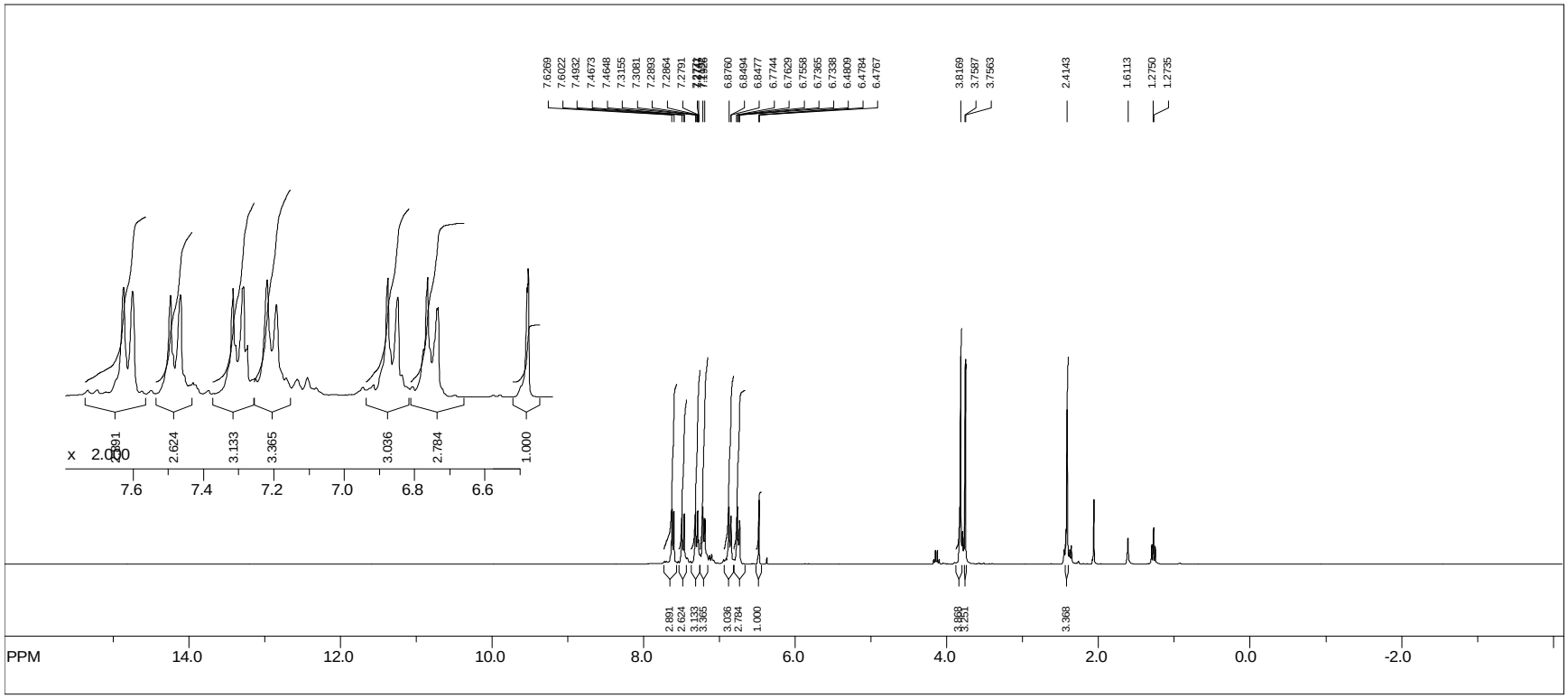
file: Z:\Laina\lmgxl\lmgxl_56d\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 910

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(Z)-N-(2-Chloro-1-(4-methoxylphenyl)vinyl)*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide (226)



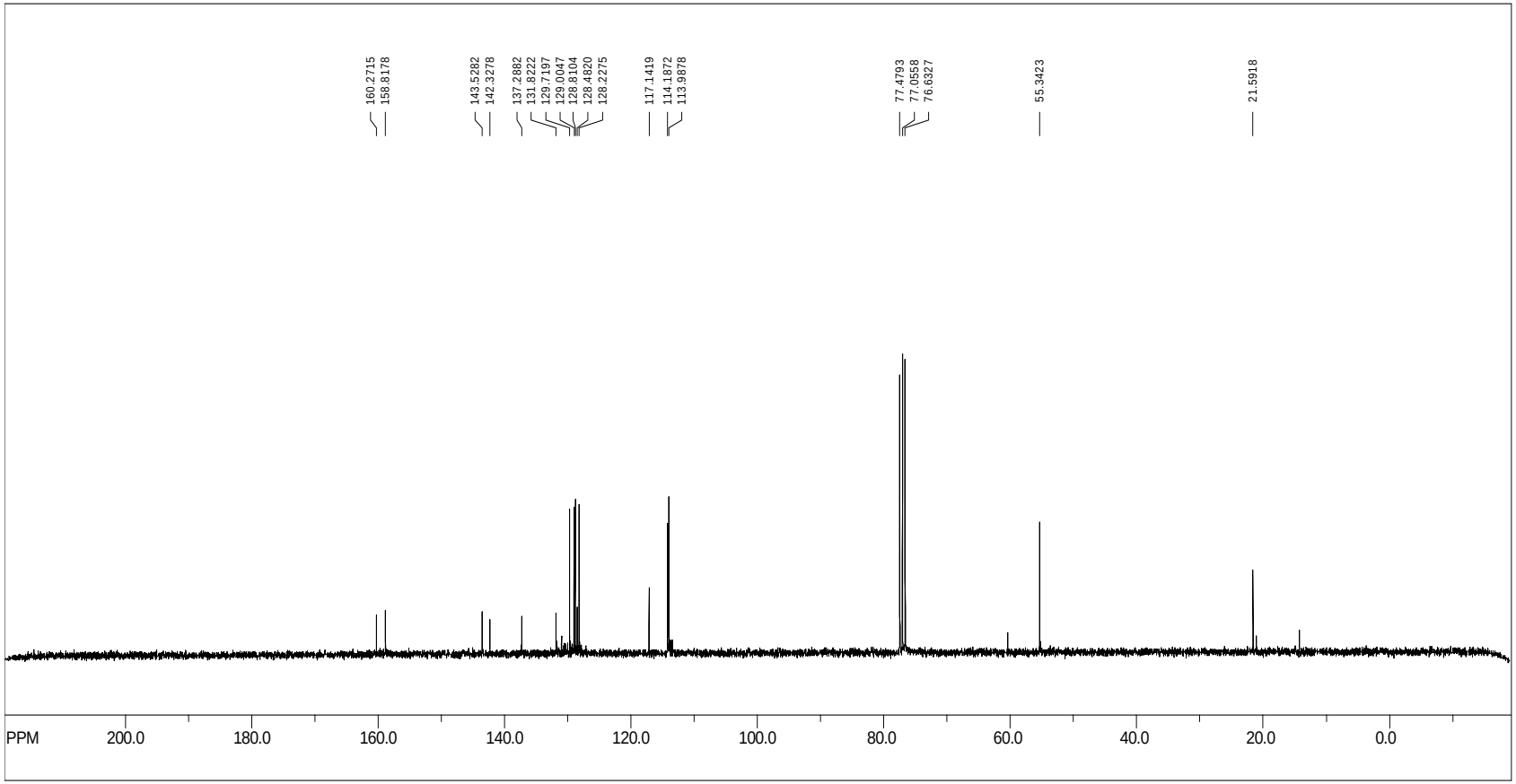
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



file: Z:\Laina\lmgxi\lmgxi_57c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

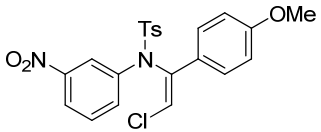
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



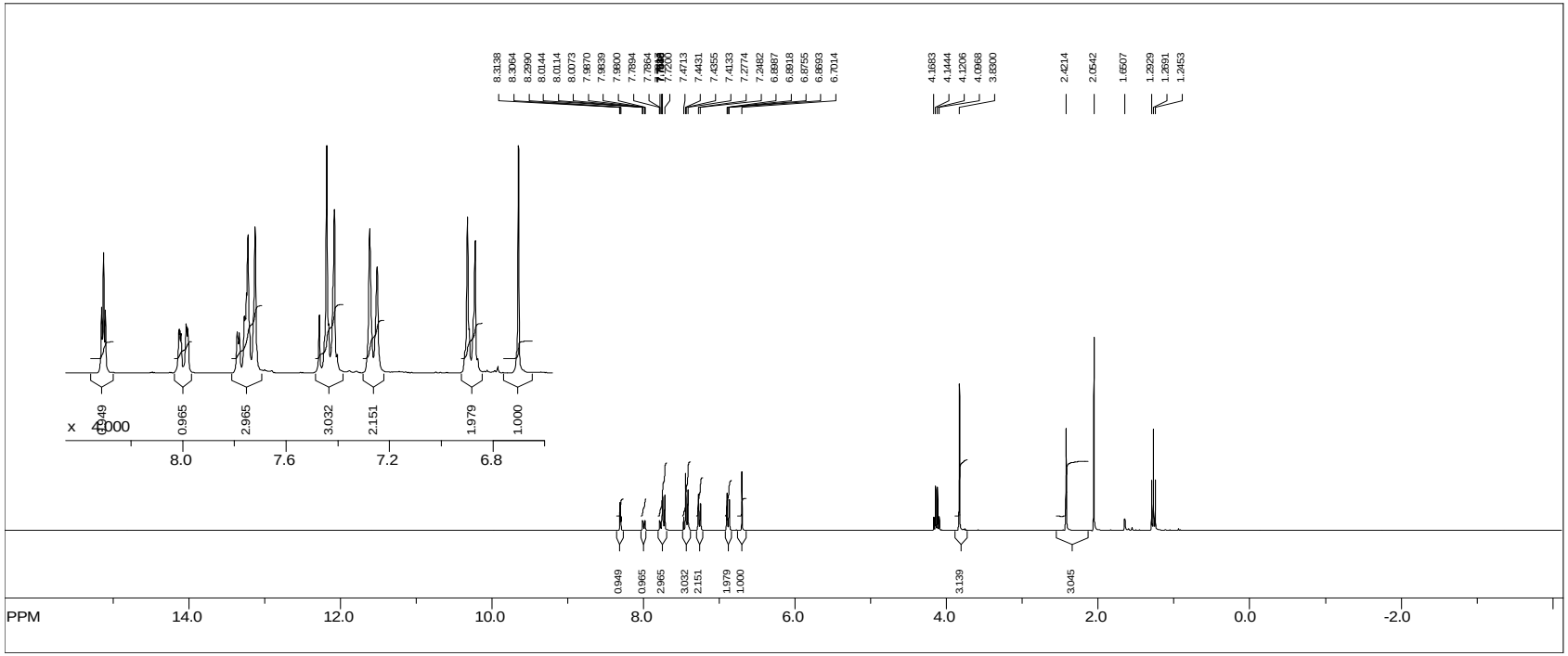
file: Z:\Laina\lmgxi\lmgxi_57c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 611

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(Z)-N-(2-Chloro-1-(4-methoxylphenyl)vinyl)*N*-(3-nitrophenyl)-4-methylbenzenesulfonamide (227)



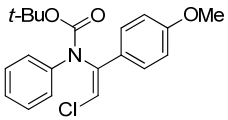
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



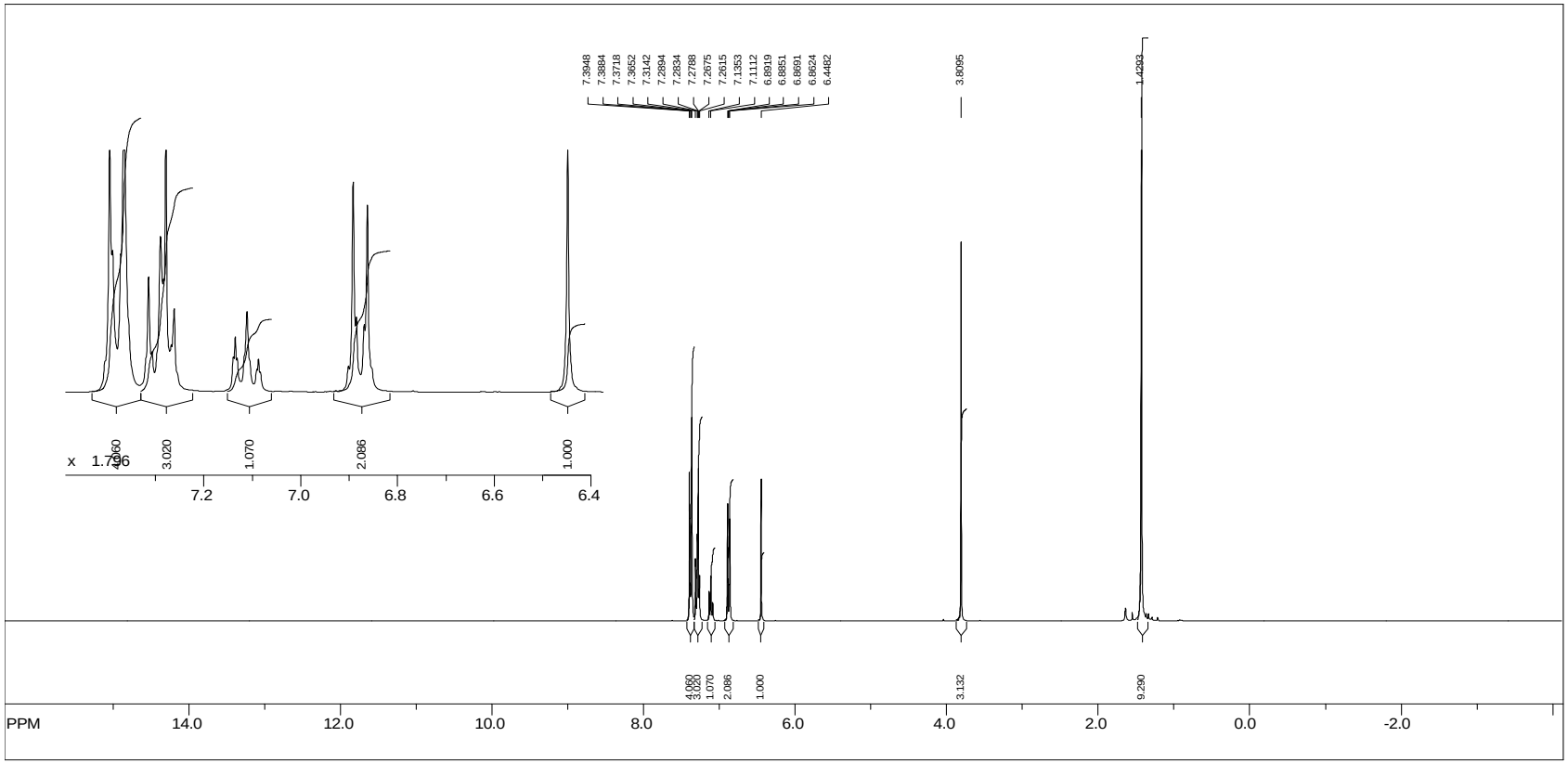
file: Z:\Laina\lmgx\lmgxi_46e\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(Z)-tert-Butyl 2-chloro-1-(4-methoxyphenyl)vinyl(phenyl)carbamate (228)



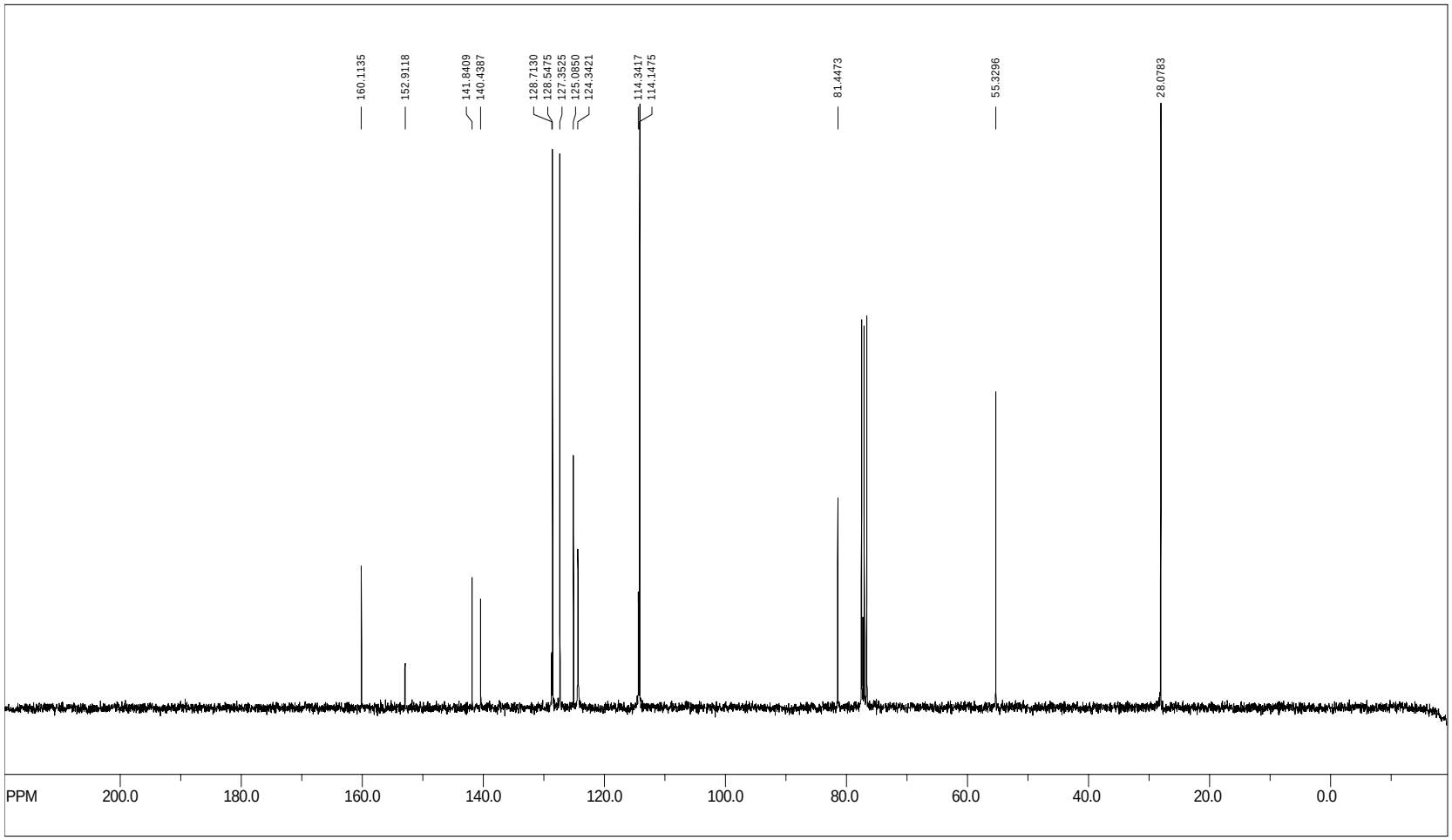
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgx\lmgx_94a\5\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

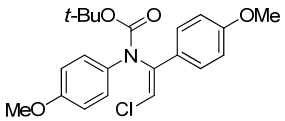
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



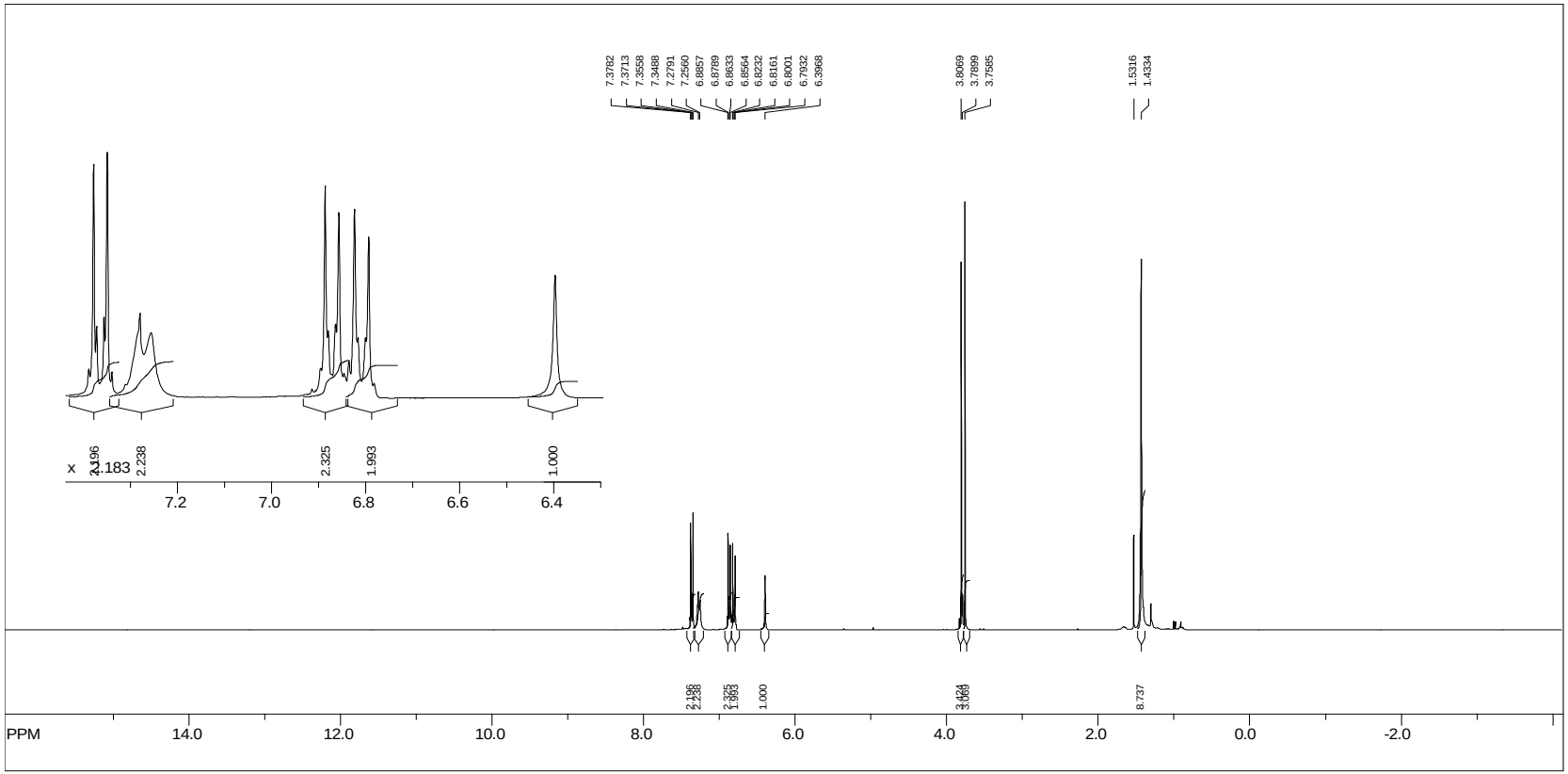
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_94a\6\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-tert-Butyl 2-chloro-1-(4-methoxyphenyl)vinyl(4-methylphenyl)carbamate (229)



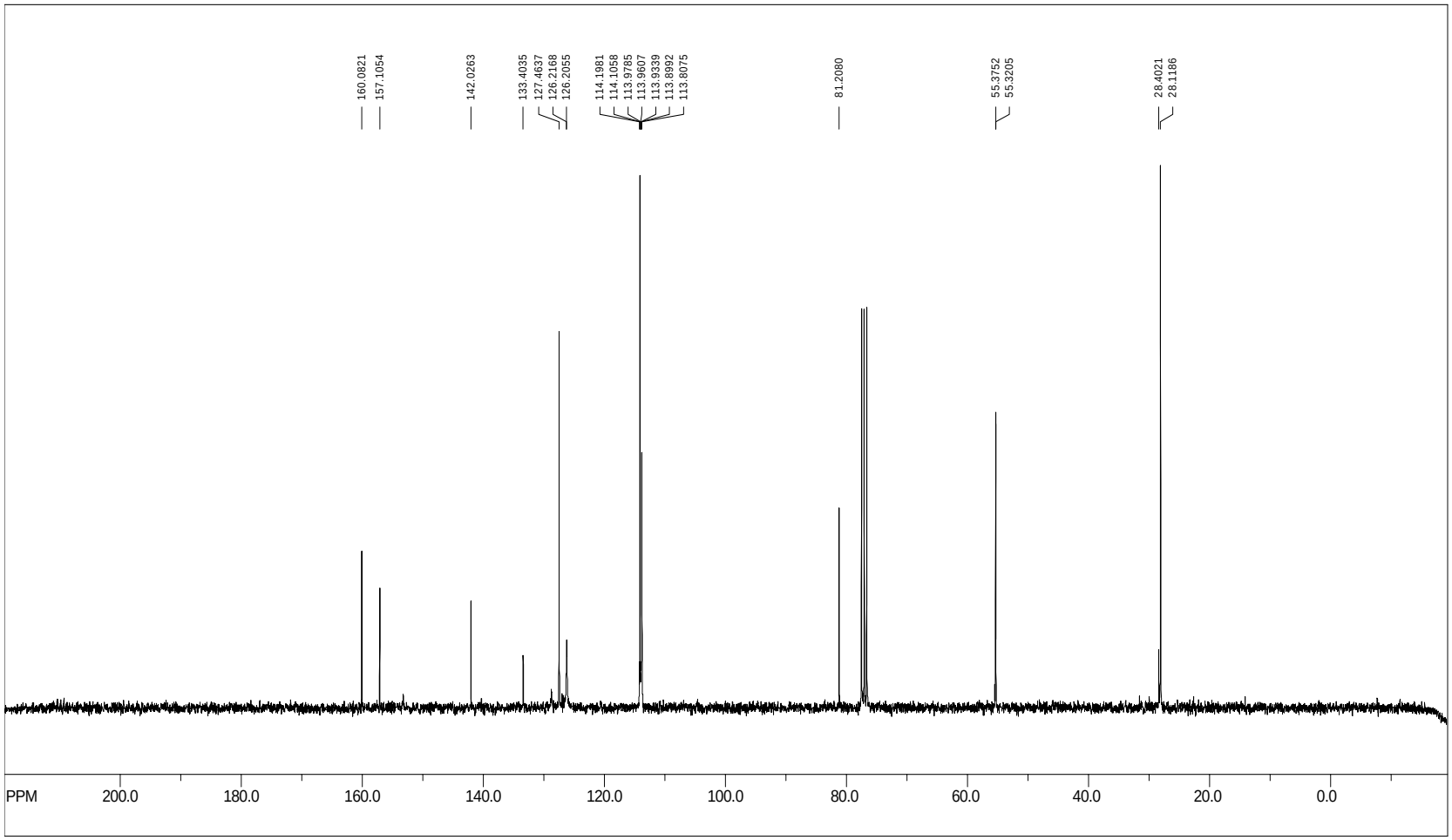
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgx\lmgx_90c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

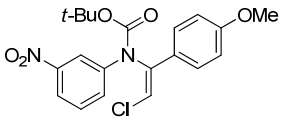
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



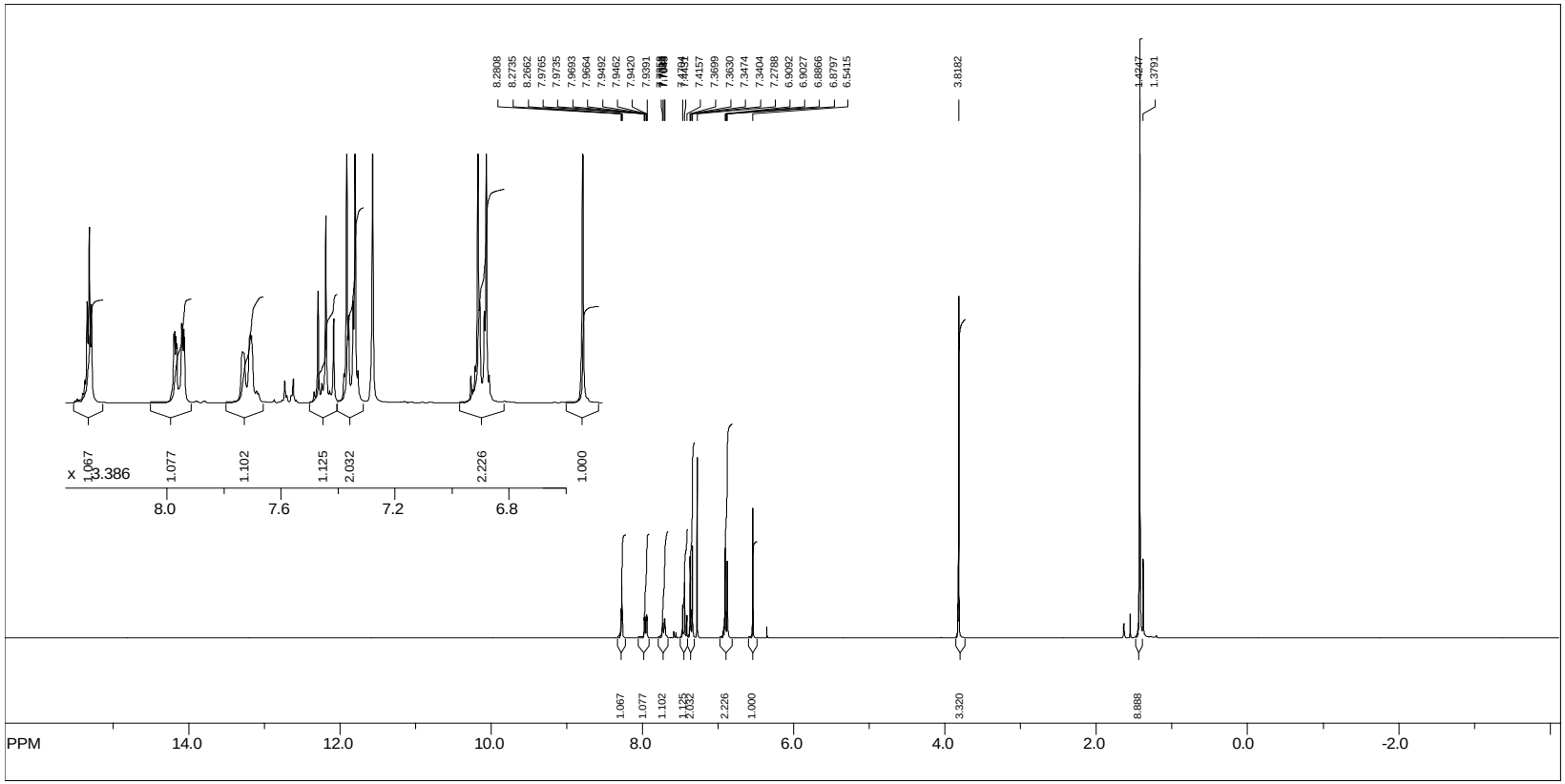
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_90c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 243

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-tert-Butyl 2-chloro-1-(4-methoxyphenyl)vinyl(3-nitrophenyl)carbamate (230)



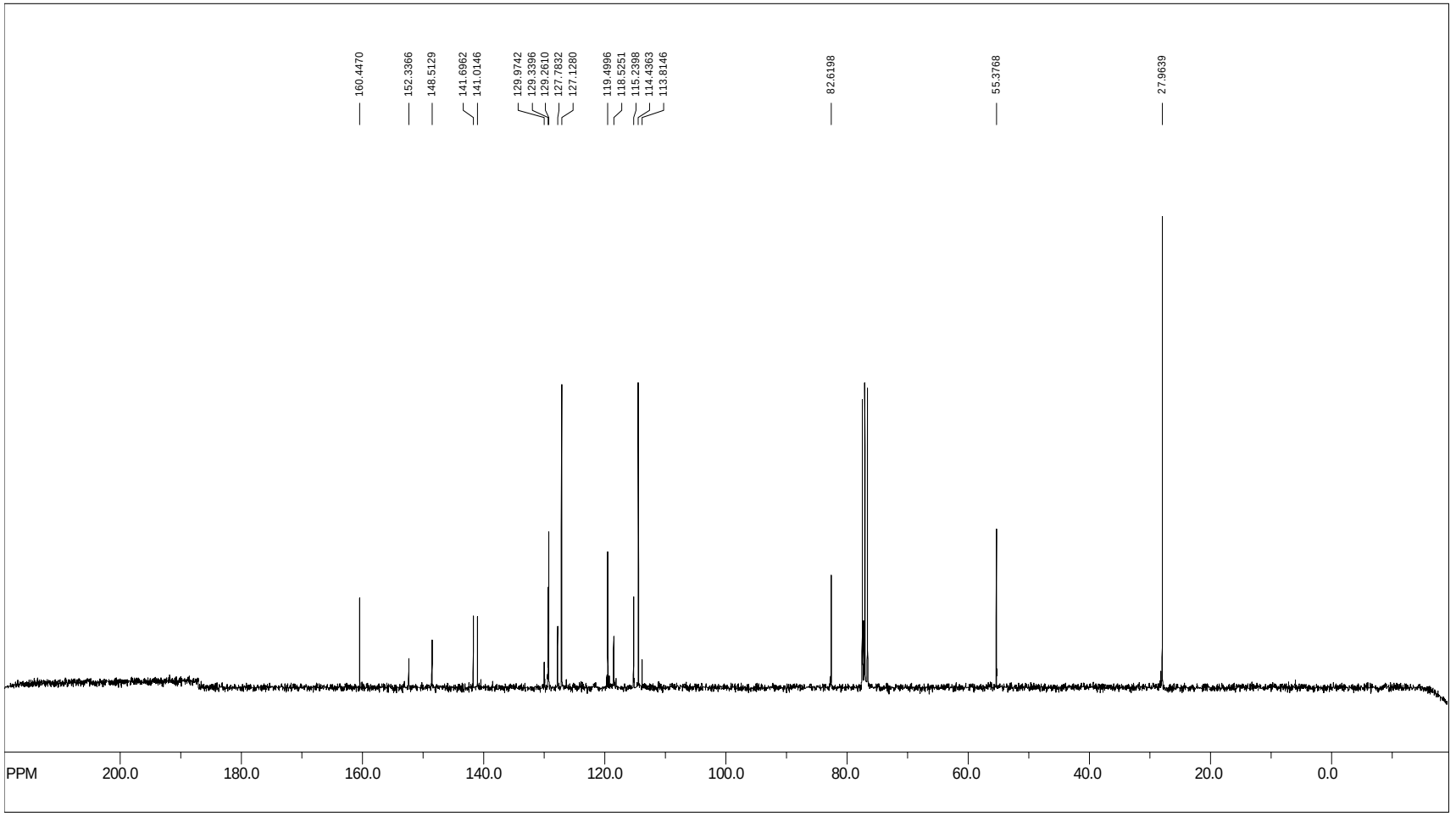
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxi\lmgxi_26b\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

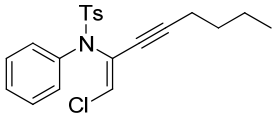
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



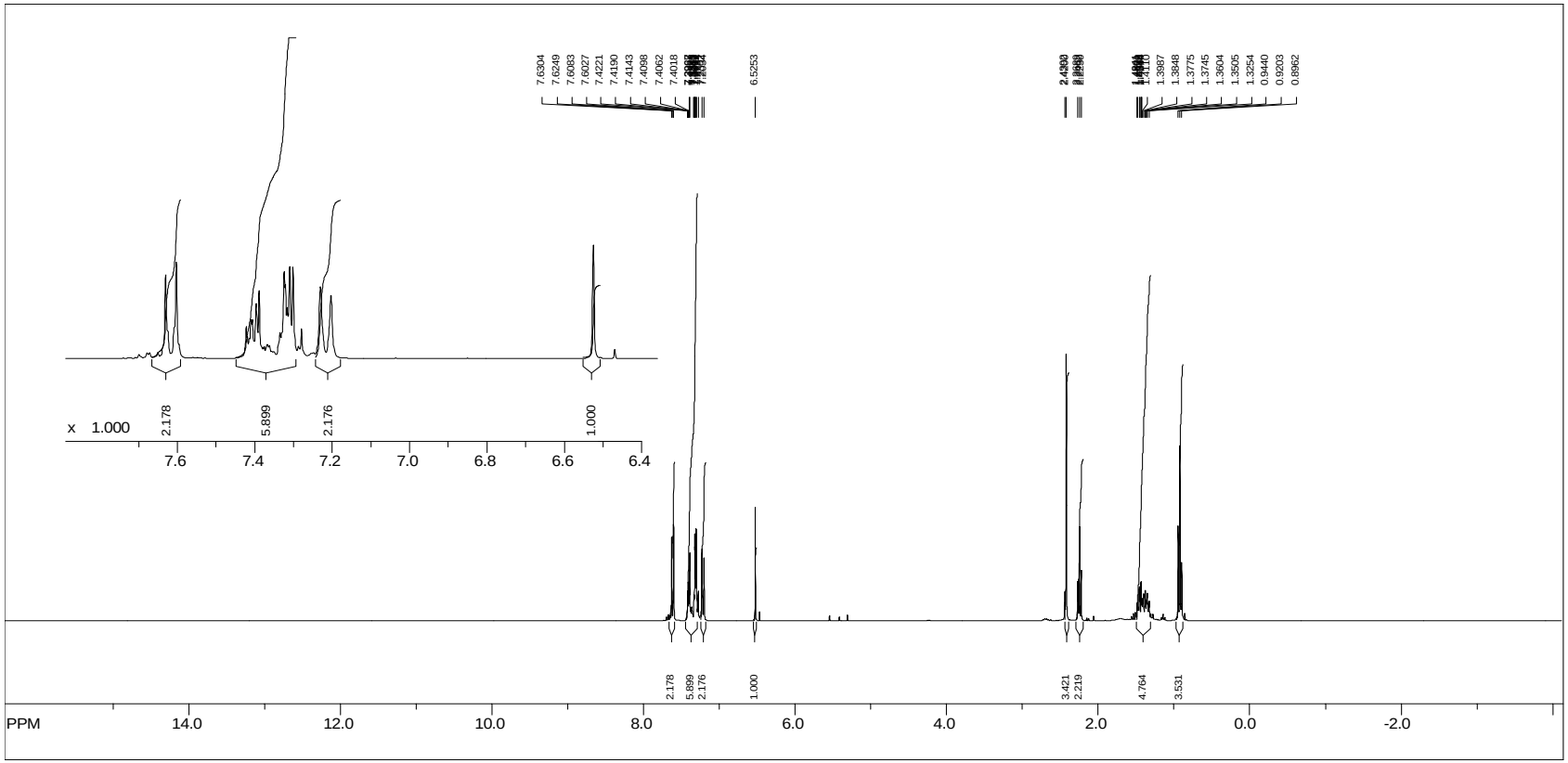
file: C:\Users\Laina\Documents\WORK\NMR\lmgxi\lmgxi_26b\4\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-*N*-(1-Chlorooct-1-en-3-yn-2-yl)-4-methyl-*N*-phenylbenzenesulfonamide (231)



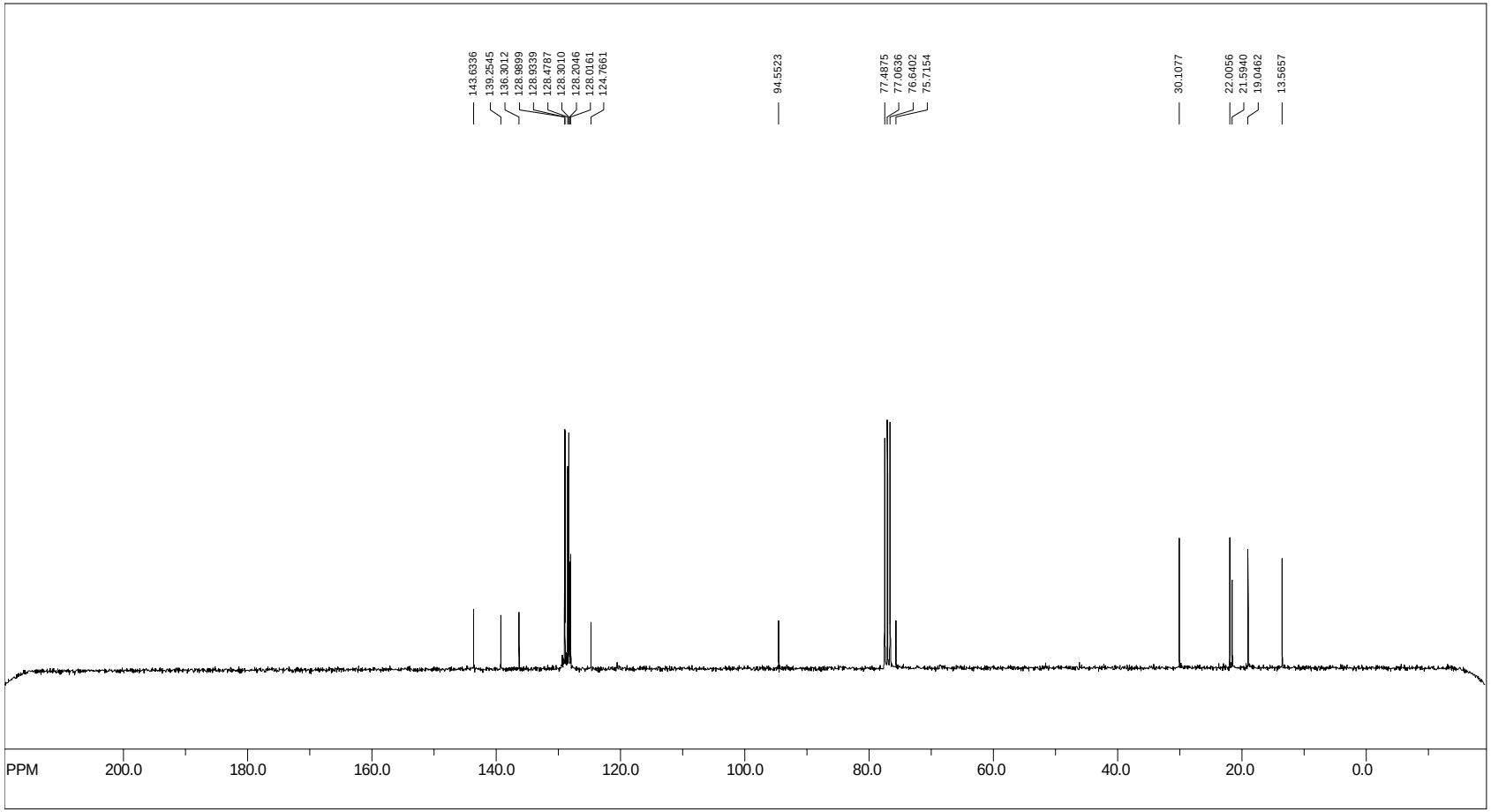
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



file: Z:\Laina\lmgx\lmgx_58a\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

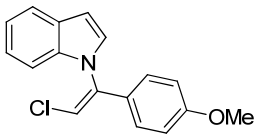
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



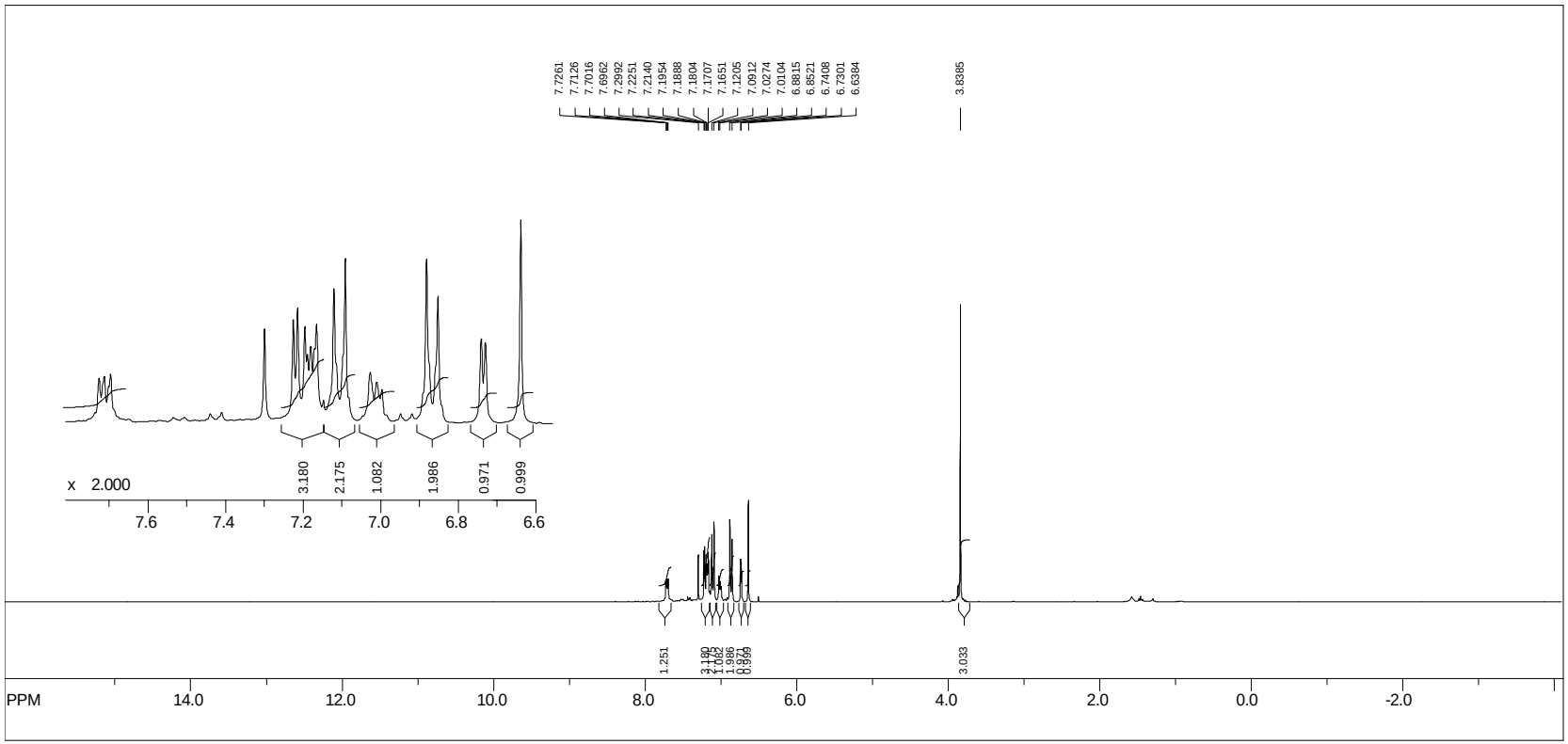
file: Z:\Laina\lmgx\lmgx_58a\4\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-1-(2-Chloro-1-(4-methoxyphenyl)vinyl)-1*H*-indole (232**)**



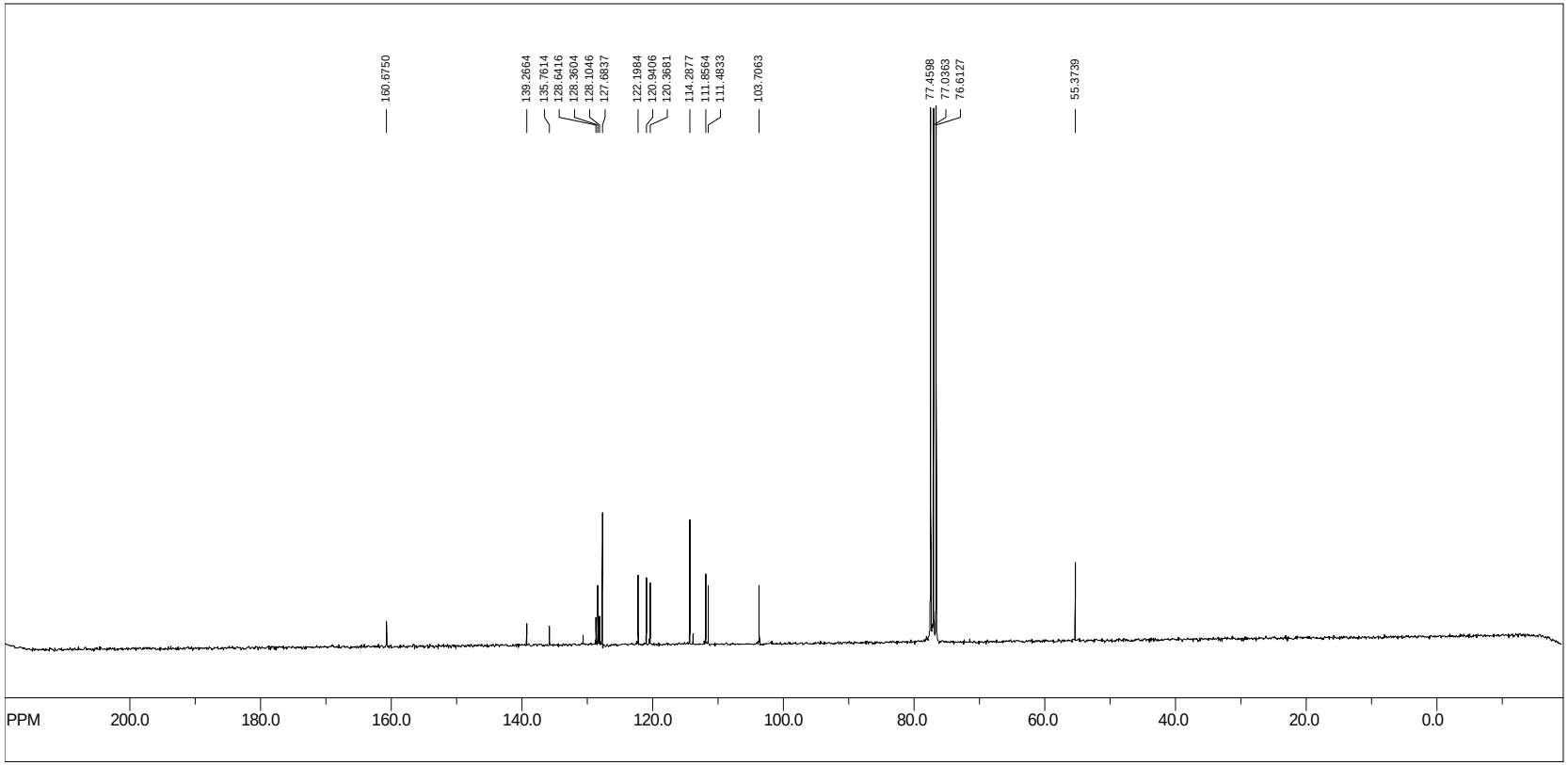
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgvii\lmgvii_51b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

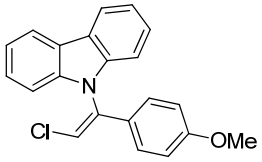
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



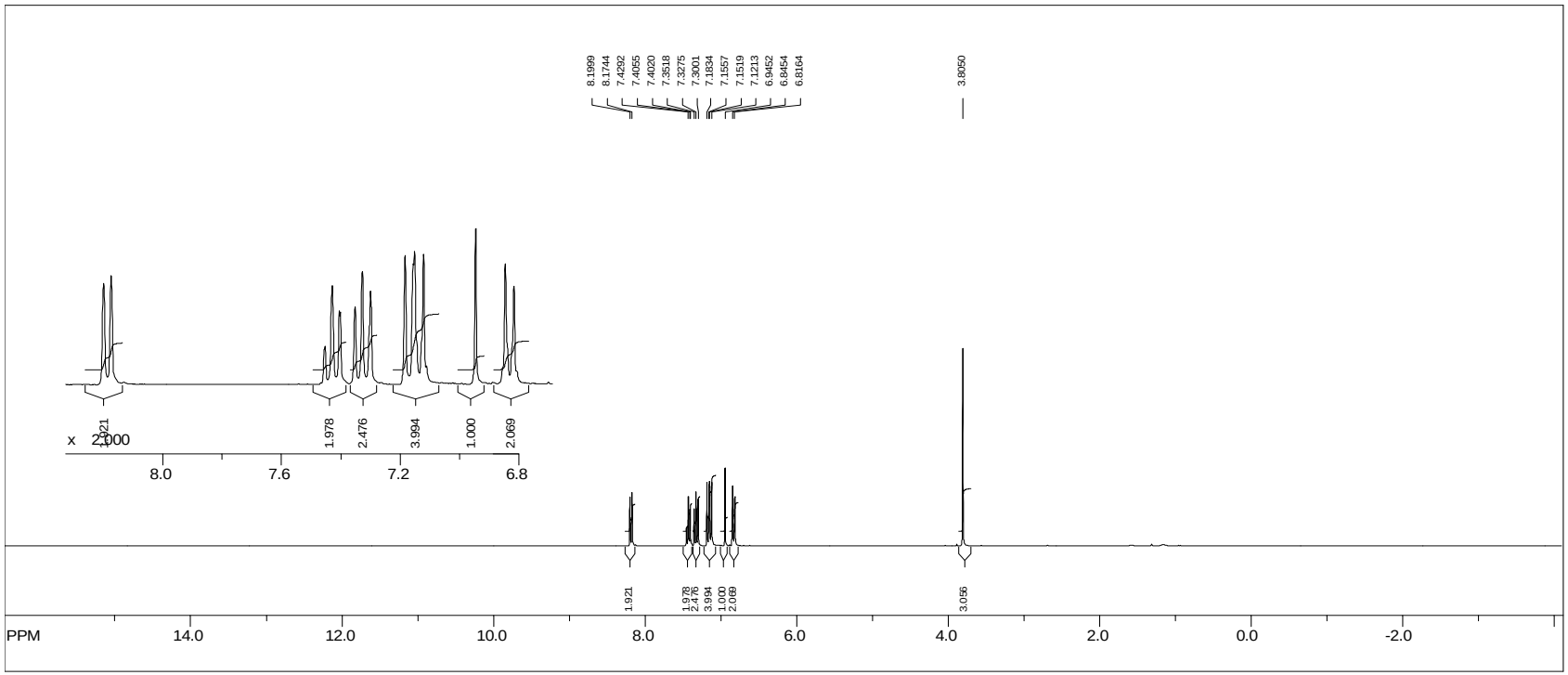
file: Z:\Laina\lmgwi\lmgwi_51b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4096

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-9-(2-Chloro-1-(4-methoxyphenyl)vinyl)-9*H*-carbazole (233)



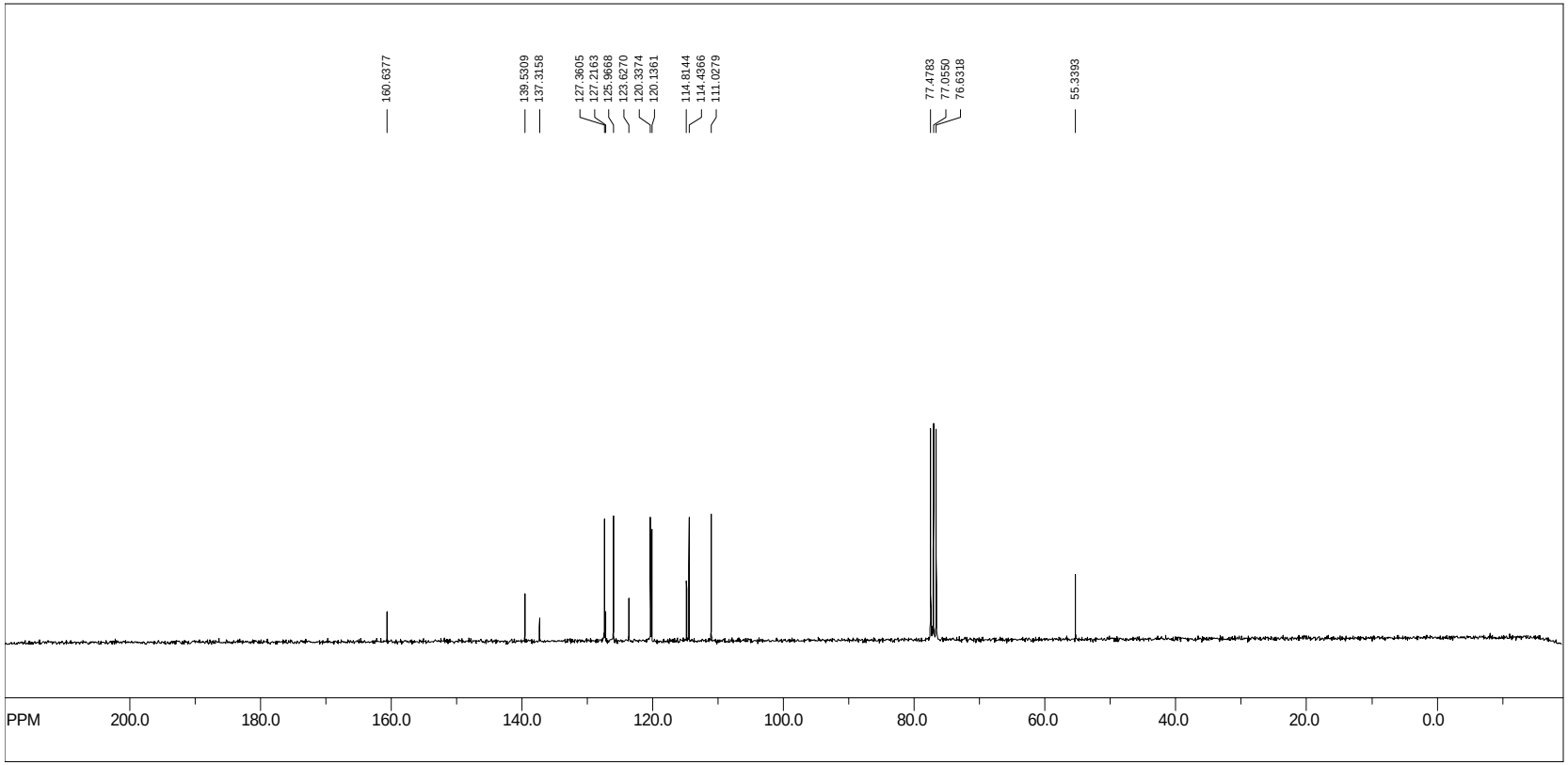
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgvii\lmgvii_52b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 21

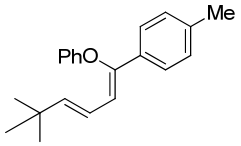


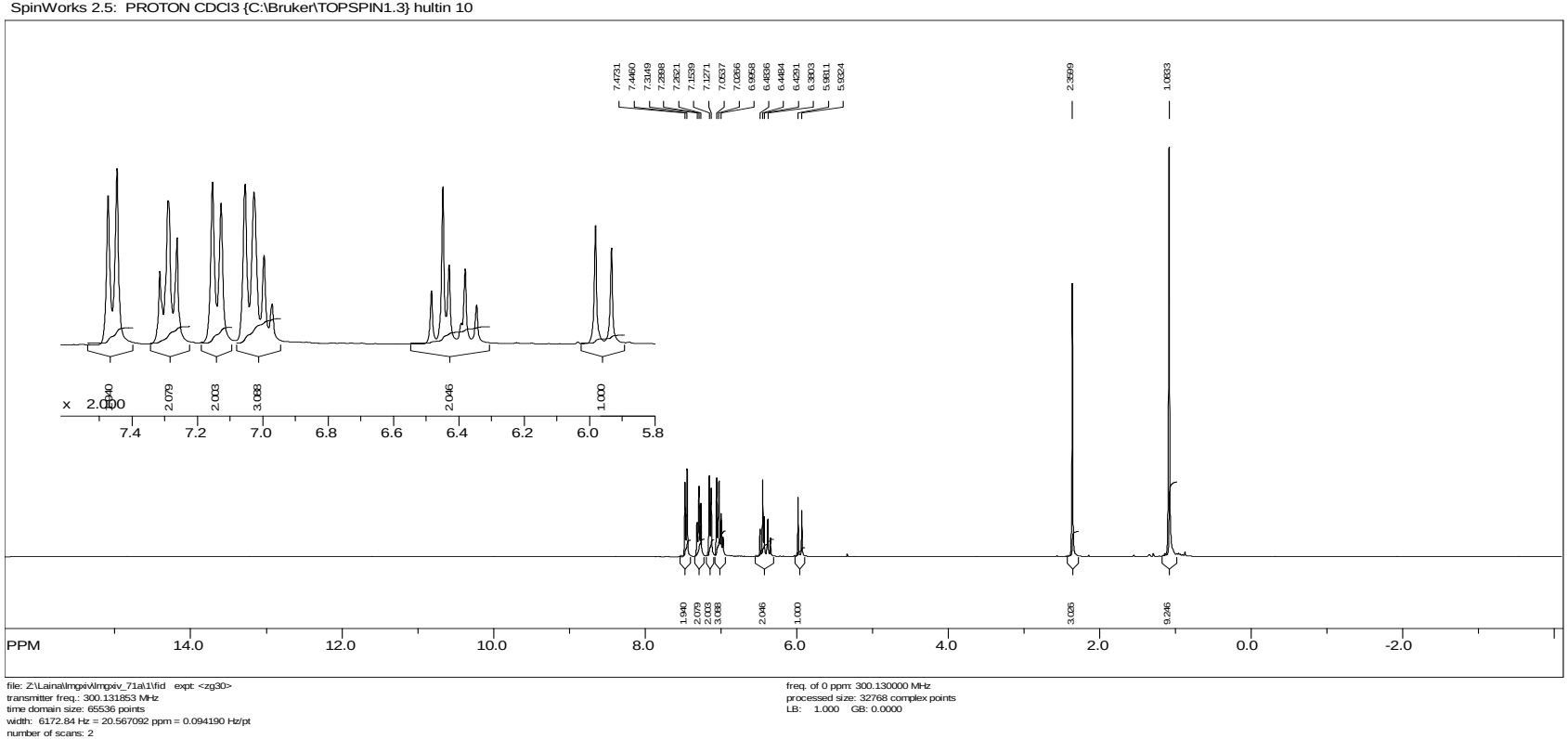
file: Z:\Laina\lmgwi\lmgwi_52b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 481

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

6.3: Section 2.4 – Trisubstituted Alkenes

1-((1*Z*,3*E*)-5,5-dimethyl-1-phenoxyhexa-1,3-dienyl-4-methylbenzene (234)

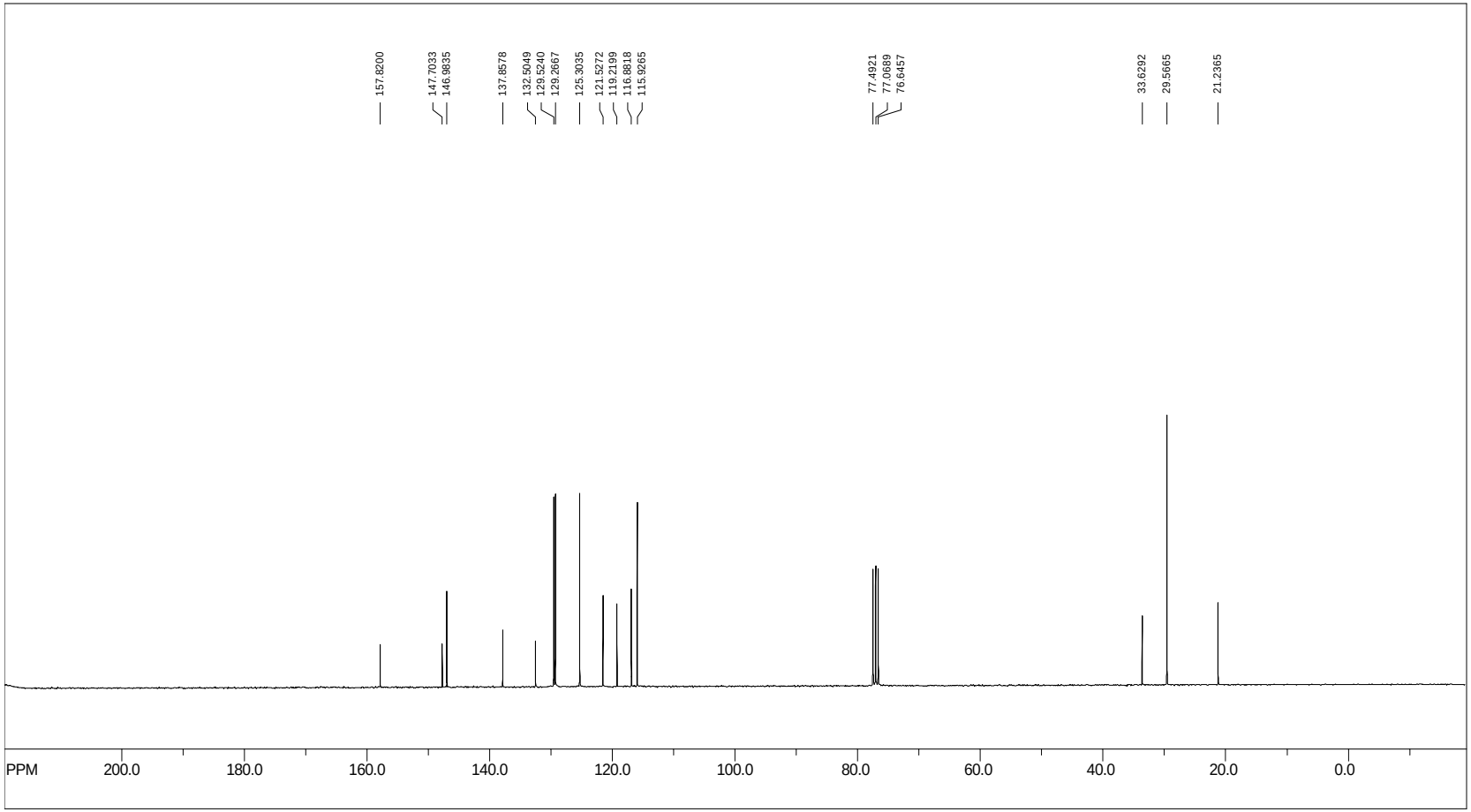




file: Z:\Laina\lmgxv\lmgxv_71a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

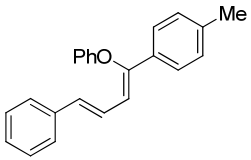
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



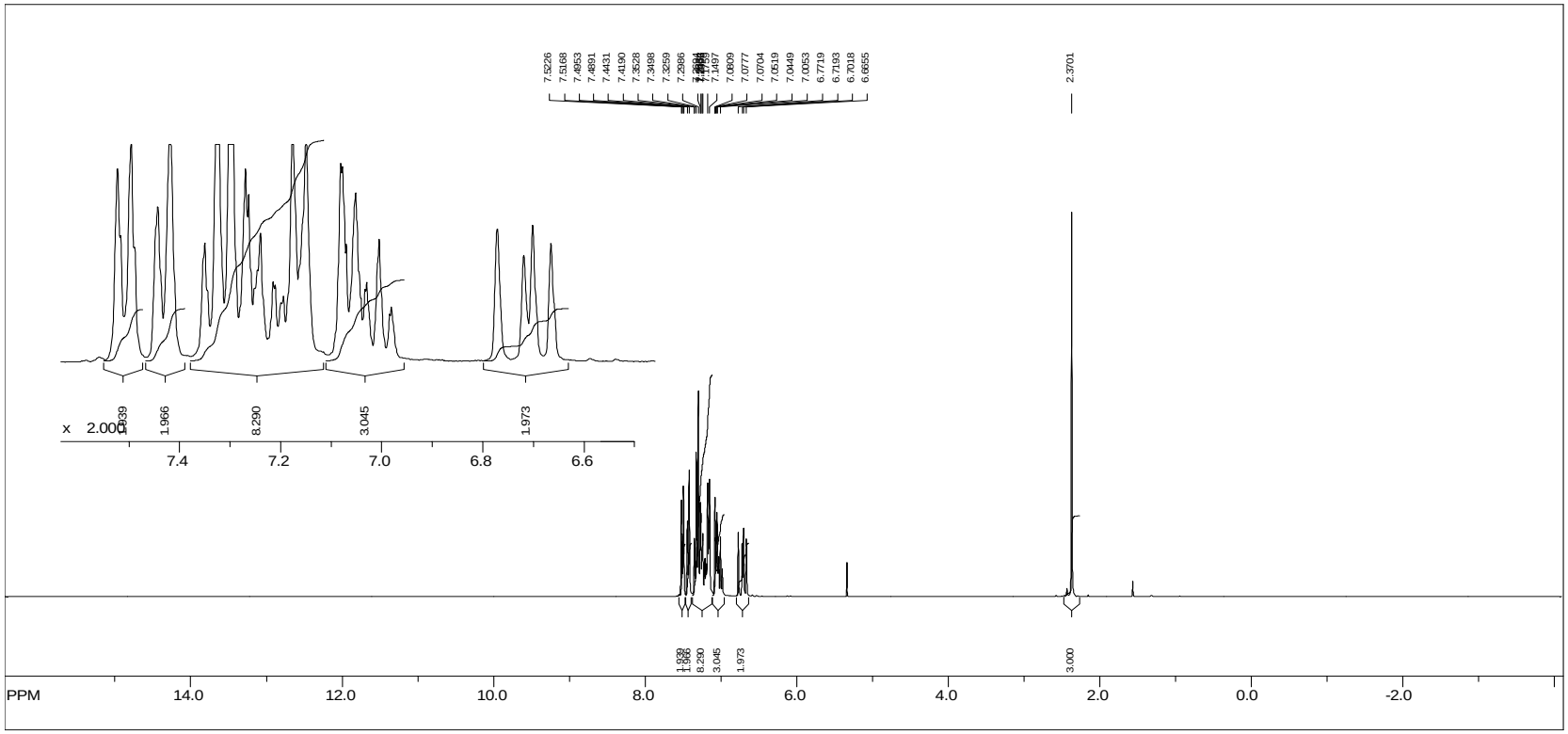
file: Z:\Laina\lmgxiv\lmgxiv_71a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-Methyl-4-((1*Z*,3*E*)-1-phenoxy-4-1,3-dienyl)benzene (235)



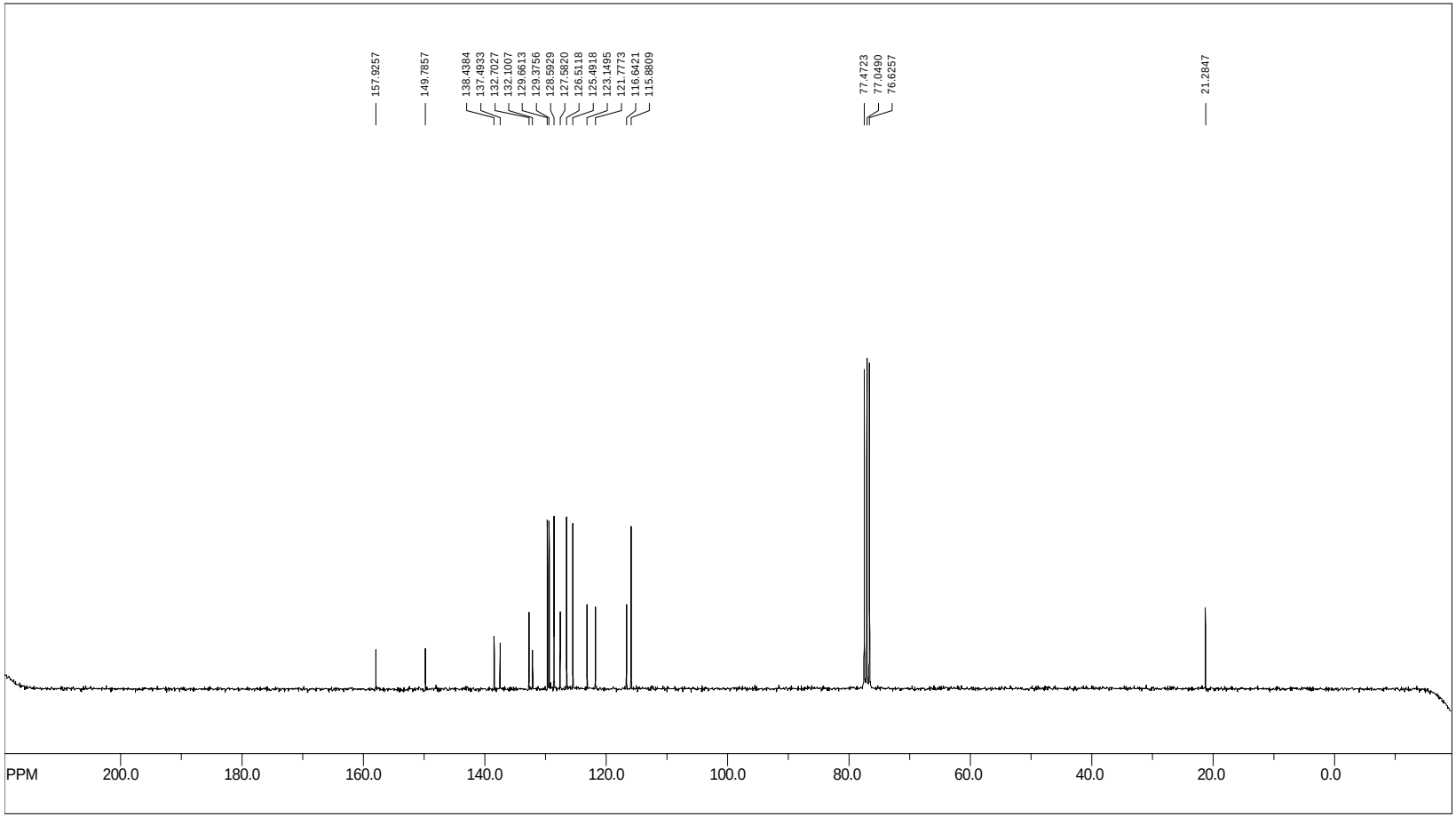
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgxiv\lmgxiv_69d\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

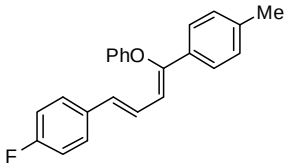
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



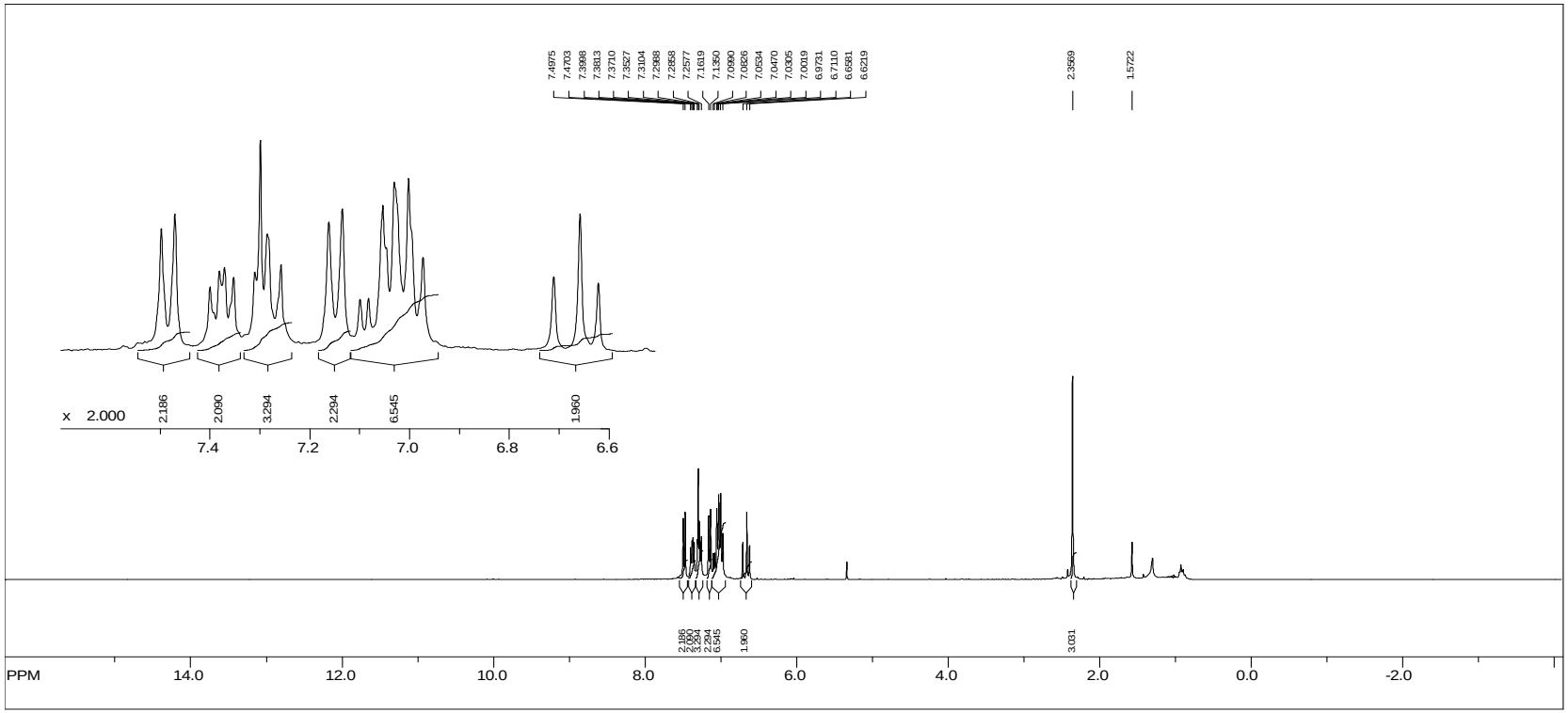
file: Z:\Laina\lmgxiv\lmgxiv_69d\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-((1*Z*,3*E*)-4-(4-fluorophenyl)-1-phenoxybuta-1,3-dienyl)-4-methylbenzene (236)



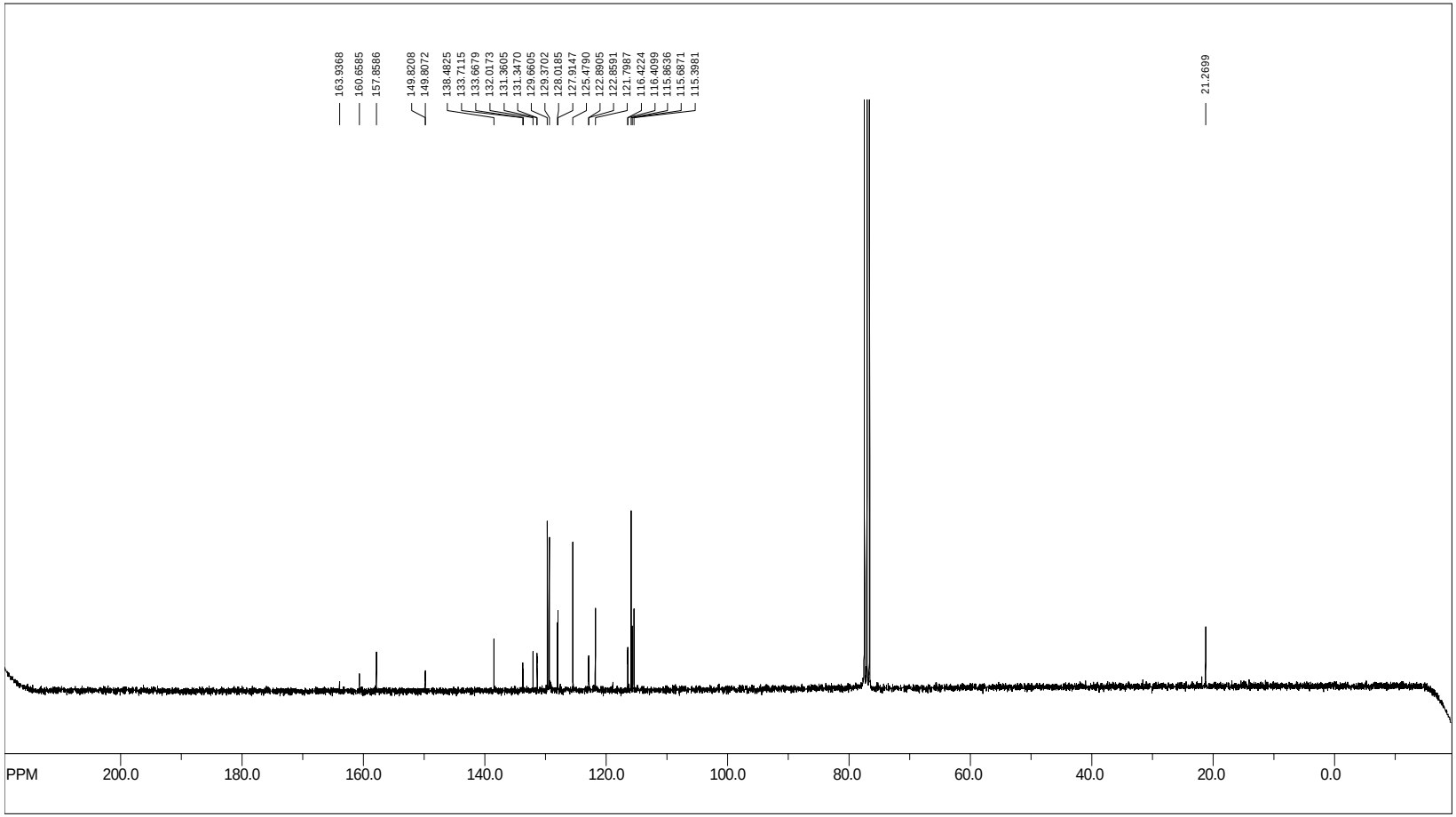
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 19



file: Z:\Laina\lmgxiv\lmgxiv_68d\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

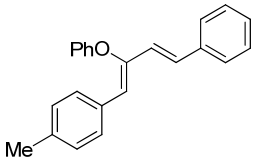
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



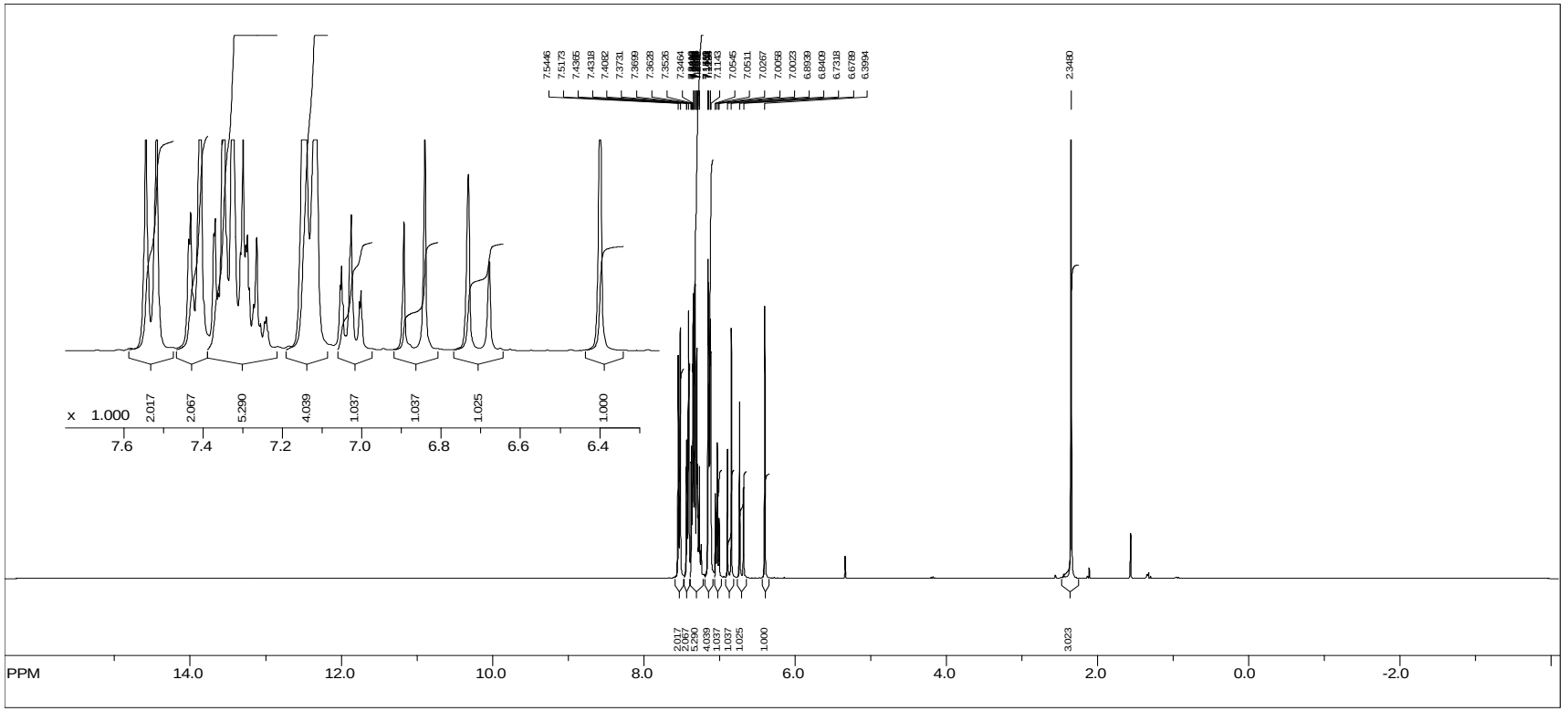
file: Z:\Laina\lmgxiv\lmgxiv_68d\6\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4196

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

1-((1*E*,3*Z*)-3-phenoxy-4-*p*-tolylbuta-1,3-dienyl)benzene (237)



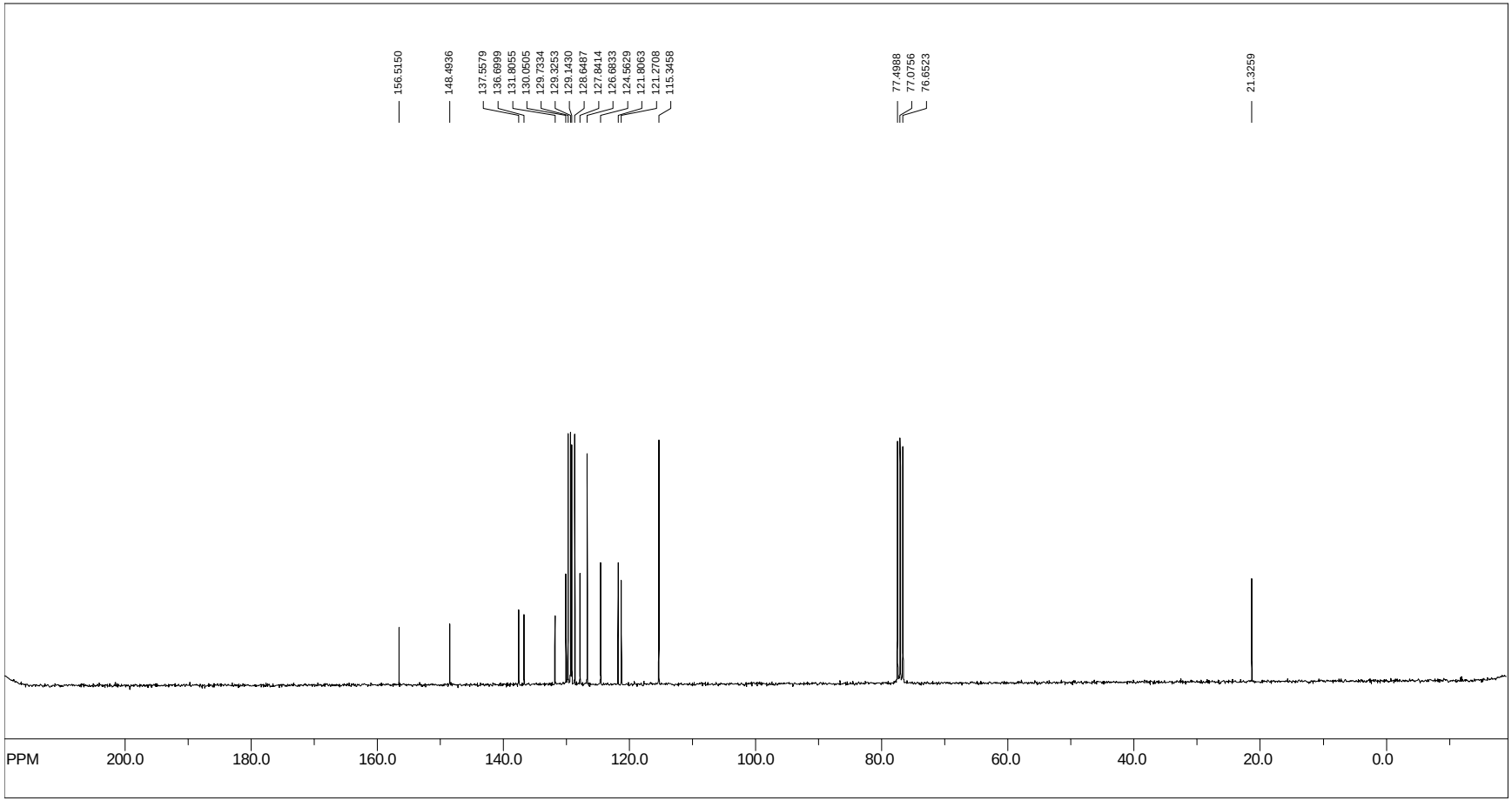
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



file: Z:\Laina\lmgxiv\lmgxiv_12c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

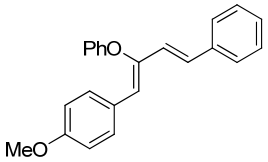
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



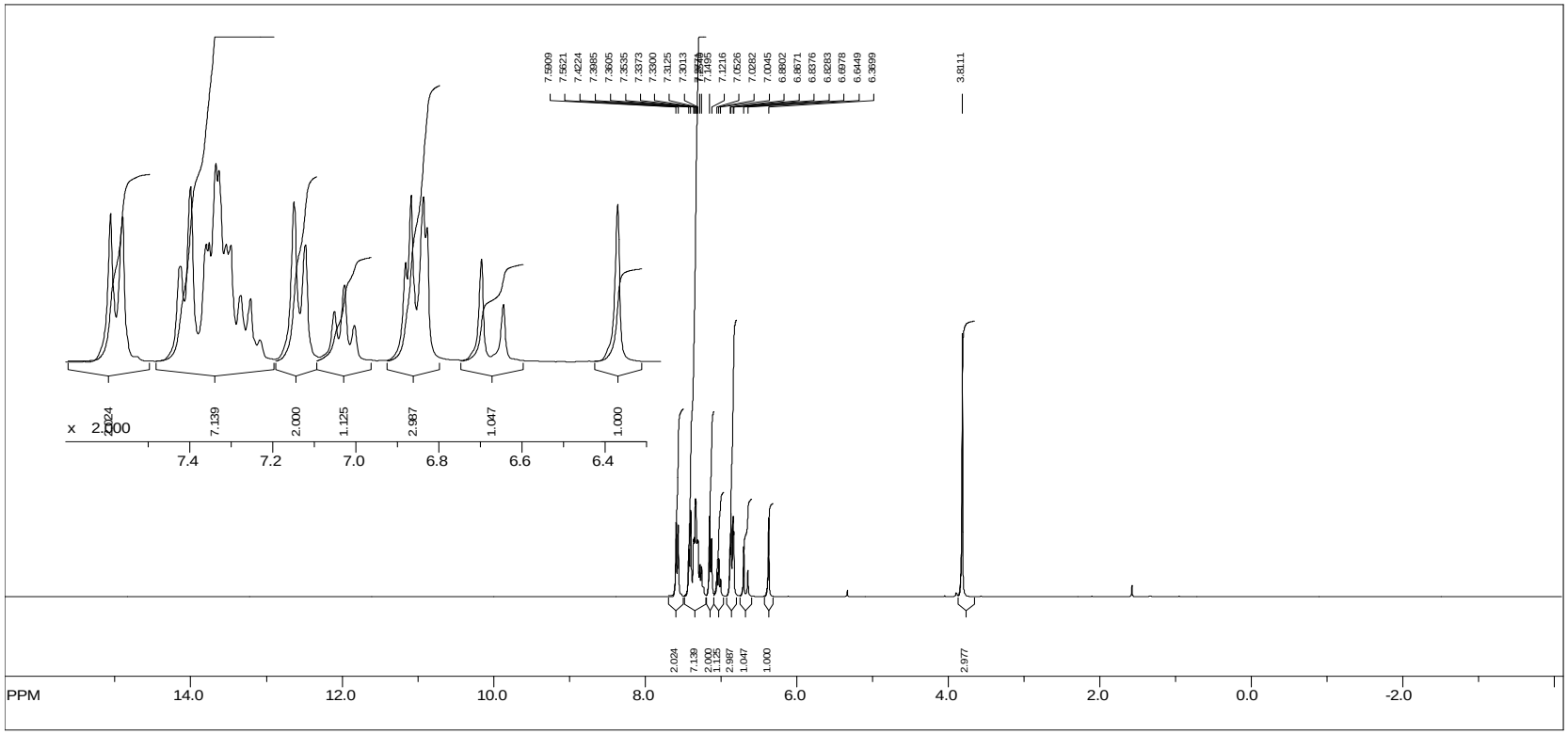
file: Z:\Laina\lmgxiv\lmgxiv_12c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-Methoxy-4-((1*Z*,3*E*)-2-phenoxy-4-phenylbuta-1,3-dienyl)benzene (238)



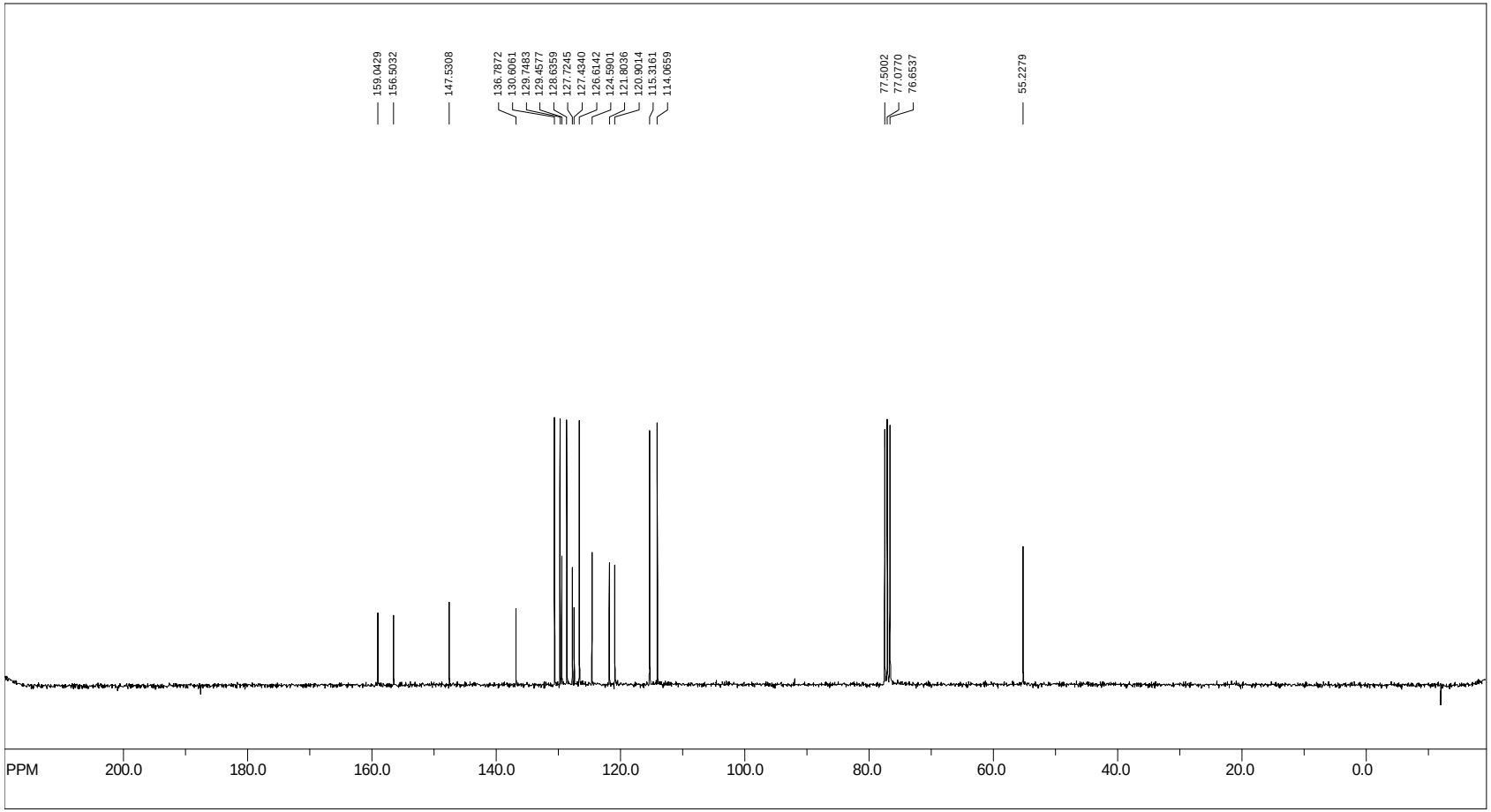
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



file: Z:\Laina\lmgxiv\lmgxiv_11d\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

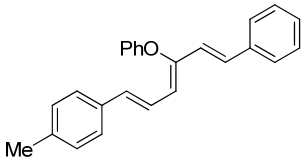
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



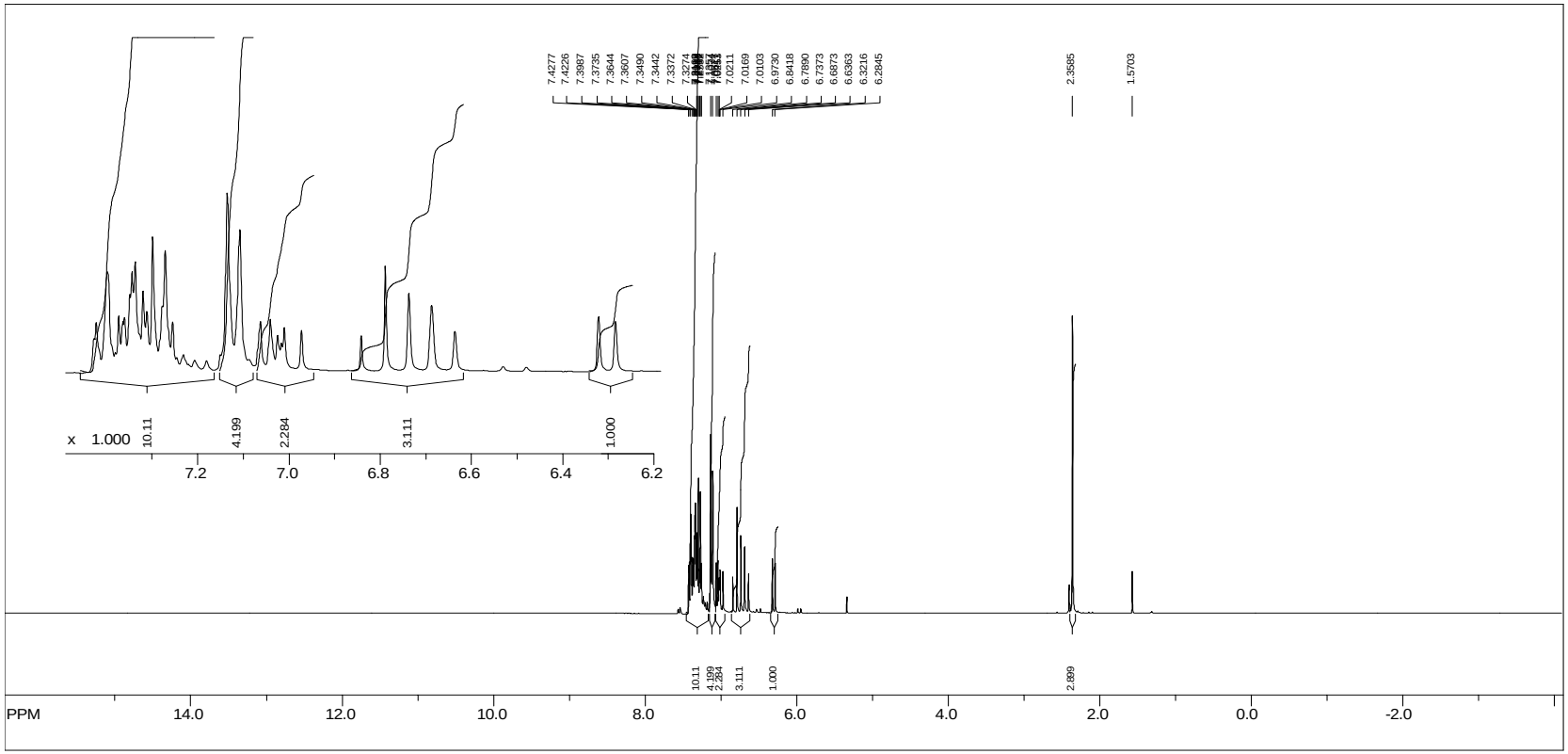
file: Z:\Laina\lmgxiv\lmgxiv_11ch\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-((1*E*,3*Z*,5*E*)-3-phenoxy-6-*p*-tolylhexa-1,3,5-trienyl)benzene (239)



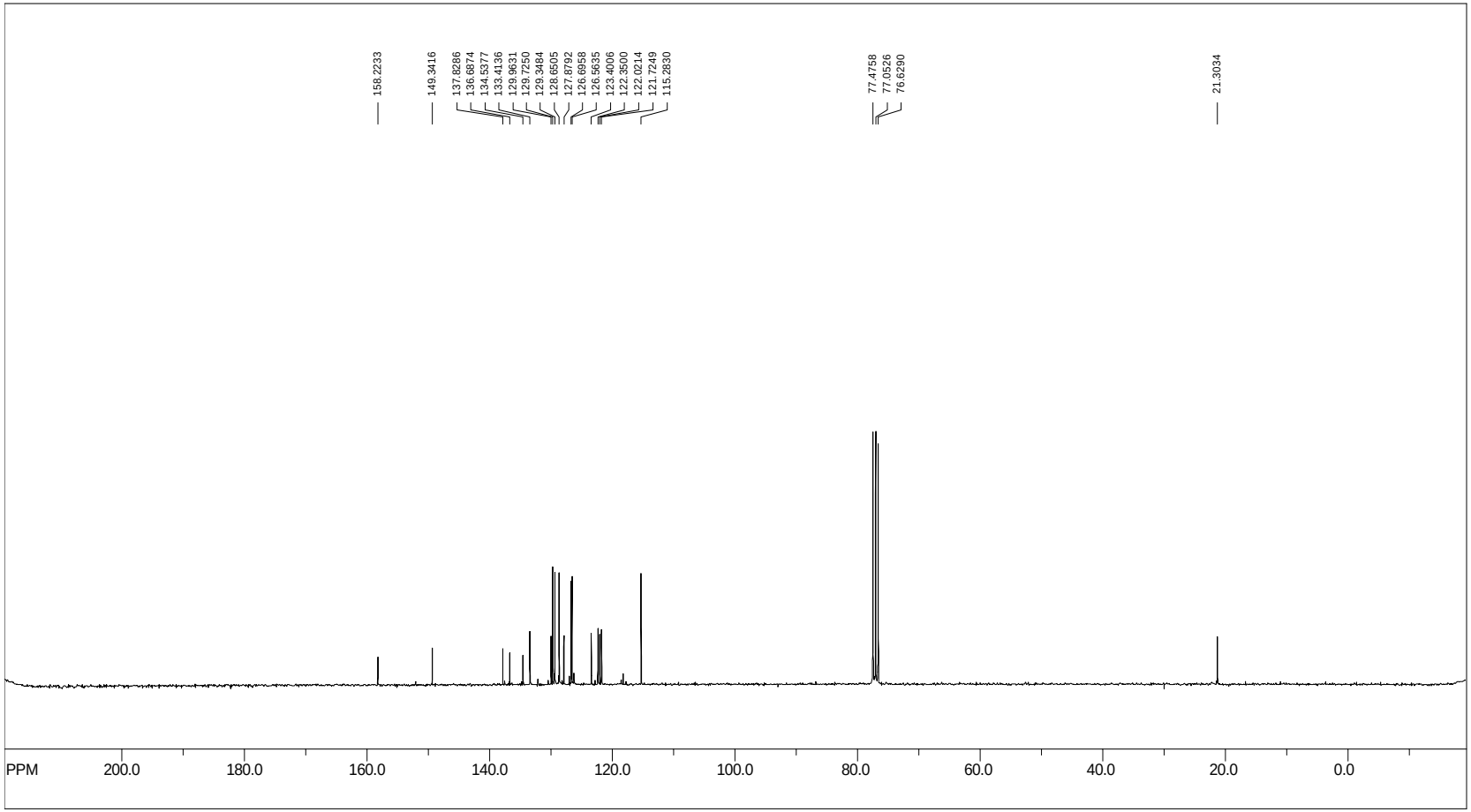
SpinWorks 2.5: triene from xiii_93a and 4-methylstyrylboronic acid



file: Z:\Laina\lmgxiv\lmgxiv_21b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

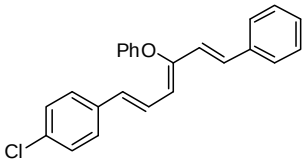
SpinWorks 2.5: triene from xiii_93a and 4-methylstyrylboronic acid



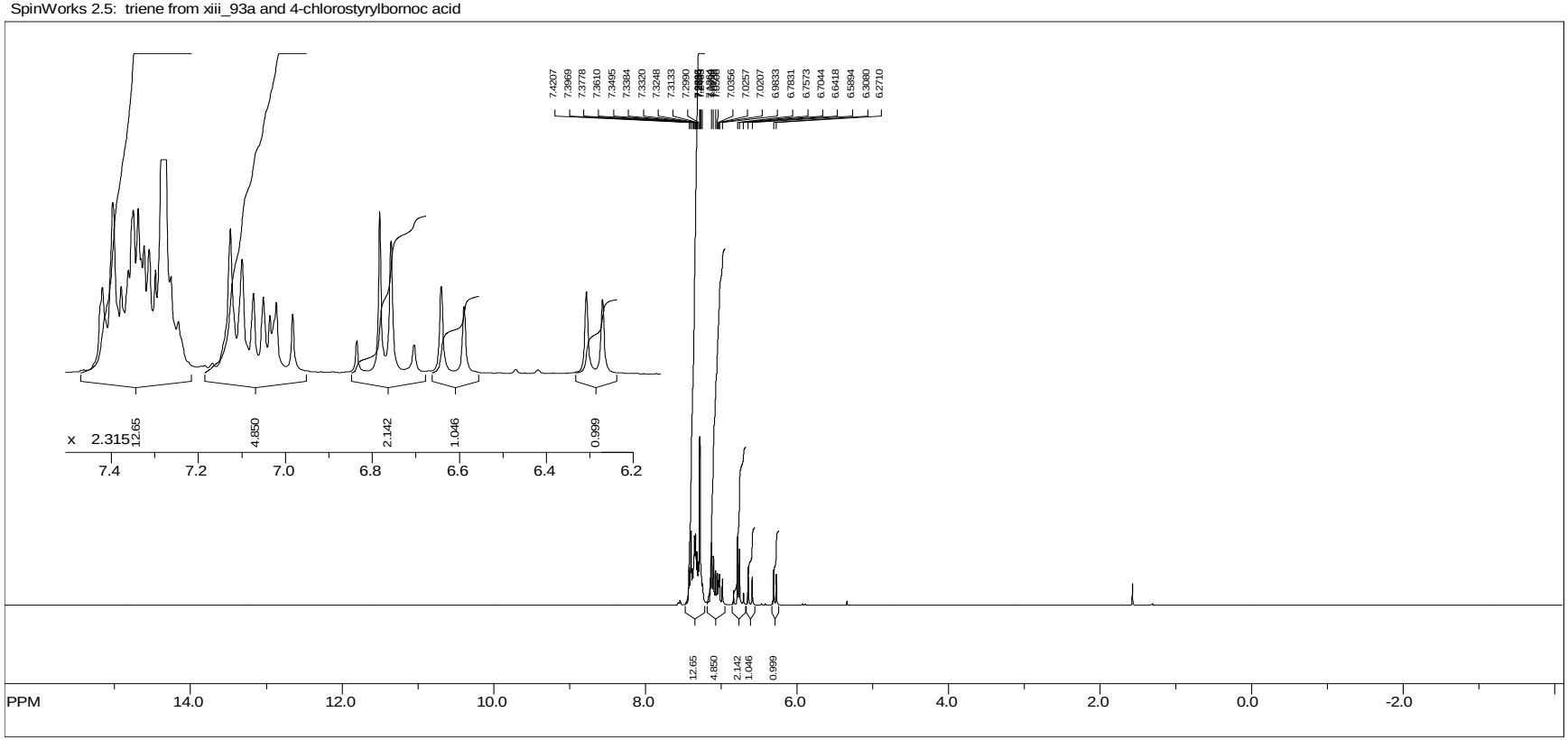
file: Z:\Laina\lmgxiv\lmgxiv_21b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-((1*E*,3*Z*,5*E*)-6-(4-Chlorophenyl)-3-phenoxy-1,3,5-trienyl)benzene (240)



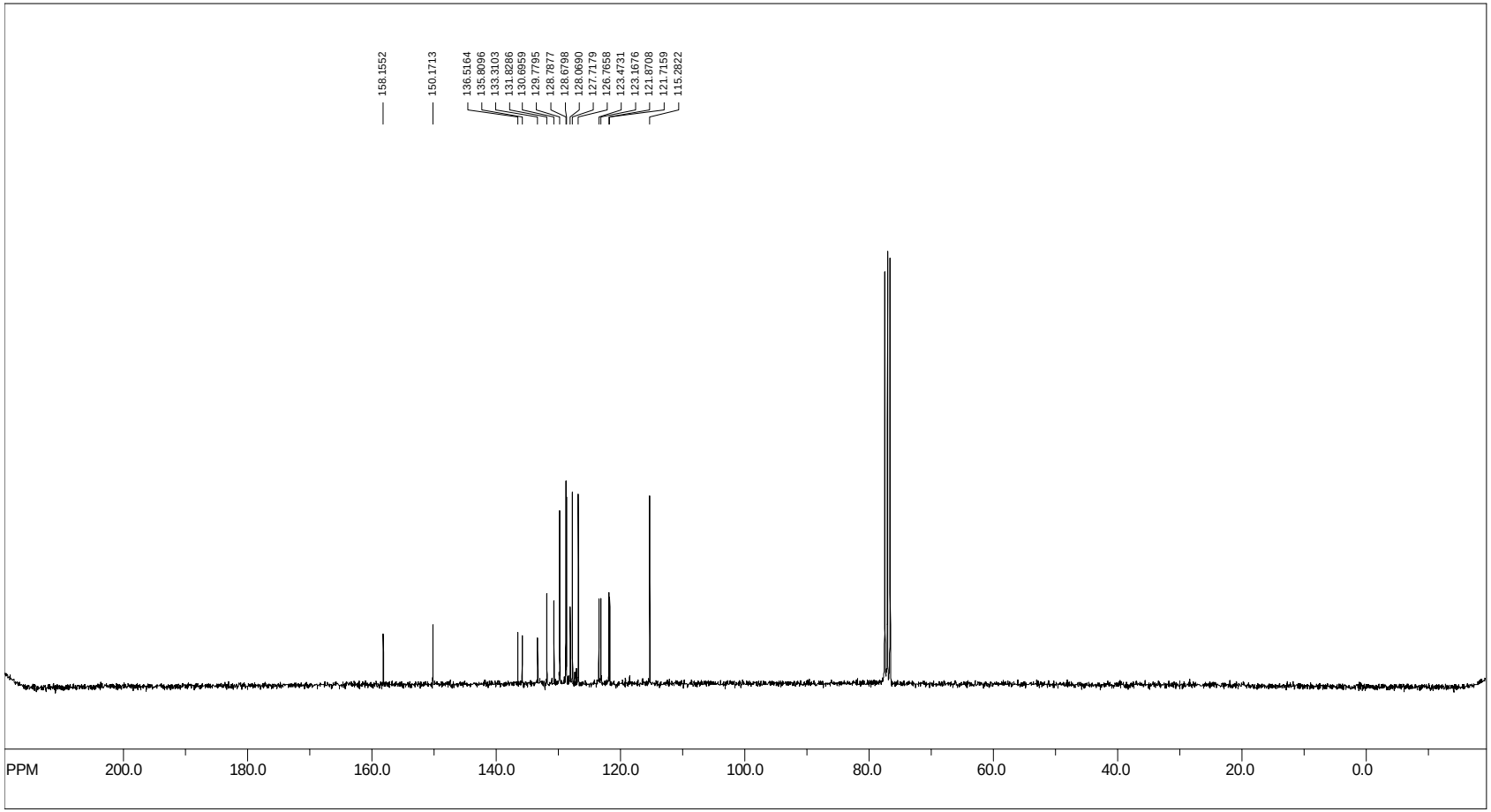
SpinWorks 2.5: triene from xiii_93a and 4-chlorostyrylbornoc acid



file: Z:\Laina\lmgxiv\lmgxiv_22a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

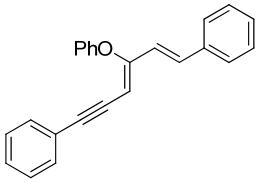
SpinWorks 2.5: triene from xiii_93a and 4-chlorostyrylbornoc acid



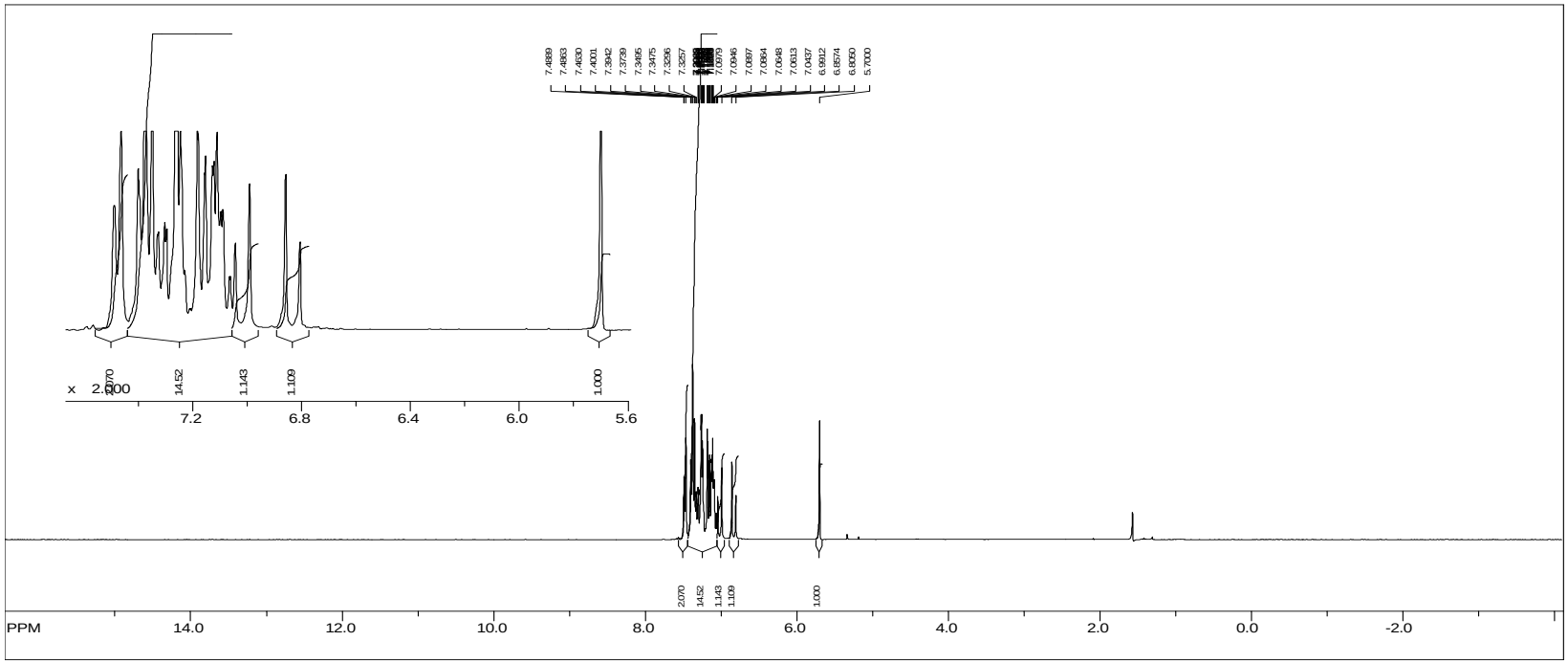
file: Z:\Laina\lmgxiv\lmgxiv_22a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 764

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(1*E*,3*Z*)-3-phenoxy-1,6-diphenylhexa-1,3-dien-5-yn (241**)**



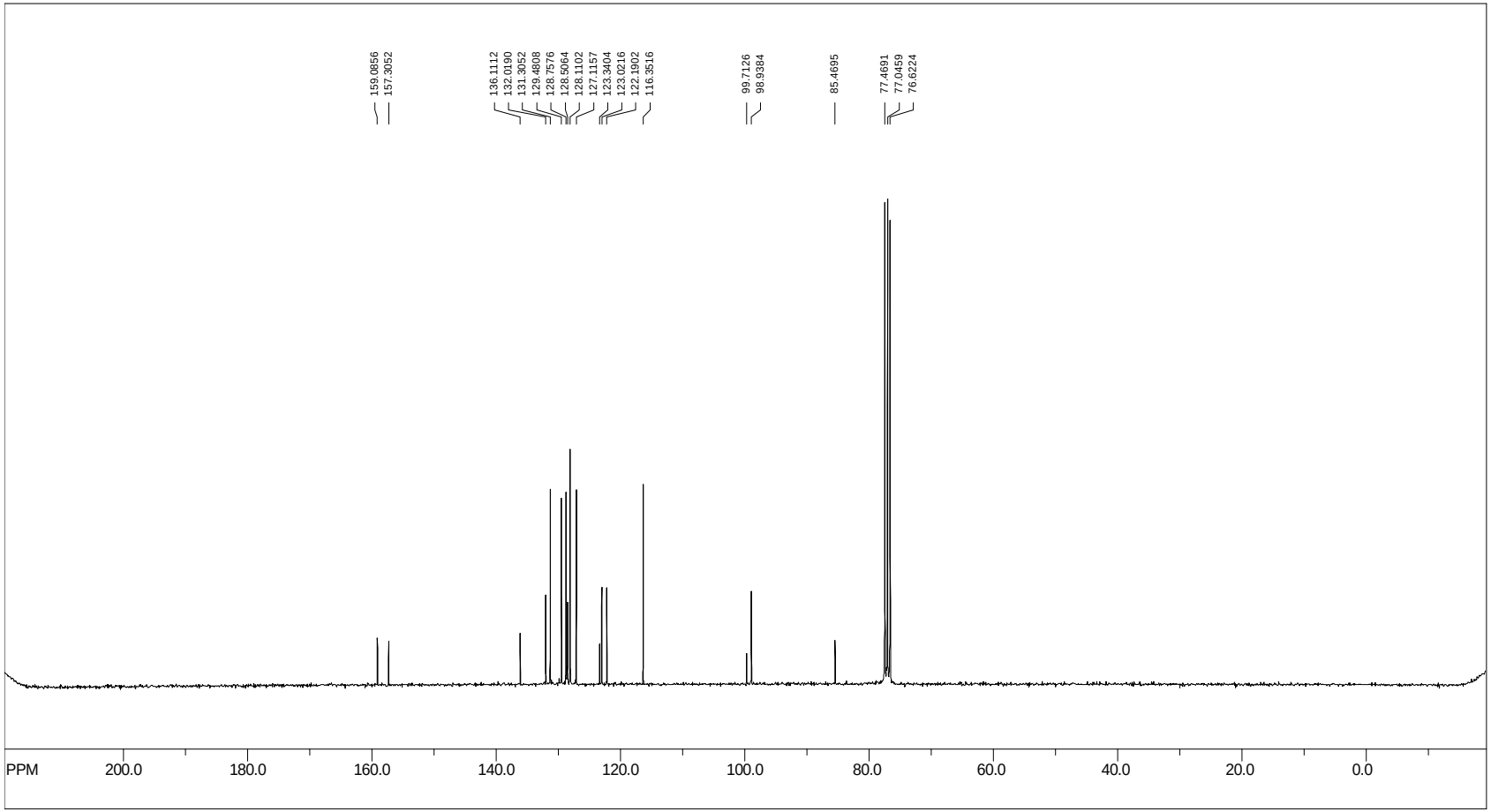
SpinWorks 2.5: Dienyne from xiii_93a and PhCCBF3K



file: Z:\Laina\lmgxiv\lmgxiv_24b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

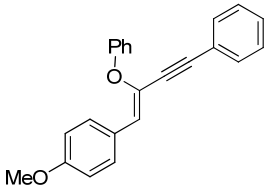
SpinWorks 2.5: Dienyne from xiii_93a and PhCCBF3K



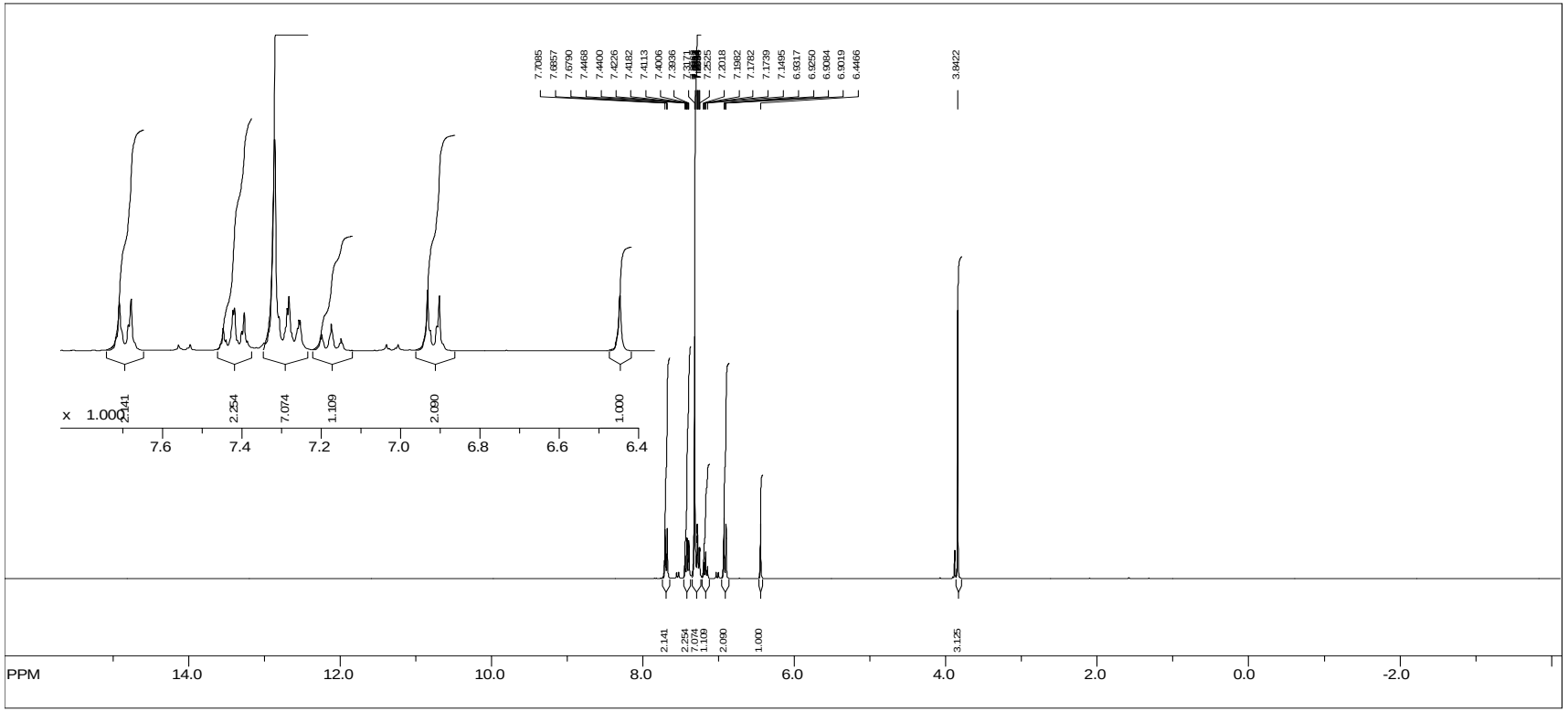
file: Z:\Laina\lmgxiv\lmgxiv_24b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 3000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-Methoxy-4-(2-phenoxy-4-phenylbut-1-en-3-ynyl)benzene (242)



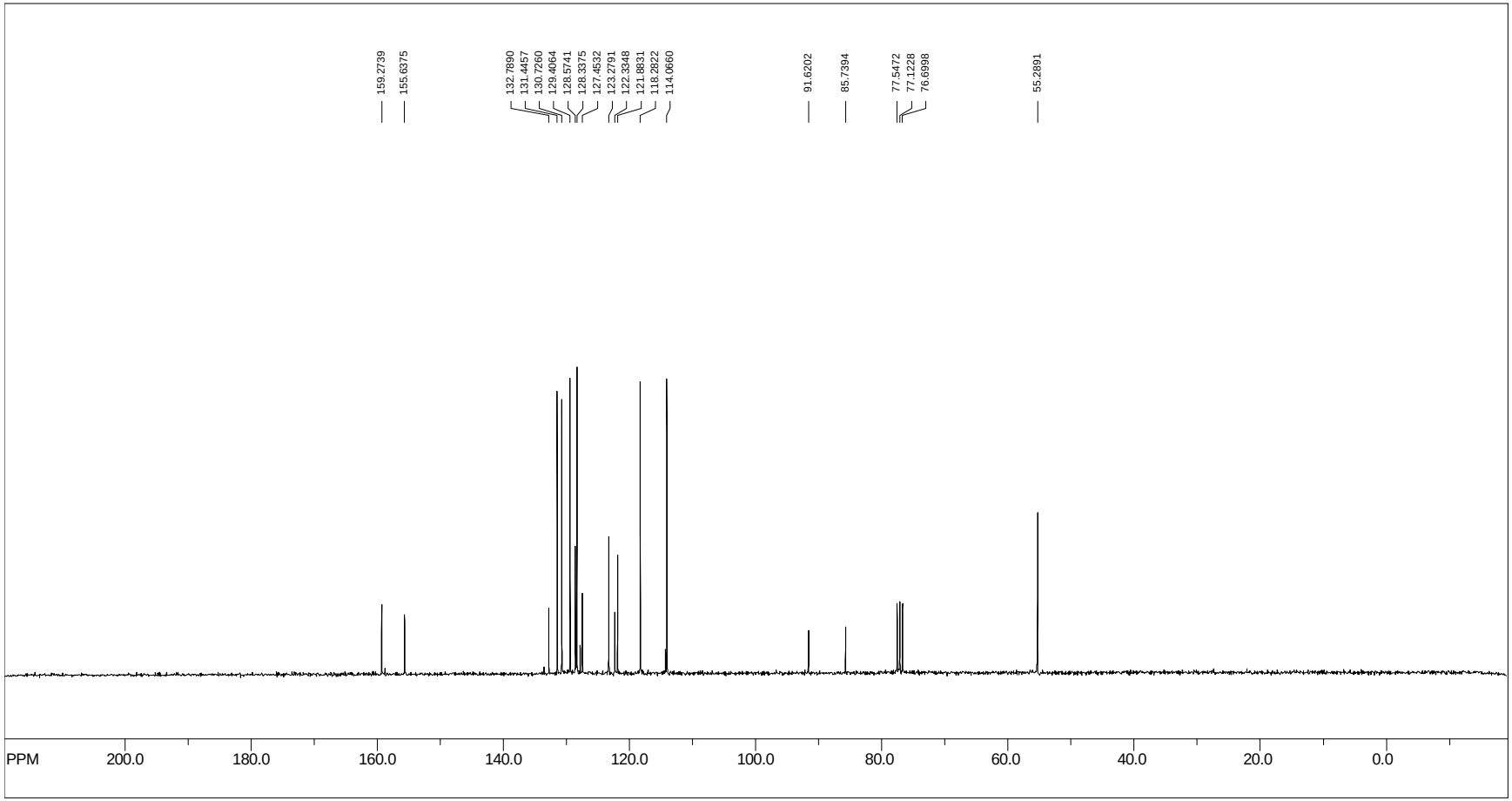
SpinWorks 2.5: suzuki on sonogashira adduct with p-methoxyphenylboronic acid



file: Z:\Laina\lmgix\lmgix_28c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

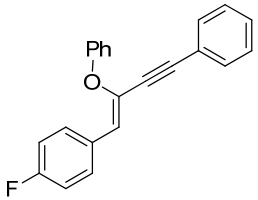
SpinWorks 2.5: suzuki on sonogashira adduct with p-methoxyphenylboronic acid



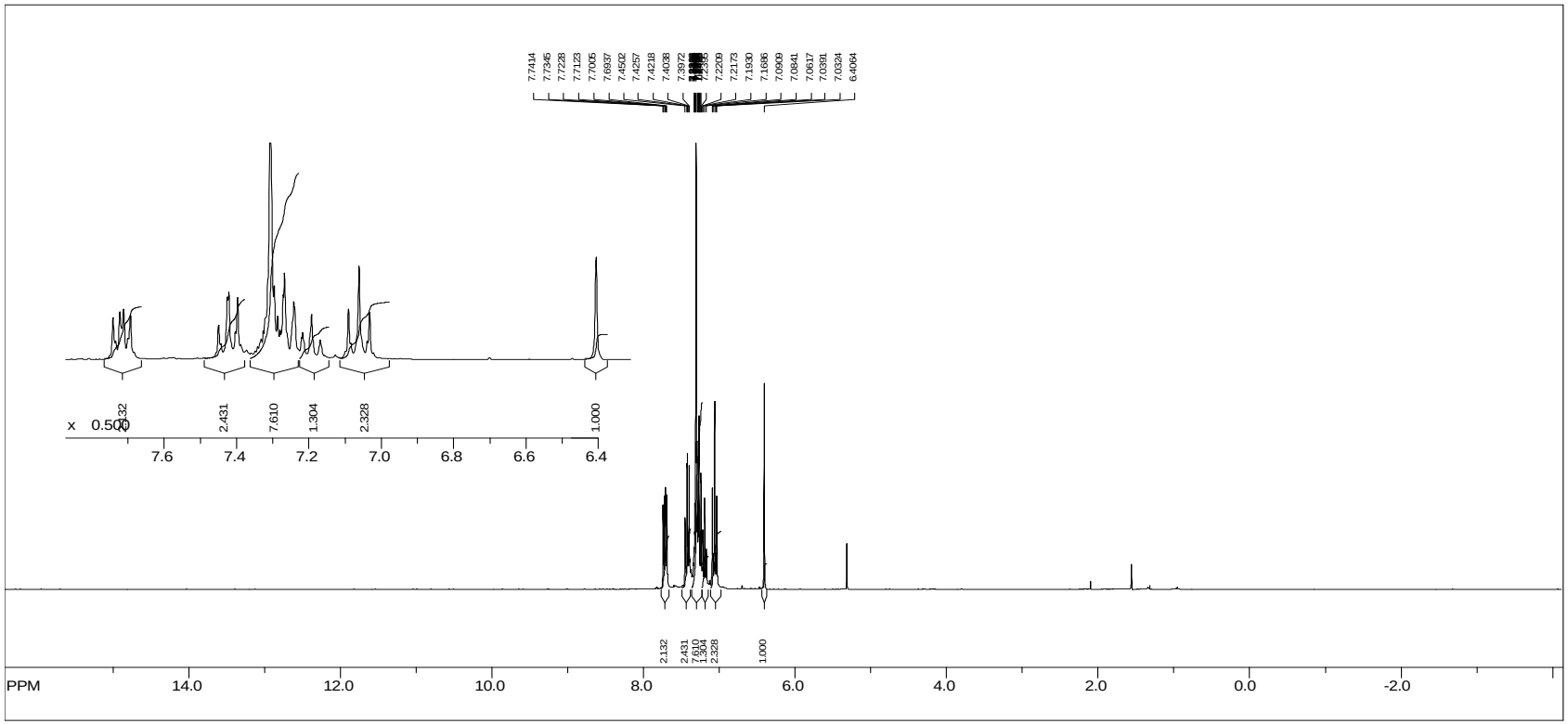
file: Z:\Laina\lmgix\lmgix_28c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 240

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(4-(4-Fluorophenyl)-3-phenoxybut-3-en-1-ynyl)benzene (243)



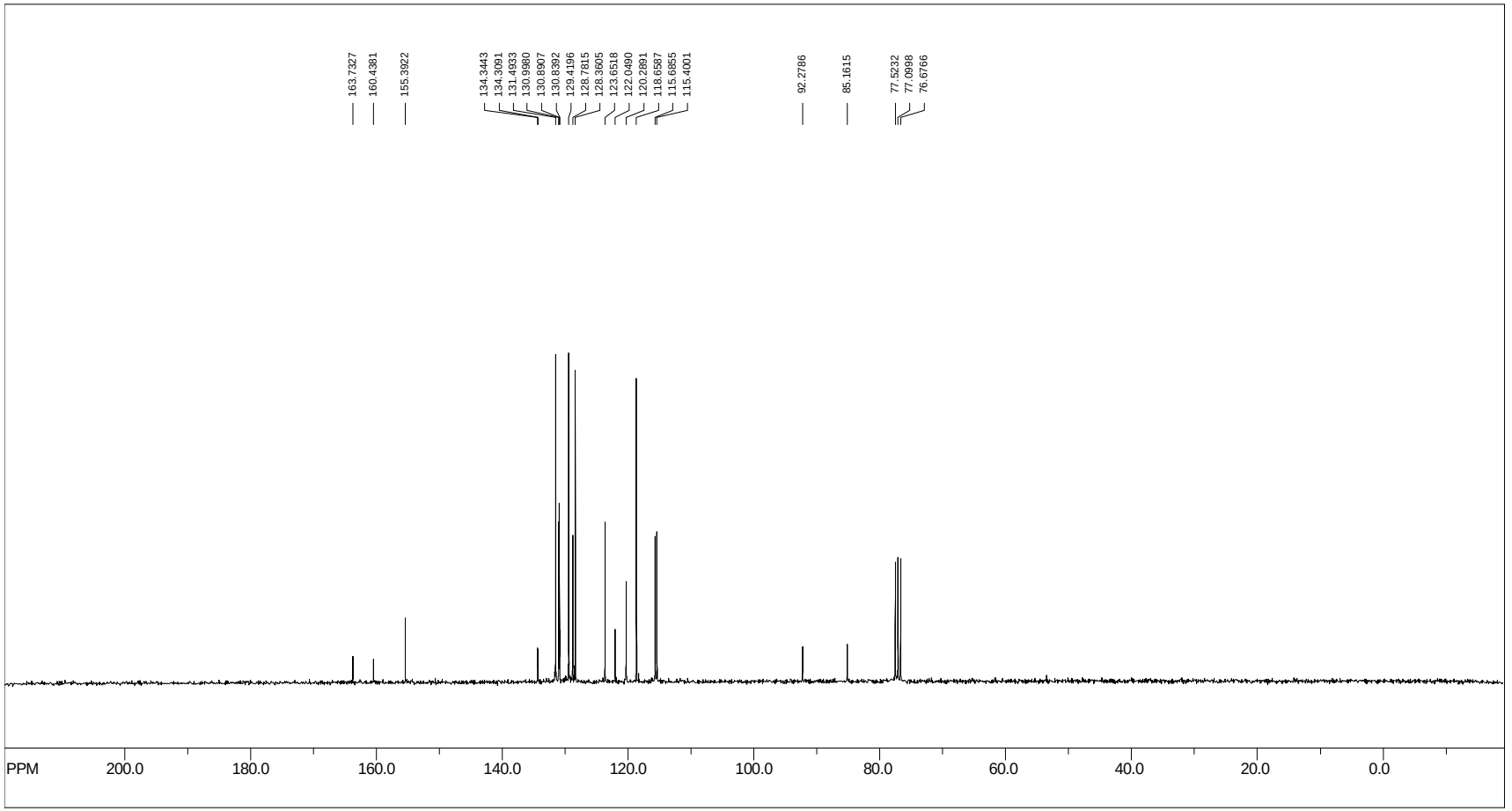
SpinWorks 2.5: suzuki on sonogashira adduct with p-fluorophenylboronic acid



file: Z:\Laina\lmgix\lmgix_29b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

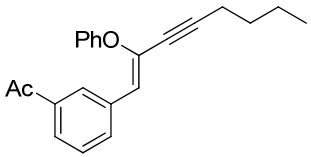
SpinWorks 2.5: suzuki on sonogashira adduct with p-fluorophenylboronic acid



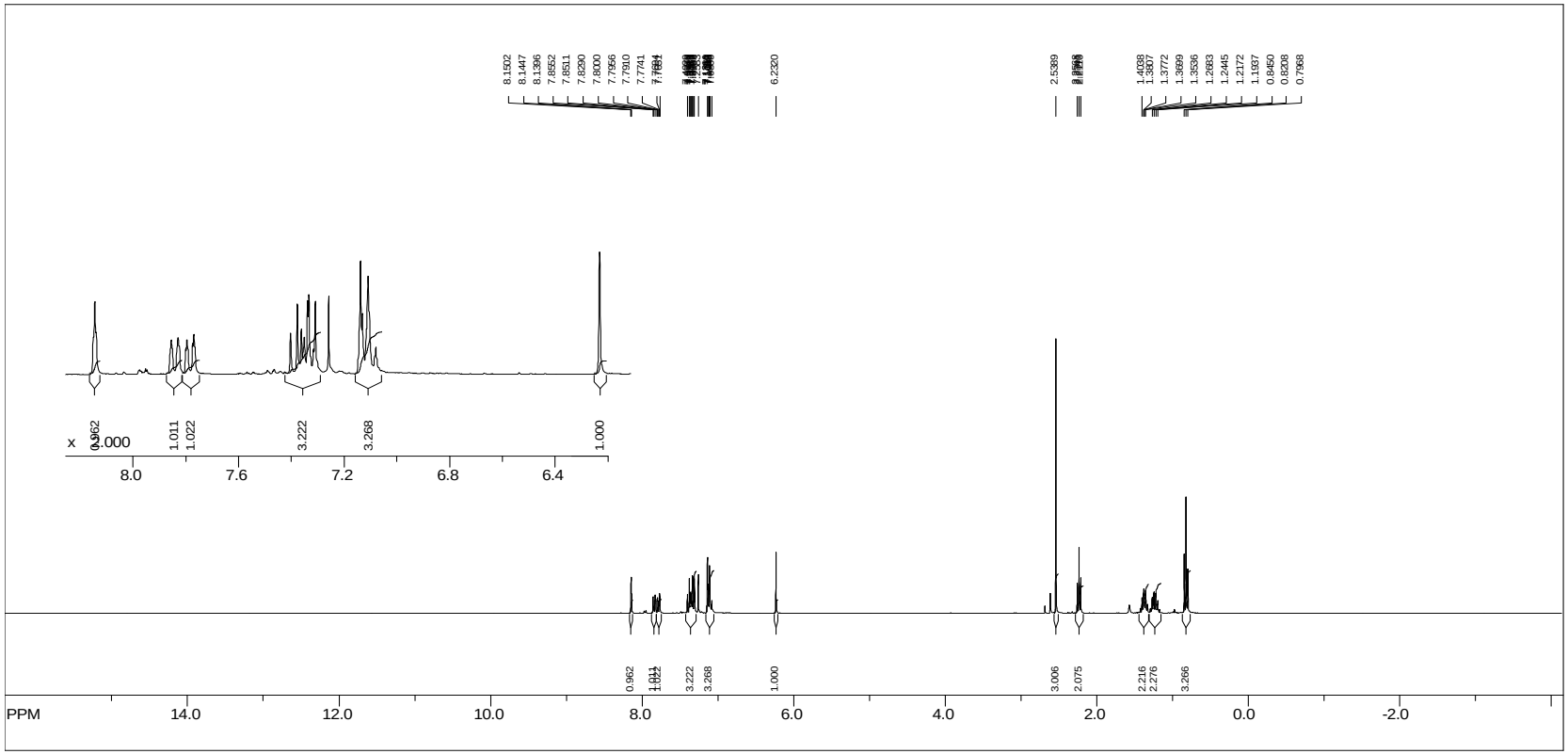
file: Z:\Laina\lmgix\lmgix_29b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 220

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(3-(2-Phenoxyoct-1-en-3-ynyl)phenyl)ethanone (245)



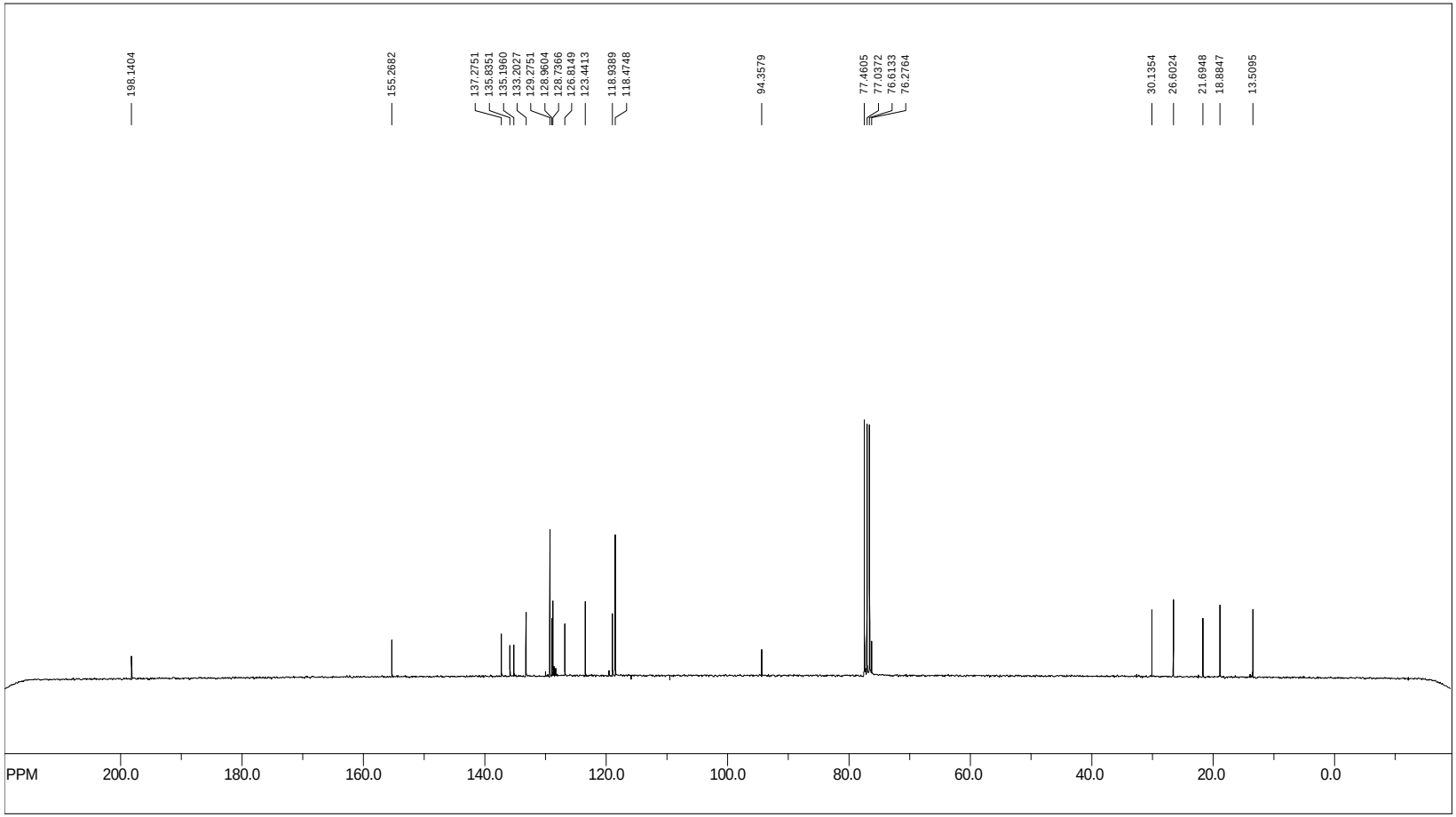
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxiii\lmgxiii_65b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

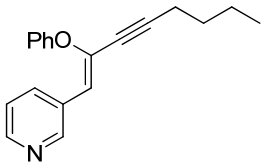
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



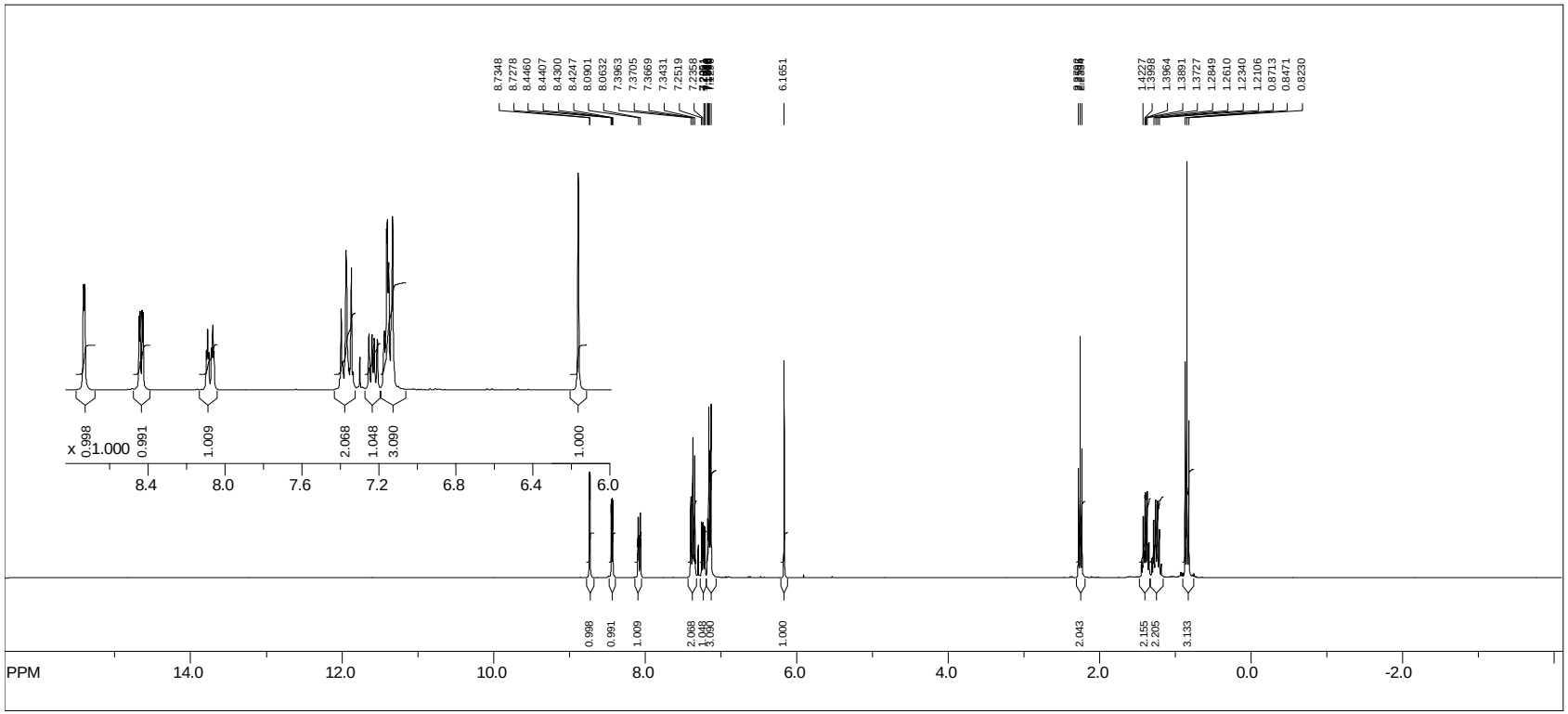
file: Z:\Laina\lmgxiii\lmgxiii_65b\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 5500

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*Z*)-3-(2-Phenoxyoct-1-en-3-ynyl)pyridine (246)



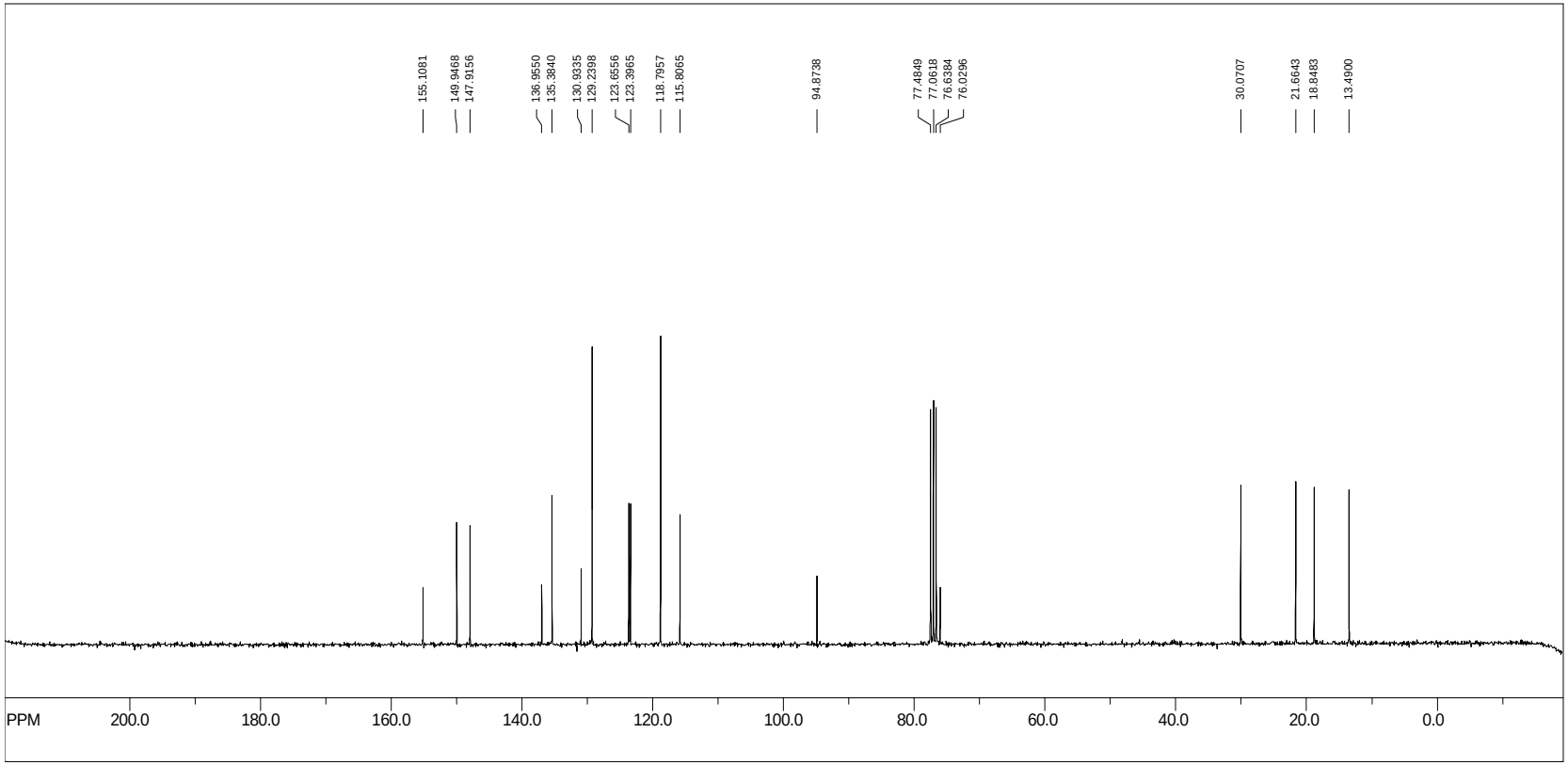
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 9



file: Z:\Laina\lmgw\lmgw_87b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

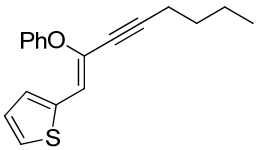
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



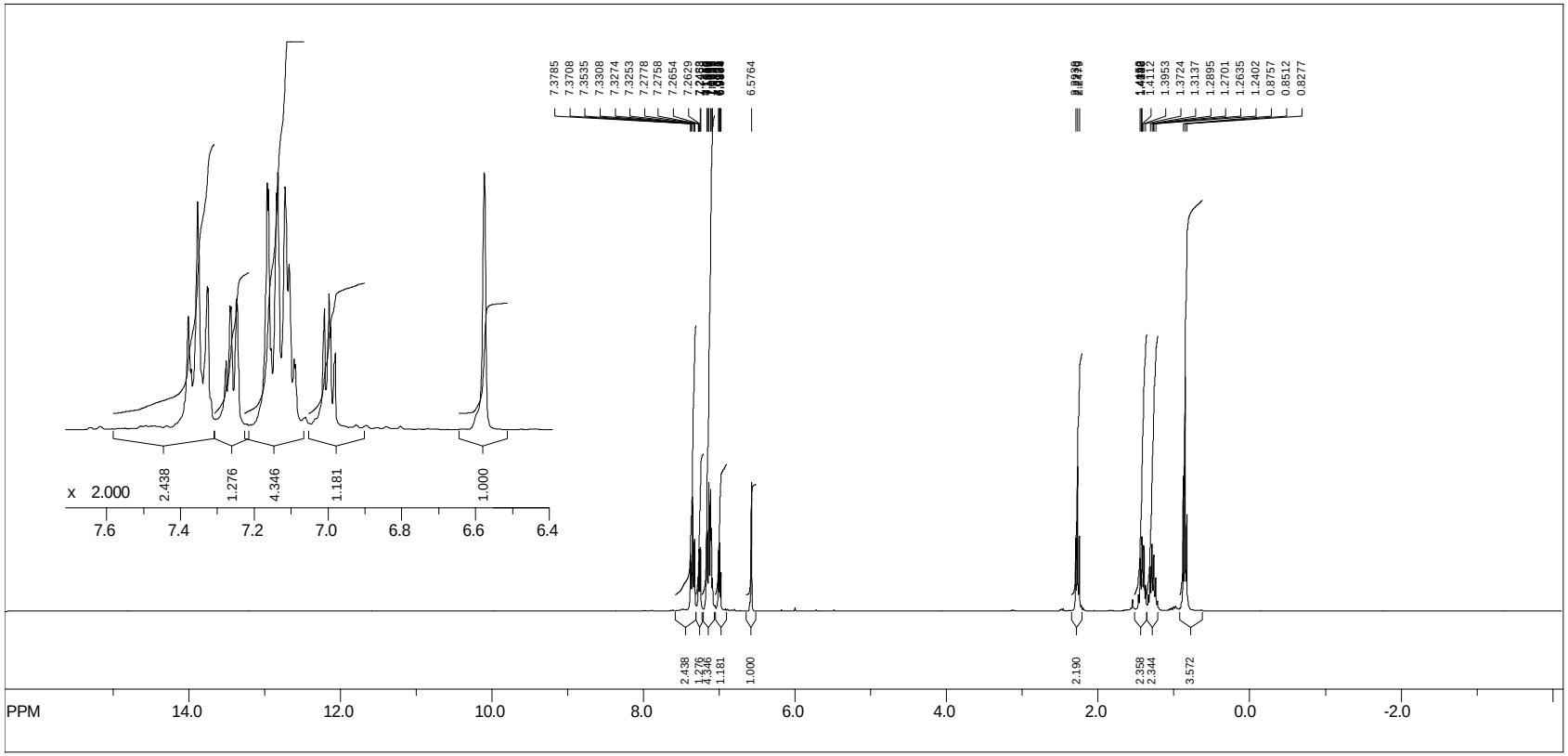
file: Z:\Laina\lmgx\lmgxv_87b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-2-(2-Phenoxyoct-1-en-3-ynyl)thiophene (247)



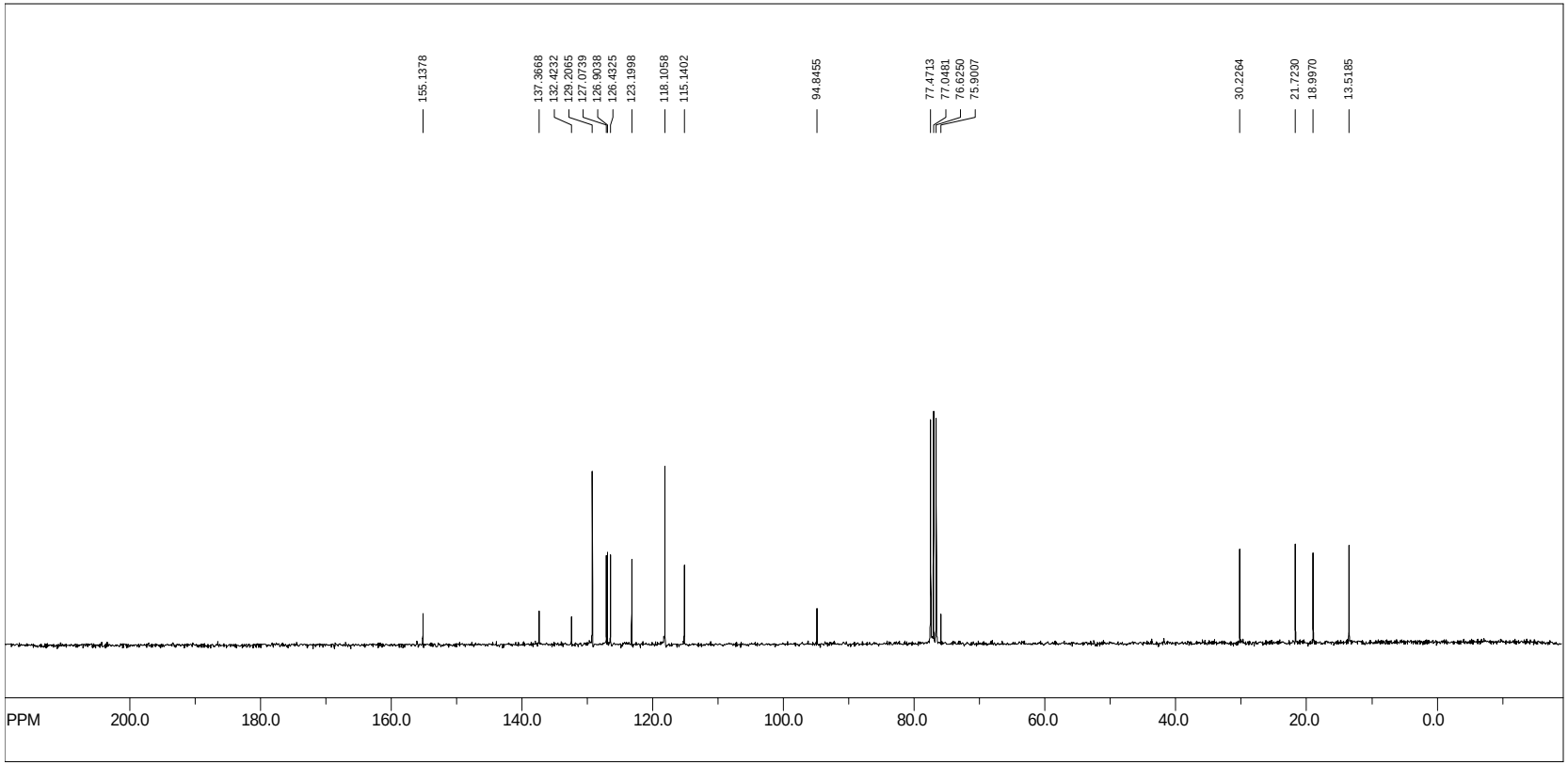
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgx\lmgxv_86b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

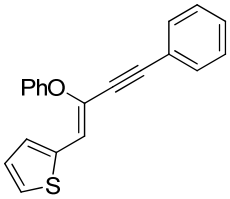
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



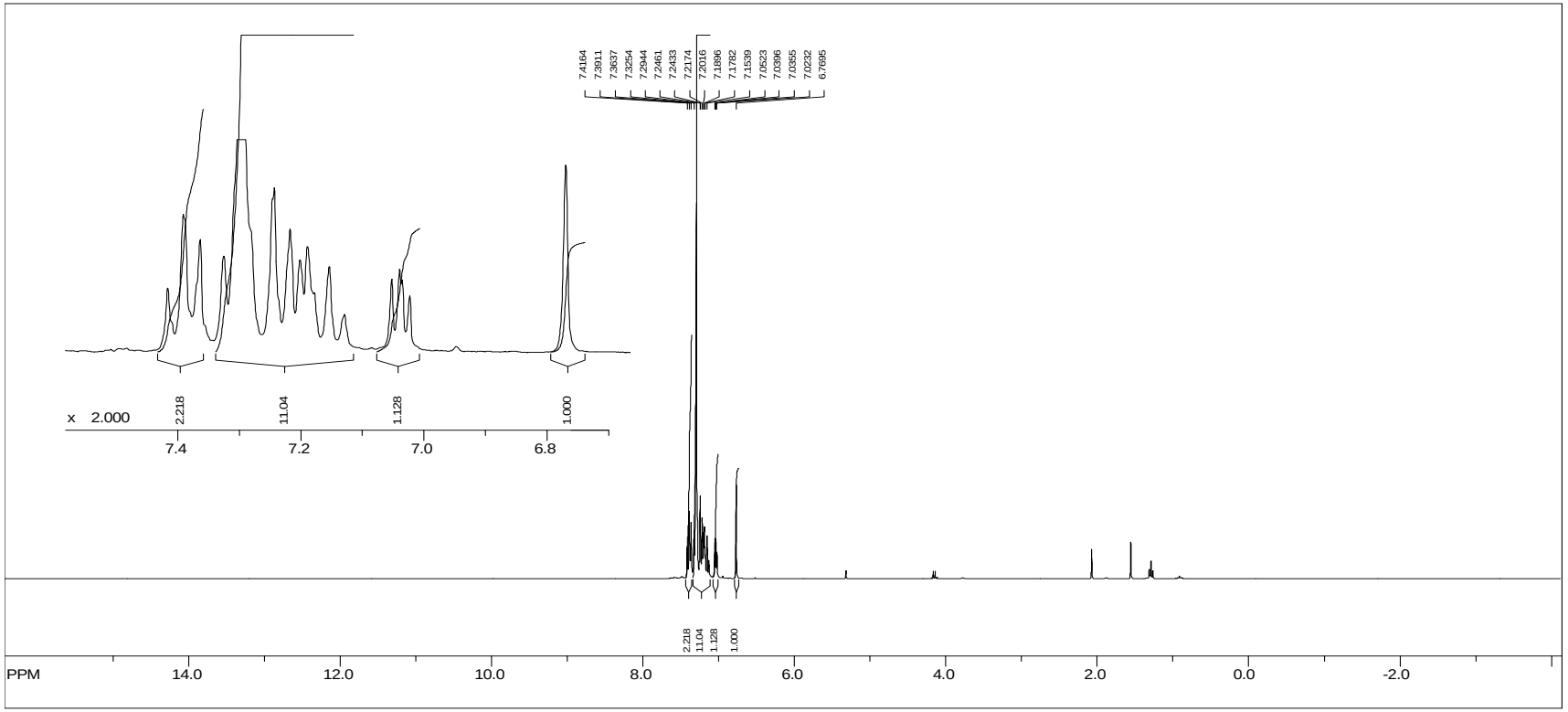
file: Z:\Laina\lmgx\lmgxv_86b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 558

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-2-(2-Phenoxy-4-phenylbut-1-en-3-ynyl)thiophene (248)



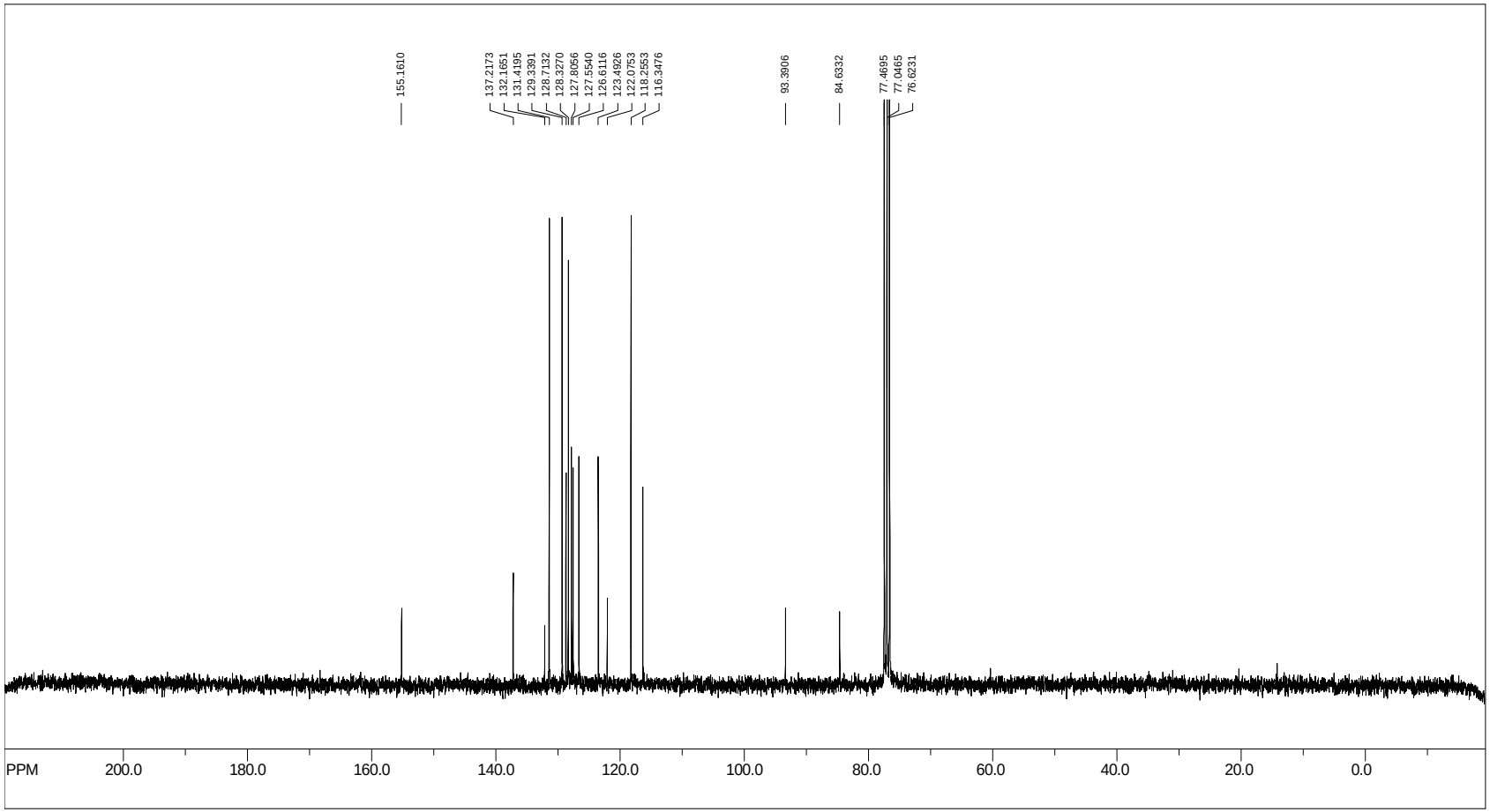
SpinWorks 2.5: suzuki on sonogashira adduct with 2-thiopheneboronic acid



file: Z:\Laina\lmgjx\lmgjx_30c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

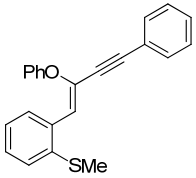
SpinWorks 2.5: suzuki on sonogashira adduct with 2-thiopheneboronic acid



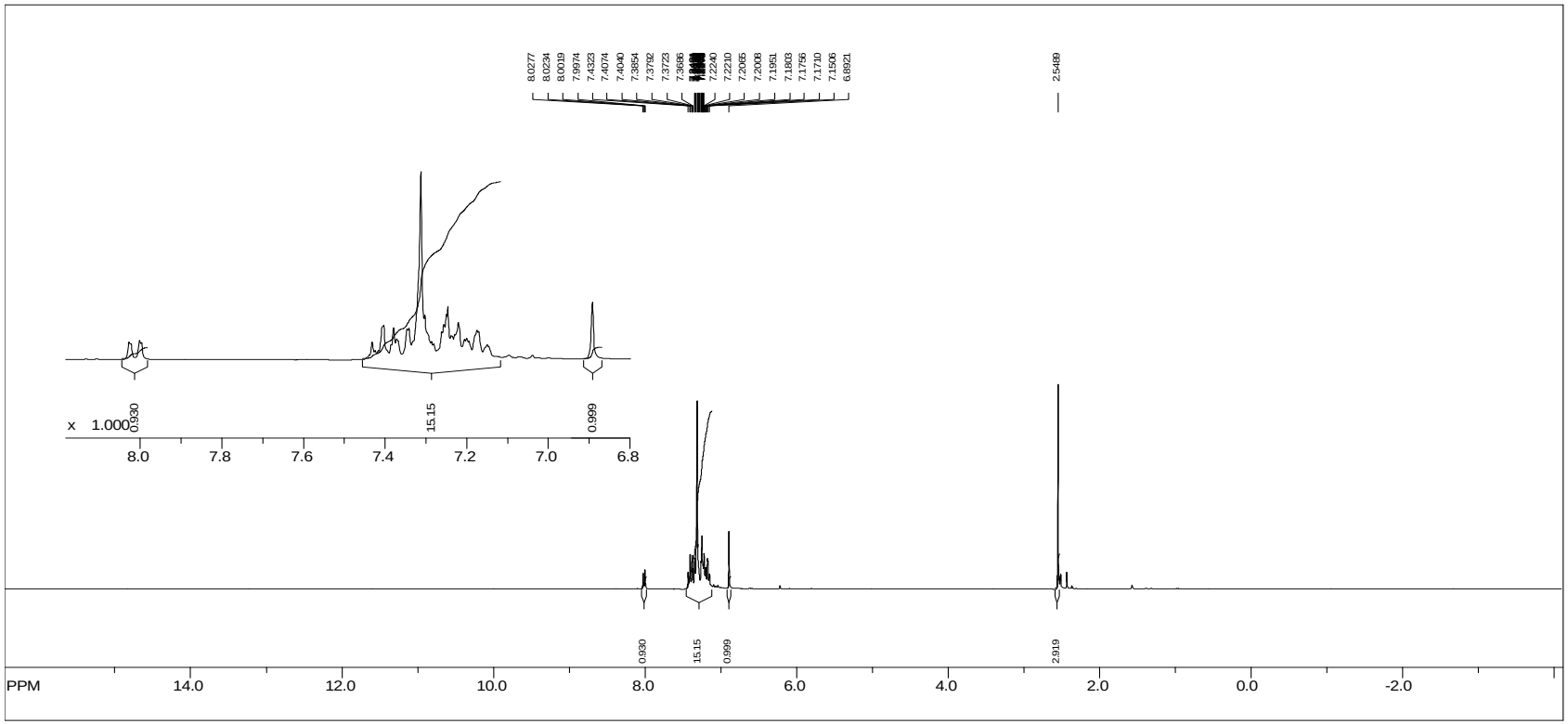
file: Z:\Laina\lmgix\lmgix_30c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 450

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-Methyl(2-(2-phenoxy-4-phenylbut-1-en-3-ynyl)phenyl)sulfane (244)



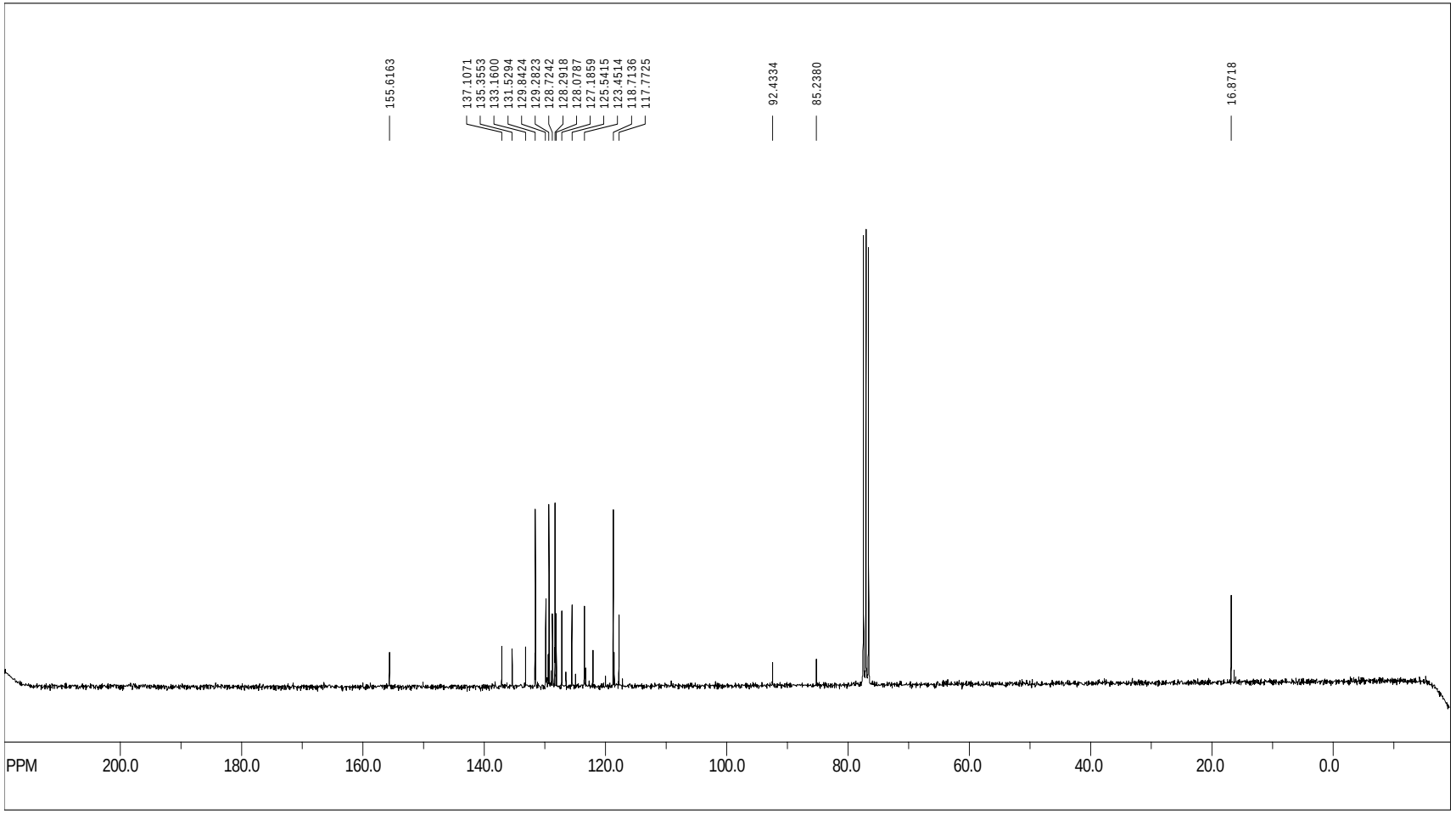
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 16



file: Z:\Laina\lmgxii\lmgxii_48e\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

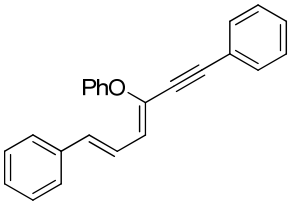
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



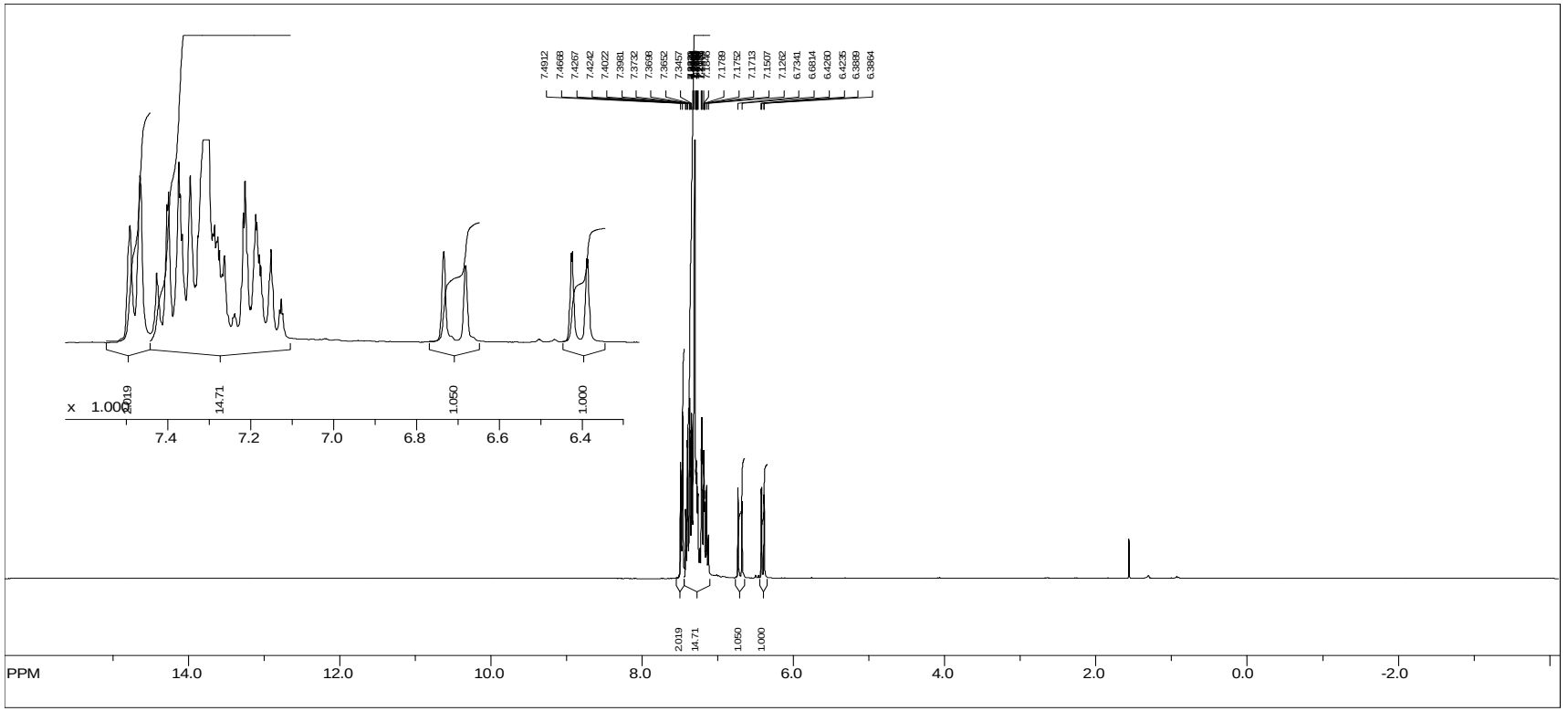
file: Z:\Laina\lmgxii\lmgxii_48eii\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 992

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(1*E*,3*Z*)-3-Phenoxy-1,6-diphenylhexa-1,3-dien-5-yne (249)



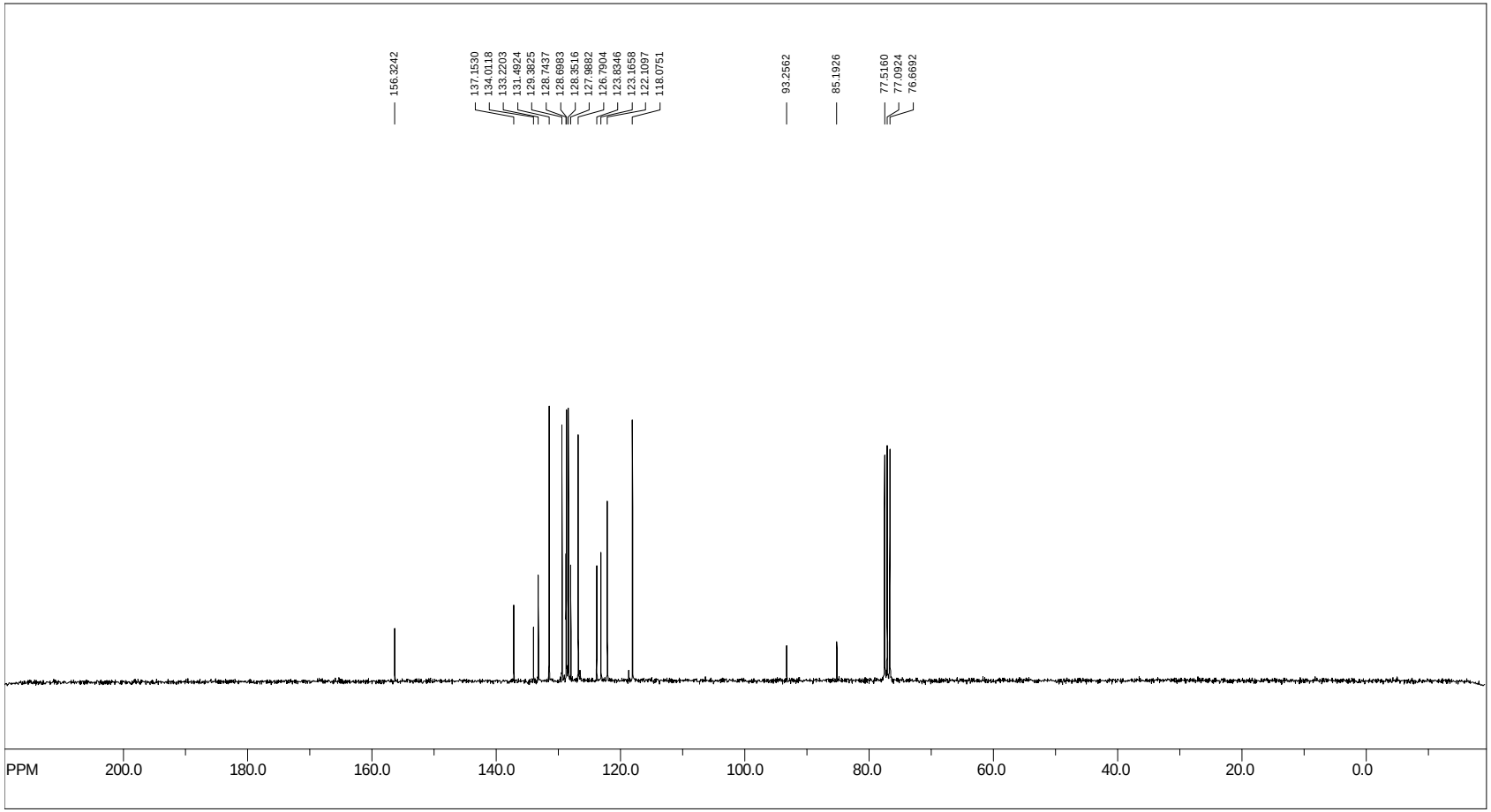
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgxiii\lmgxiii_30ci\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

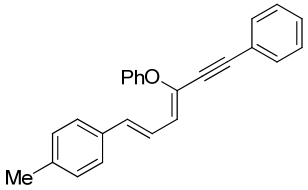
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



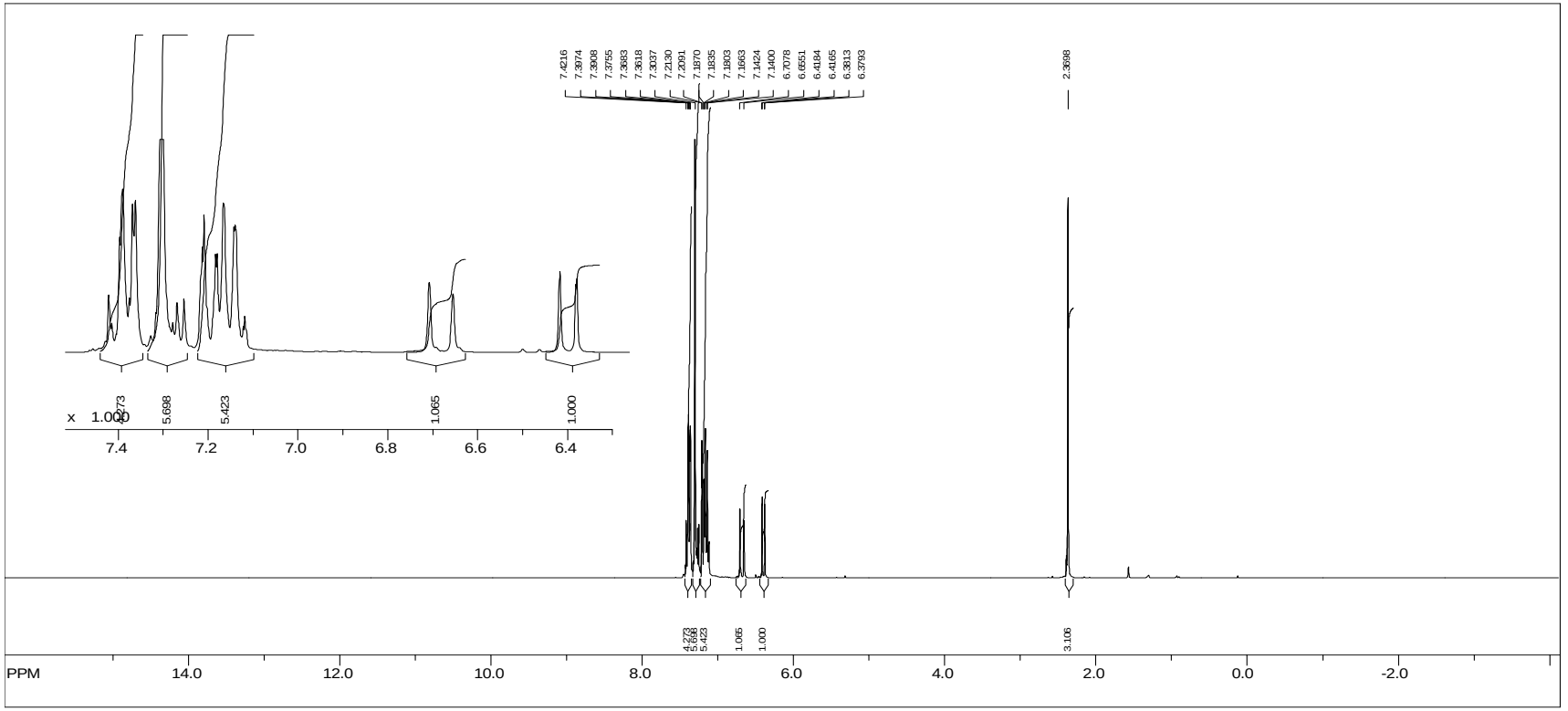
file: Z:\Laina\lmgxiii\lmgxiii_30ci\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-((3*Z*,5*E*)-3-Phenoxy-6-*p*-tolylhexa-3,5-dien-1-ynyl)benzene (250)



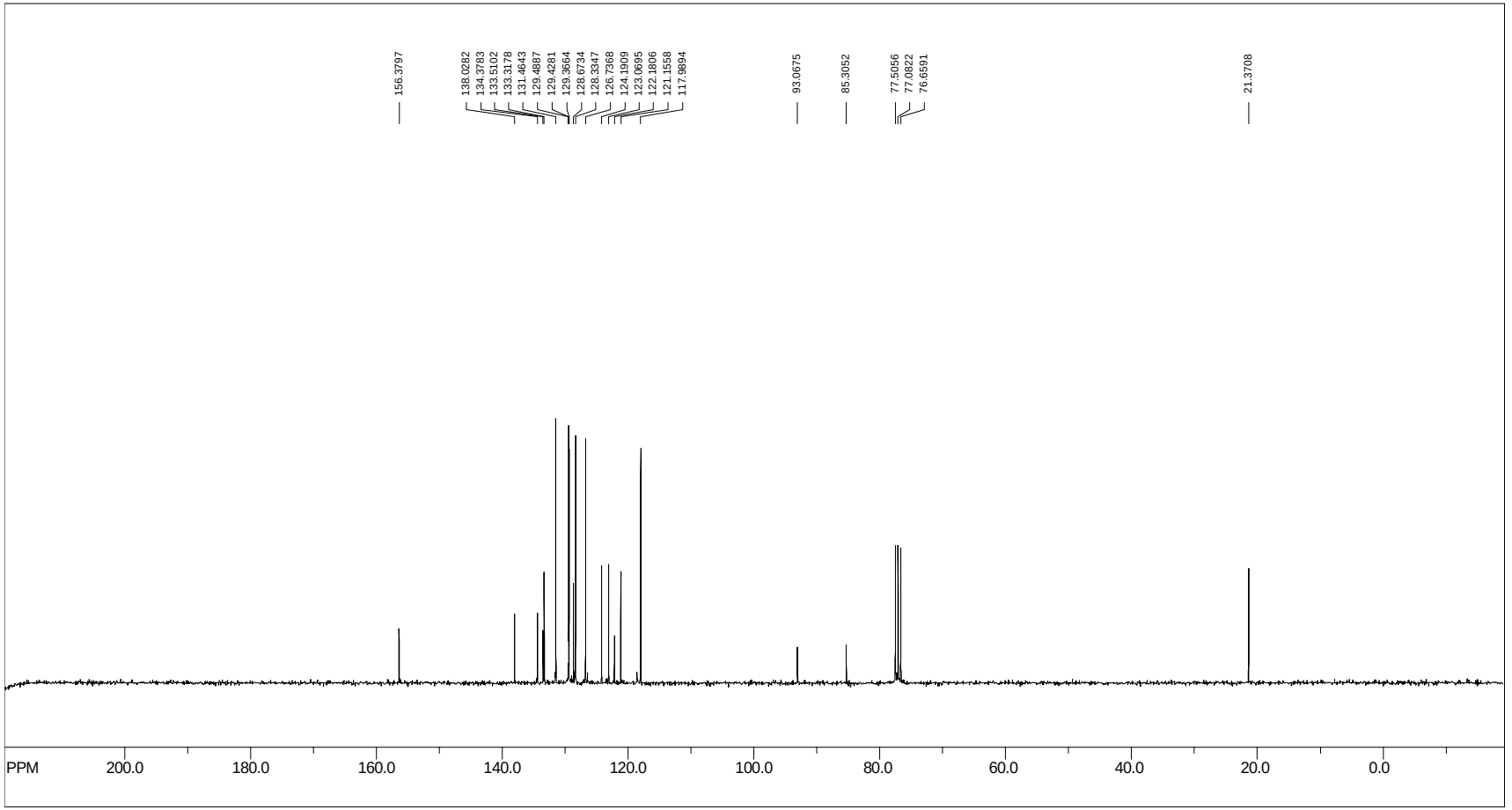
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 9



file: Z:\Laina\lmgxiii\lmgxiii_31c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

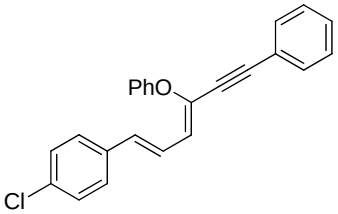
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 9

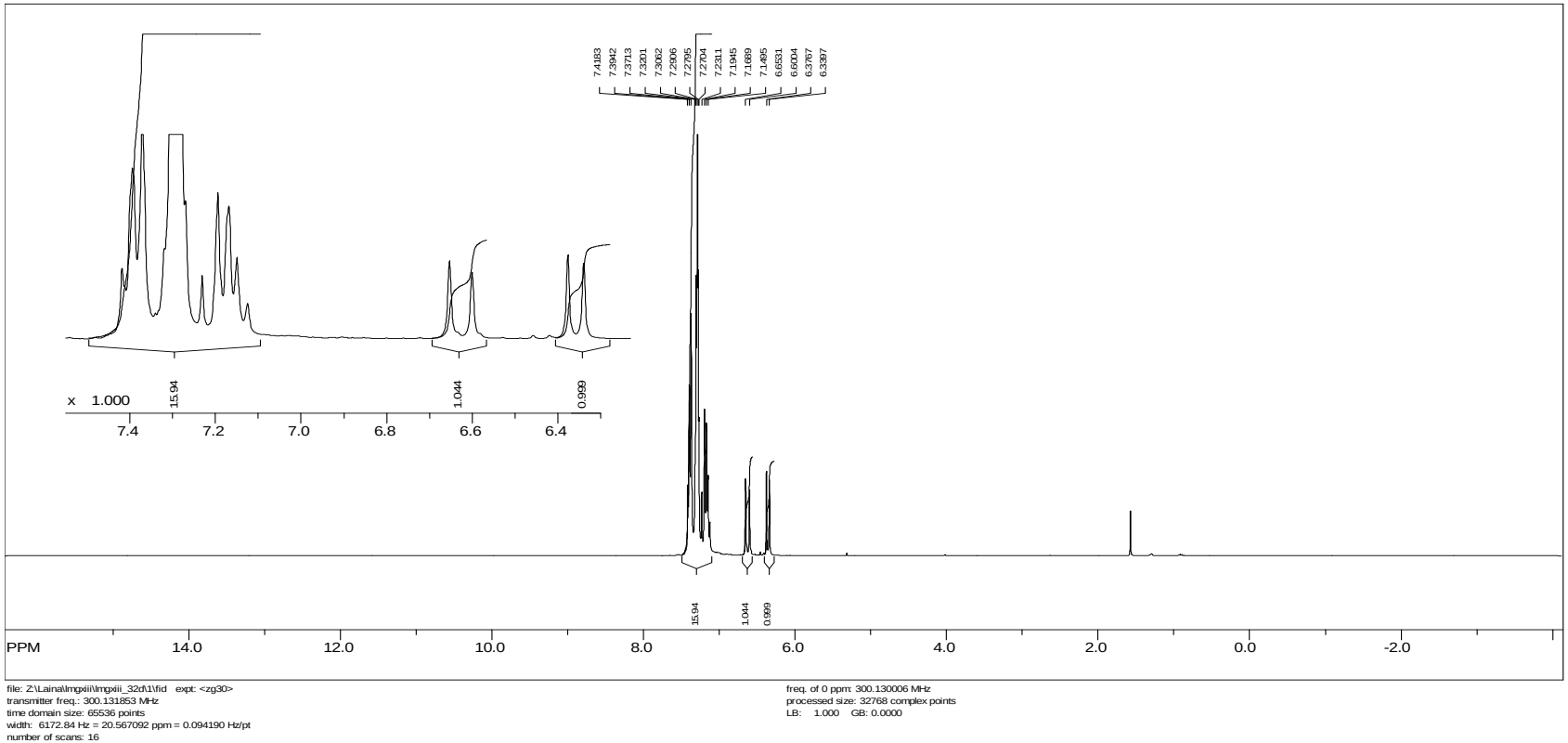


file: Z:\Laina\lmgxiii\lmgxiii_31c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 418

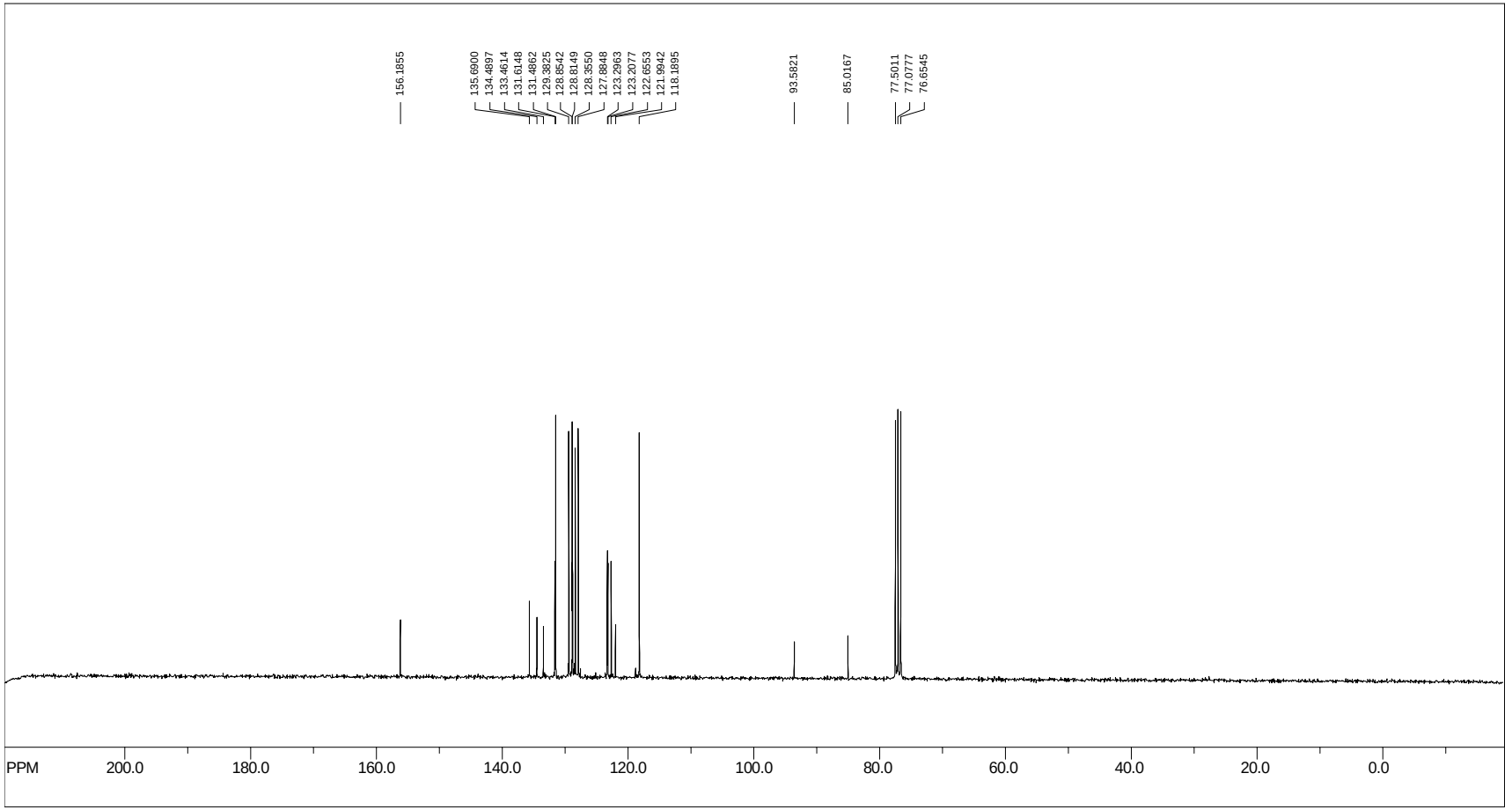
freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-((3*Z*,5*E*)-6-(4-Chlorophenyl)-3-phenoxyhexa-3,5-dien-1-ynyl)benzene (251)





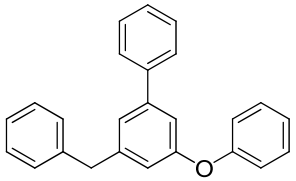
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



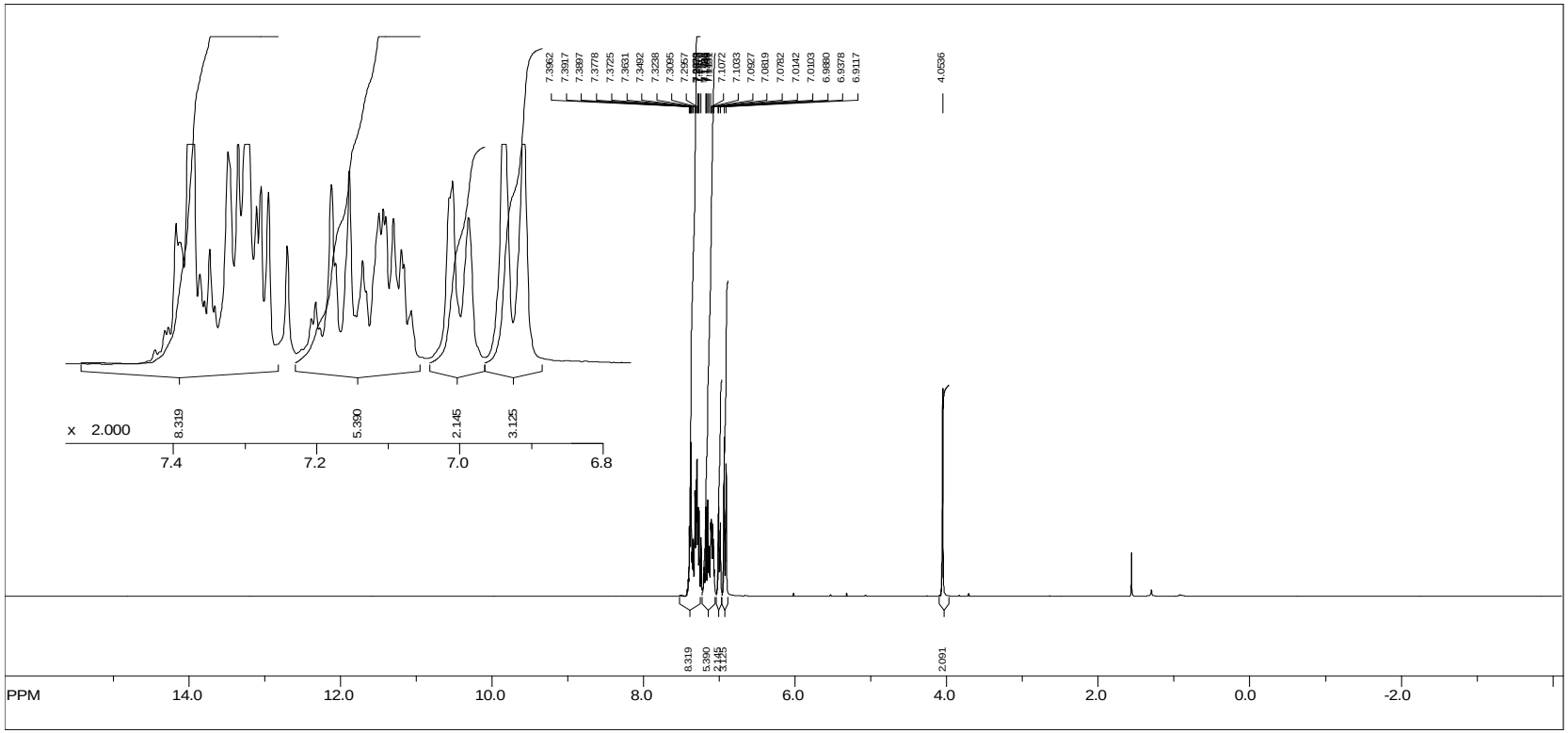
file: Z:\Laina\lmgxiii\lmgxiii_32d\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(3-Benzyl-5-phenoxy)biphenyl (253)



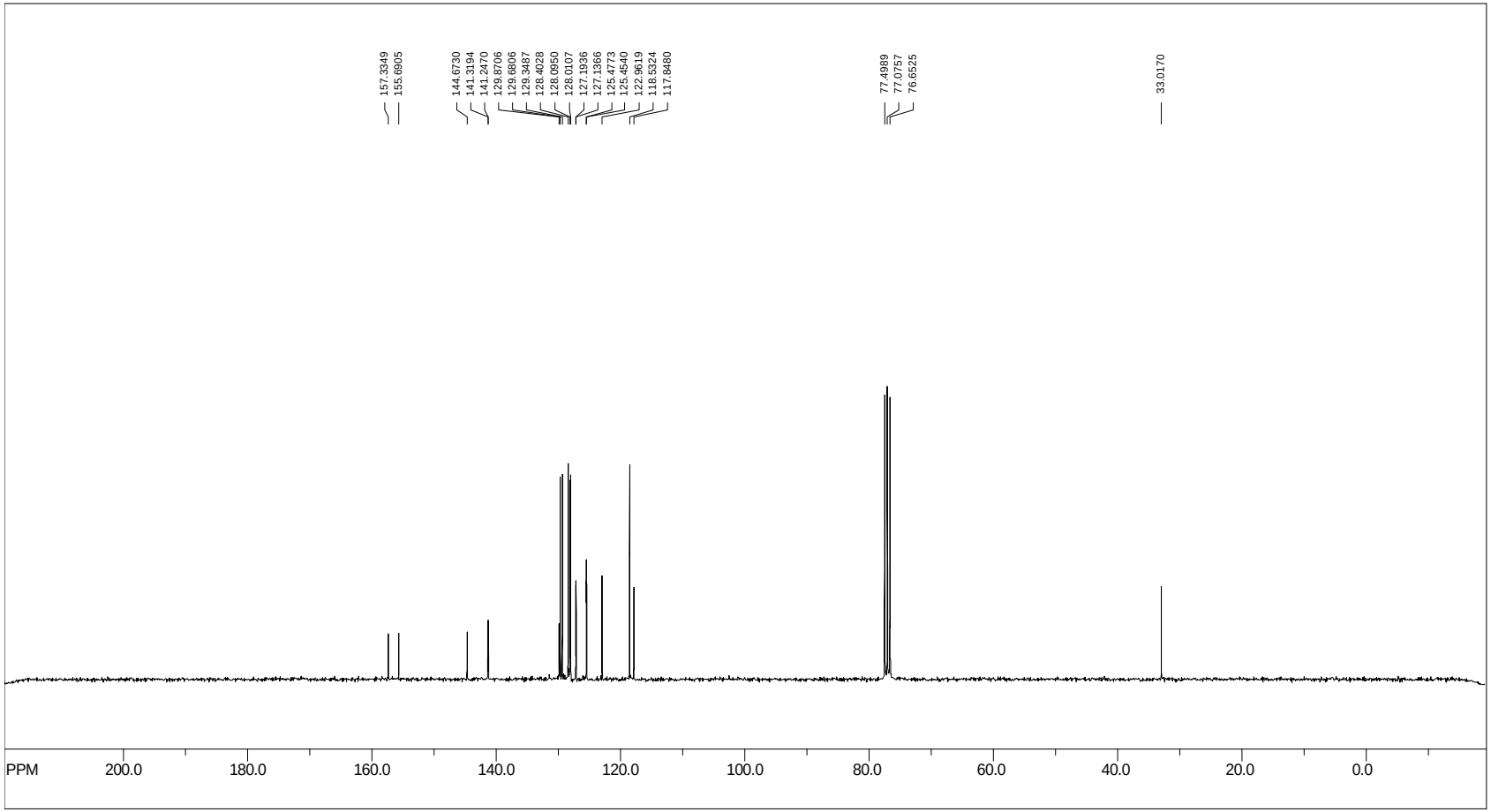
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



file: Z:\Laina\lmgxiii\lmgxiii_33c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

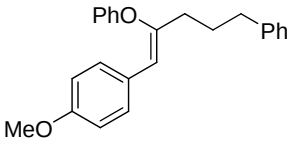
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



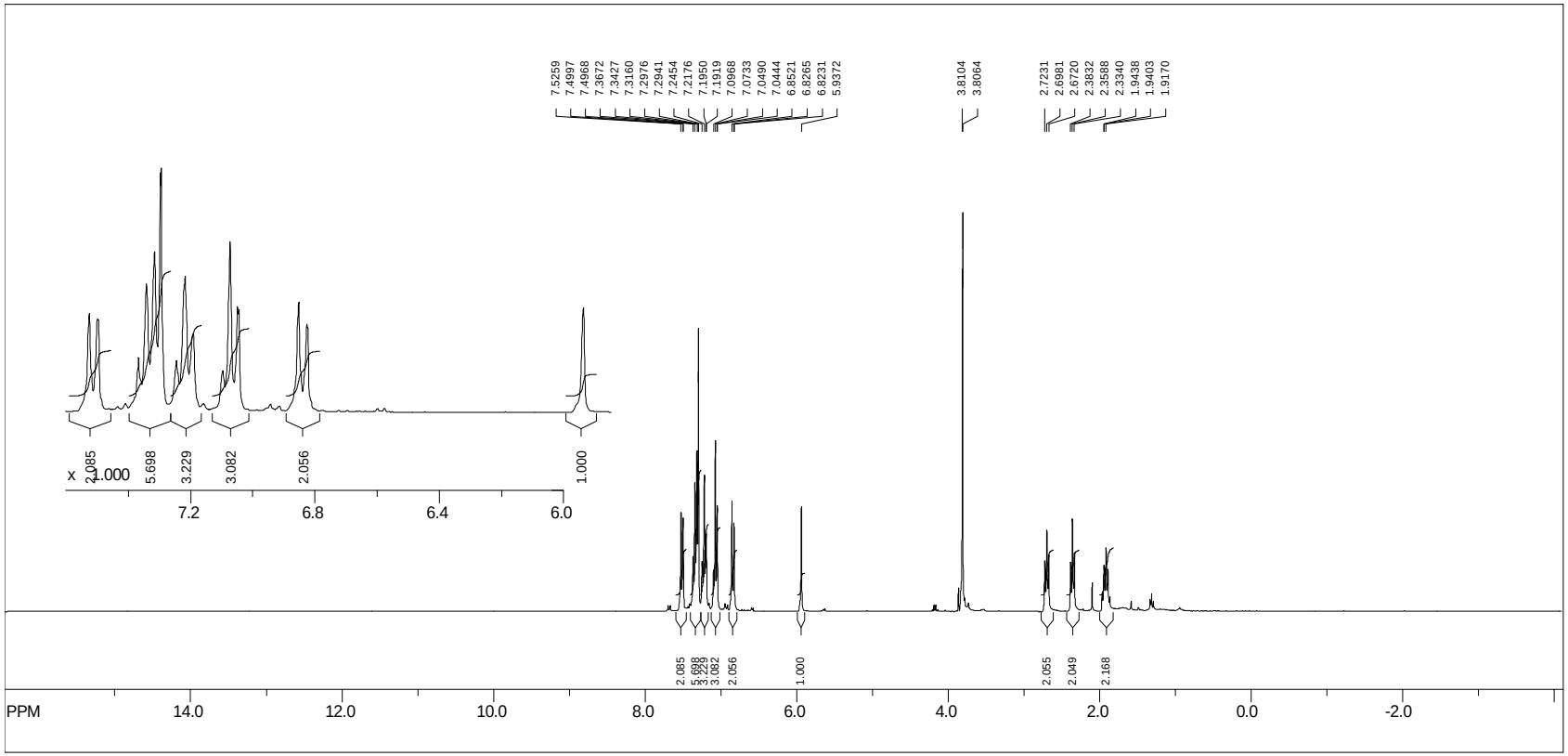
file: Z:\Laina\lmgxiii\lmgxiii_33c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1005

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-Methoxy-4-(2-phenoxy-5-phenylpent-1-enyl)benzene (254)



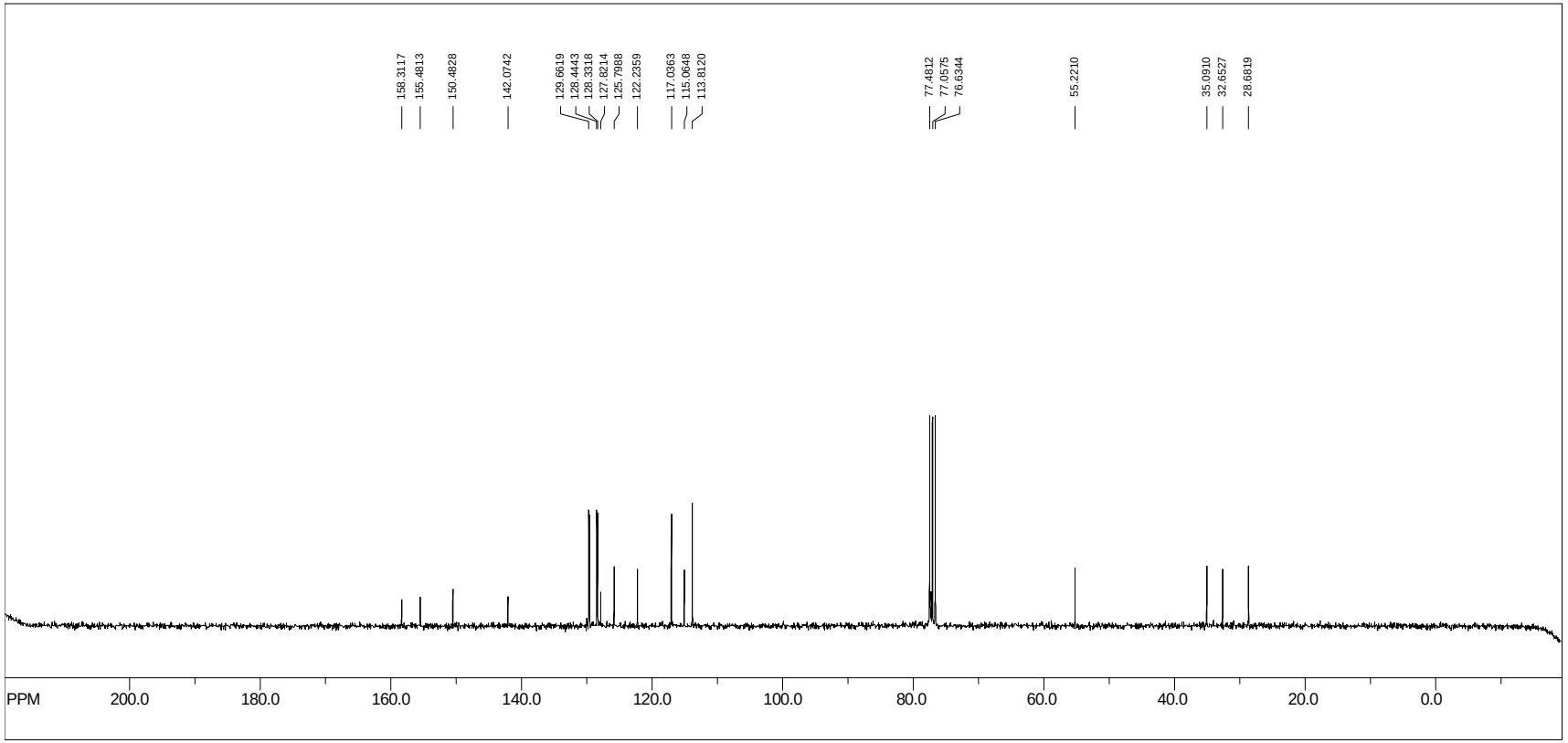
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxv\lmgxv_69b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

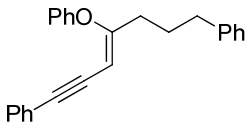
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



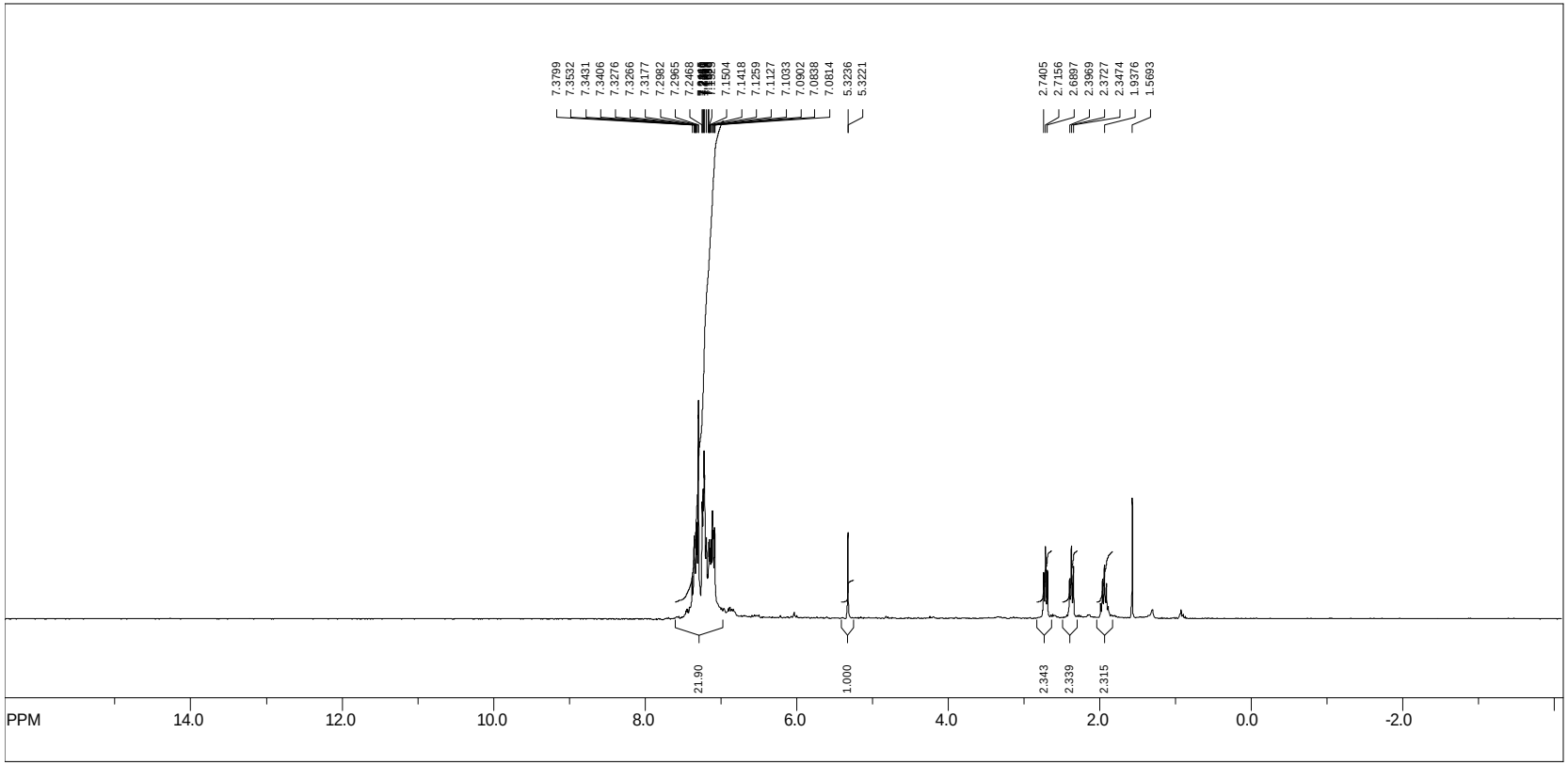
file: Z:\Laina\lmgx\lmgxv_69b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 234

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-4-Phenoxy-1,7-diphenylhept-3-en-1-yne (255)



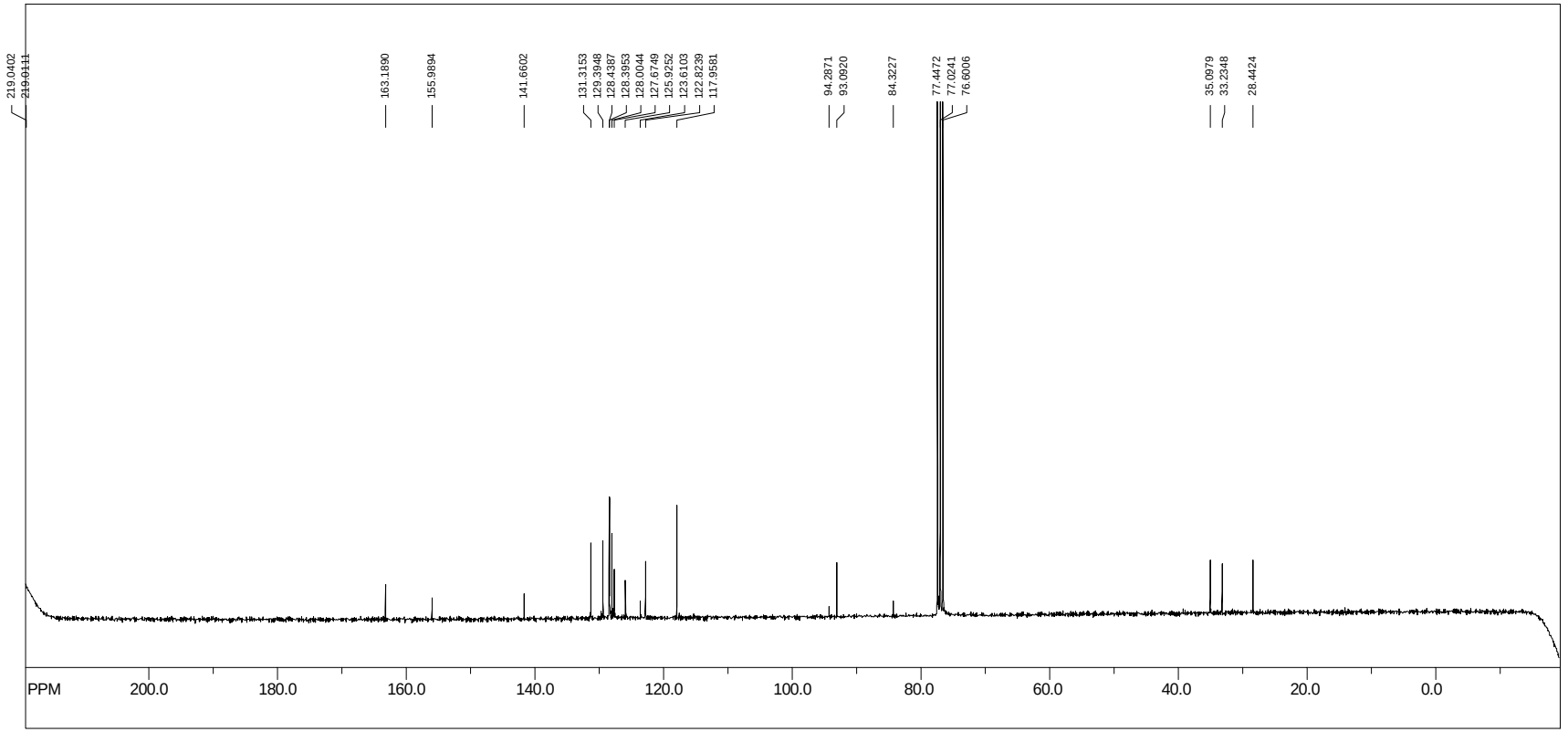
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



file: Z:\Laina\lmgxv\lmgxv_71b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 9

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

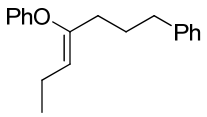
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



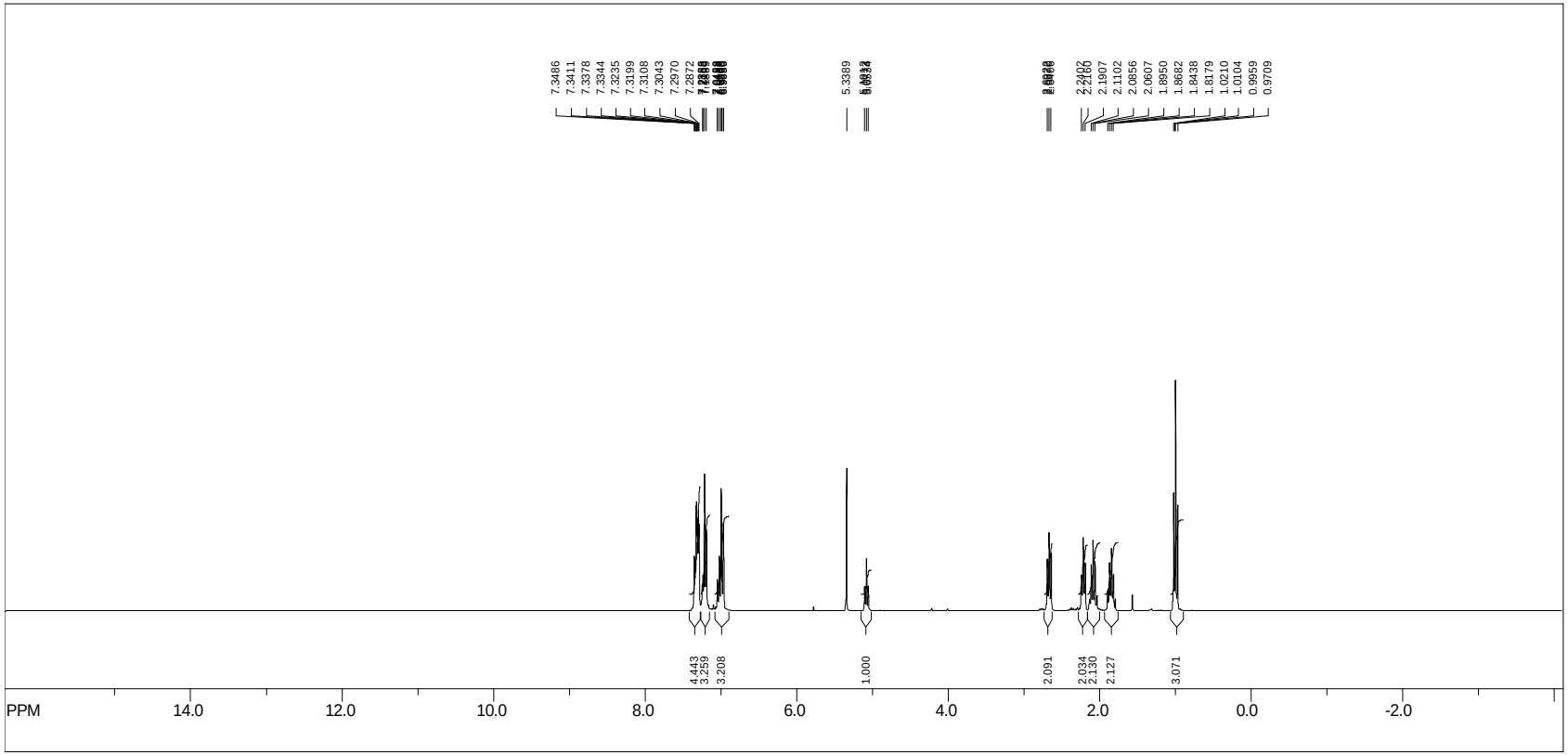
file: Z:\Laina\lmgxv\lmgxv_71b\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 11000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*Z*)-1-(1-Phenylhept-4-en-4-yloxy)benzene (257)



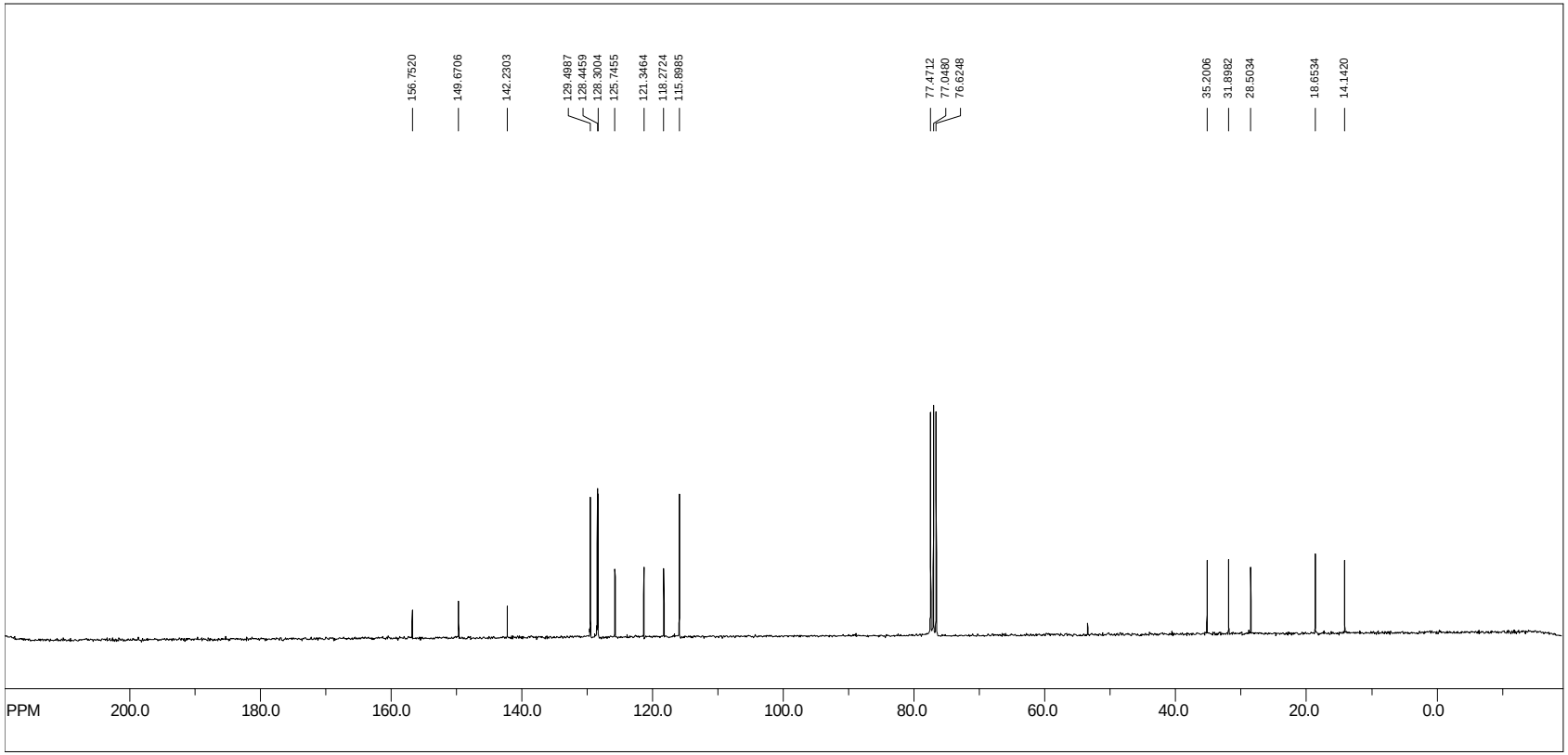
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgxv\lmgxv_72bi\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

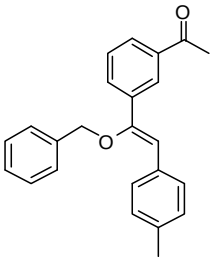
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



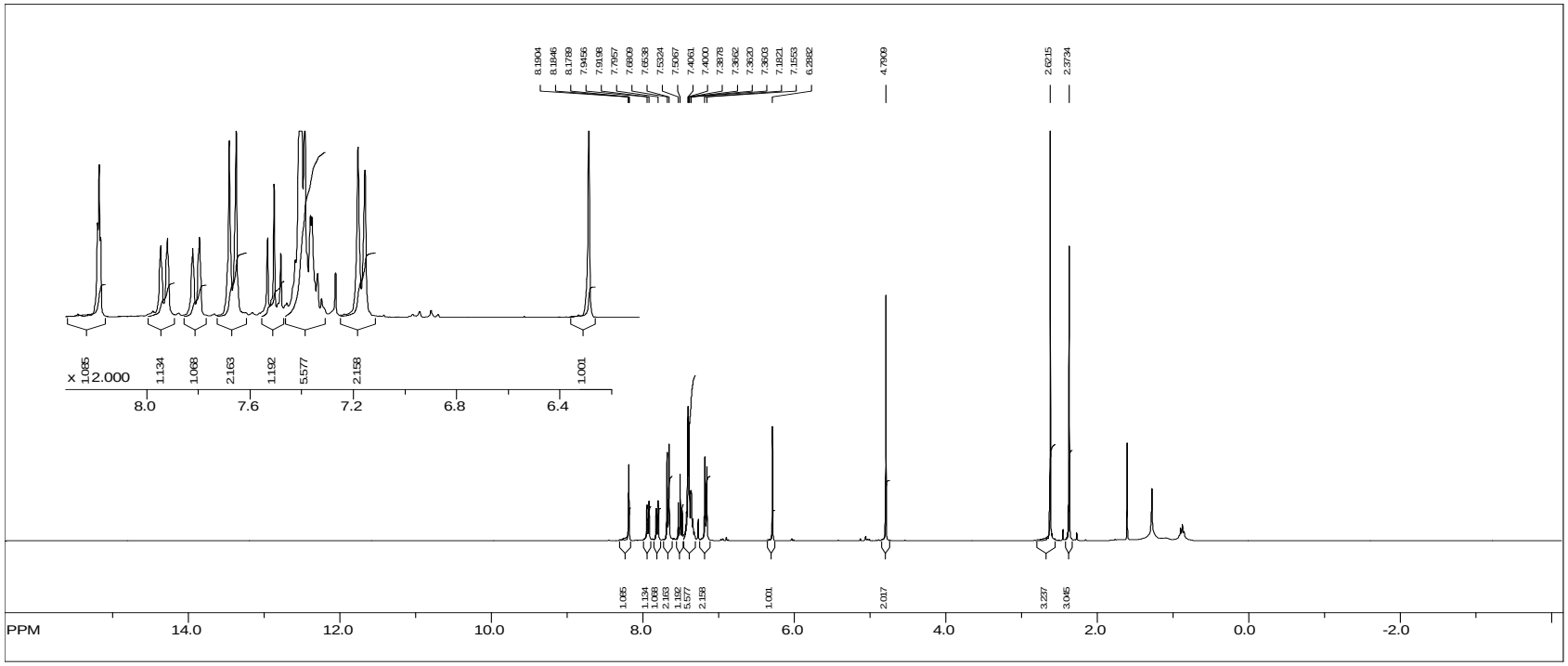
file: Z:\Laina\lmgxv\lmgxv_72bi\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-1-(3-(1-Benzyloxy)-2-*p*-tolylvinyl)phenyl)ethanone (258)



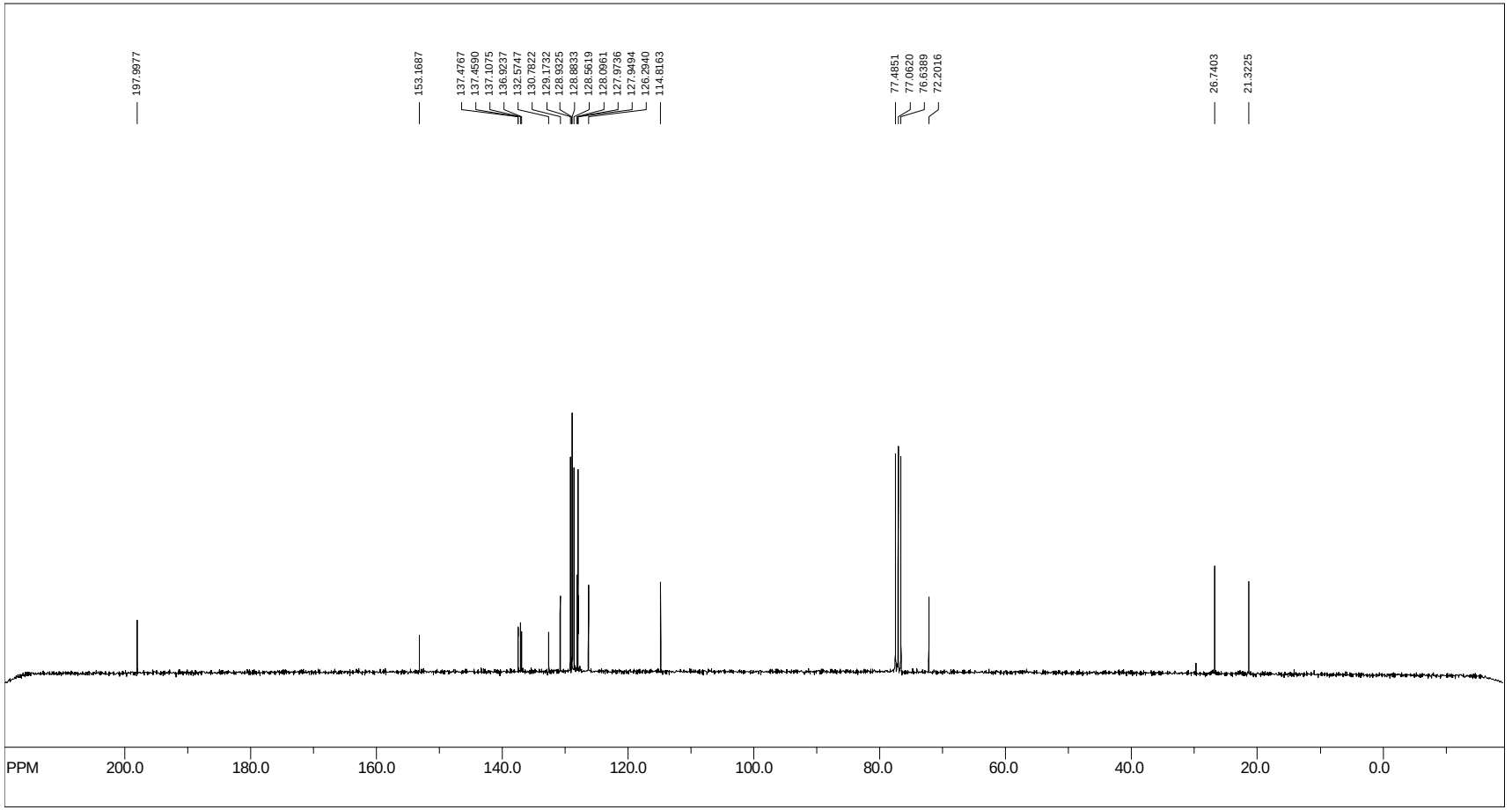
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 13



file: Z:\Laina\lmgxii\lmgxii_91c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 8

freq. of 0 ppm: 300.130009 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

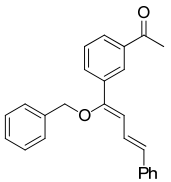
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 17



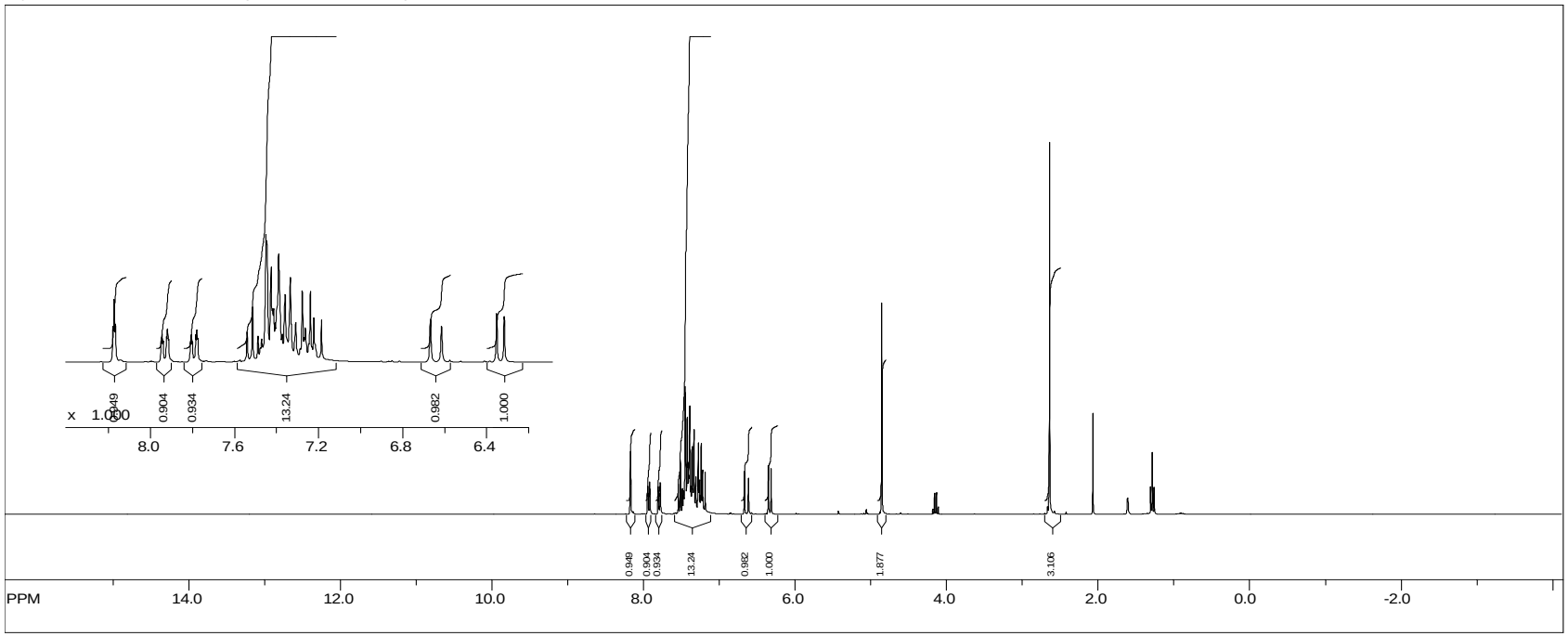
file: Z:\Laina\lmgxii\lmgxii_91c\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1005

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

1-(3-(1*Z*,3*E*)-1-(Benzyloxy)-4-phenylbuta-1,3-dienyl)phenyl)ethanone (259)



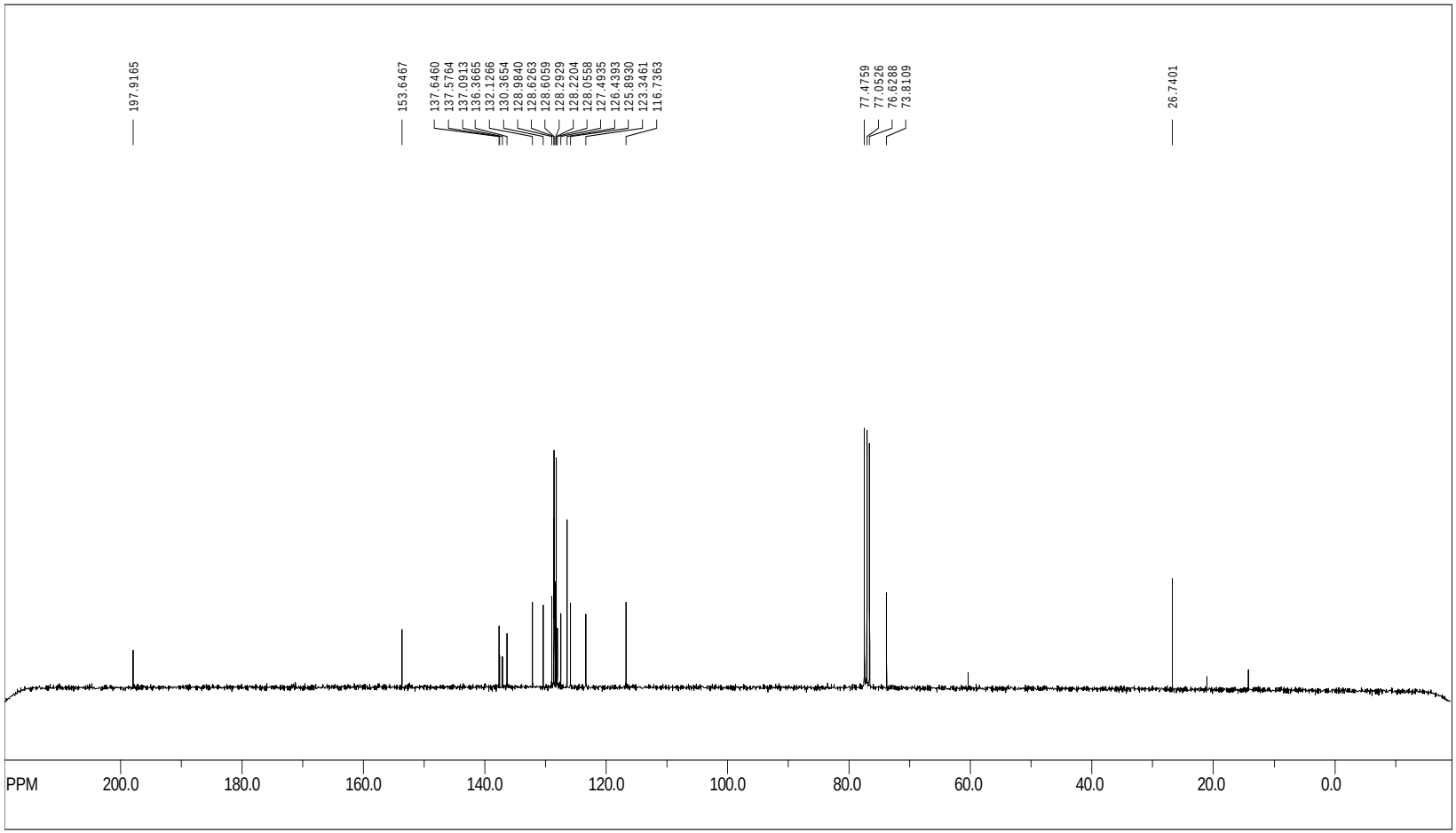
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



file: Z:\Laina\lmgxiii\lmgxiii_10c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10

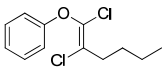


file: Z:\Laina\lmgxiii\lmgxiii_10c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

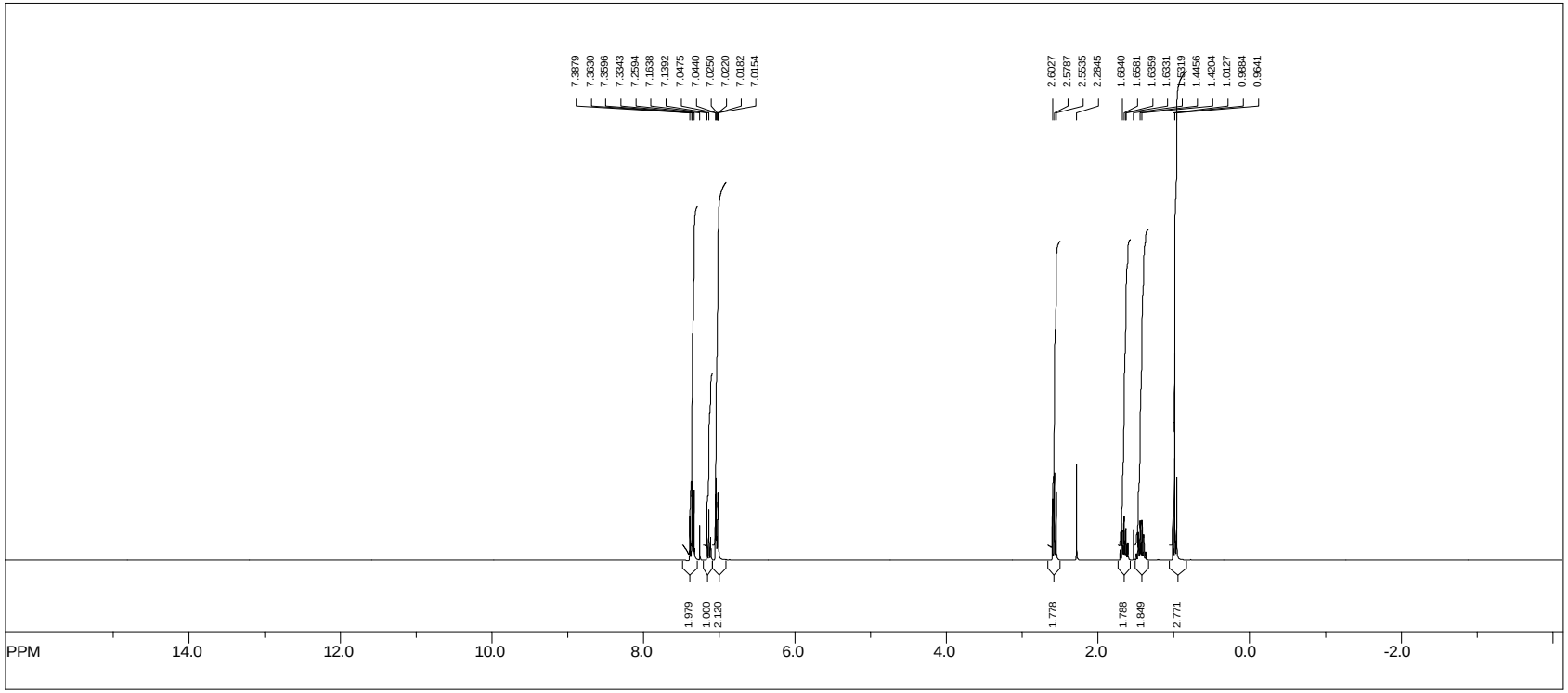
freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

6.4: Section 2.4.3 – Tetrasubstituted Alkenes

(*E*)-1-(1,2-Dichlorohex-1-enyloxy)benzene (260)



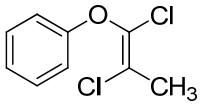
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4

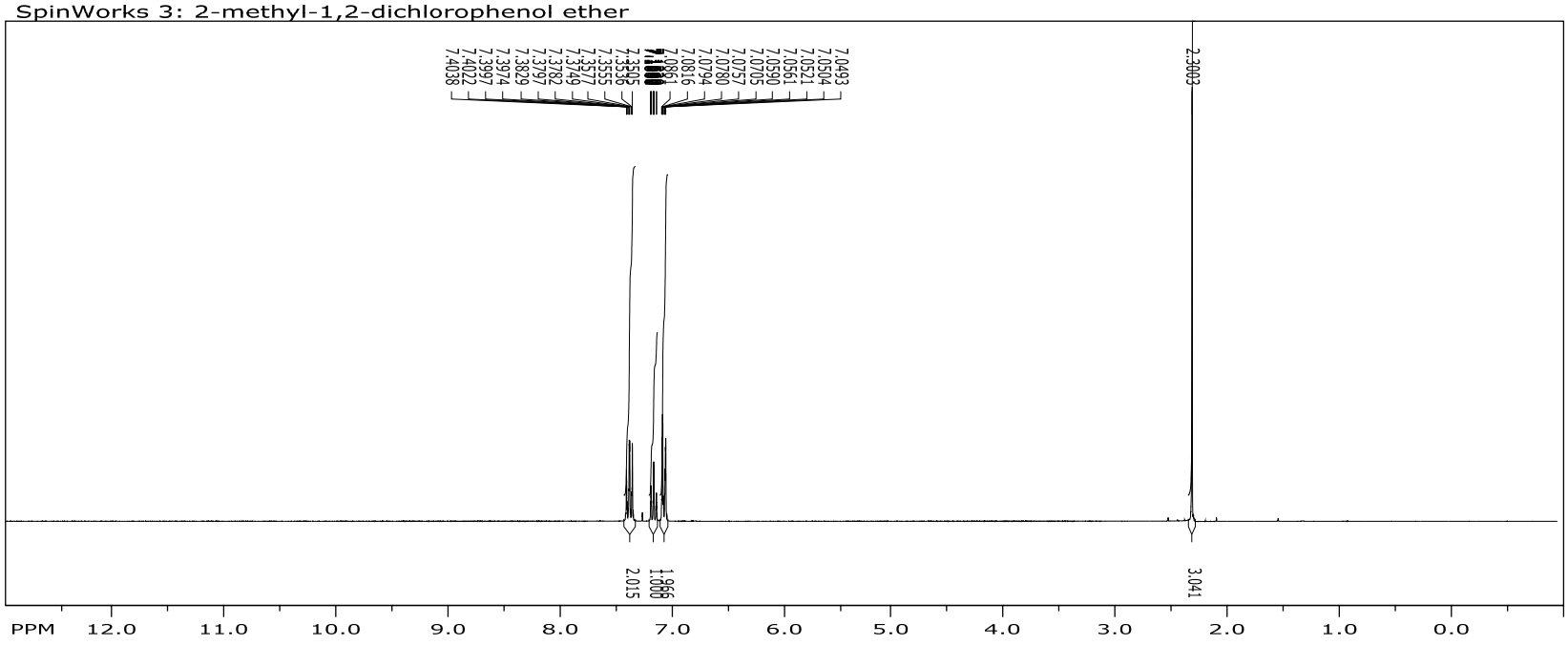


file: Z:\Laina\lmgvi\lmgvi_14a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-1-(1,2-Dichloroprop-1-enyloxy)benzene (261)

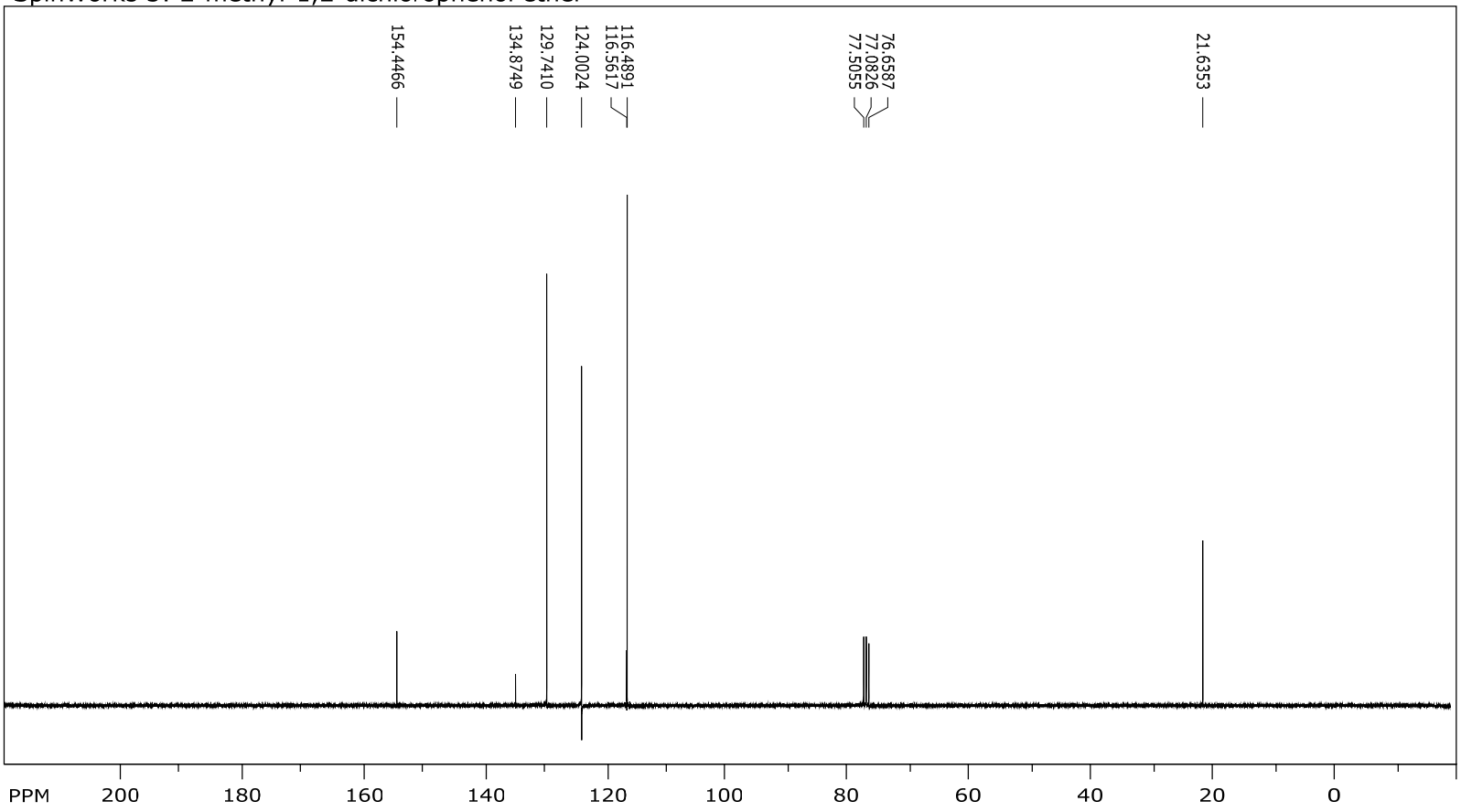




file: Z:\Laina\lmgxv\lmgxv_51a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 168.111 ppm/cm: 0.56013

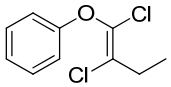
SpinWorks 3: 2-methyl-1,2-dichlorophenol ether



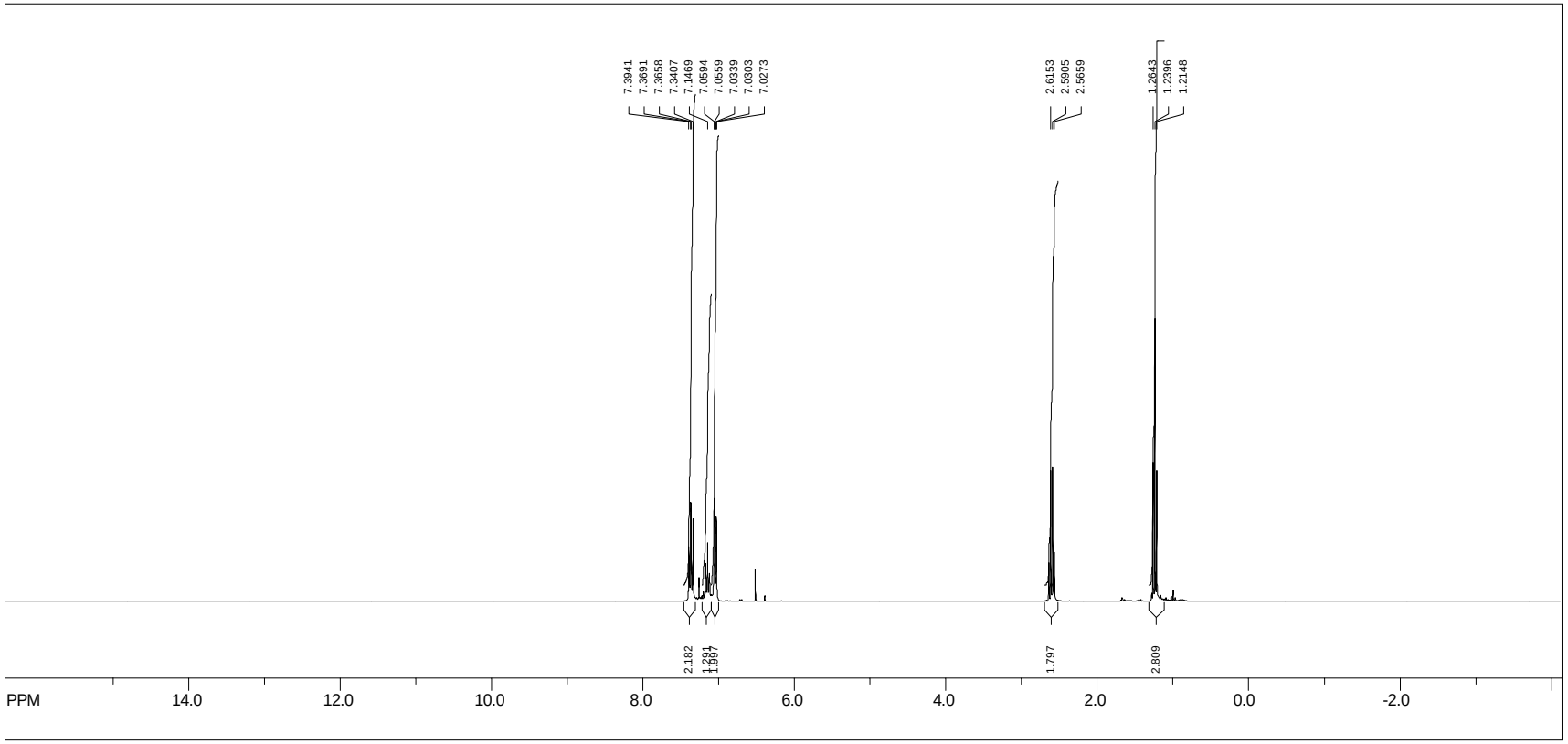
file: Z:\Laina\lmgxv\lmgxv_51a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.2980 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 719.424 ppm/cm: 9.53192

(*E*)-1-(1,2-Dichlorobut-1-enyloxy)benzene (264)



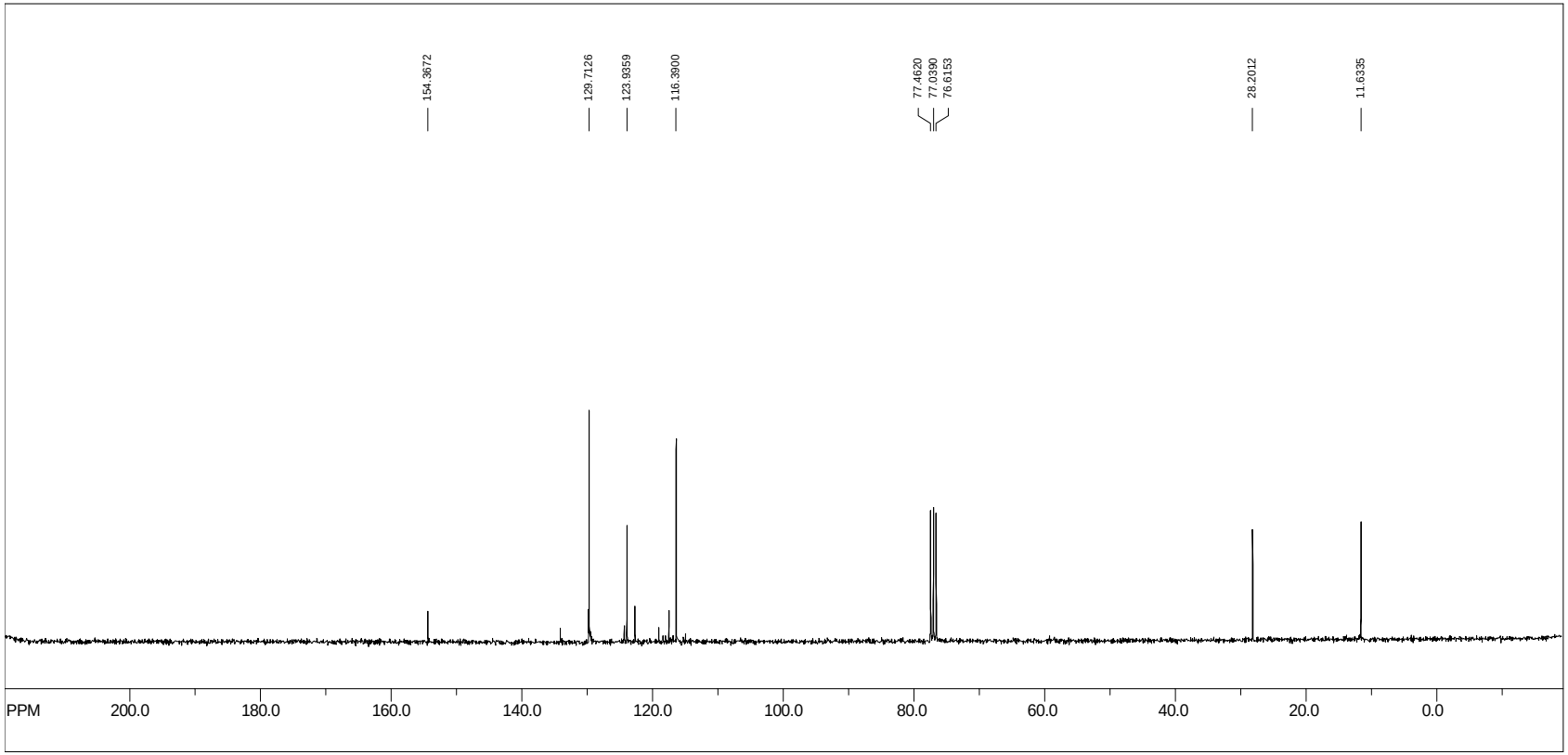
SpinWorks 2.5: ethylation



file: Z:\Laina\lmgvii\lmgvii_19\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

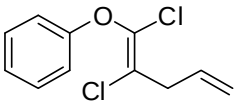
SpinWorks 2.5: ethylation

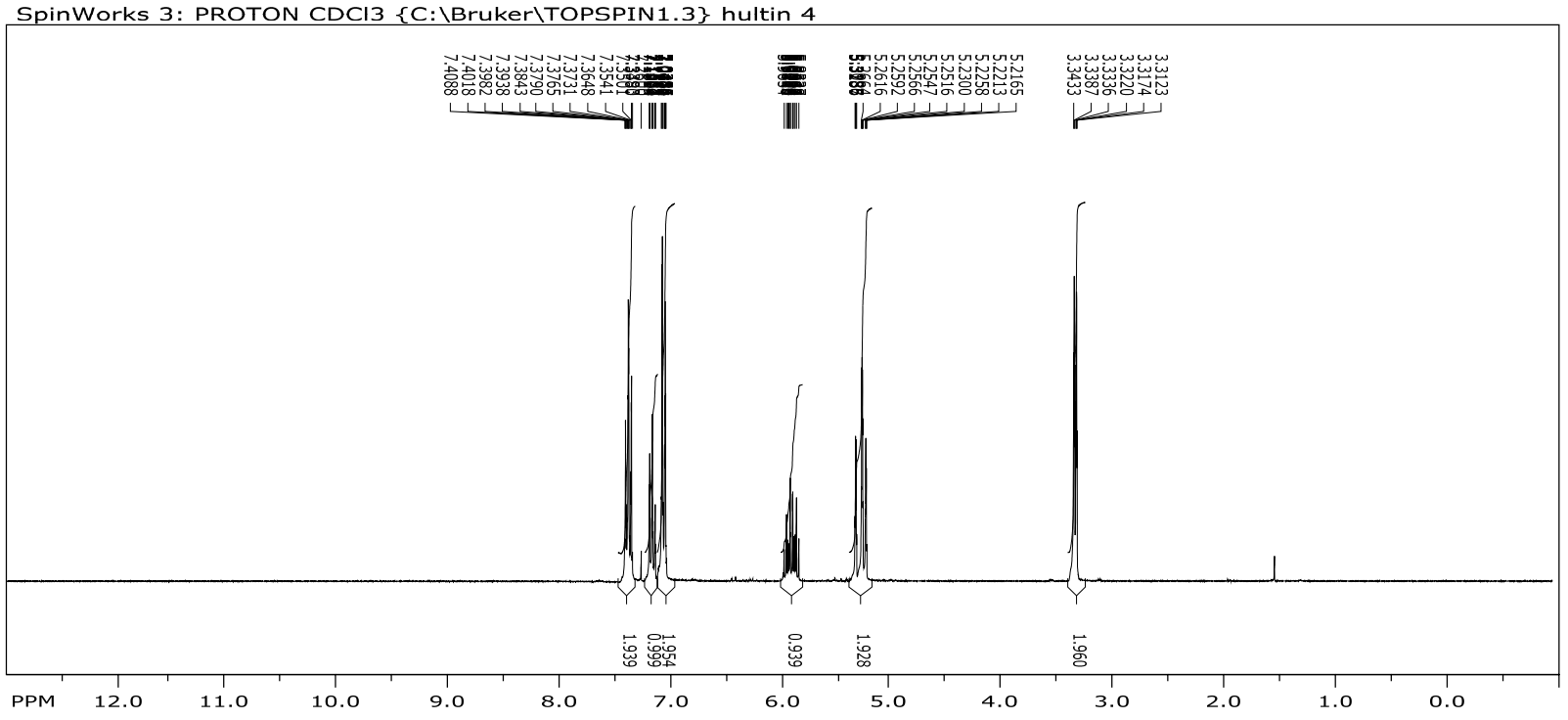


file: Z:\Laina\lmgvii\lmgvii_19\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 128

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-(1,2-Dichloropenta-1,4-dienyloxy)benzene (265)

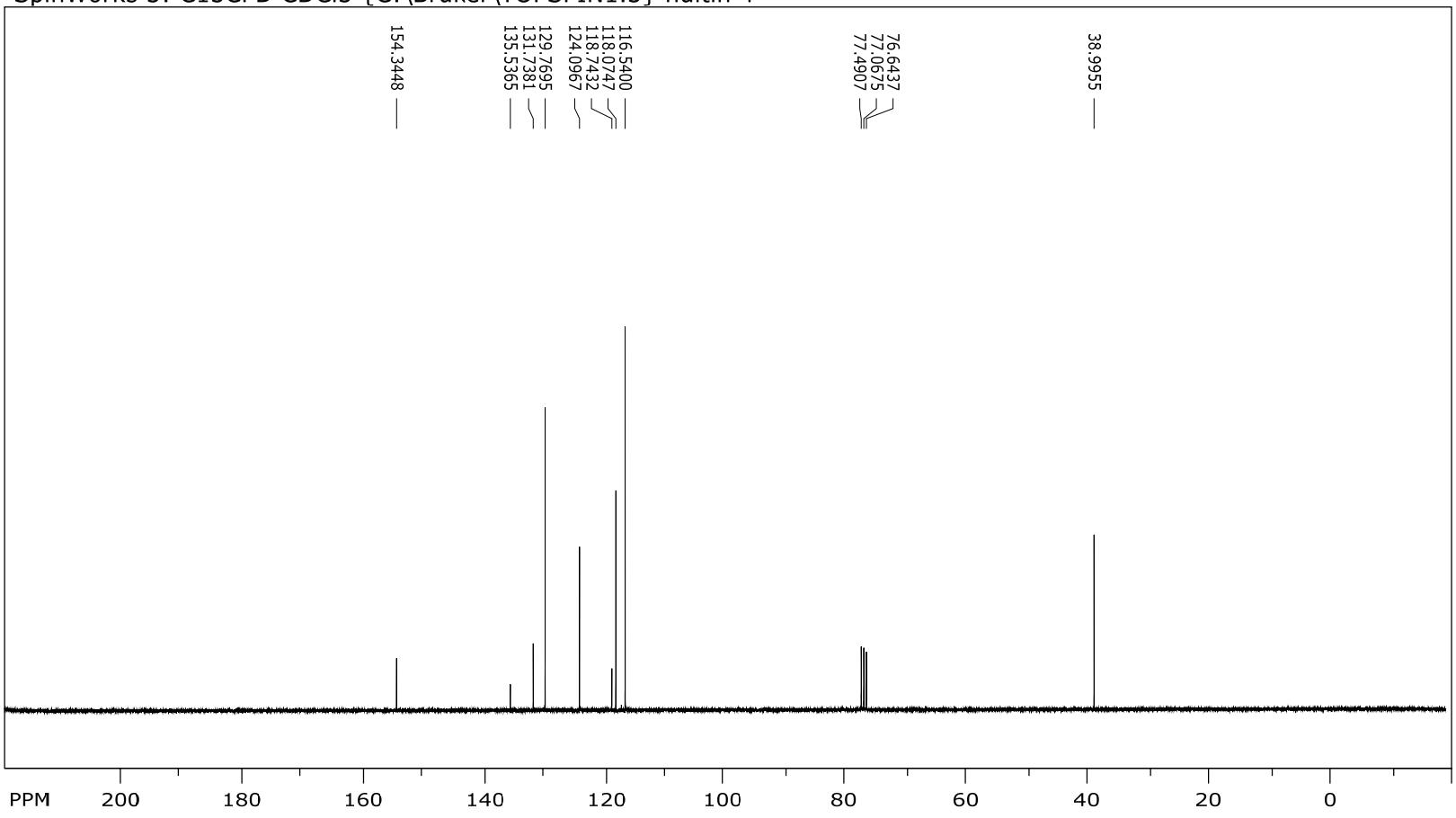




file: Z:\Laina\lmgxv\lmgxv_53a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130011 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 168.111 ppm/cm: 0.56013

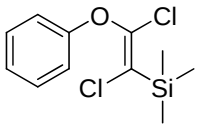
SpinWorks 3: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4

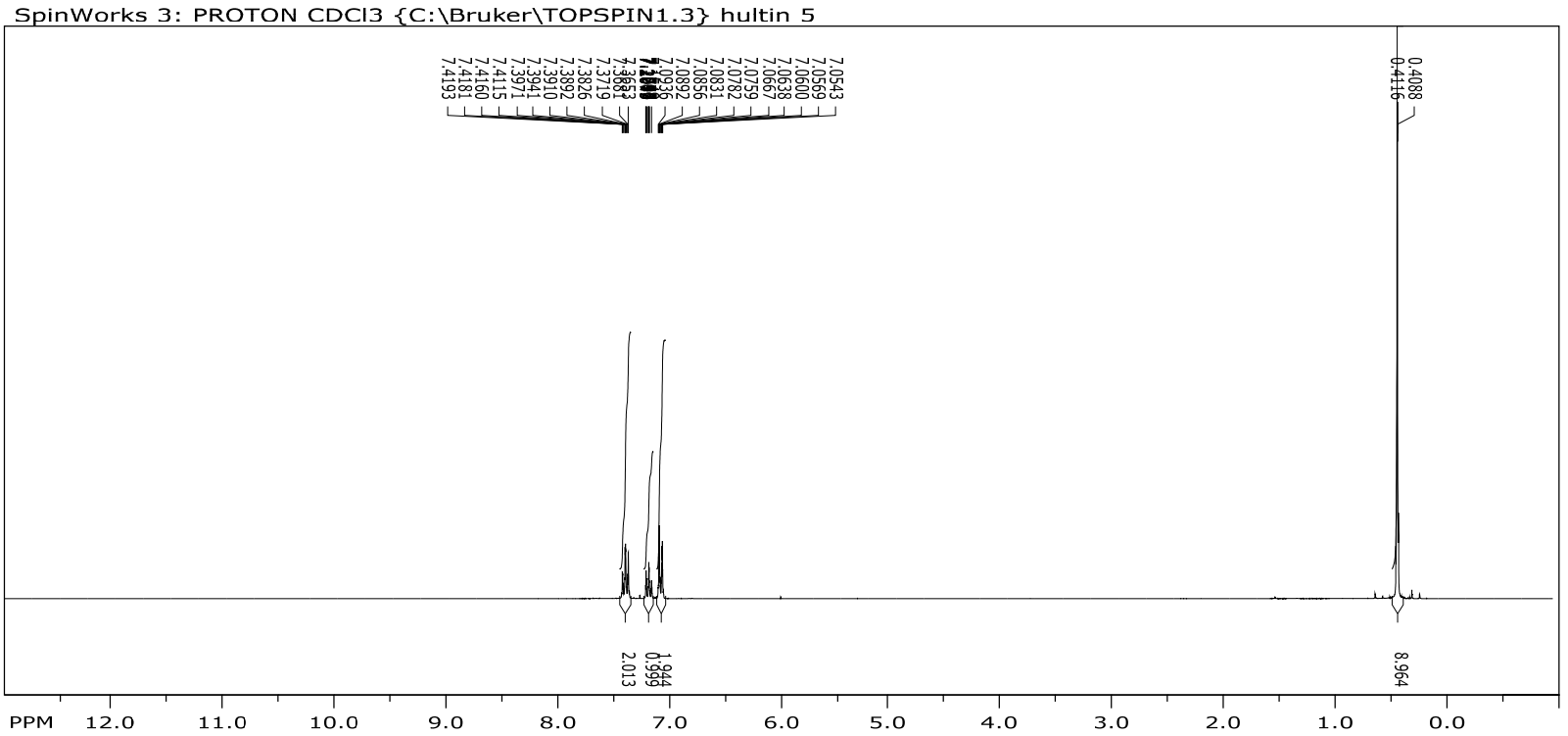


file: Z:\Laina\lmgxv\lmgxv_53a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.2980 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 719.424 ppm/cm: 9.53192

(*E*)-(1,2-Dichloro-2-phenoxyvinyl)trimethylsilane (266)

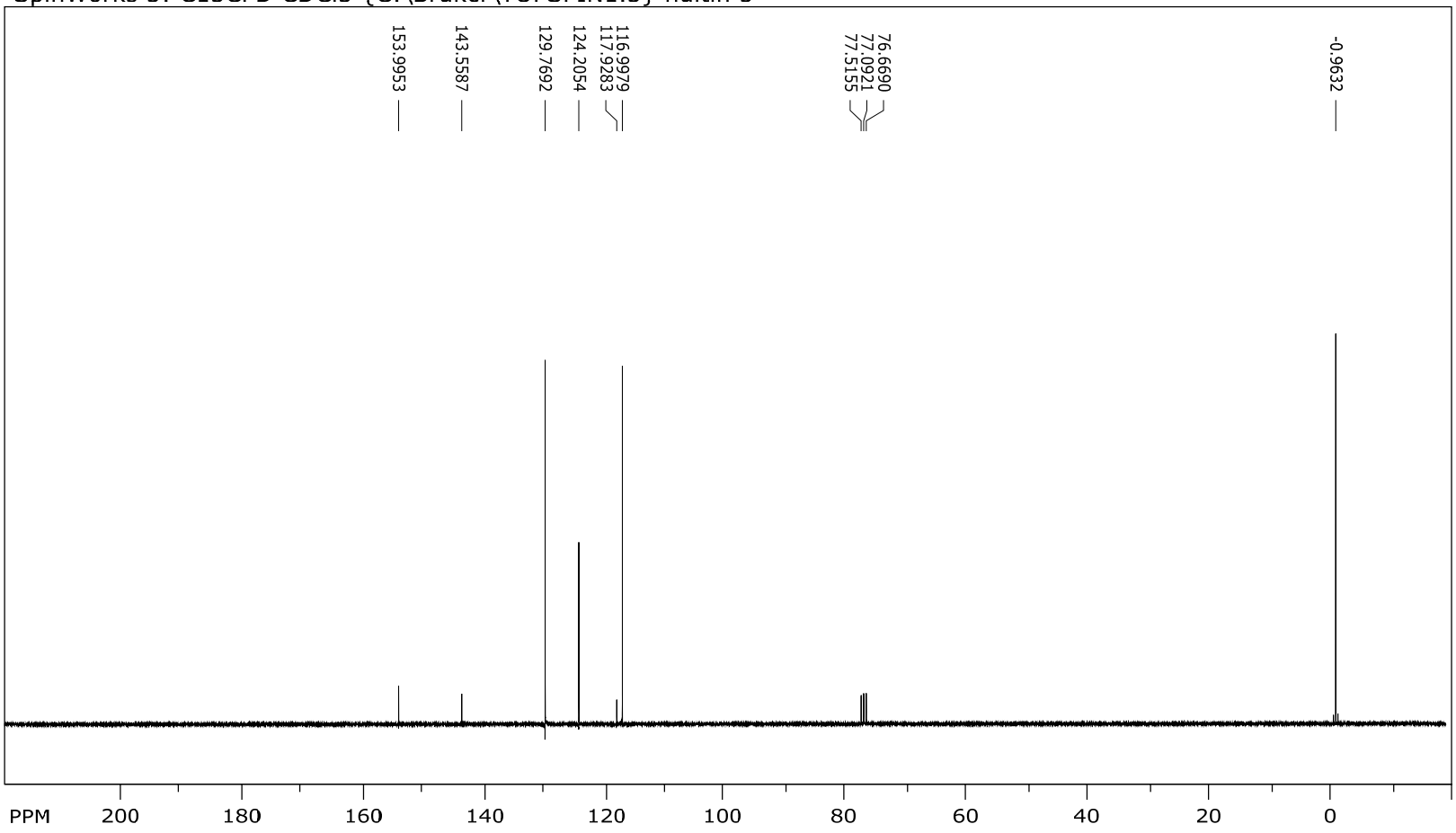




file: Z:\Laina\lmgxv\lmgxv_54a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130011 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 168.111 ppm/cm: 0.56013

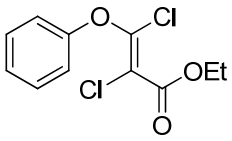
SpinWorks 3: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5

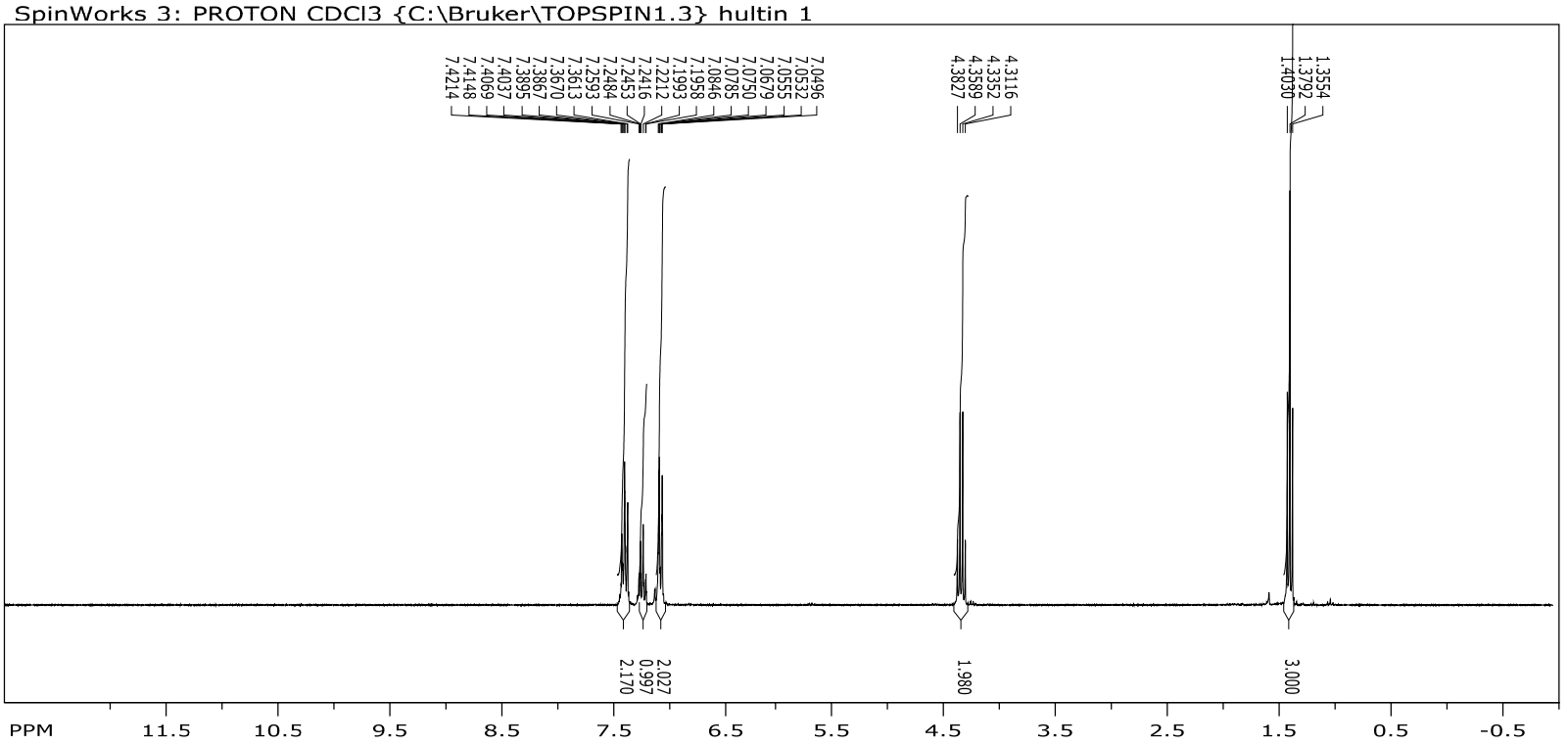


file: Z:\Laina\lmgxv\lmgxv_54a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.2980 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 719.424 ppm/cm: 9.53192

(E)-Ethyl 2,3-dichloro-3-phenoxyacrylate (267)

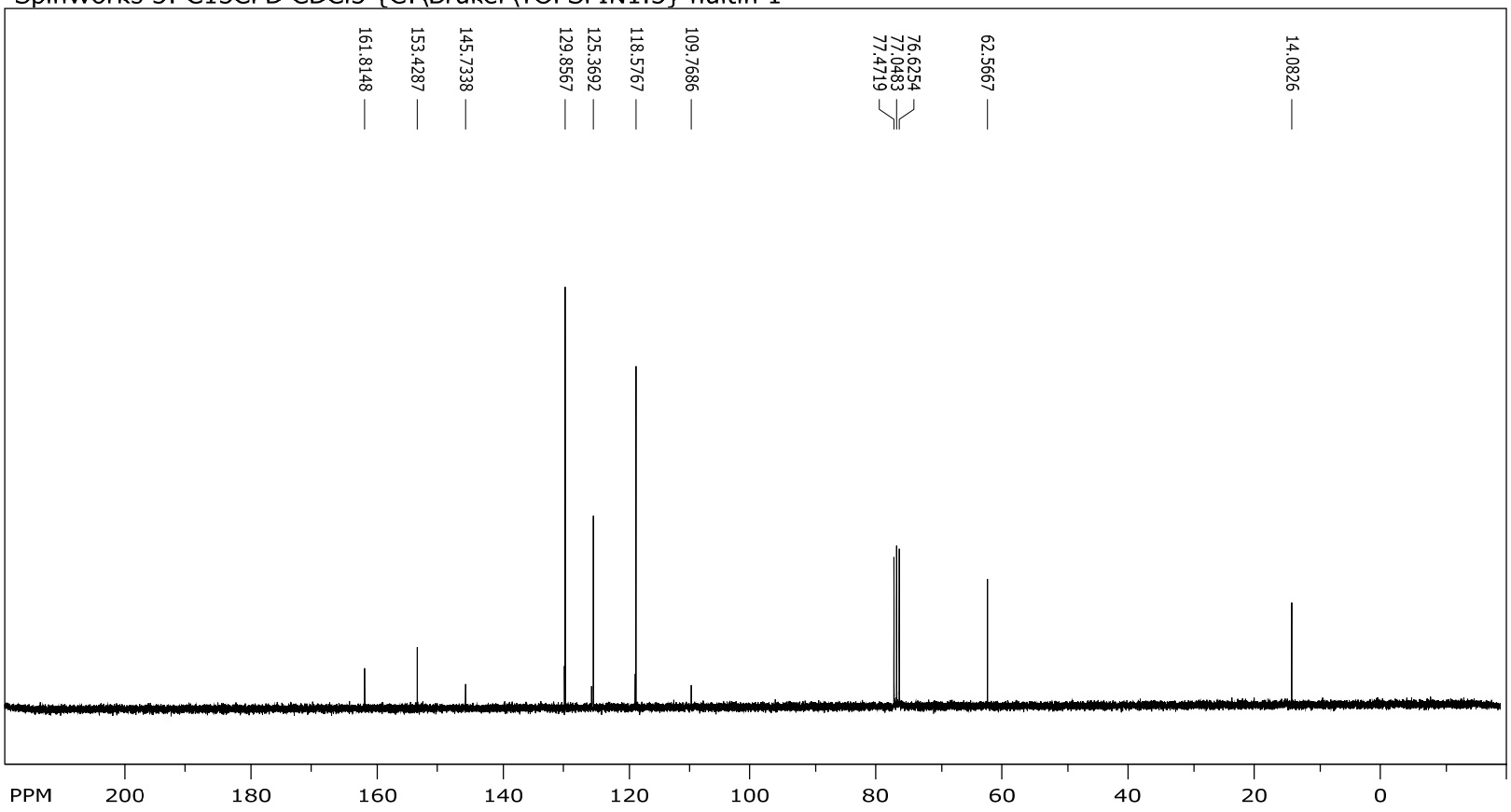




file: Z:\Laina\lmgxv\lmgxv_55a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130011 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 167.901 ppm/cm: 0.55942

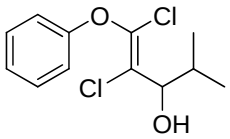
SpinWorks 3: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1

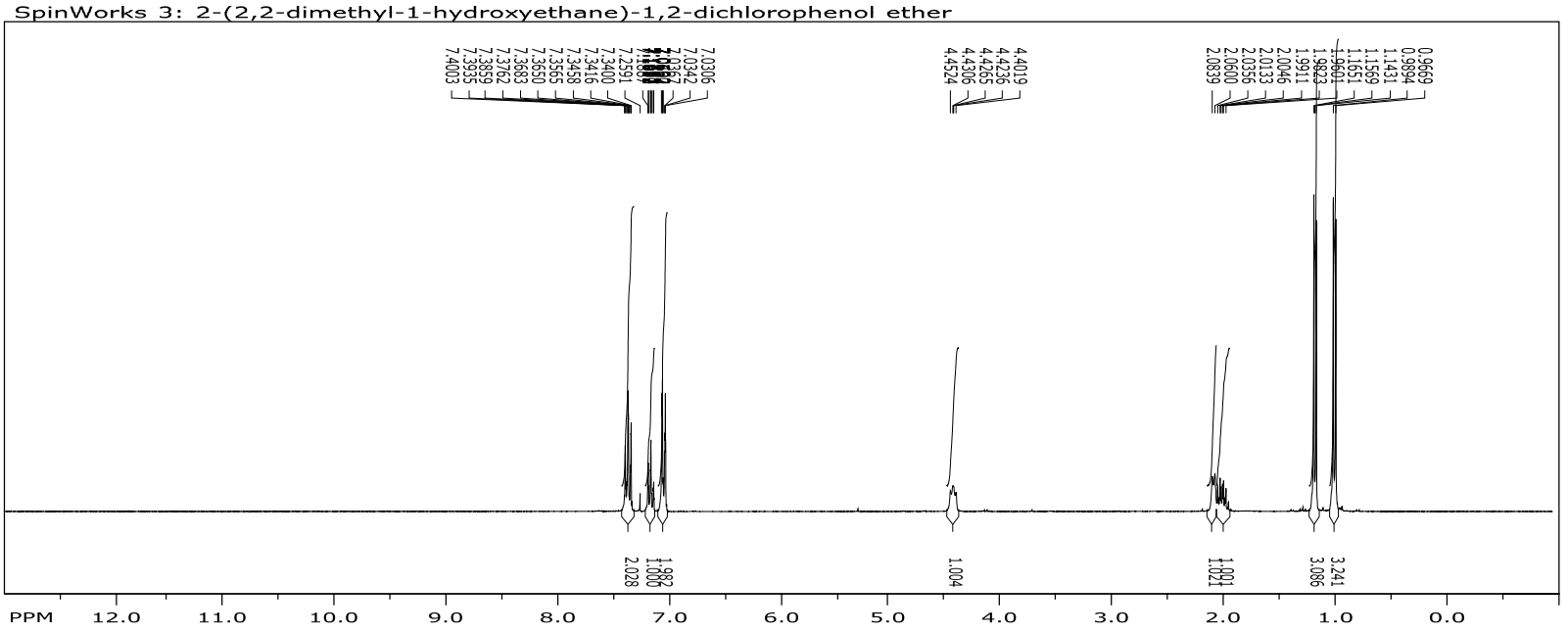


file: Z:\Laina\lmgxv\lmgxv_55a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.2980 ppm = 0.274439 Hz/pt
number of scans: 317

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 719.424 ppm/cm: 9.53192

(*E*)-1,2-Dichloro-4-methyl-1-phenoxypent-1-en-3-ol (268)

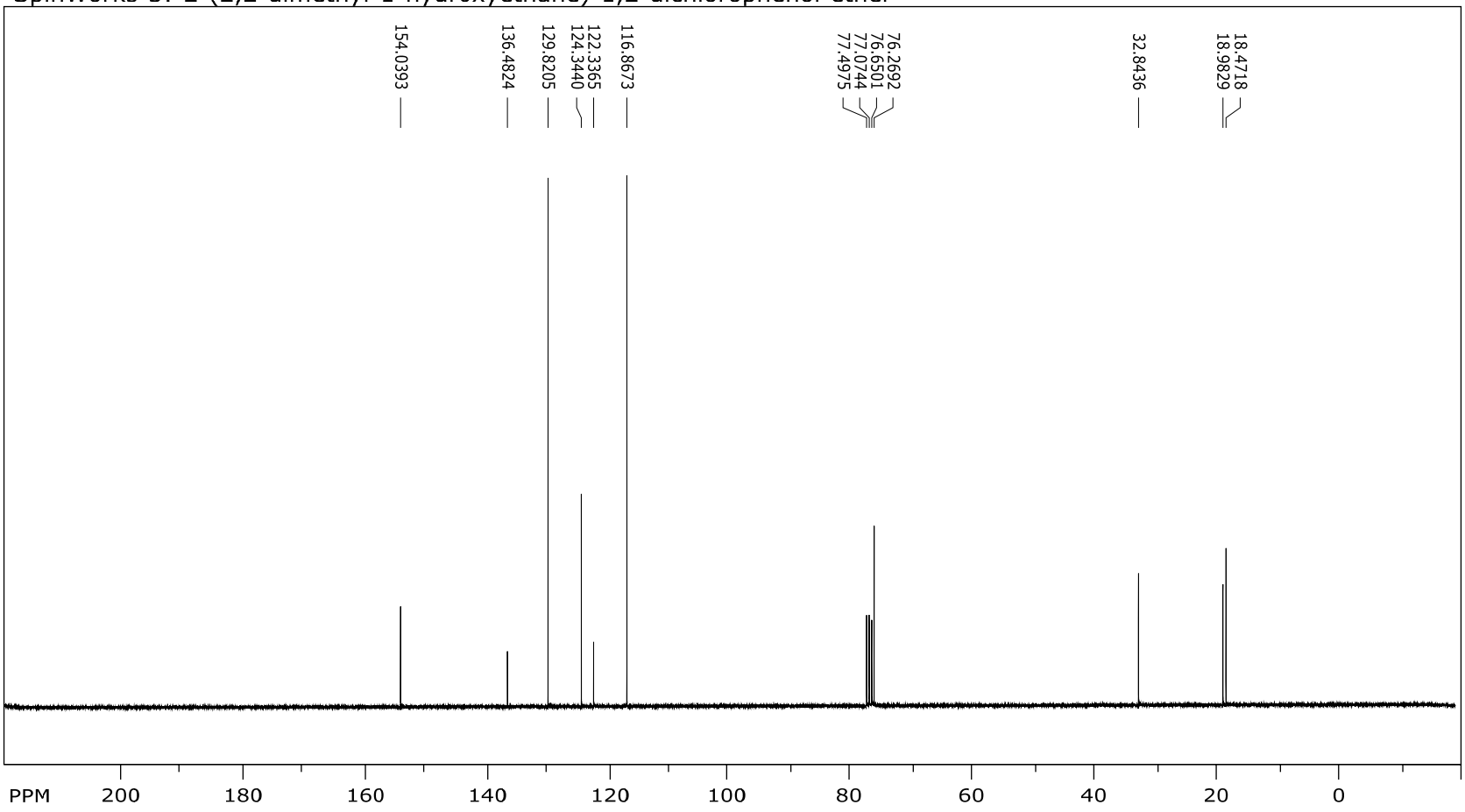




file: Z:\Laina\lmgxv\lmgxv_52a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130011 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 168.111 ppm/cm: 0.56013

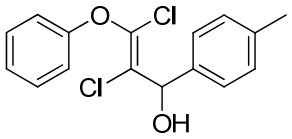
SpinWorks 3: 2-(2,2-dimethyl-1-hydroxyethane)-1,2-dichlorophenol ether

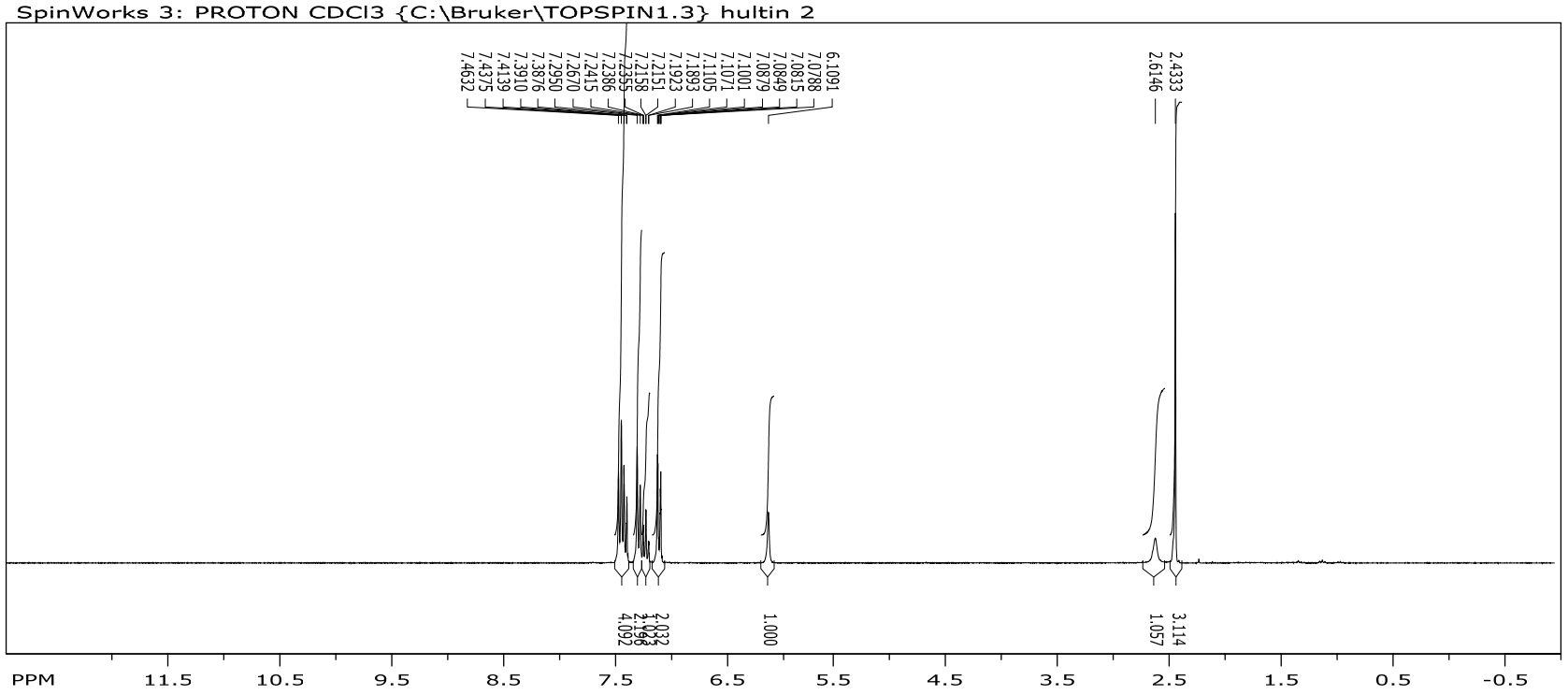


file: Z:\Laina\lmgxv\lmgxv_52a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.2980 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 719.424 ppm/cm: 9.53192

(*E*)-2,3-Dichloro-3-phenoxy-1-*p*-tolylprop-2-en-1-ol (265)

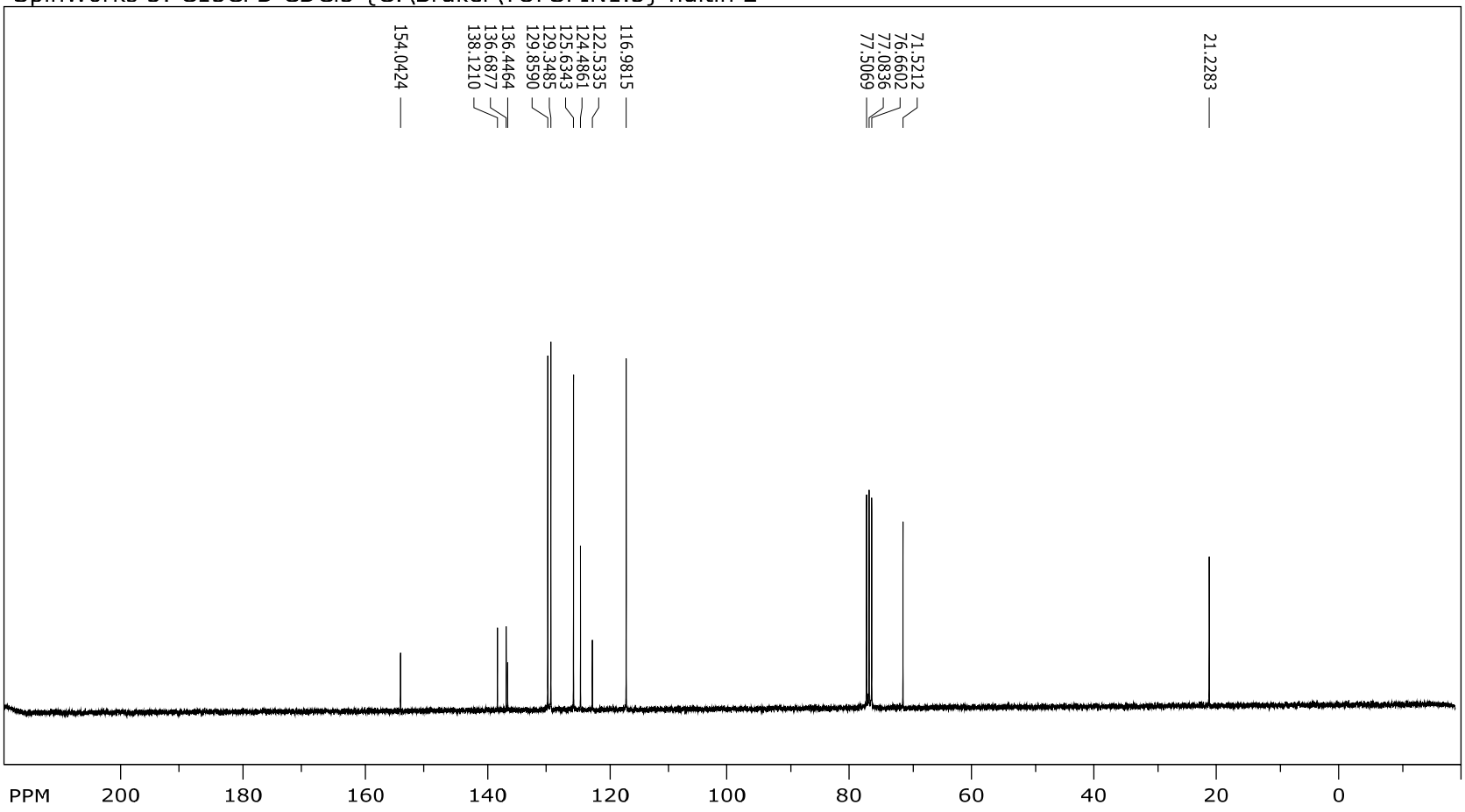




file: Z:\Laina\lmgxv\lmgxv_56a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000
Hz/cm: 167.901 ppm/cm: 0.55942

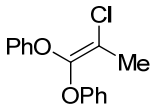
SpinWorks 3: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



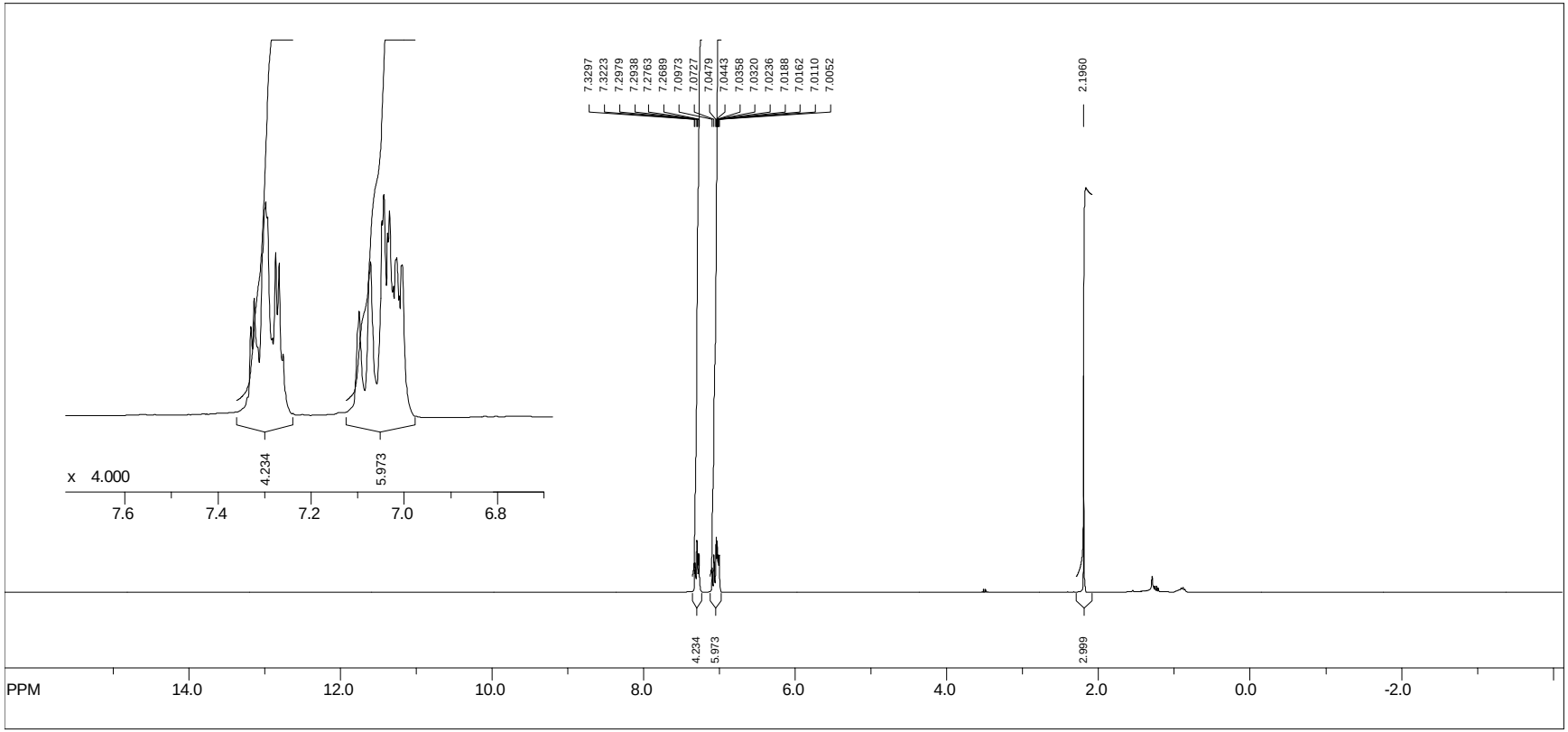
file: Z:\Laina\lmgxv\lmgxv_56a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.2980 ppm = 0.274439 Hz/pt
number of scans: 331

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 719.424 ppm/cm: 9.53192

1-(2-chloro-1phenoxy-1-enyloxy)benzene (270)



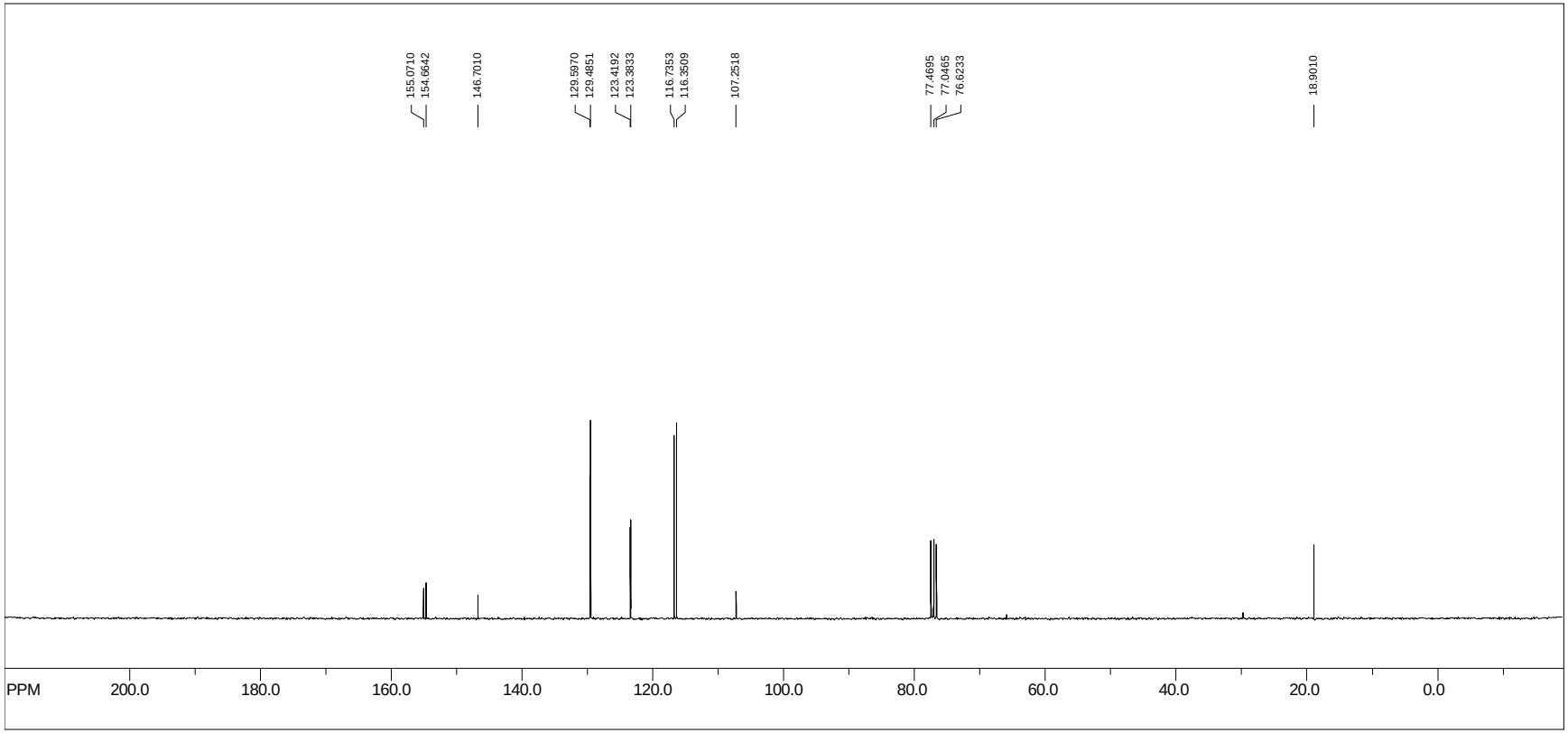
SpinWorks 2.5: methylation of vii_25



file: Z:\Laina\lmgvi\lmgvii_30\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

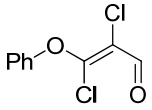
SpinWorks 2.5: methylation of vii_25

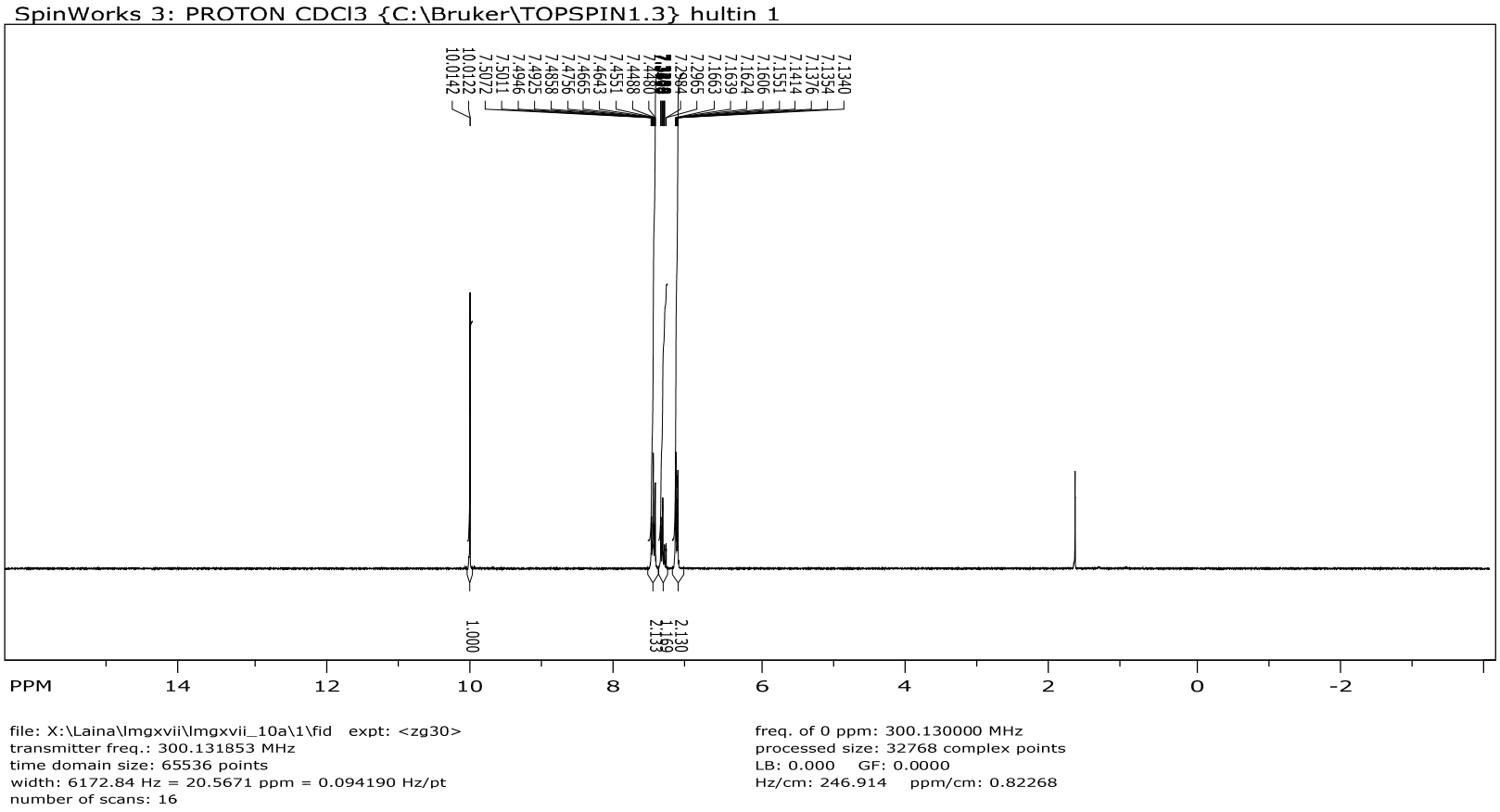


file: Z:\Laina\lmgvii\lmgvii_30\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 438

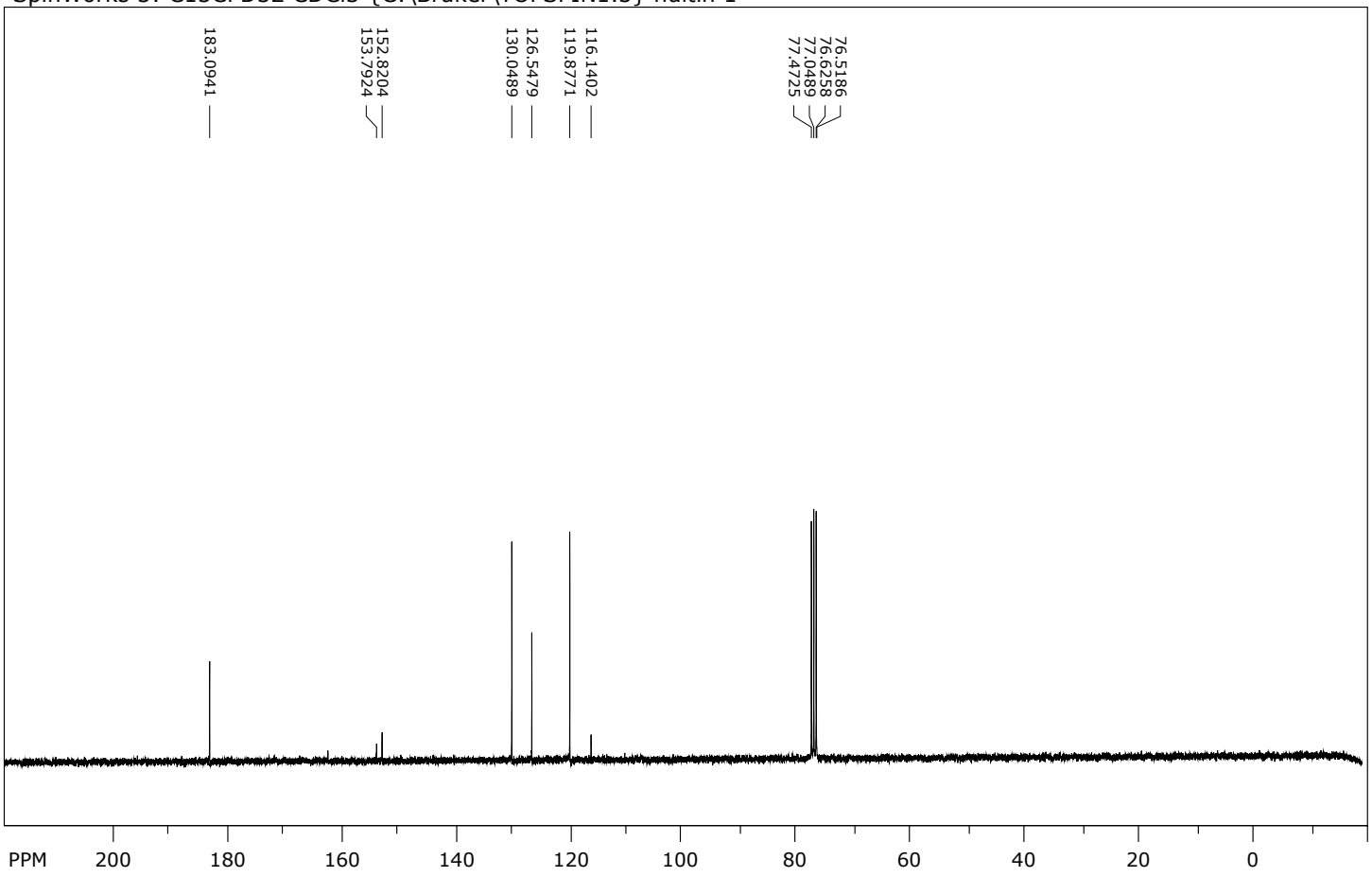
freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-2,3-Dichloro-3-phenoxyacrylaldehyde (271)





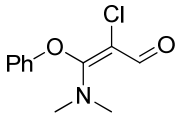
SpinWorks 3: C13CPD32 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1

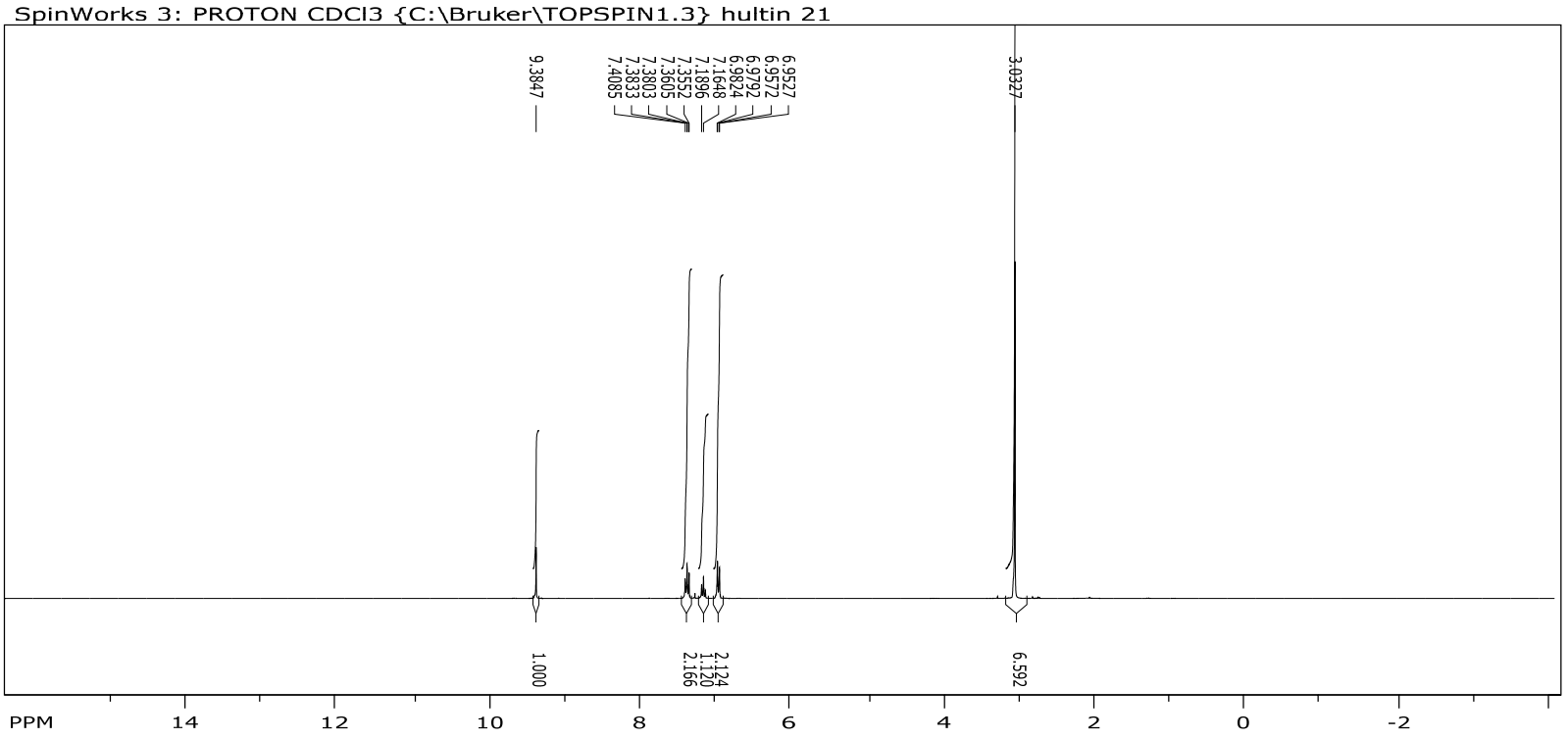


file: X:\Laina\lmgxvii\lmgxvii_10a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.2980 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 719.424 ppm/cm: 9.53192

2-Chloro-3-(dimethylamino)-3-phenoxyacrylaldehyde (272)

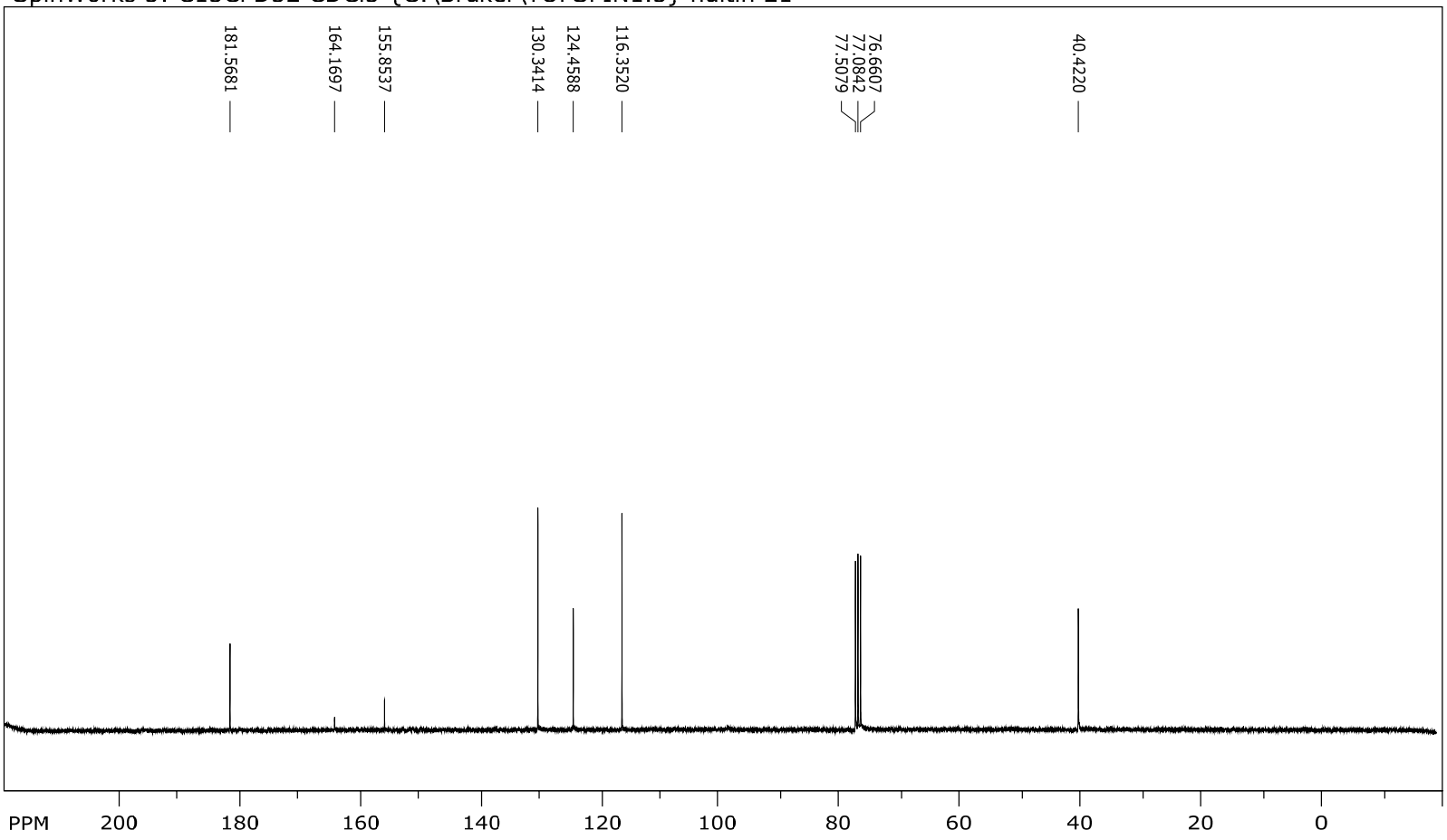




file: X:\Laina\lmgxvii\lmgxvii_15b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.5671 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000
Hz/cm: 246.914 ppm/cm: 0.82268

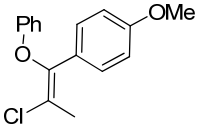
SpinWorks 3: C13CPD32 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 21



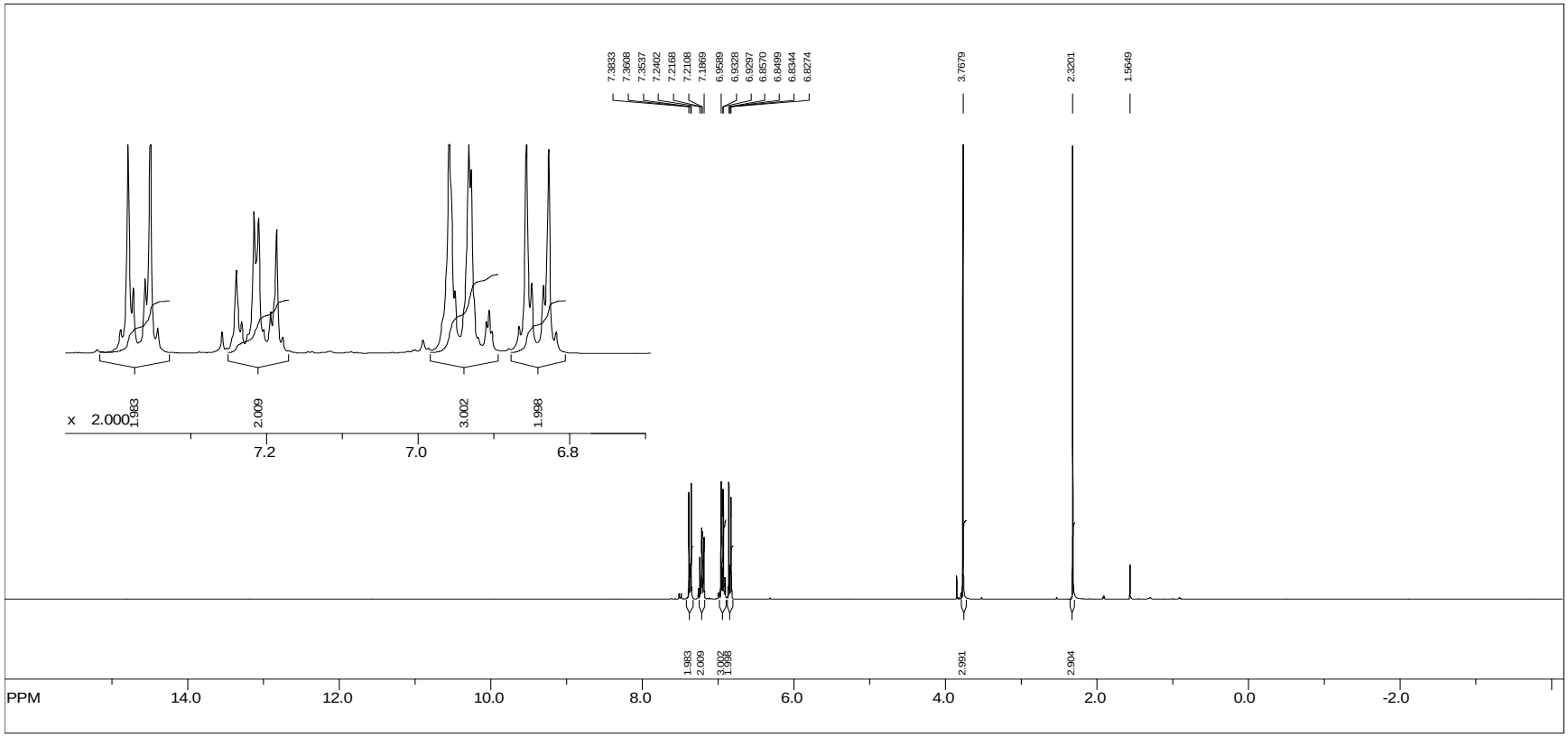
file: X:\Laina\lmgxvii\lmgxvii_15b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.2980 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000
Hz/cm: 719.424 ppm/cm: 9.53192

(Z)-1-(2-Chloro-1-(4-methoxyphenyl)prop-1-enyloxy)benzene ((Z)-276)



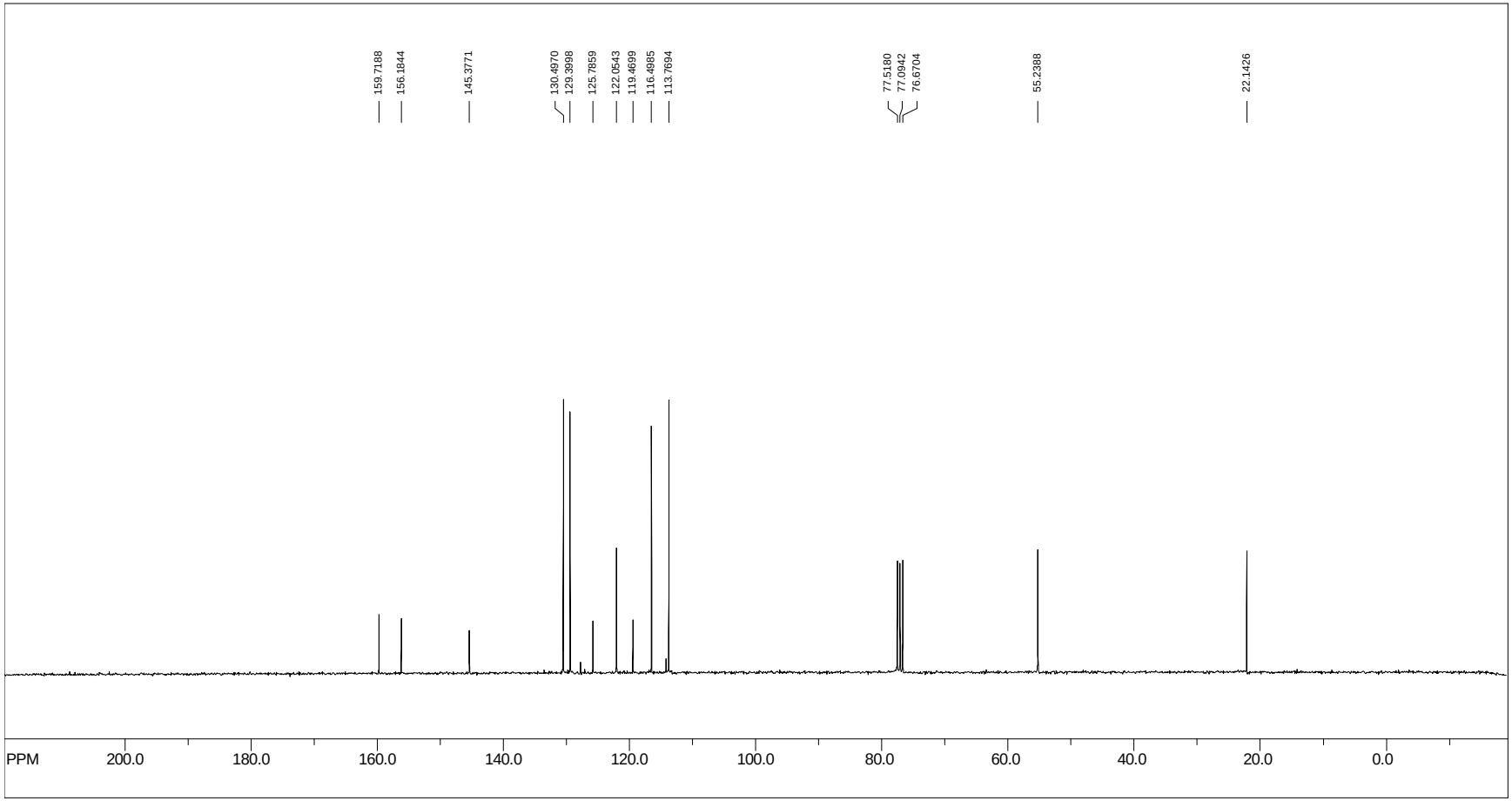
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxi\lmgxi_90a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

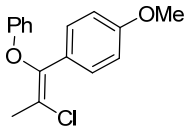
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



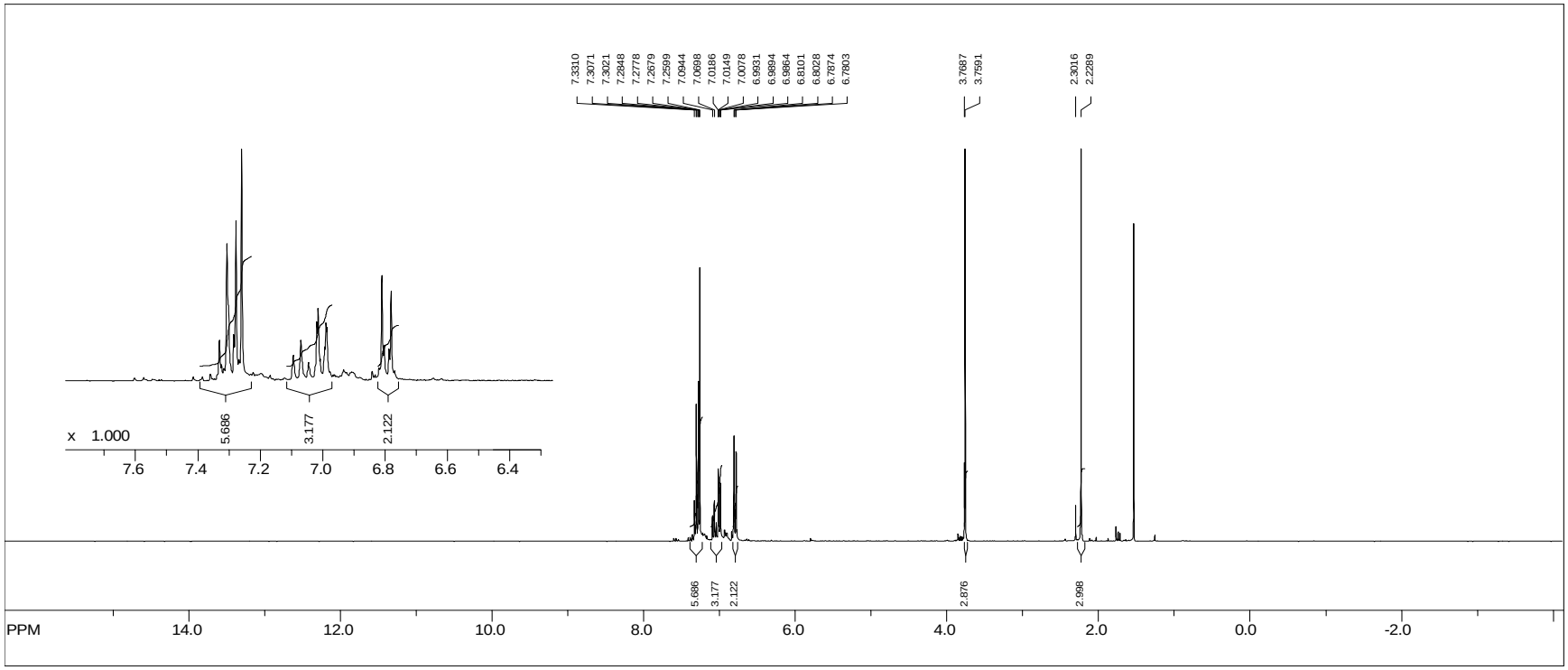
file: Z:\Laina\lmgxi\lmgxi_90a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-(2-Chloro-1-(4-methoxyphenyl)prop-1-enyloxy)benzene ((E)-276)



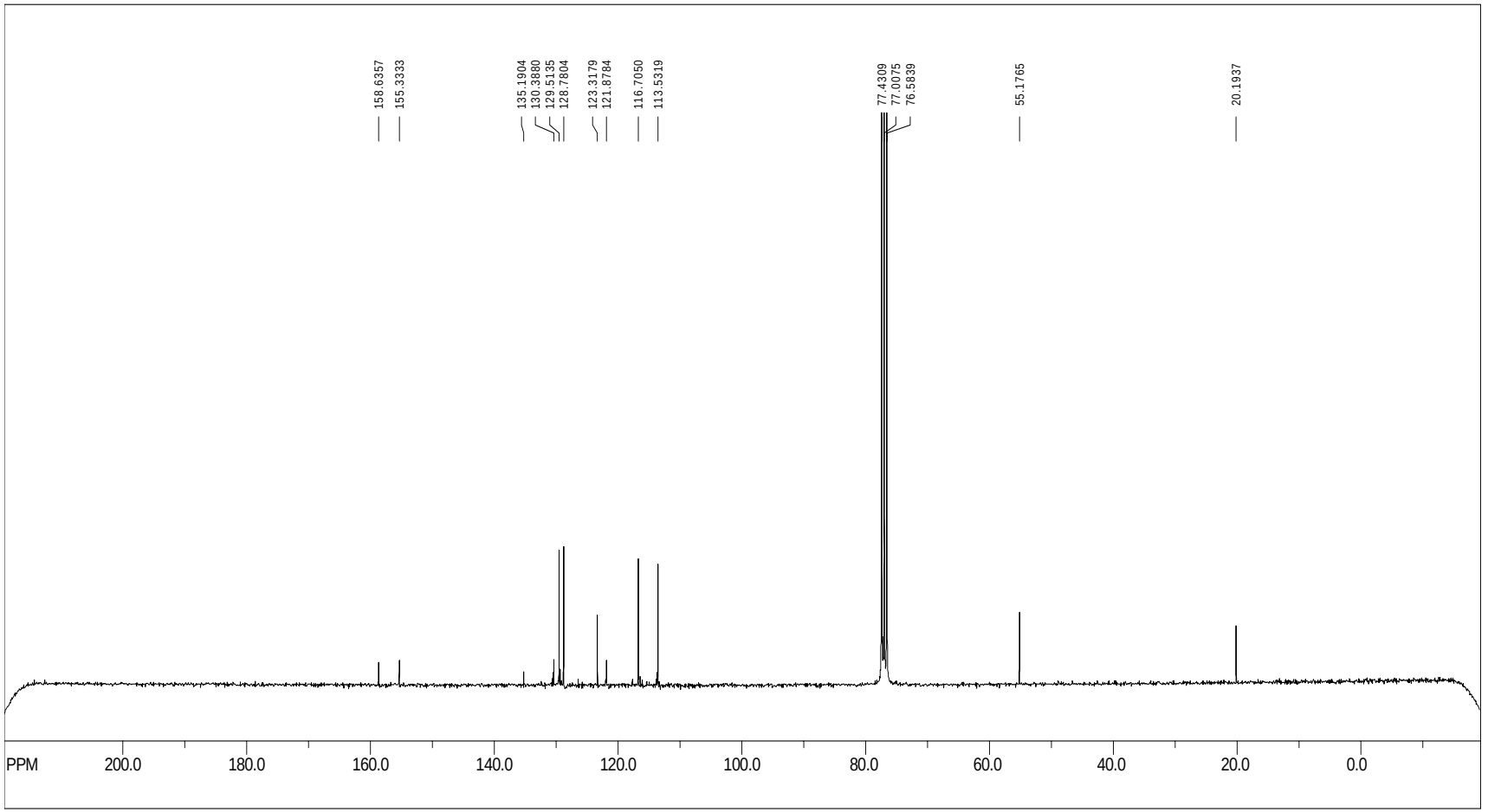
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



file: C:\Users\Laina\Desktop\viii_68\lmgviii_68b\1 HMfid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 6

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

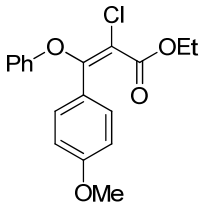
SpinWorks 2.5: C13CPD32 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



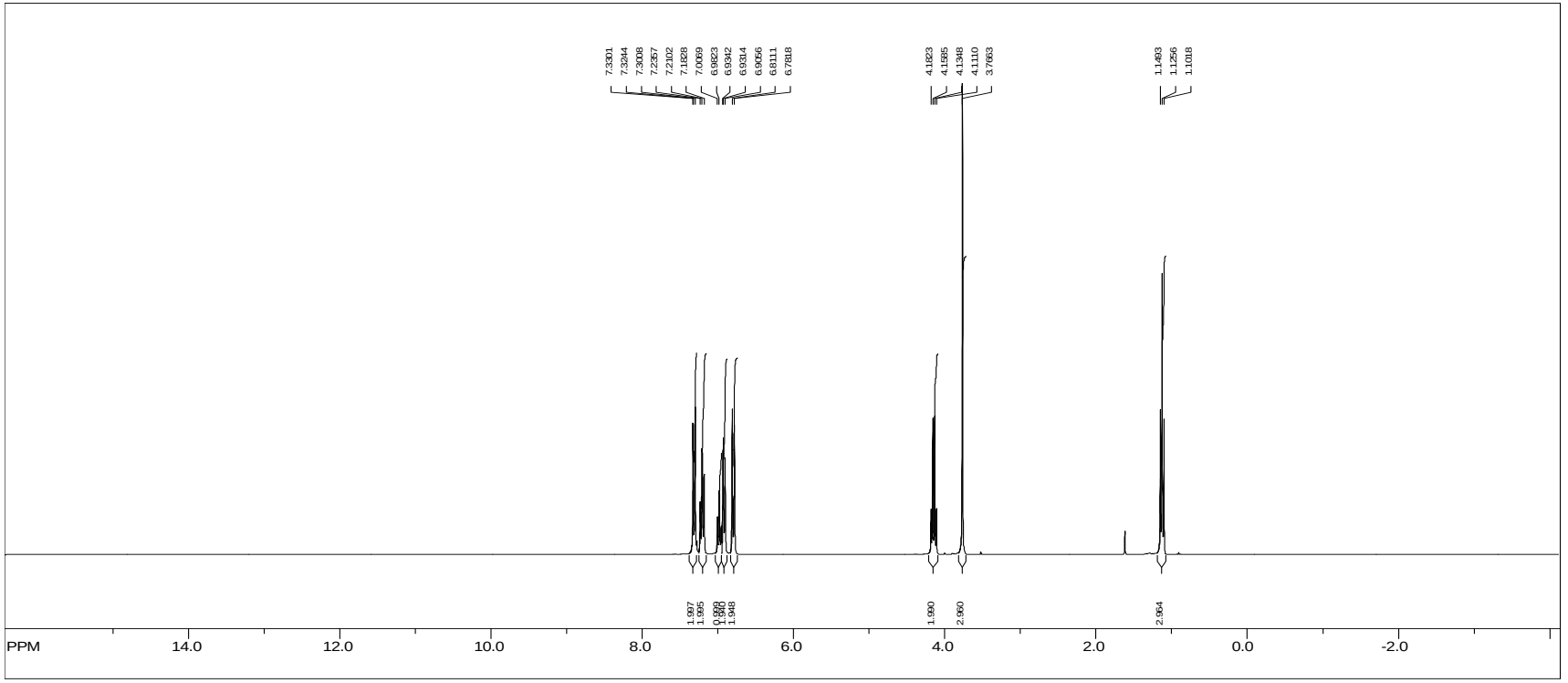
file: C:\Users\Laina\Desktop\viii_68\lmgviii_68b\3 C\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 12000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*Z*)-Ethyl 2-chloro-3-(4-methoxyphenyl)-3-phenoxyacrylate (277)



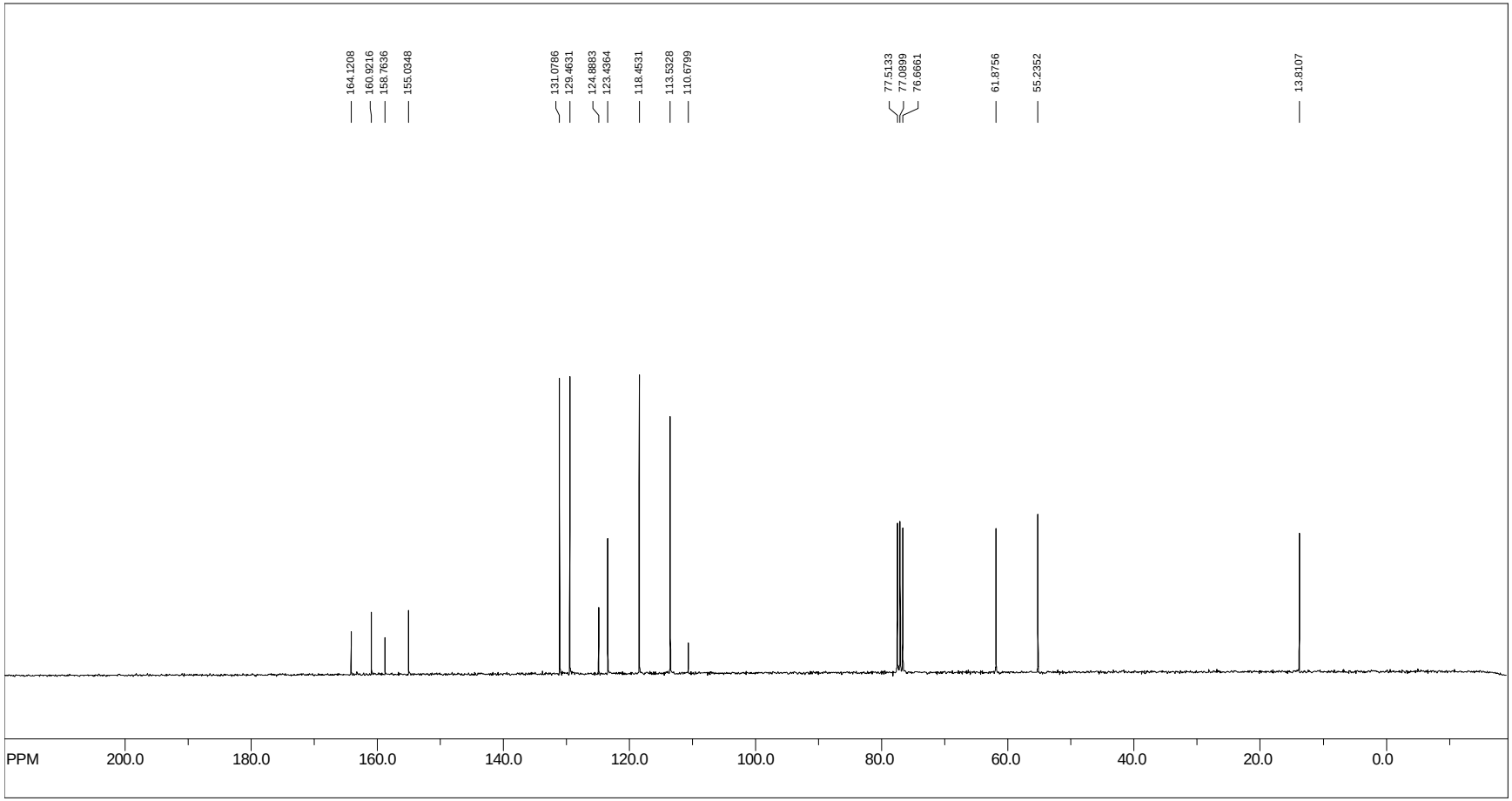
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgxl\lmgxl_79b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

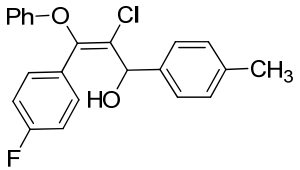
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



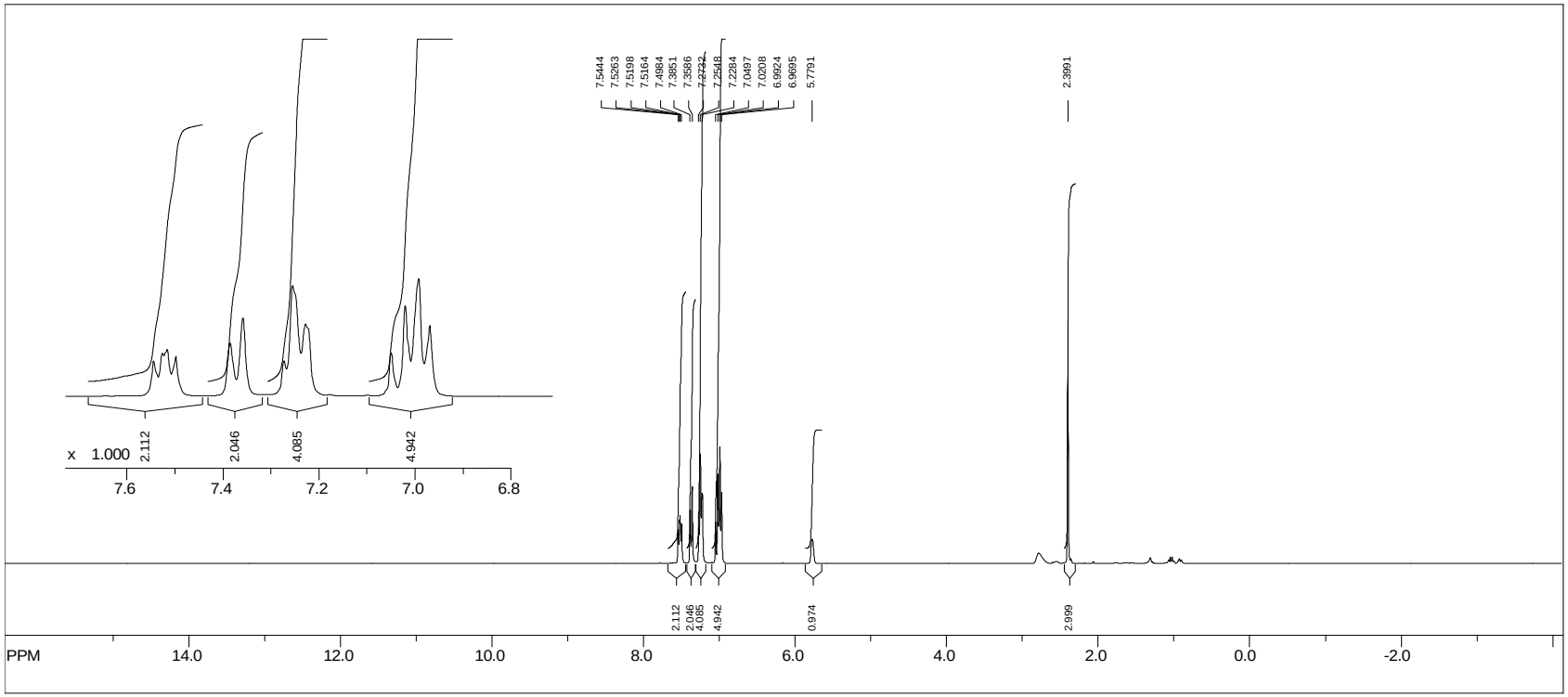
file: Z:\Laina\lmgxi\lmgxi_79b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 417

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-2-Chloro-3-(4-fluorophenyl)-3-phenoxy-1-*p*-tolylprop-2-en-1-ol (278)



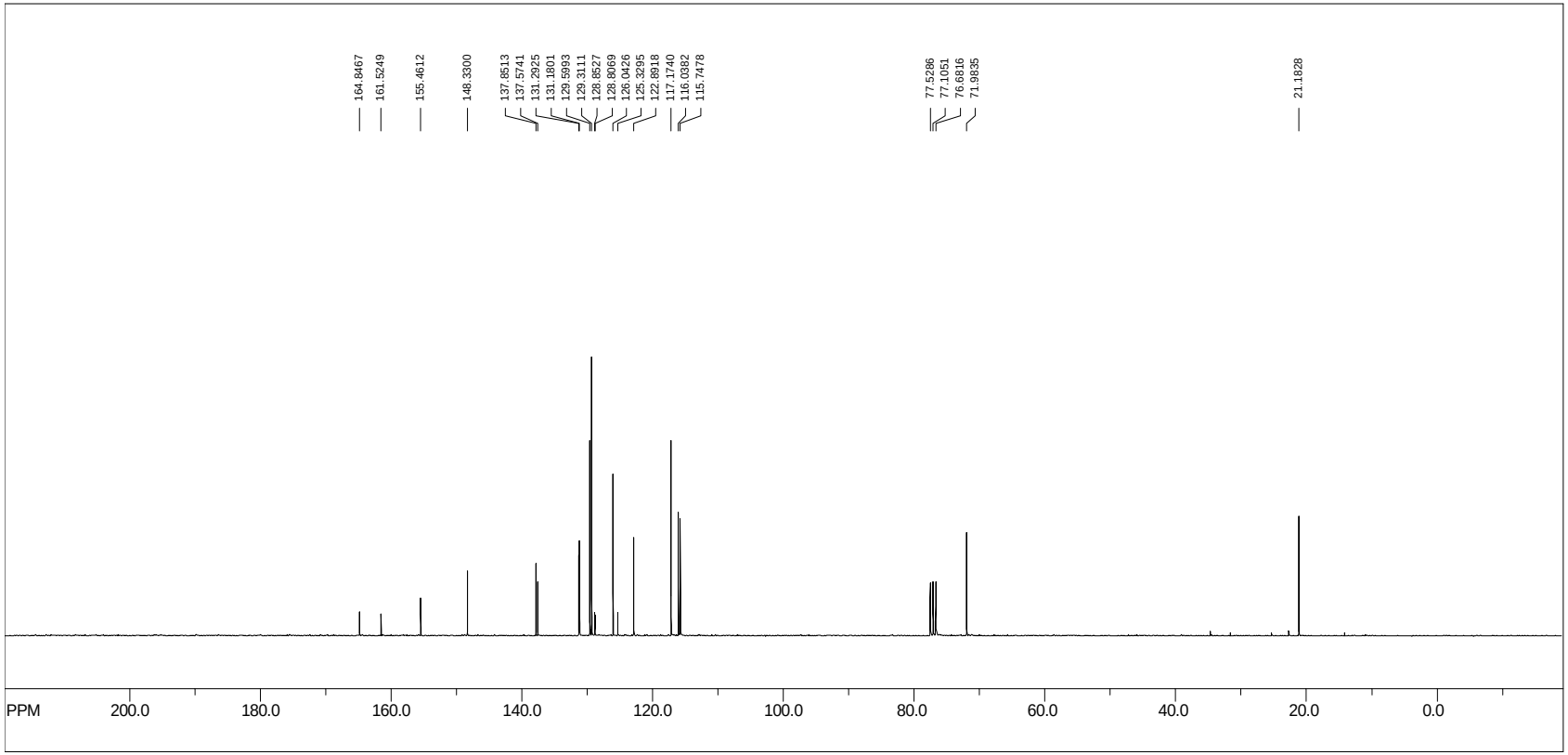
SpinWorks 2.5: phenol ether - p-fluorophenyl - addition to p-tolualdehyde



file: Z:\Laina\lmgviii\lmgviii_53d\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

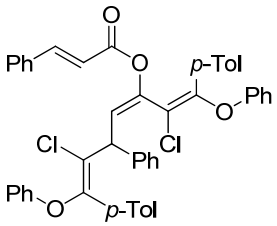
SpinWorks 2.5: phenol ether - p-fluorophenyl - addition to p-tolualdehyde



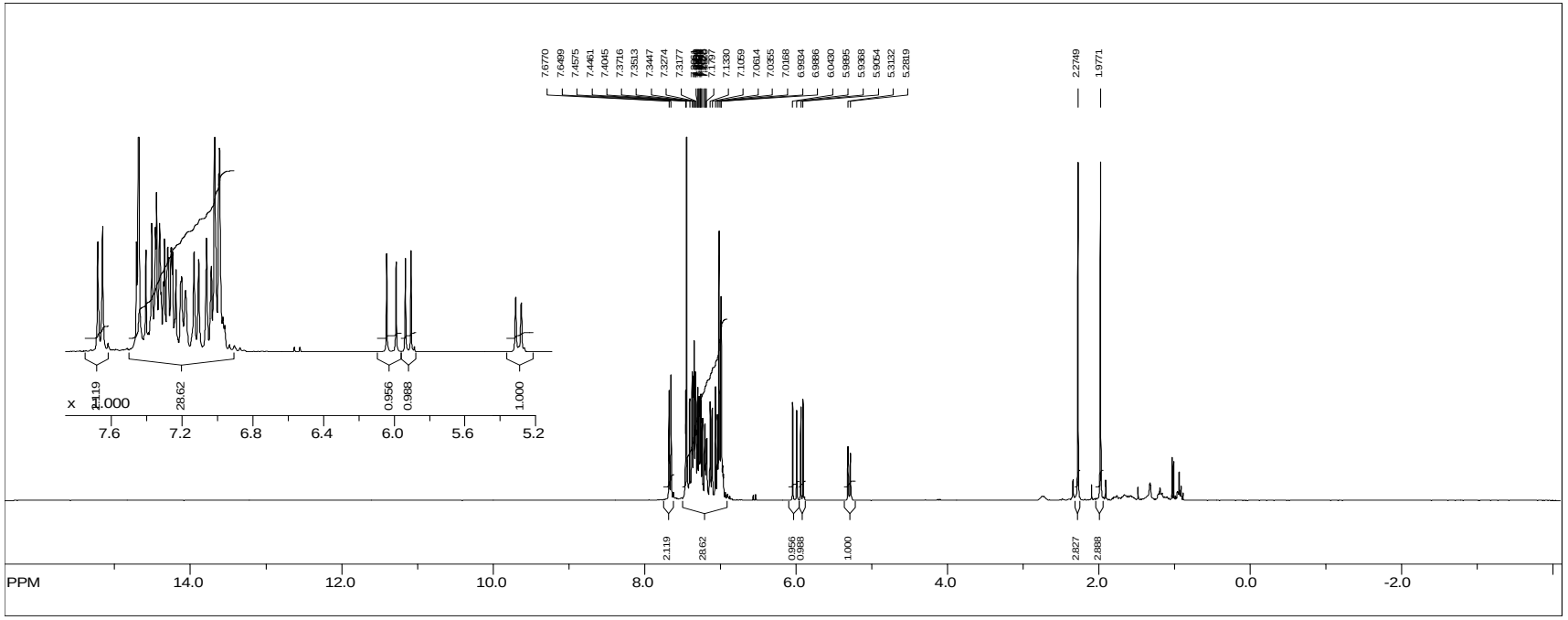
file: Z:\Laina\lmgviii\lmgviii_53d\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(1*Z*,3*E*,6*Z*)-2,6-Dichloro-1,7-diphenoxy)-5-phenyl-1,7-di*p*-tolylhepta-1,3,6-trien-3-yl cinnamate (279)



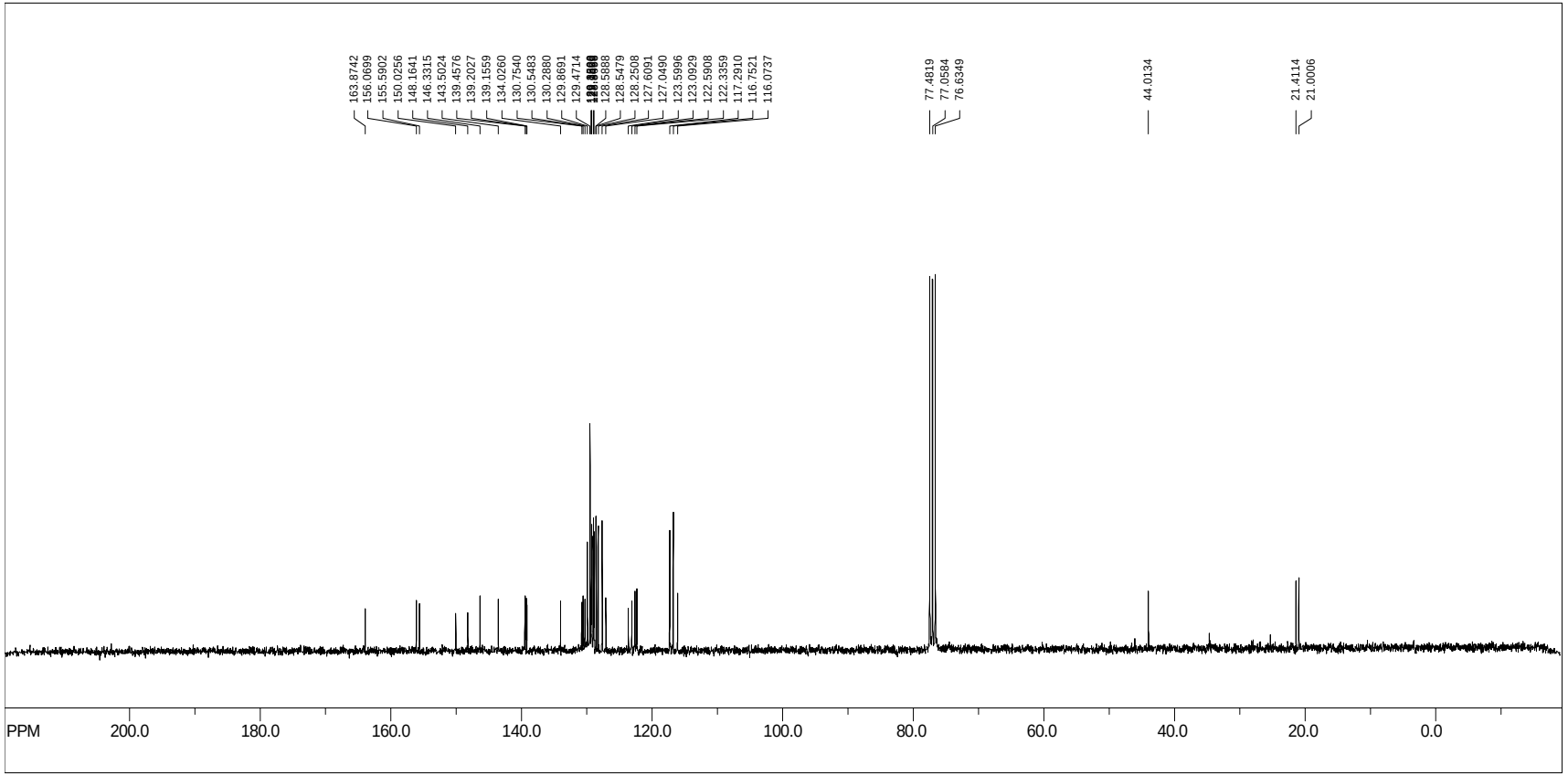
SpinWorks 2.5: repurified



file: Z:\Laina\lmgx\lmgxv_84g\Spectra of Repurified Material\300\5 H.fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

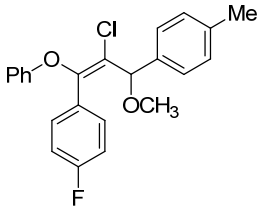
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



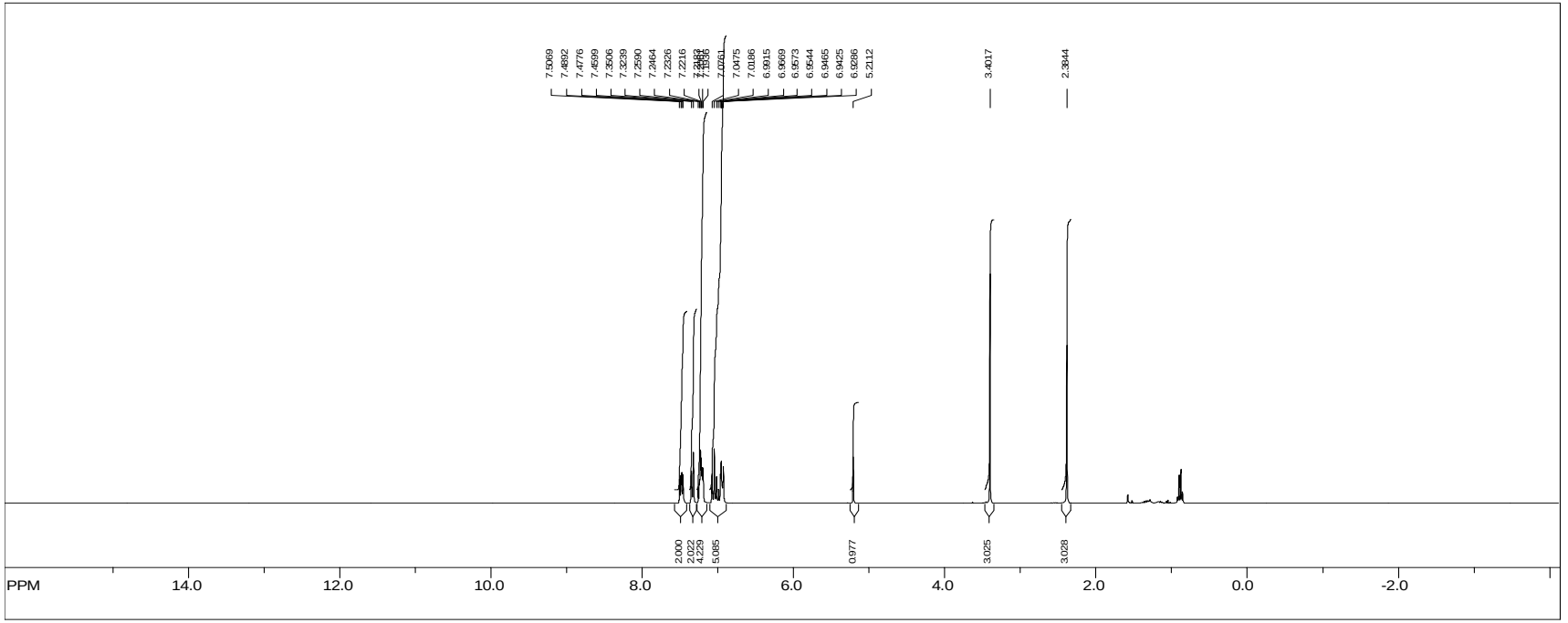
file: Z:\Laina\lmgxl\lmgxv_84g\Spectra of Repurified Material\300\6 C\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 346

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-2-Chloro-1-(4-fluorophenyl)-3-methoxy-3-*p*-tolylprop-1-enyloxy)benzene (284)



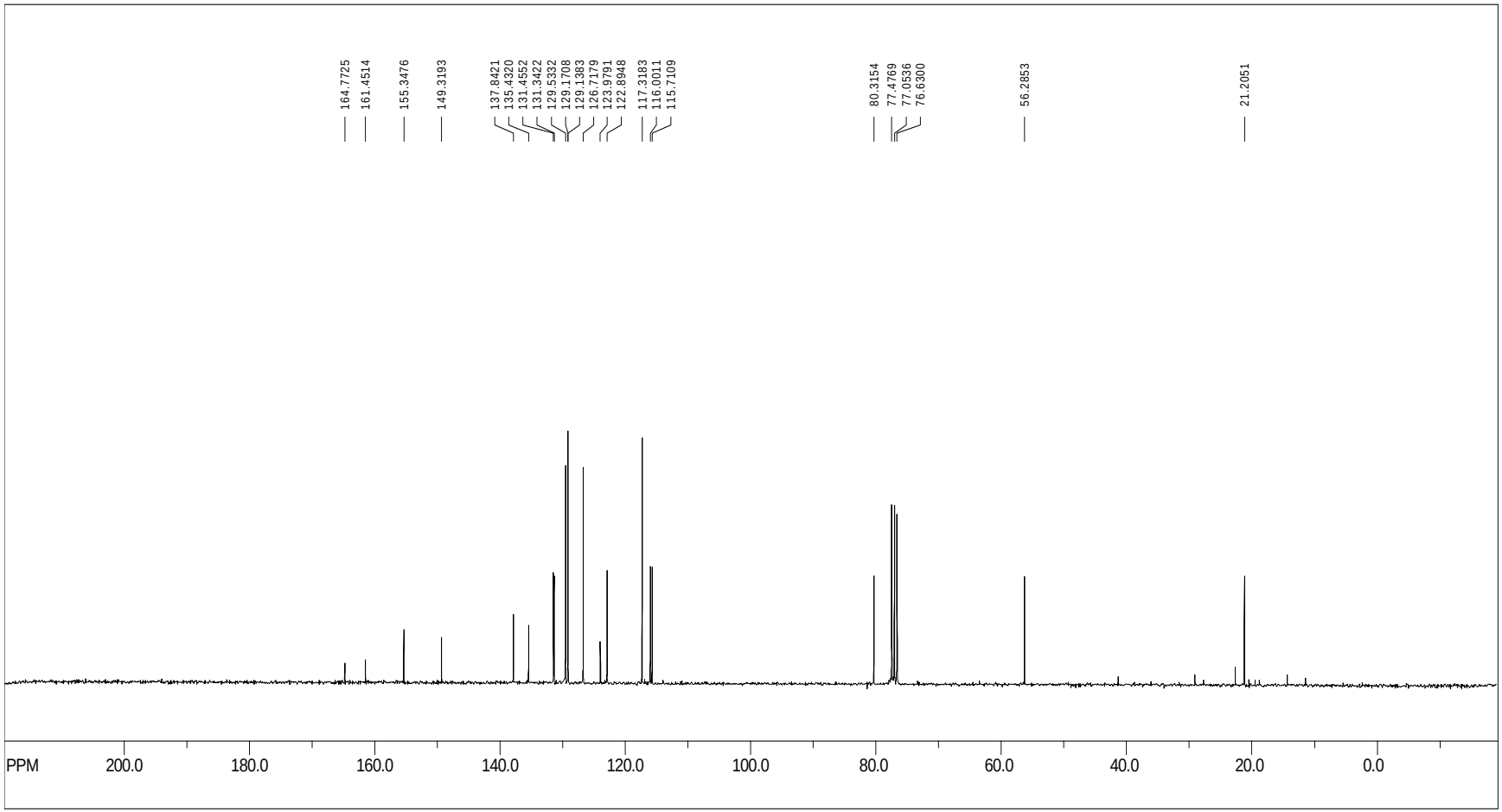
SpinWorks 2.5: methyl ether of 50



file: Z:\Laina\lmgviii\lmgviii_64a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

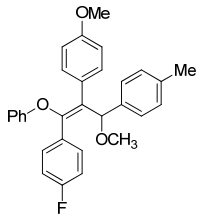
SpinWorks 2.5: methyl ether of 50



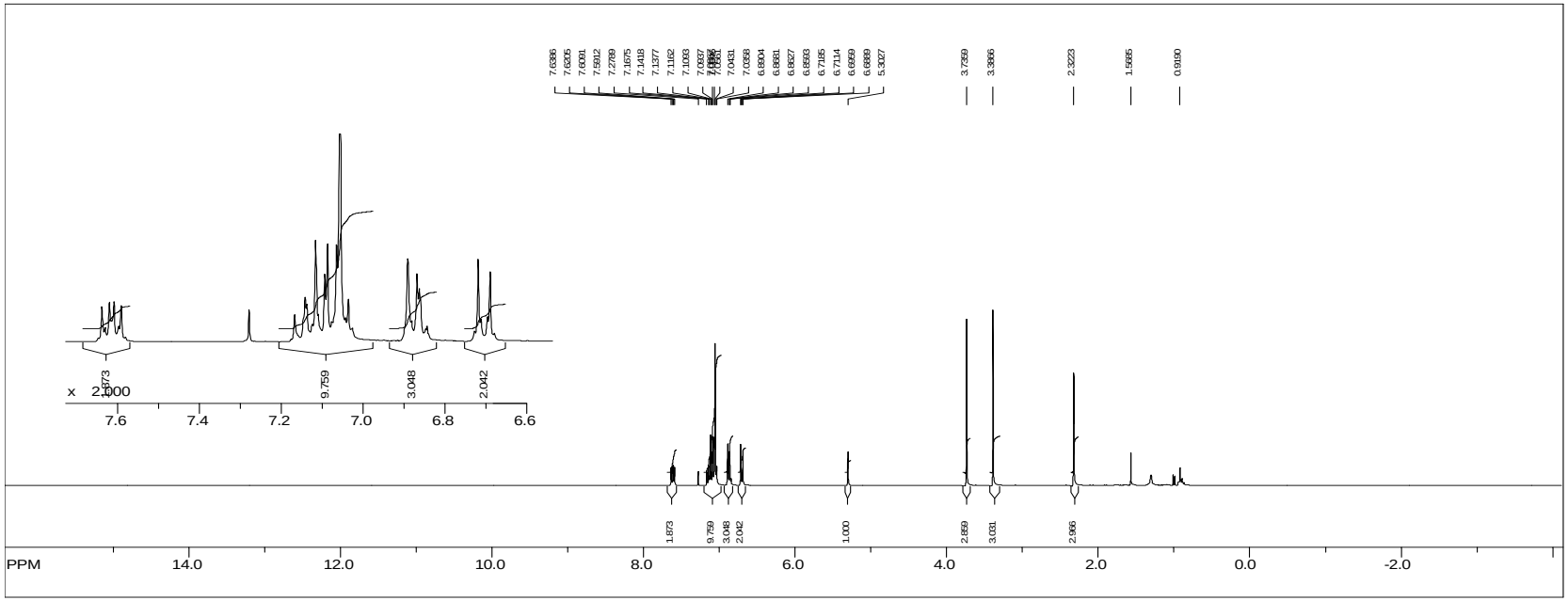
file: Z:\Laina\lmgviii\lmgviii_64a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 401

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*E*)-1-(3-(4-Fluorophenyl)-1-methoxy-2-(4-methoxyphenyl)-3-phenoxyallyl)-4-methylbenzene (285)



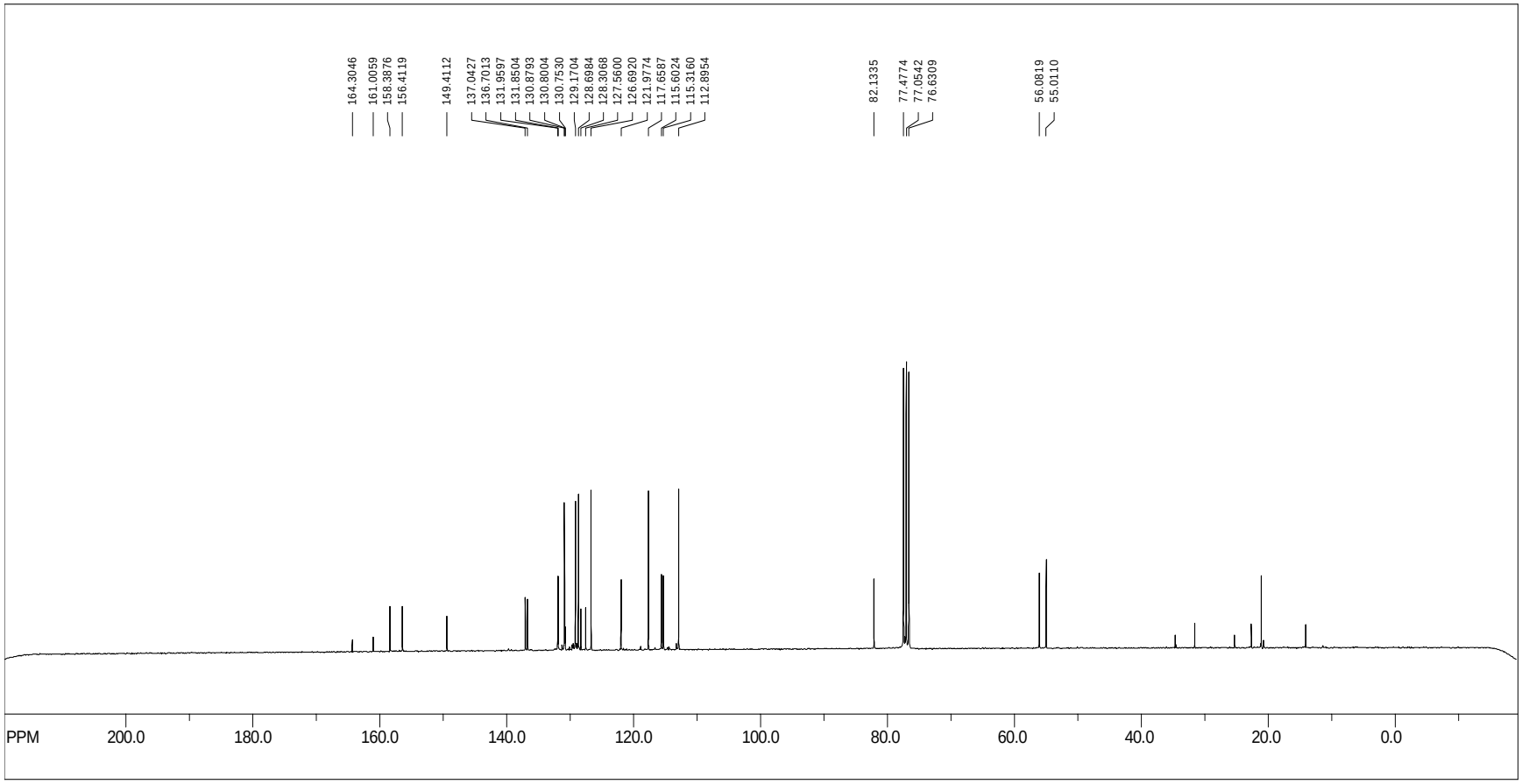
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



file: Z:\Laina\lmgix\lmgix_96b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

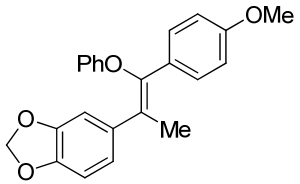
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 13



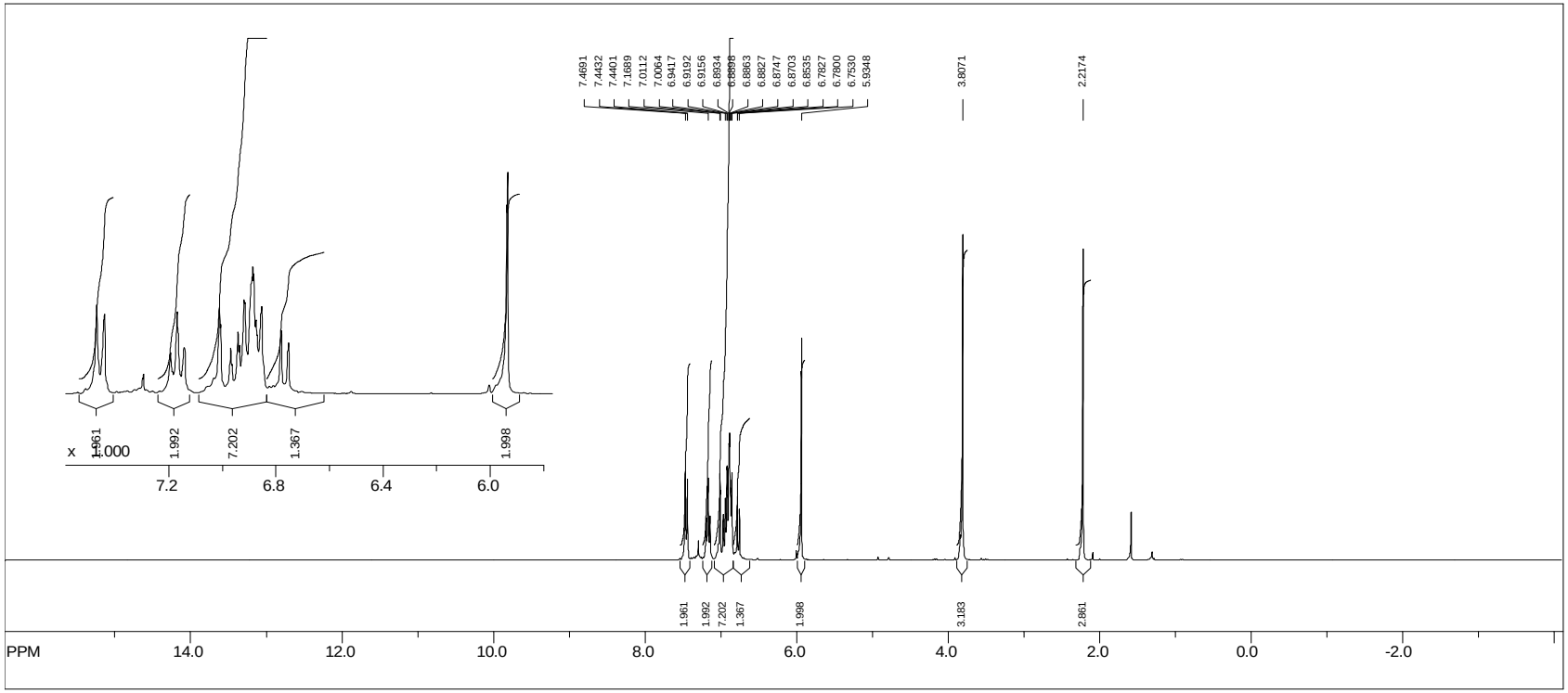
file: Z:\Laina\lmgix\lmgix_96b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 11000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(*Z*)-5-(1-(4-Methoxyphenyl)-1-phenoxyprop-1-en-2-yl)benzo[*d*][1,3]dioxole (286)



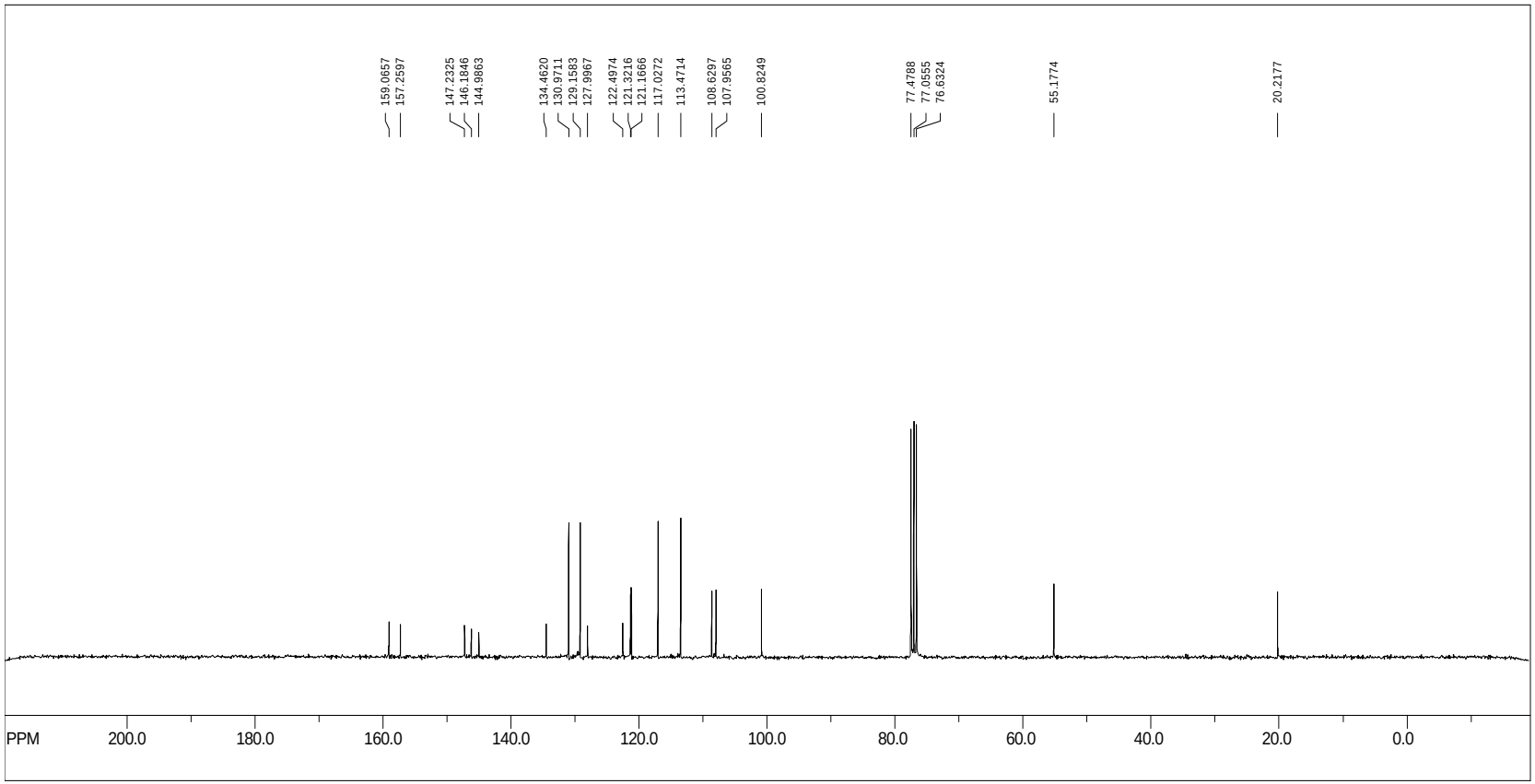
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxvi\lmgxvi_30a\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

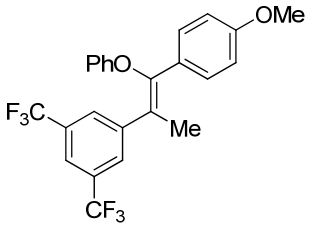
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



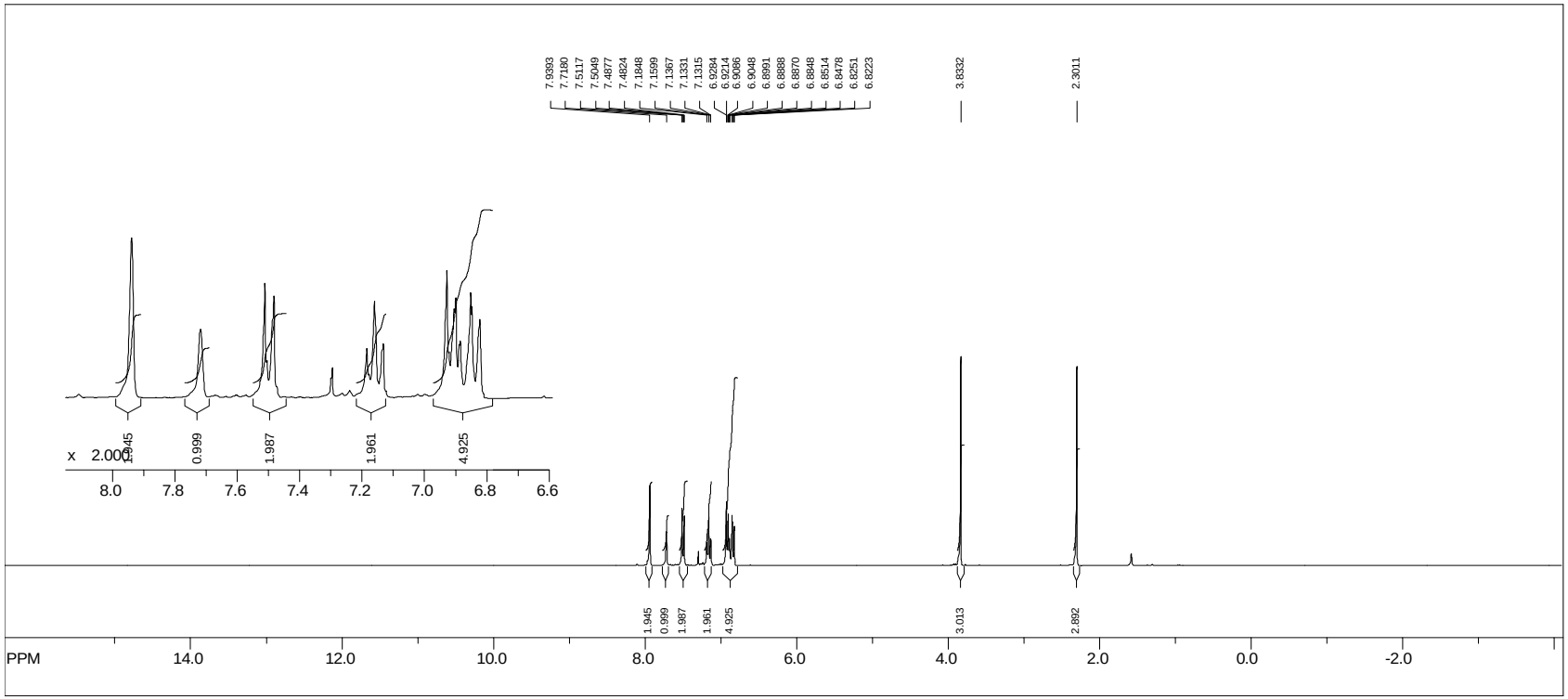
file: Z:\Laina\lmgxvi\lmgxvi_30a\4\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-1-((2-3,5-bis(Trifluoromethyl)phenyl)-1-(4-methoxyphenyl)prop-1-enyloxy)benzene (287)



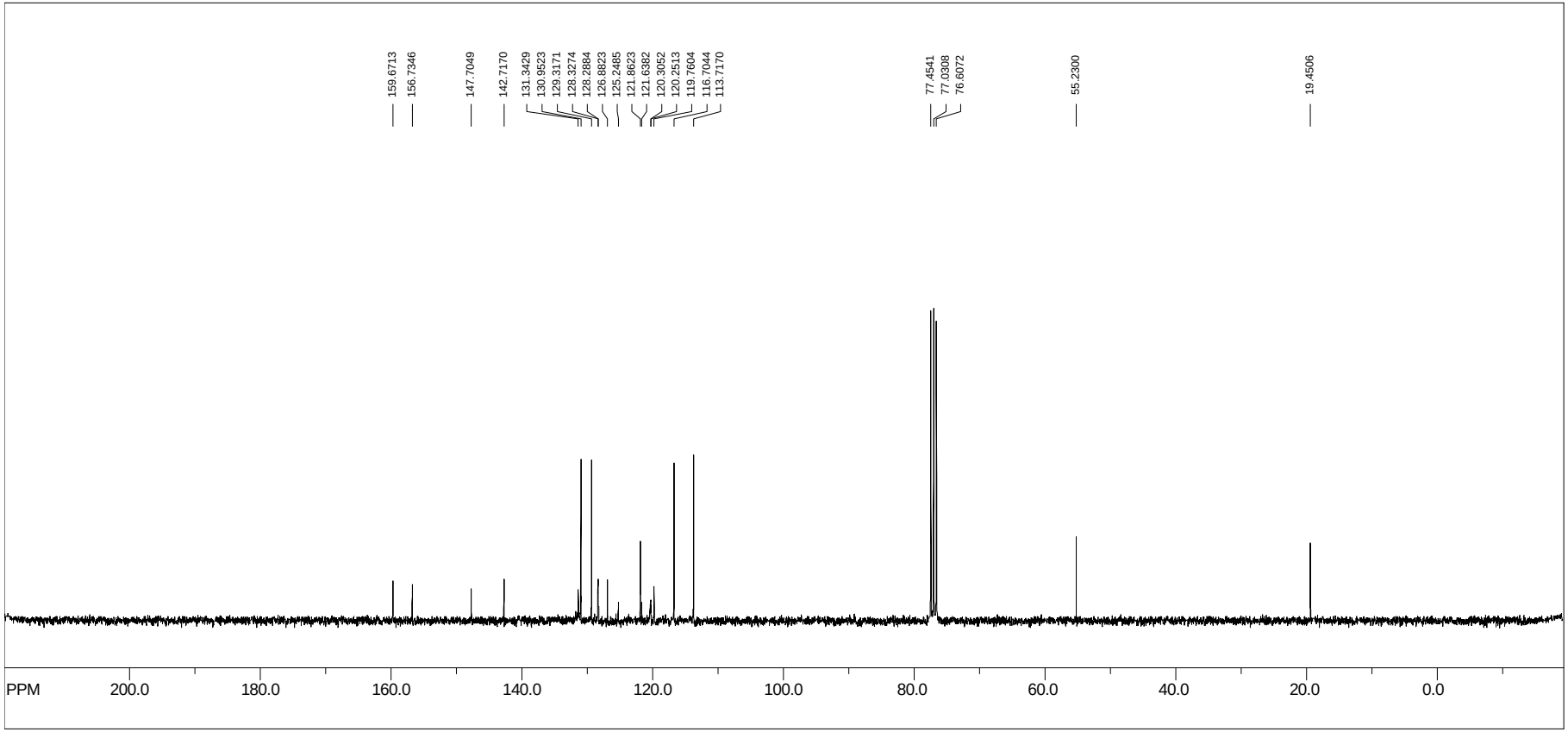
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxvi\lmgxvi_32a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

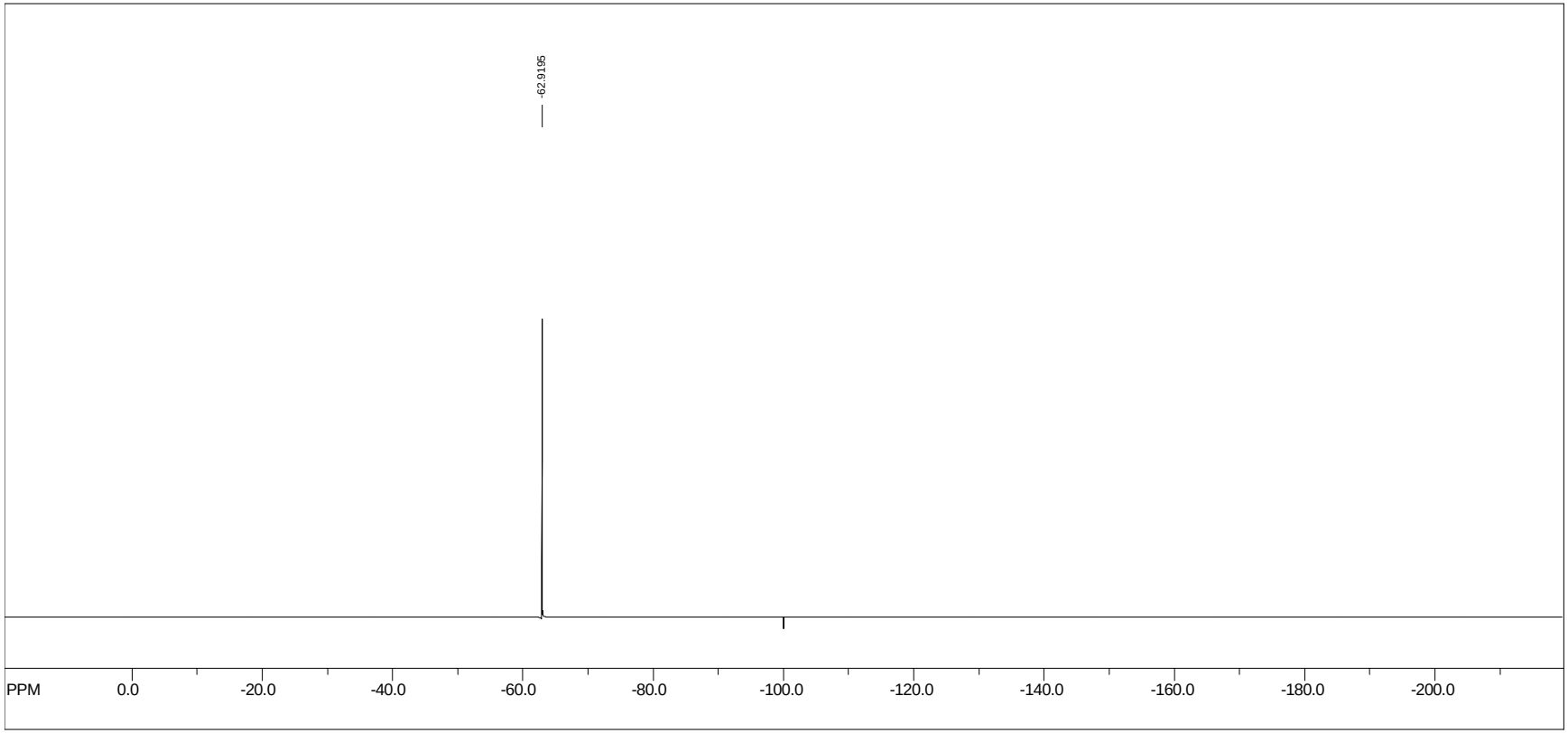
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxvi\lmgxvi_32a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

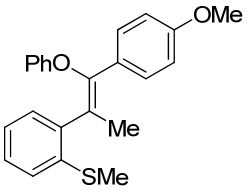
SpinWorks 2.5: F19 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



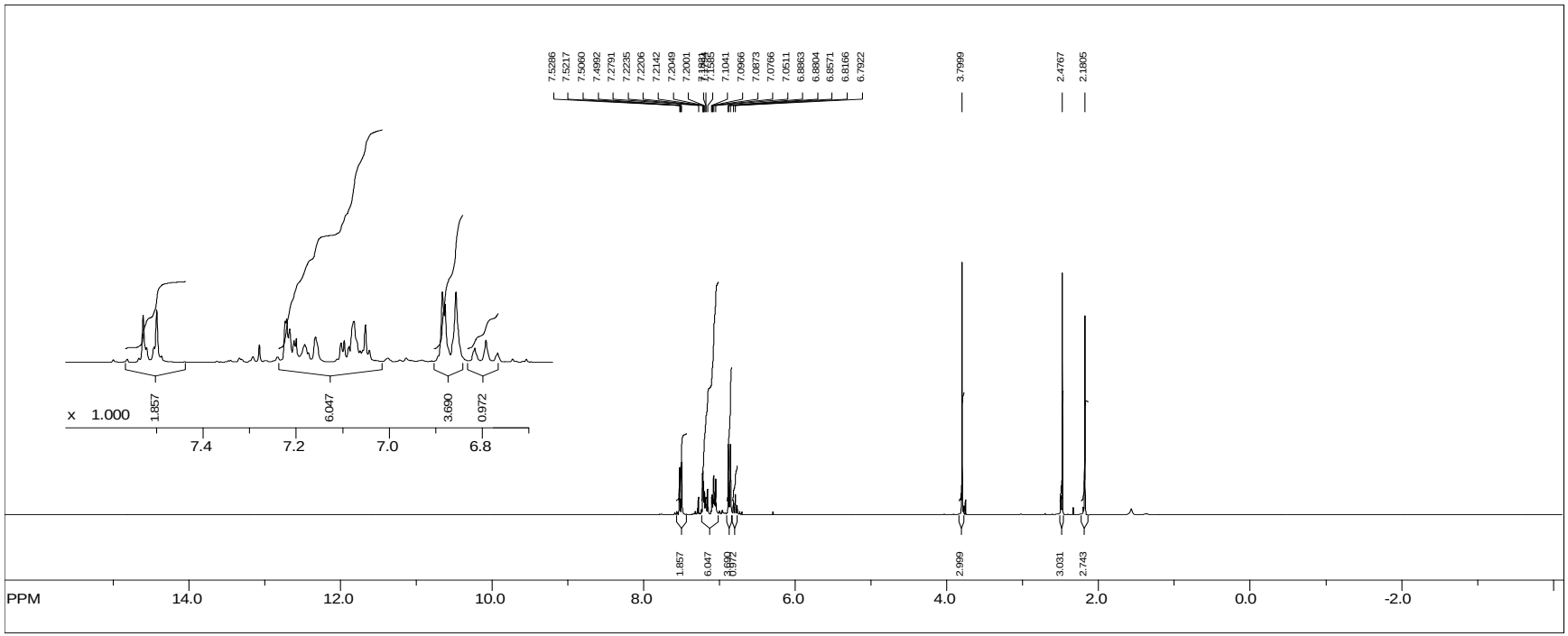
file: Z:\Laina\lmgwi\lmgwi_32a\2\fid expt: <zgflqn>
transmitter freq.: 282.376115 MHz
time domain size: 131072 points
width: 67567.57 Hz = 239.282163 ppm = 0.515500 Hz/pt
number of scans: 7

freq. of 0 ppm: 282.404355 MHz
processed size: 65536 complex points
LB: 0.300 GB: 0.0000

(*Z*)-(2-(1-Methoxyphenyl)-1-phenoxyprop-1-en-2-yl)phenyl)(methyl)sulfane (288)



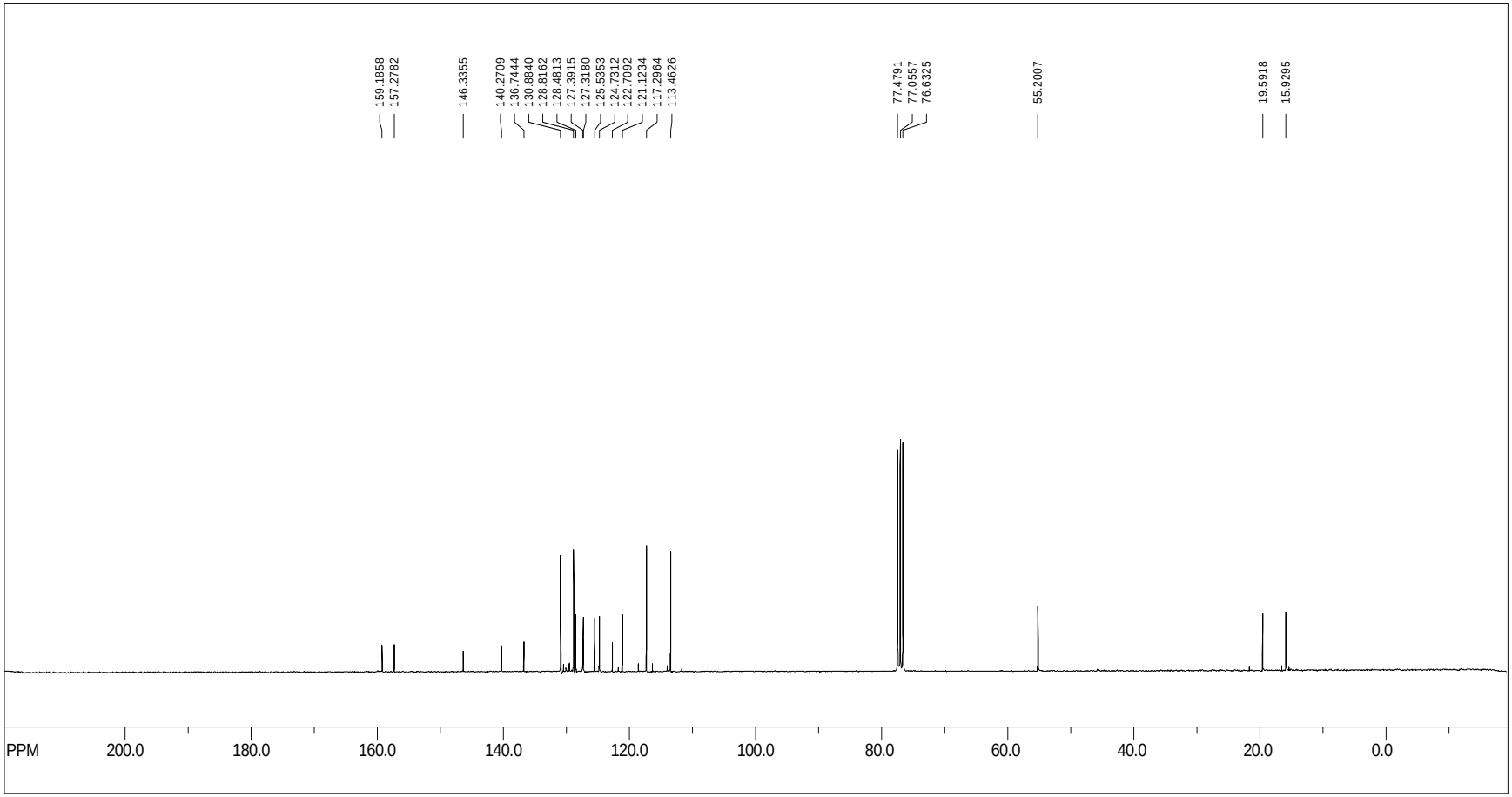
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgwi\lmgwi_33ai\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 8

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

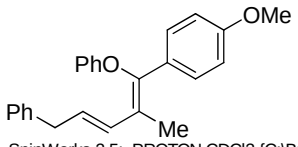
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



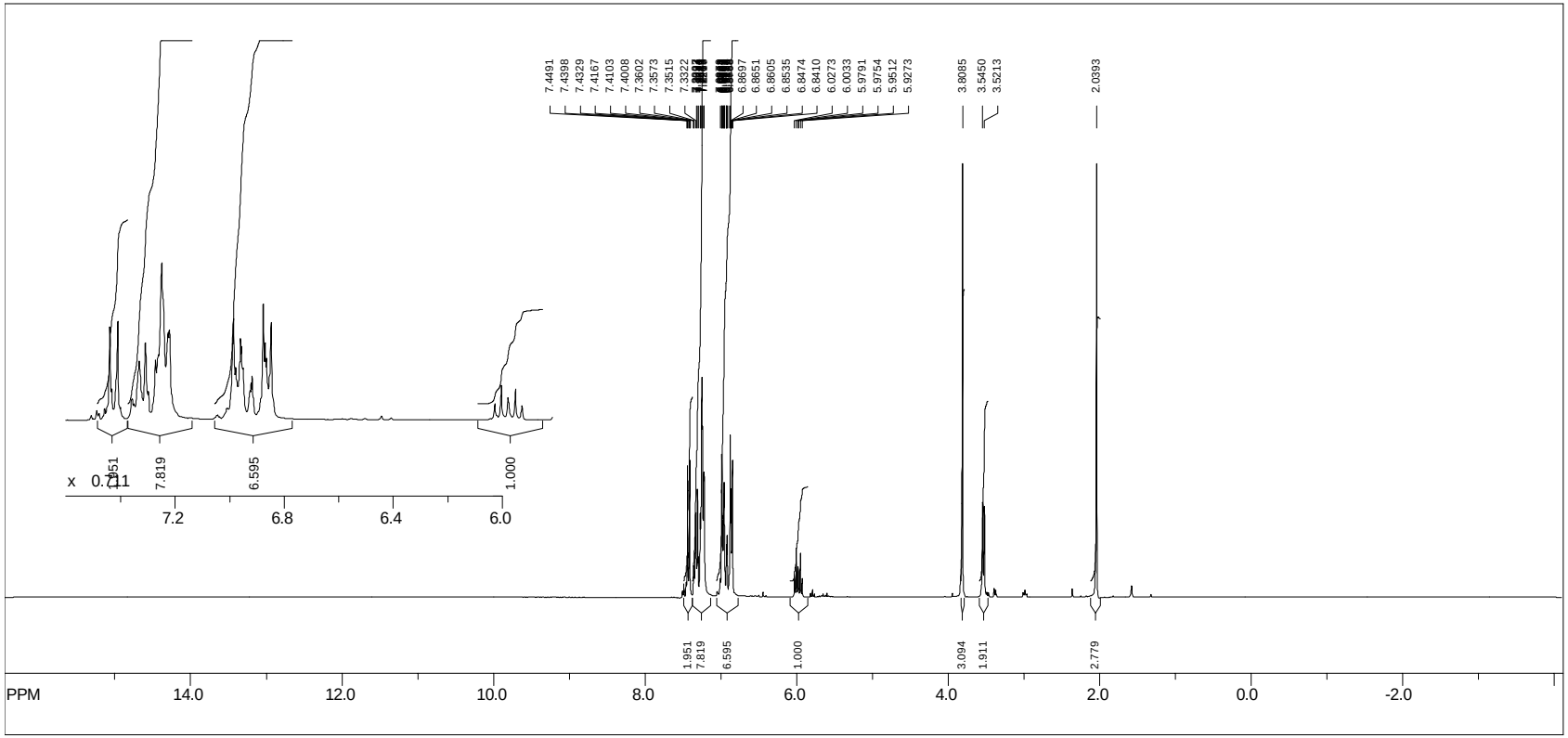
file: Z:\Laina\lmgxvi\lmgxvi_33ai\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4096

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-Methoxy-4-((1*Z*,3*E*)-2-methyl-1-phenoxy-5-phenylpenta-1,3-dienyl)benzene (289)



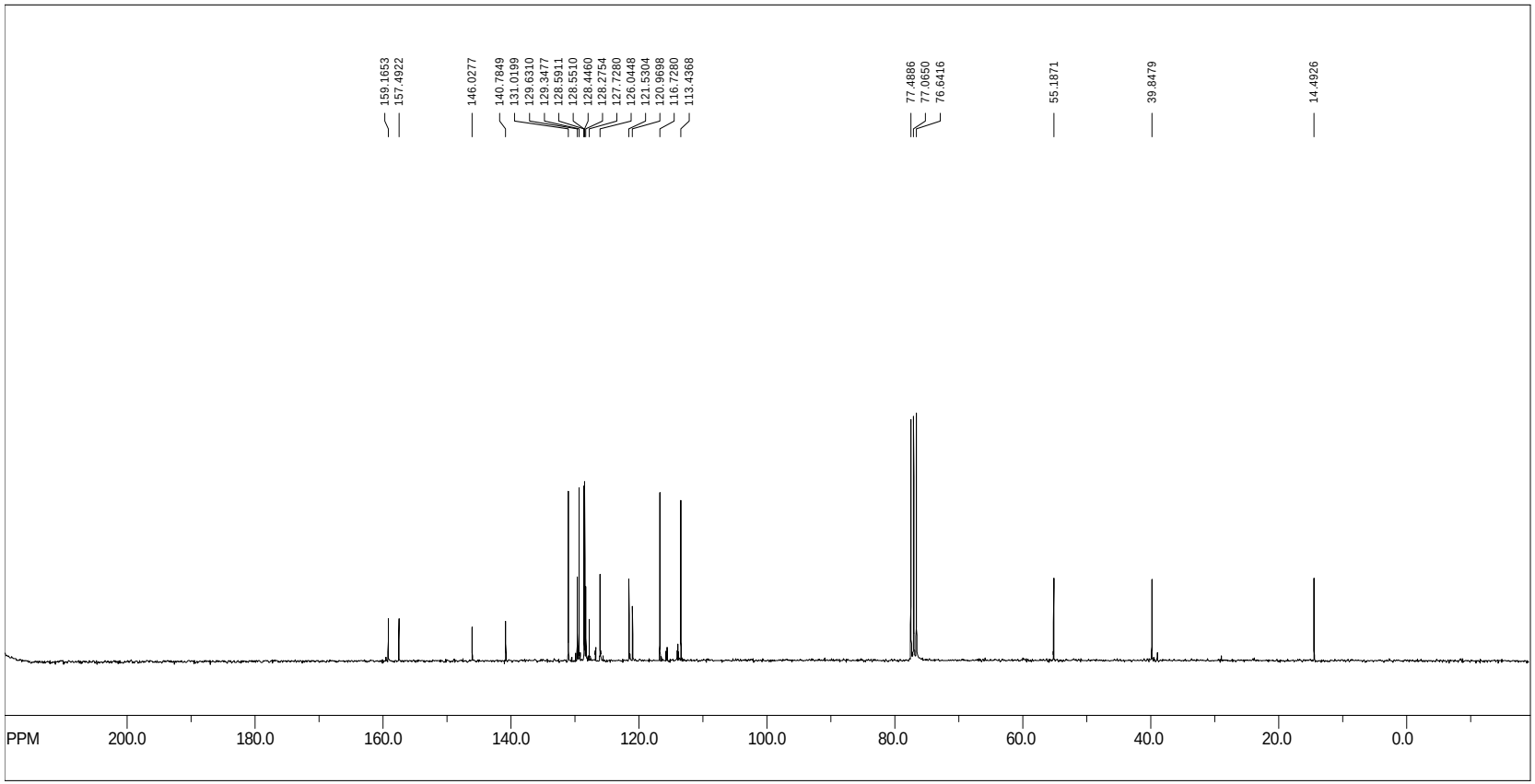
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxw\lmgxw_34a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

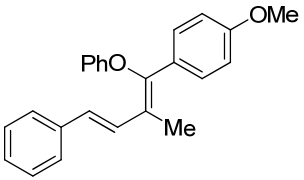
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



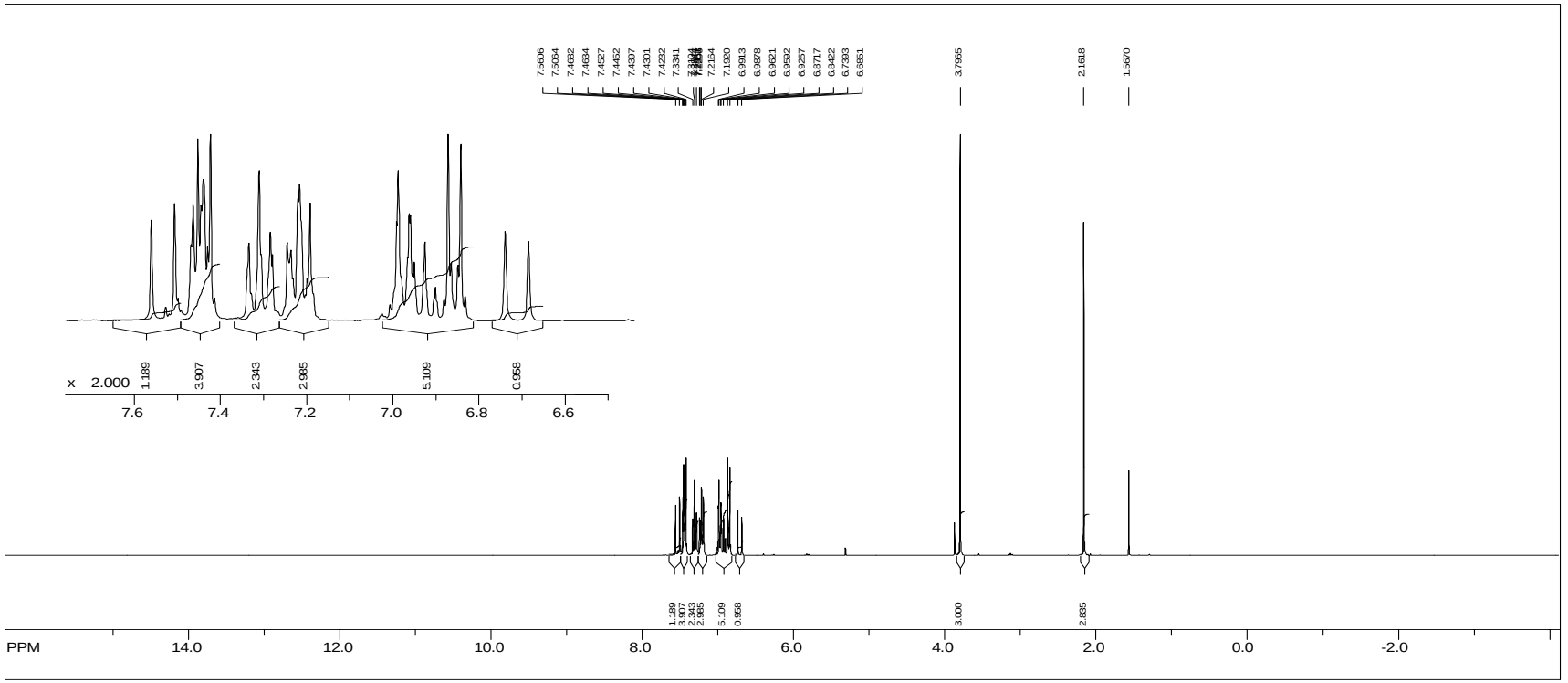
file: Z:\Laina\lmgxvi\lmgxvi_34a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 870

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

1-((1*Z*,3*E*)-1-(4-methoxyphenyl)-2-methyl-4-phenylbuta-1,3-dienyloxyl)benzene (290)



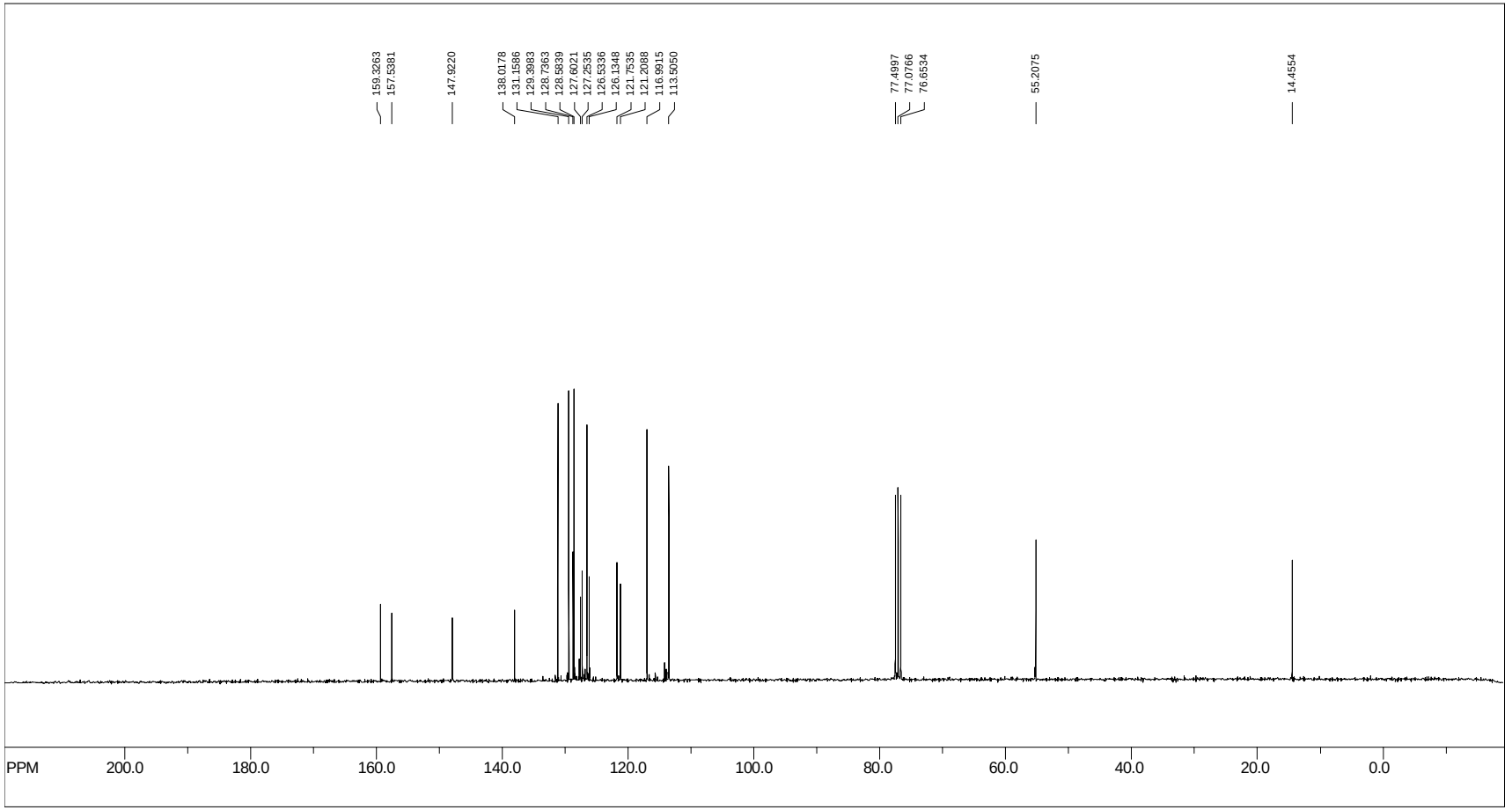
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



file: C:\Users\Laina\Desktop\Tetrasub Me\lmgxii_35b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

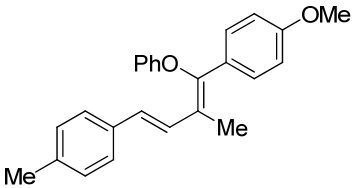
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 18



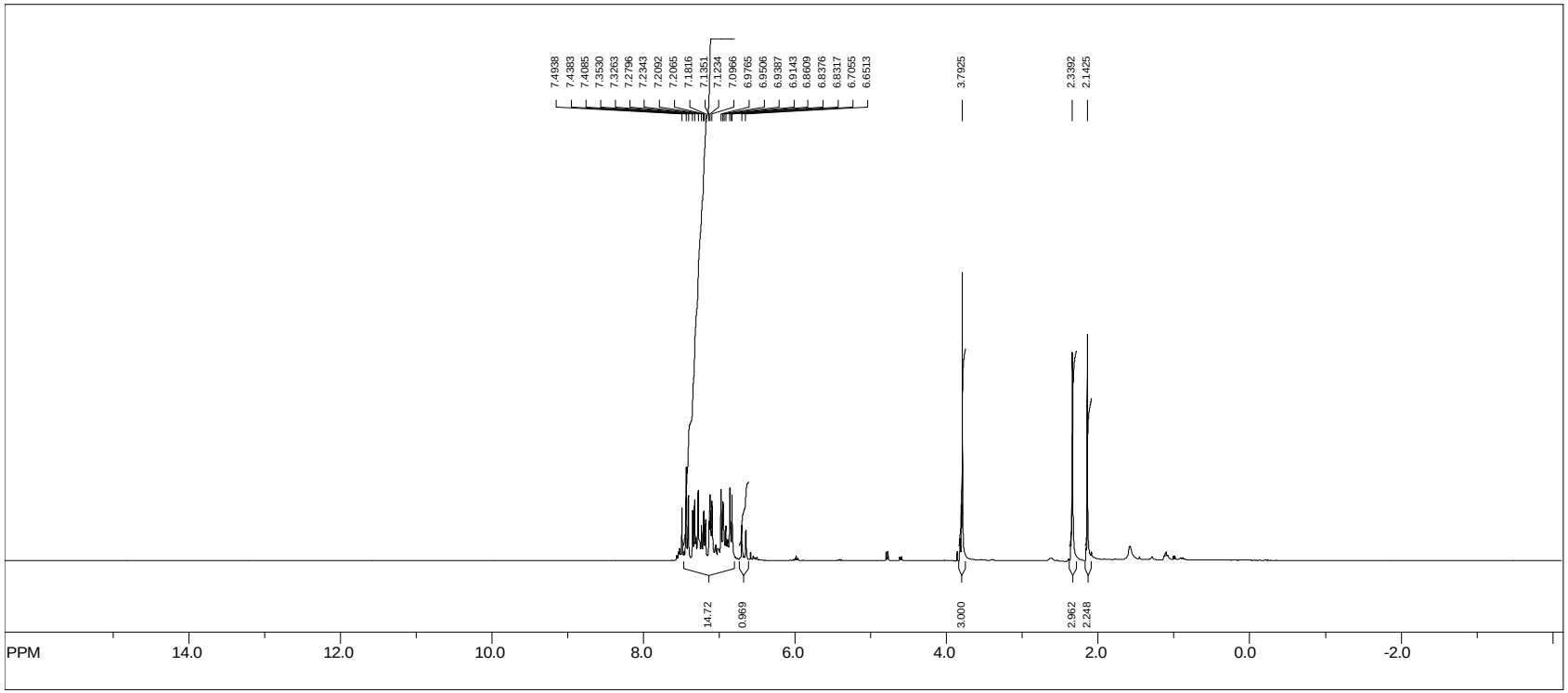
file: C:\Users\Laina\Desktop\Tetrasub Me\lmgxii_35b\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1018

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

1-((1Z,3E)-(4-methoxyphenyl)-2-methyl-4-p-tolylbuta-1,3-dienyloxy)benzene (291)



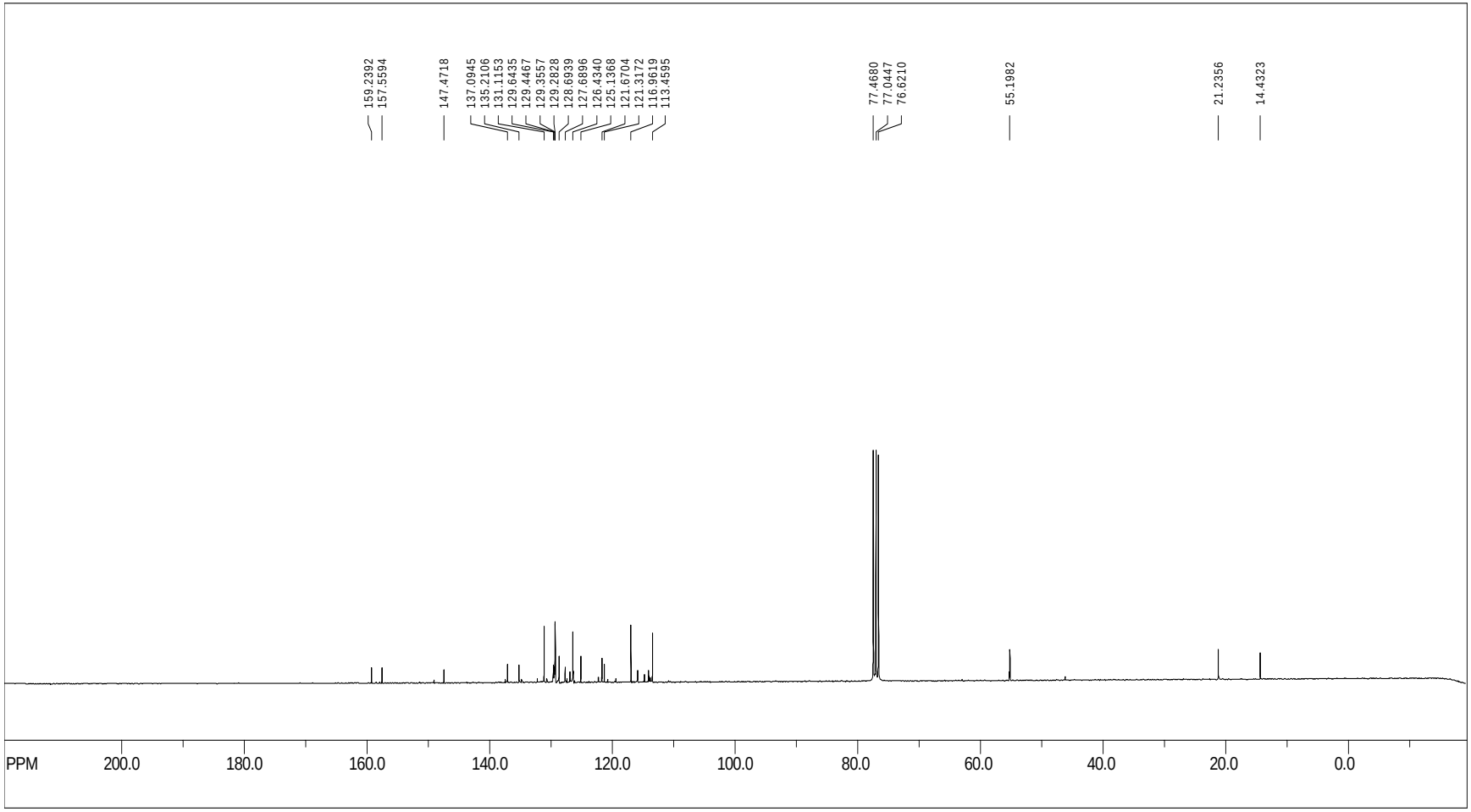
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



file: Z:\Laina\lmgxvi\lmgxvi_35aii\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

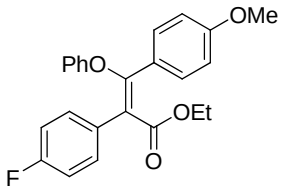
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



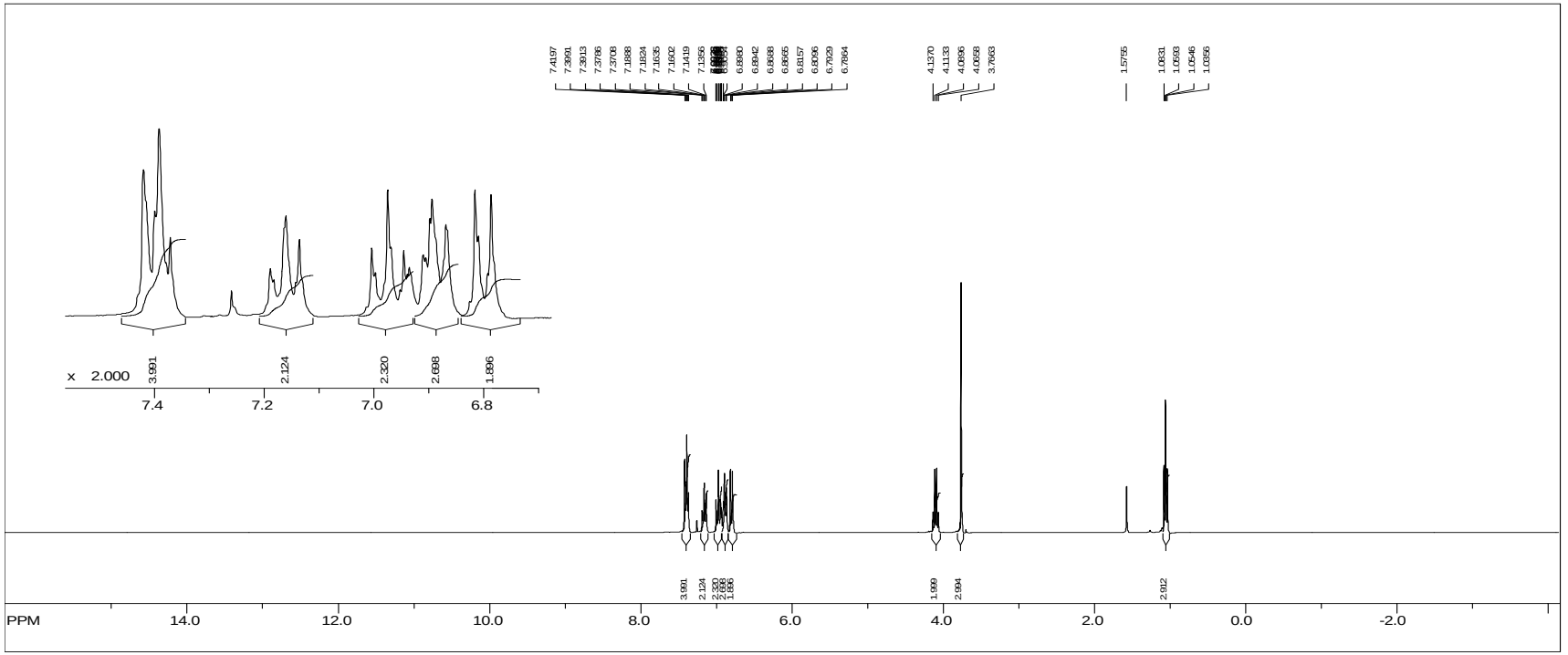
file: Z:\Laina\lmgxvi\lmgxvi_35aii\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 8000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(E)-Ethyl 2-(4-fluorophenyl)-3-(4-methoxyphenyl)-3-phenoxyacrylate (292)



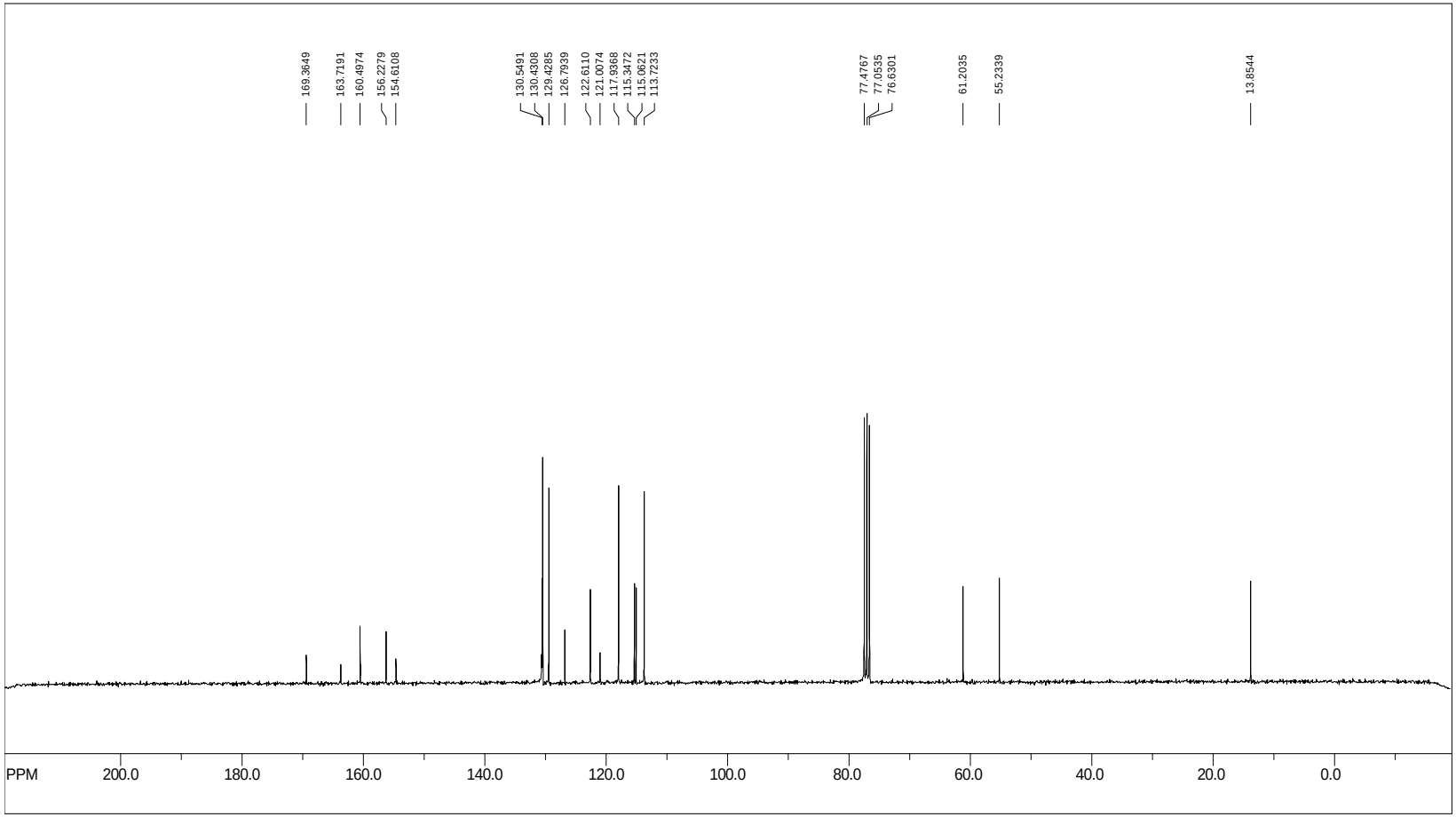
SpinWorks 2.5: tetrasub from xi_79b and pfluorophenylboronic acid



file: Z:\Laina\lmgxi\lmgxi_96a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

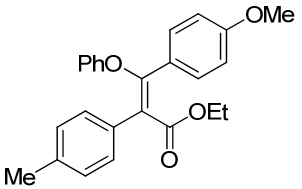
SpinWorks 2.5: tetrasub from xi_79b and pfluorophenylboronic acid



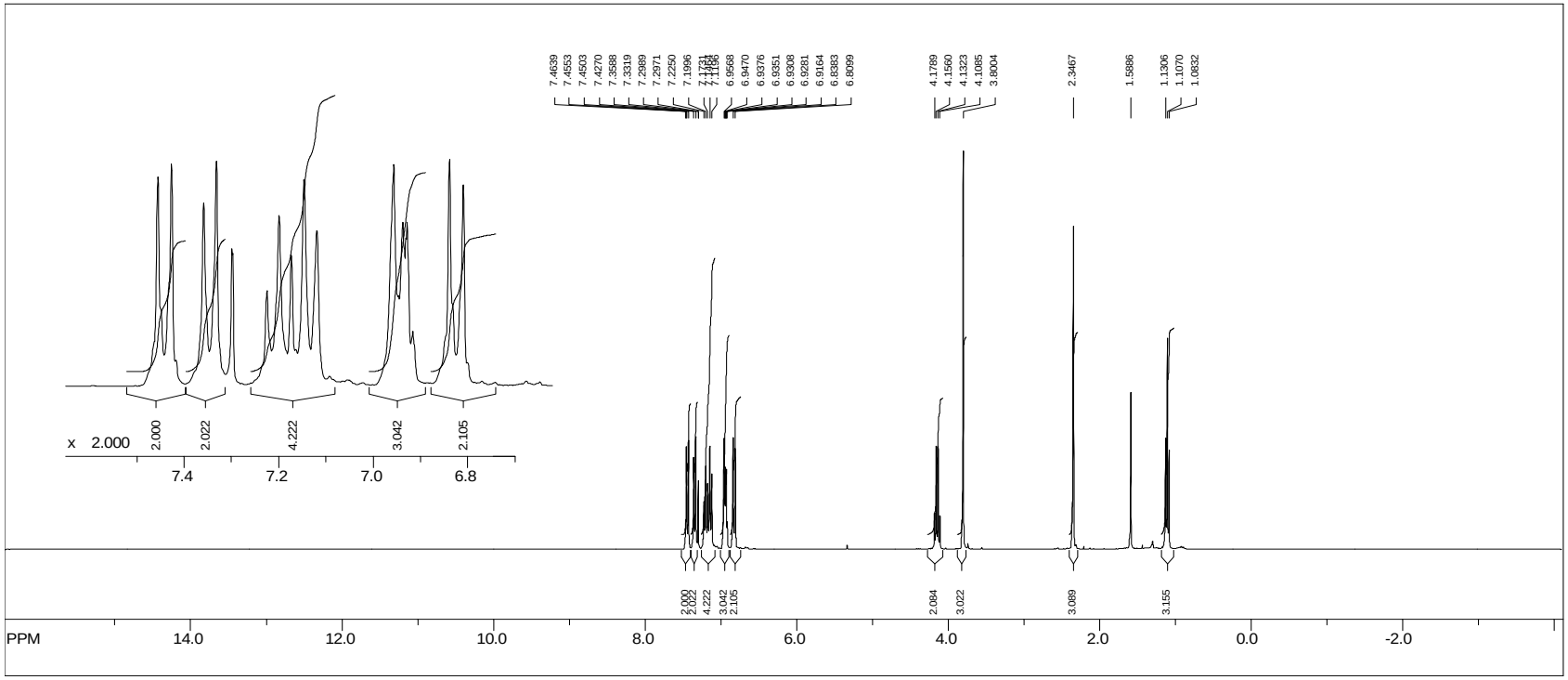
file: Z:\Laina\lmgxi\lmgxi_96a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(E)-Ethyl 3-(4-methoxyphenyl)-3-phenoxy-2-*p*-tolylacrylate (293)



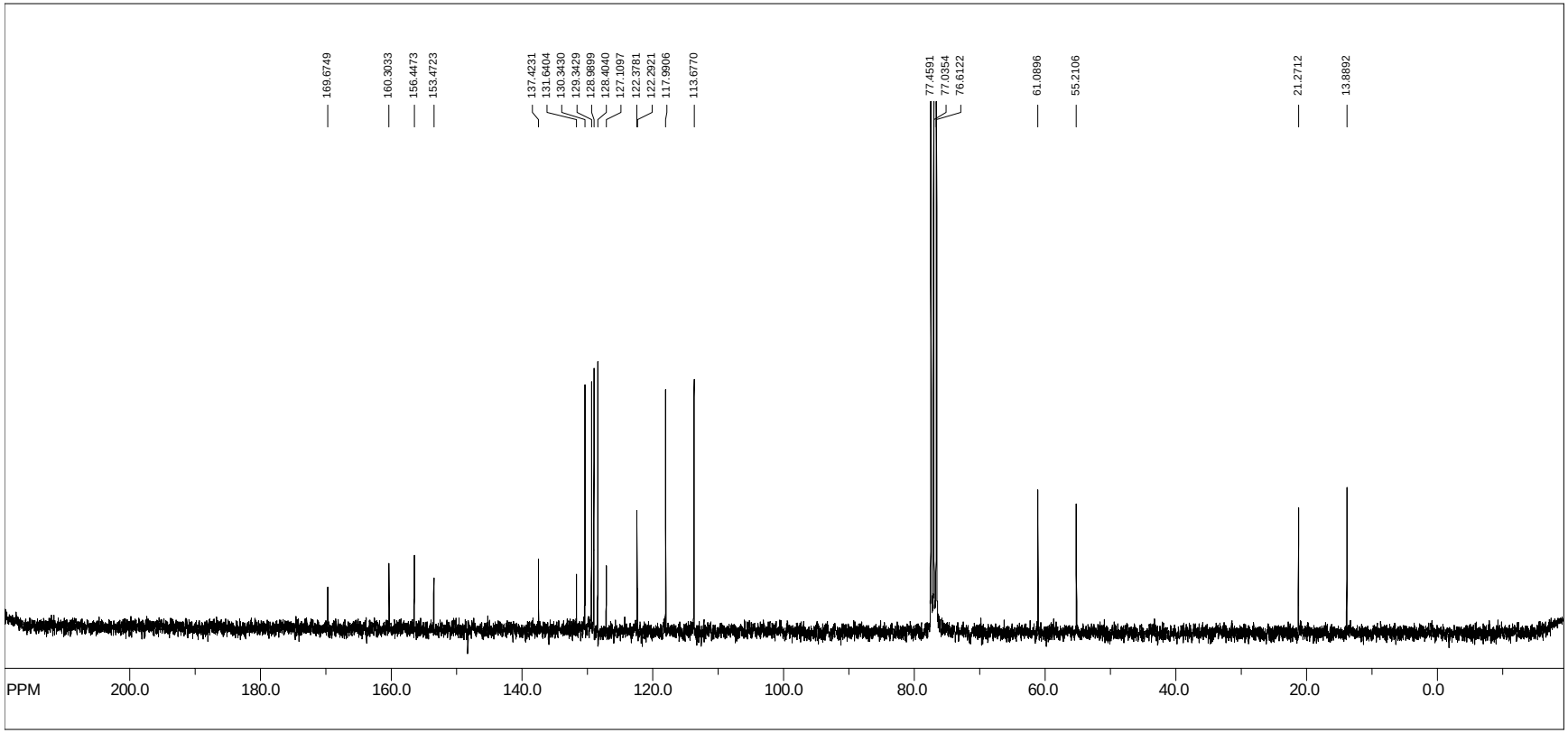
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgxvi\lmgxvi_37a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

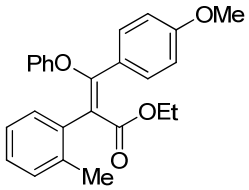
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



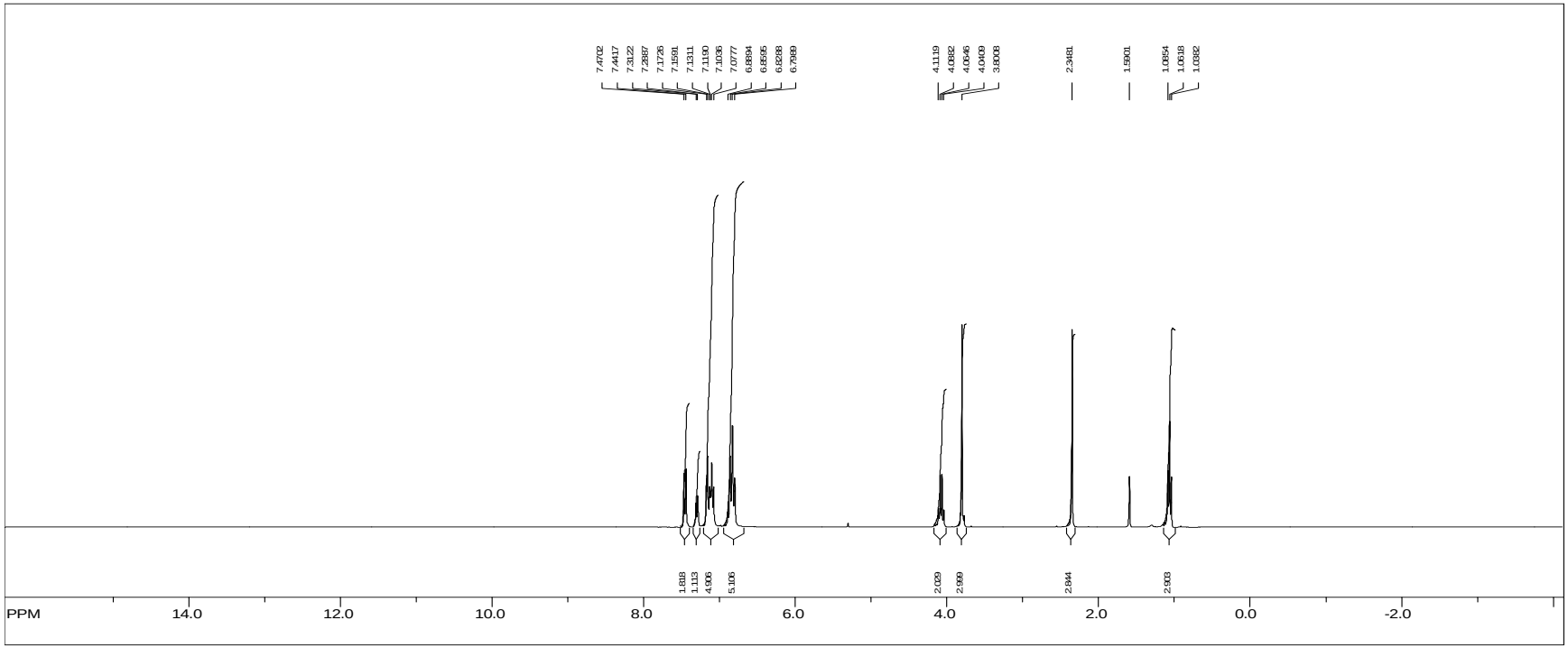
file: Z:\Laina\lmgwi\lmgwi_37a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(E)-Ethyl 3-(4-methoxyphenyl)-3-phenoxy-2-*o*-tolylacrylate (294)



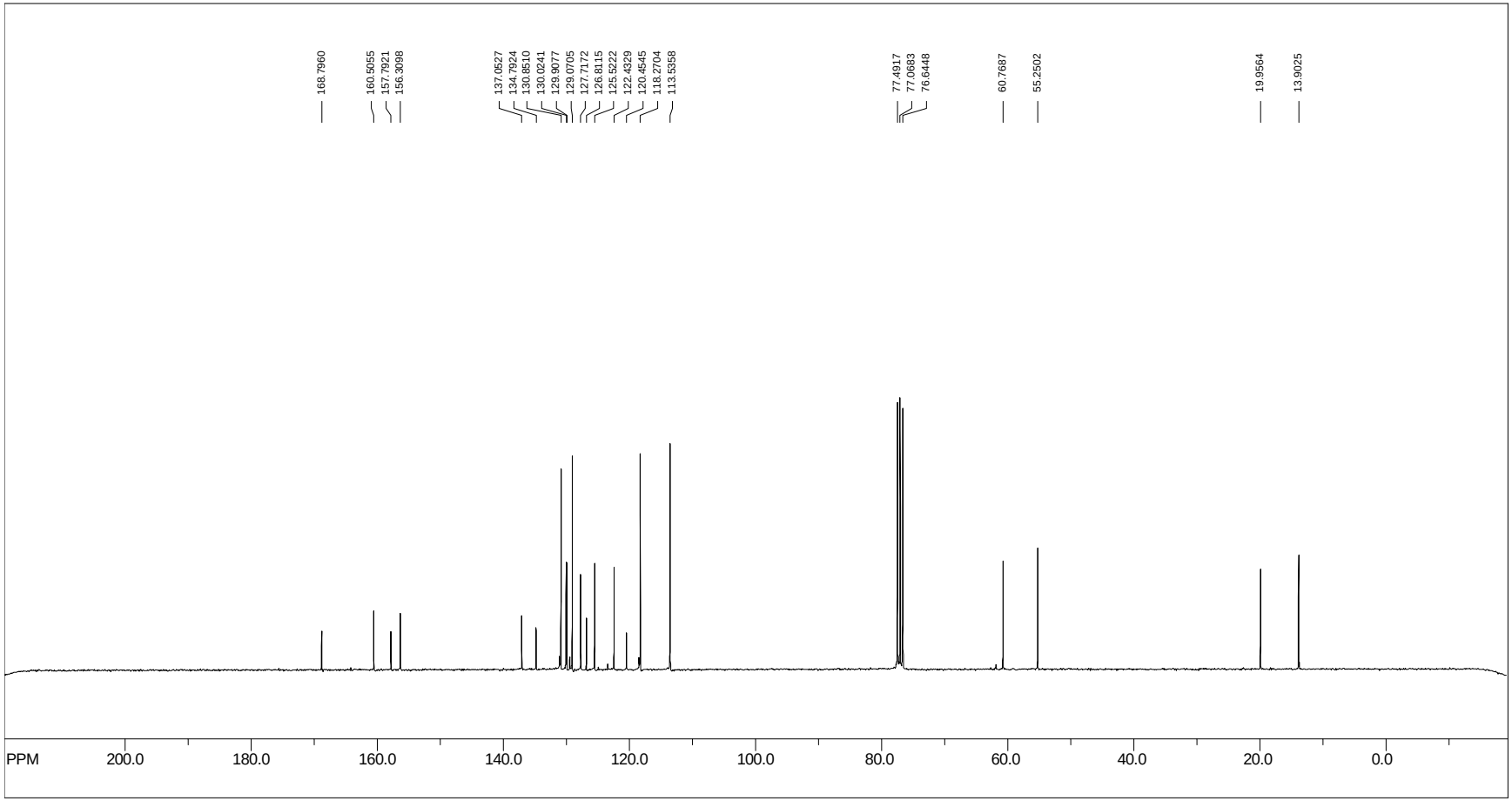
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxi\lmgxi_96cl\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

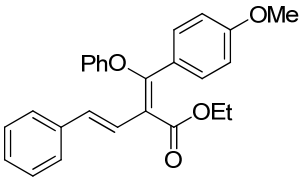
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



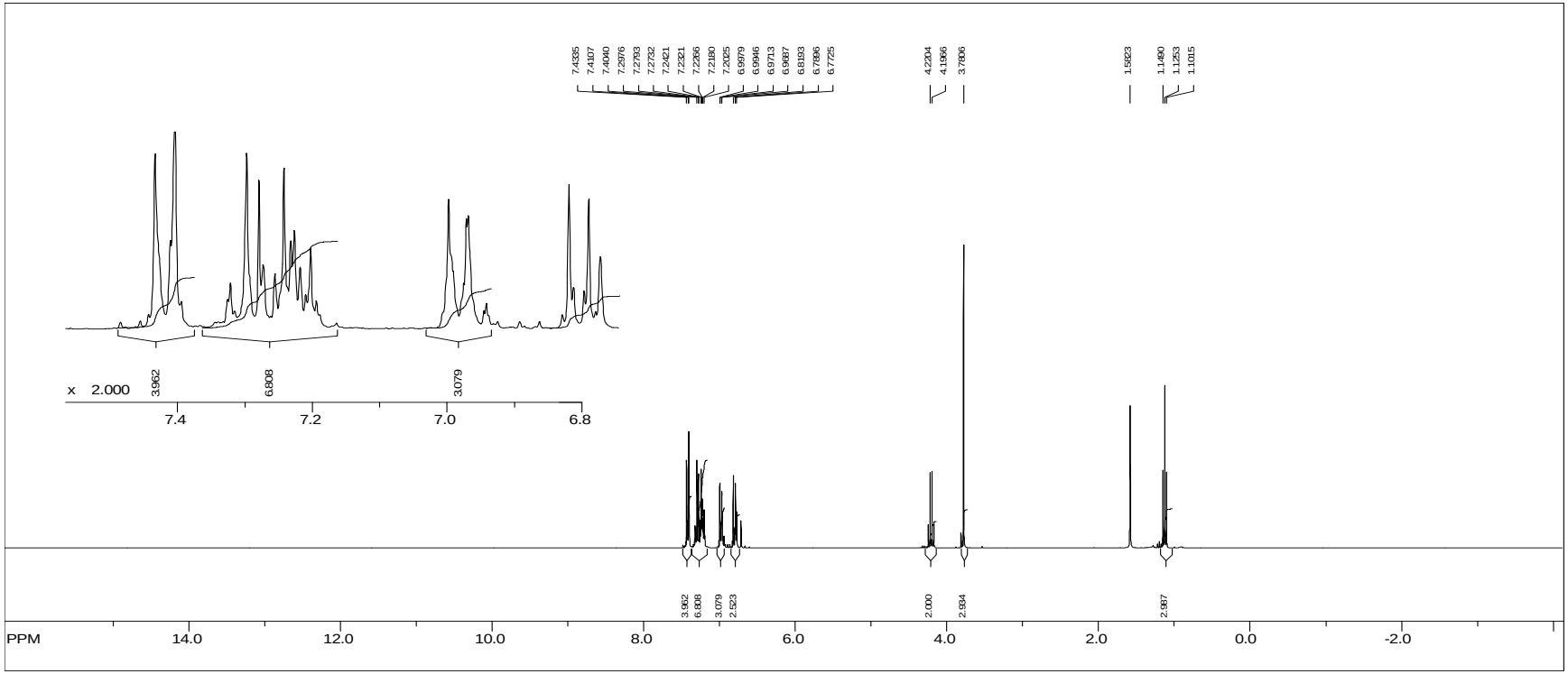
file: Z:\Laina\lmgxi\lmgxi_96d\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4096

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(2*E*,3*E*)-Ethyl 2-((4-methoxypheny)(phenoxy)methylene)-4-phenylbut-3-enoate (295)



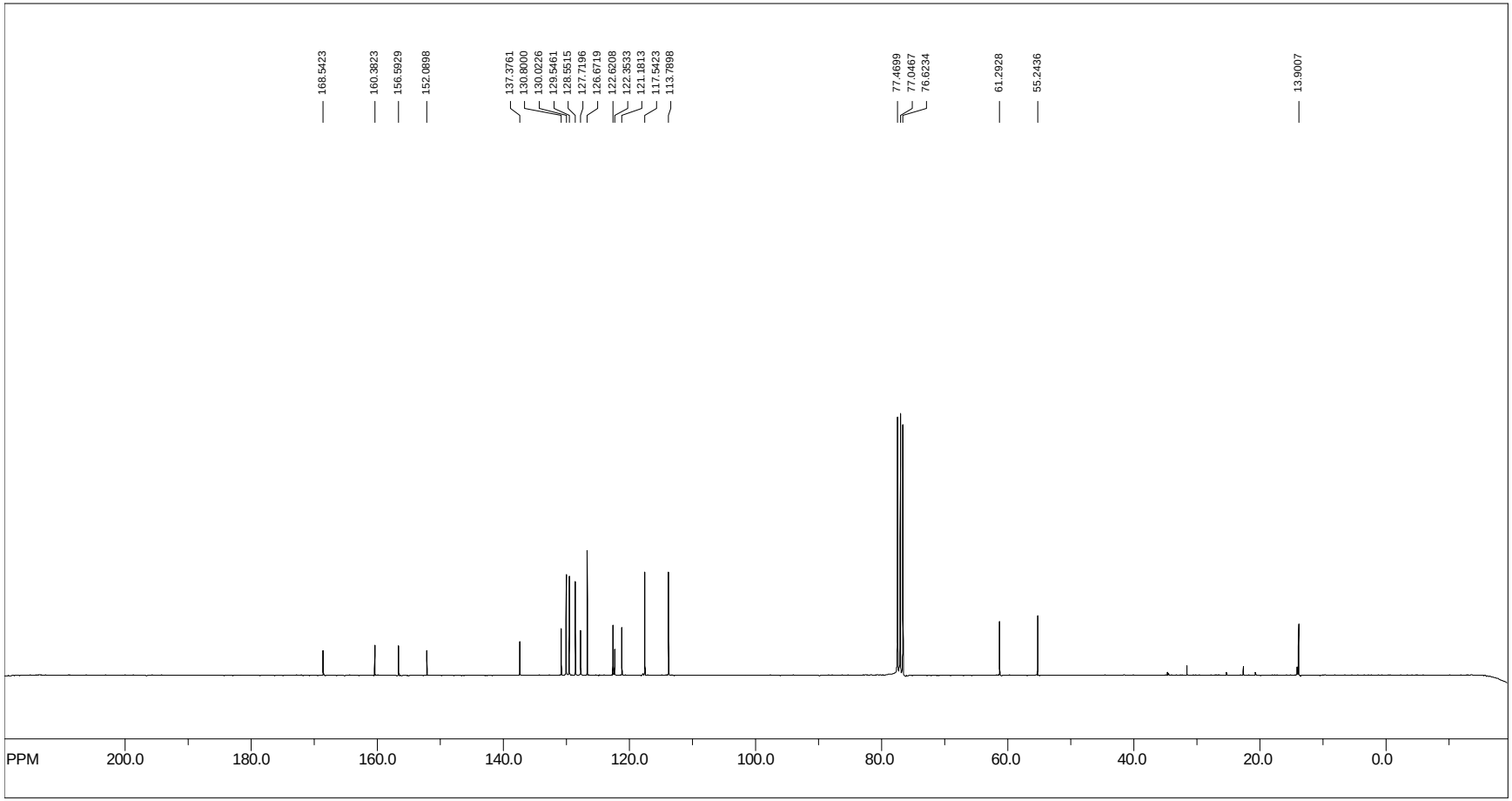
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



file: C:\Users\Laina\Desktop\Tetrasub Esters\lmgxii_30c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

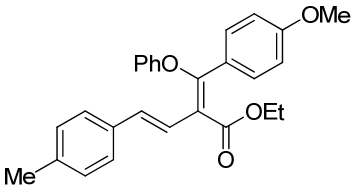
SpinWorks 2.5: fractions 28-40



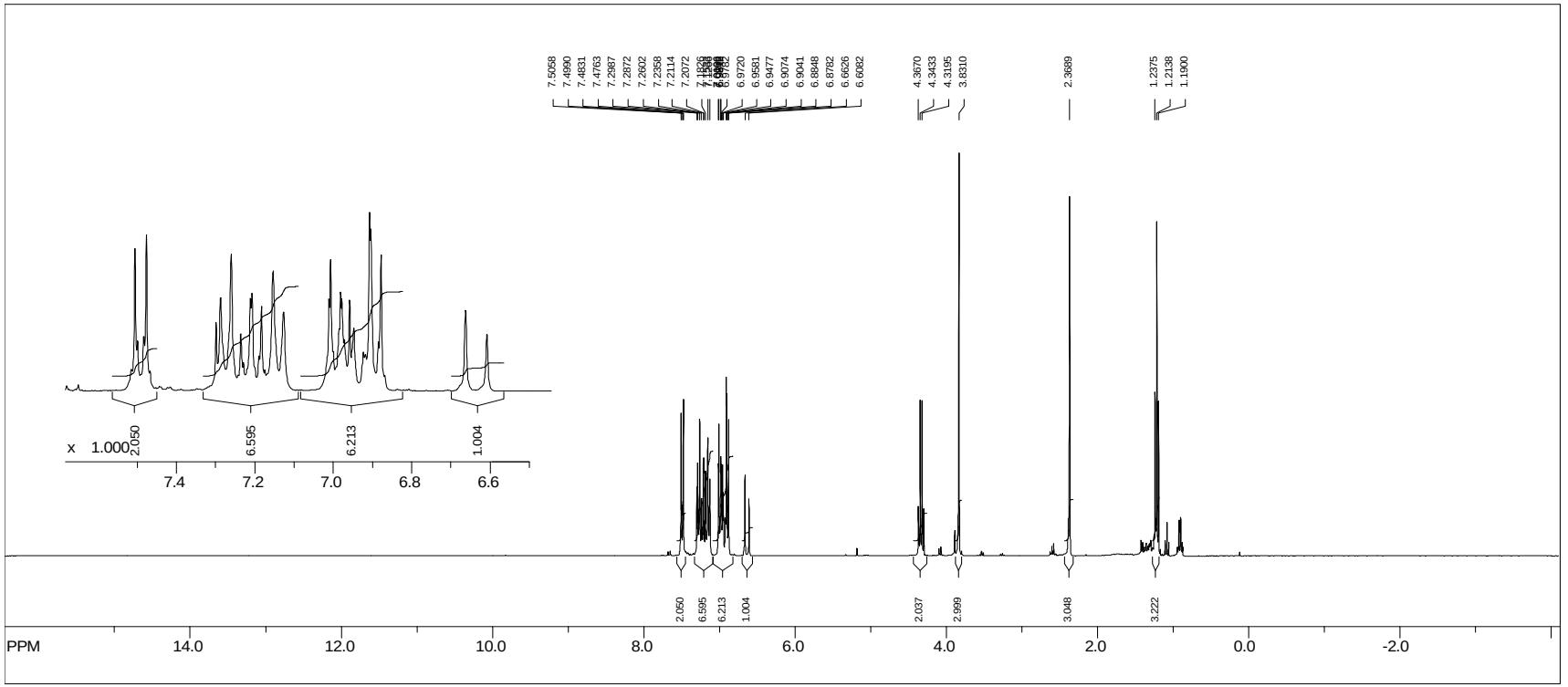
file: Z:\Laina\lmgxii\lmgxii_21b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 8000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(2*E*,3*E*)-Ethyl 2-((4-methoxyphenyl)(phenoxy)methylene)-4-*p*-tolylbut-3-enoate (296)



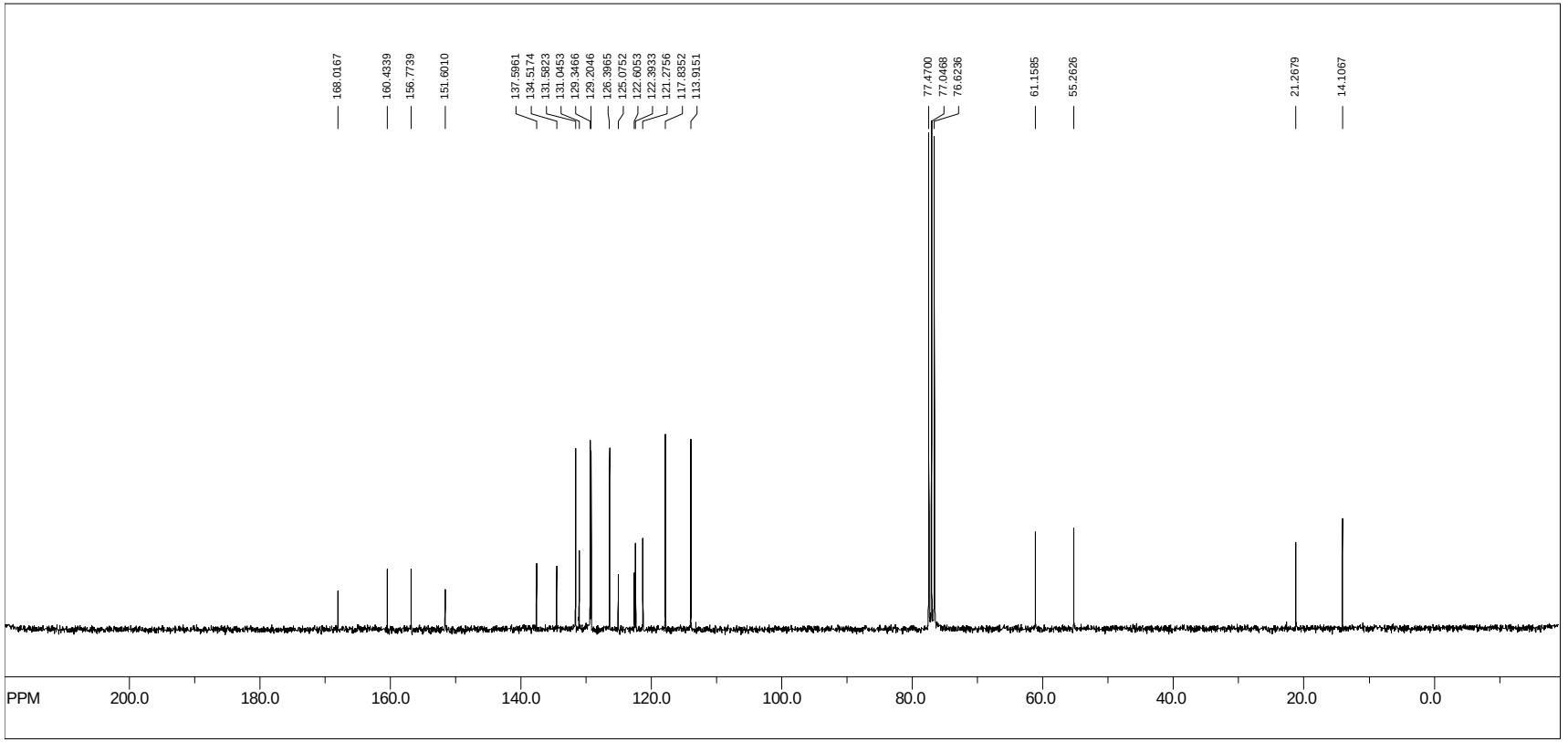
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxvi\lmgxvi_39a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

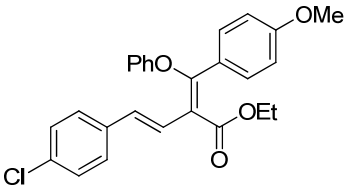
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



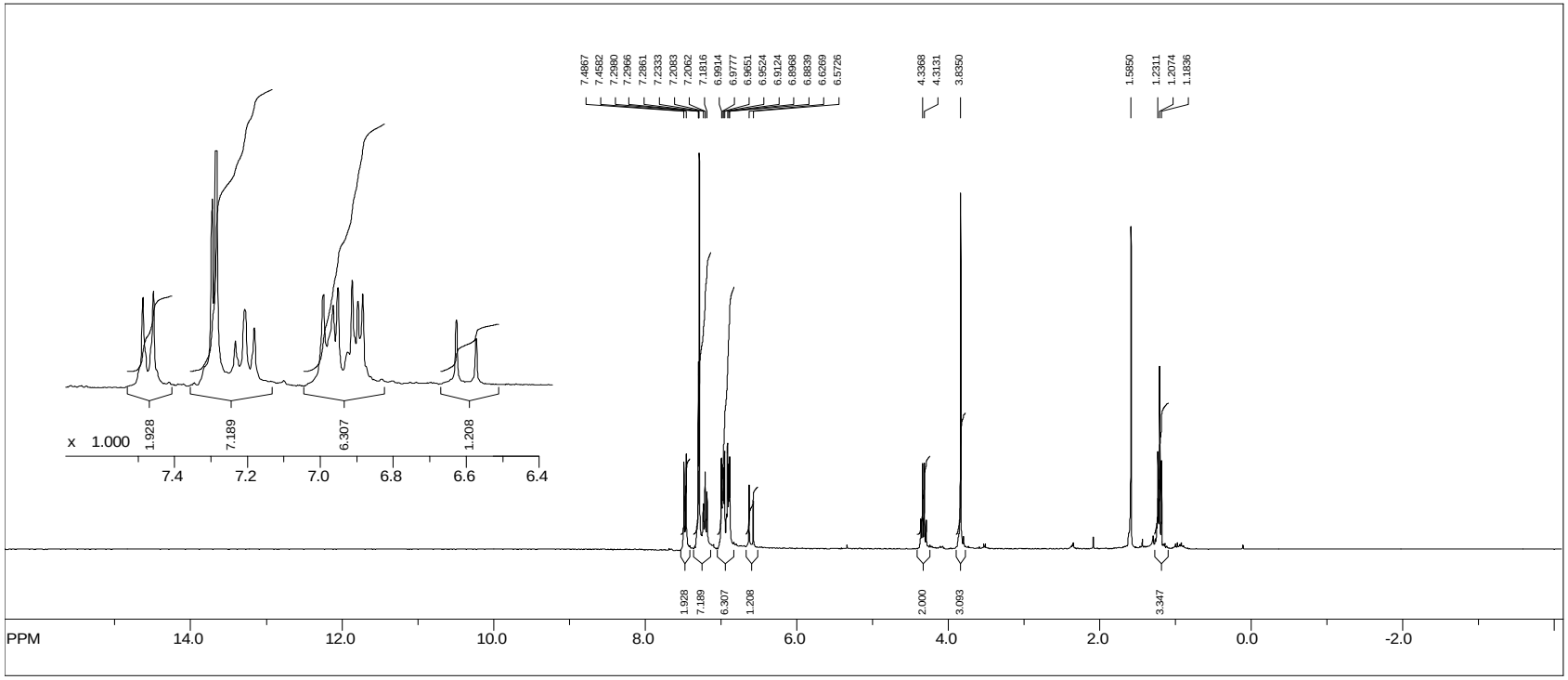
file: Z:\Laina\lmgxvi\lmgxvi_39a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 969

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(2*E*,3*E*)-Ethyl 4-(4-chlorophenyl)-2-((4-methoxyphenyl)(phenoxy)methylene)but-3-enoate (297)



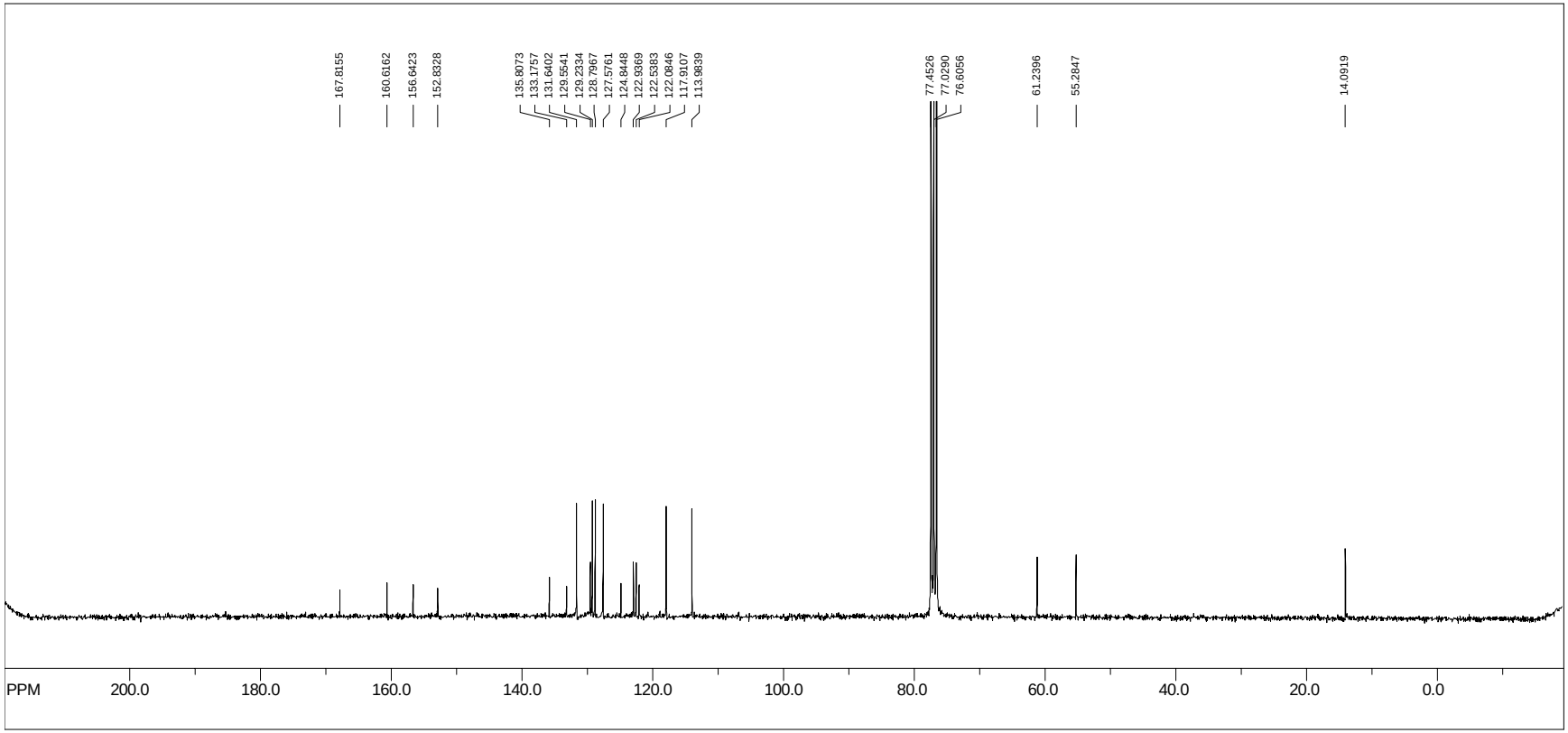
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgxvi\lmgxvi_40a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

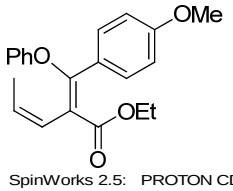
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



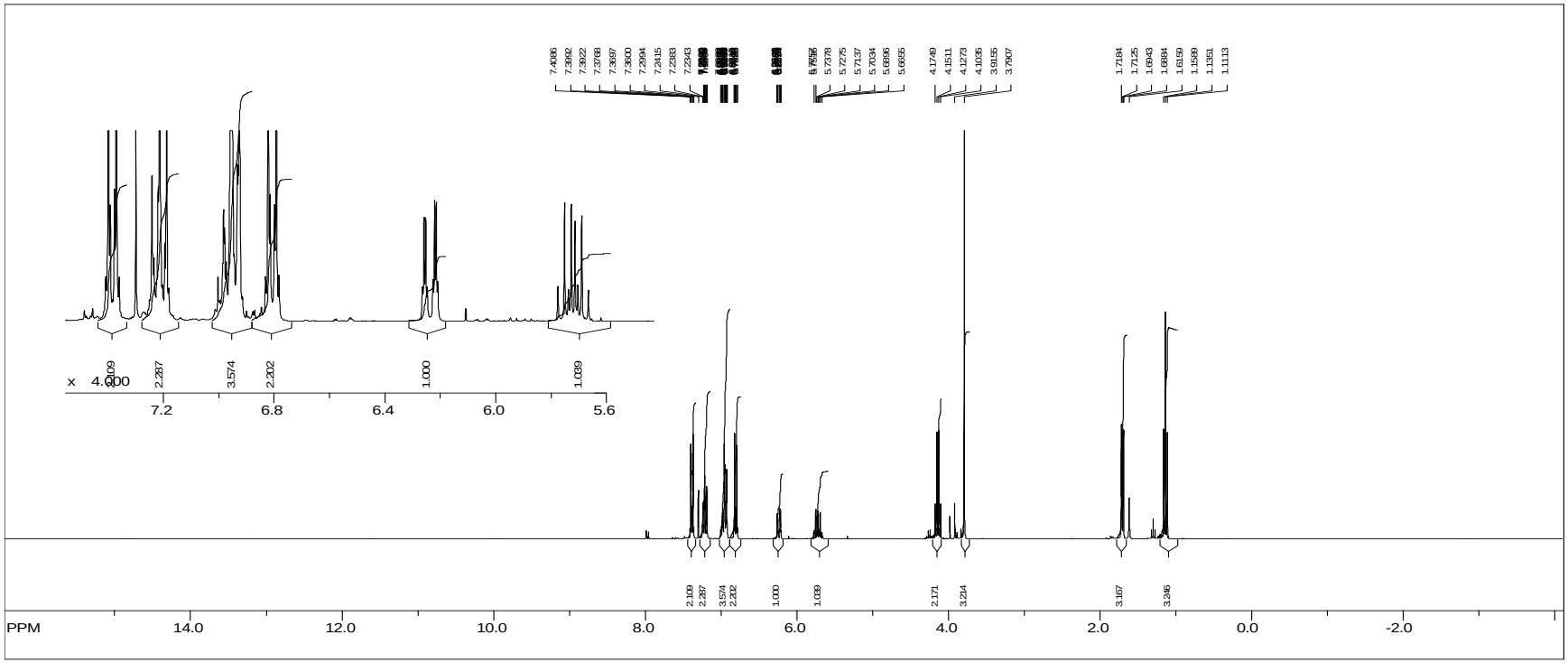
file: Z:\Laina\lmgwi\lmgwi_40a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 10500

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(2*E*,3*Z*)-Ethyl 2-((4-methoxyphenyl)(phenoxy)methylene)pent-3-enoate (298)



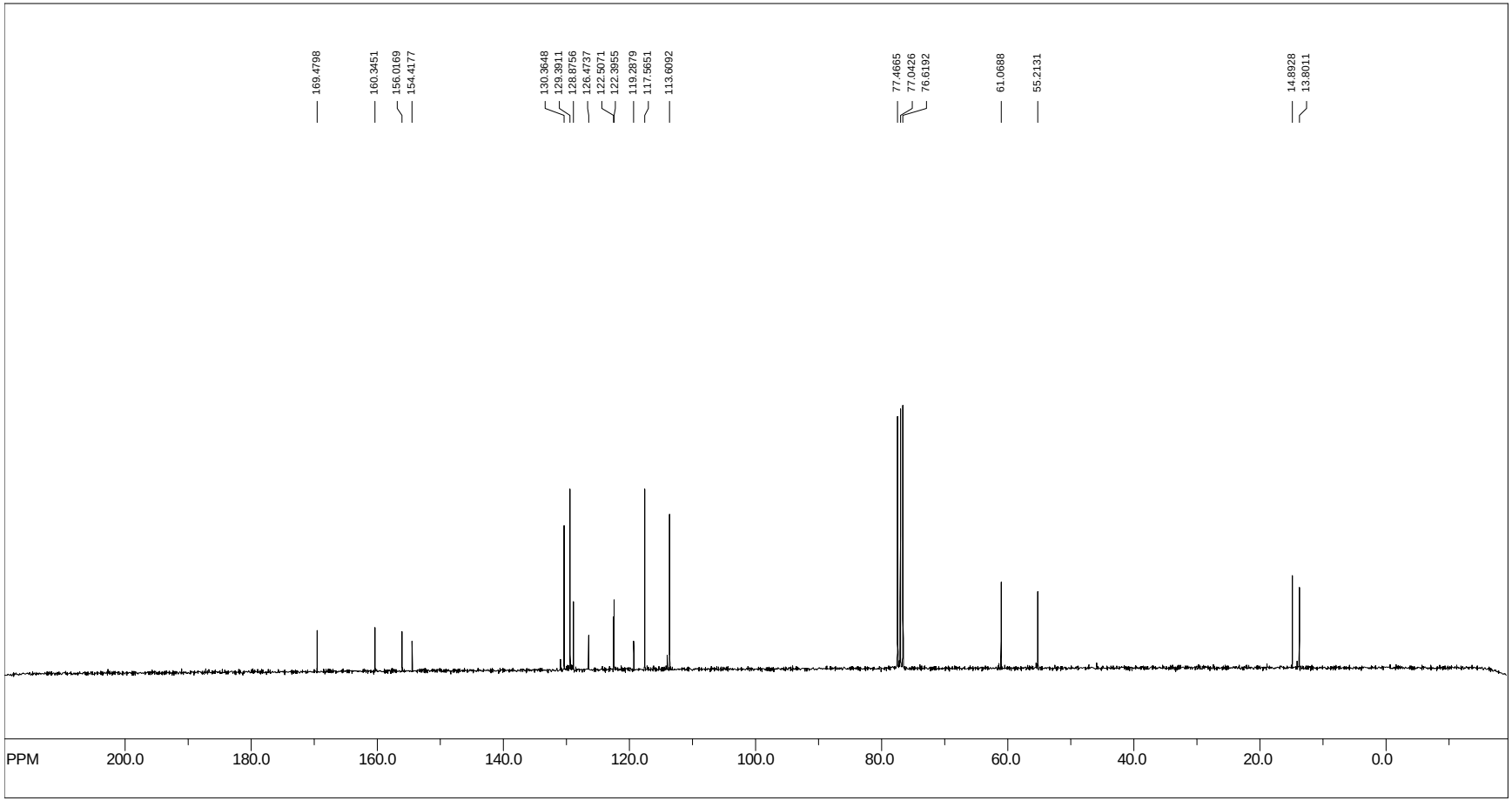
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: C:\Users\Laina\Desktop\Tetrasub Esters\lmgxi_34b\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

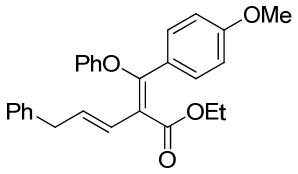
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



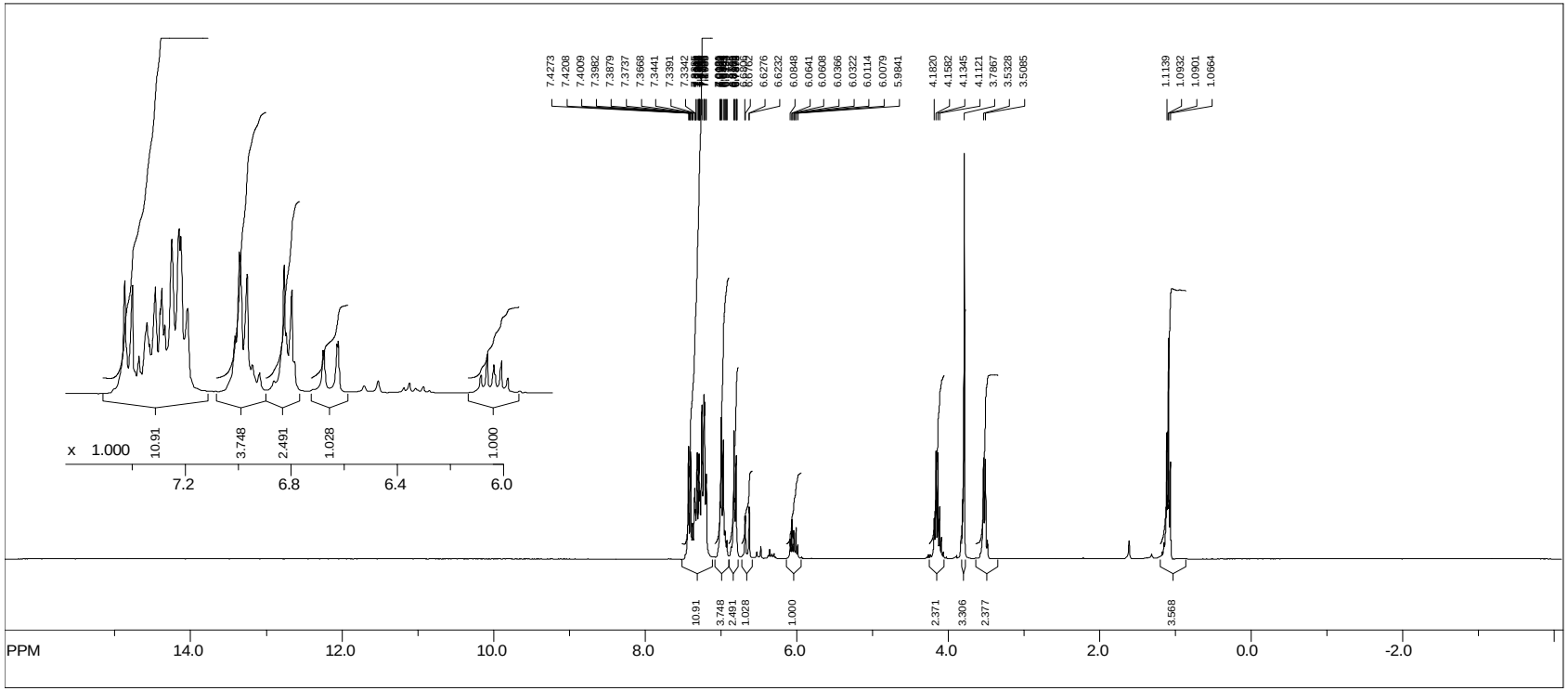
file: C:\Users\Laina\Desktop\Tetrasub Esters\lmgxii_34b\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1500

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(2*E*,3*E*)-Ethyl 2-((4-methoxyphenyl)(phenoxy)methylene)-5-phenylpent-3-enoate (299)



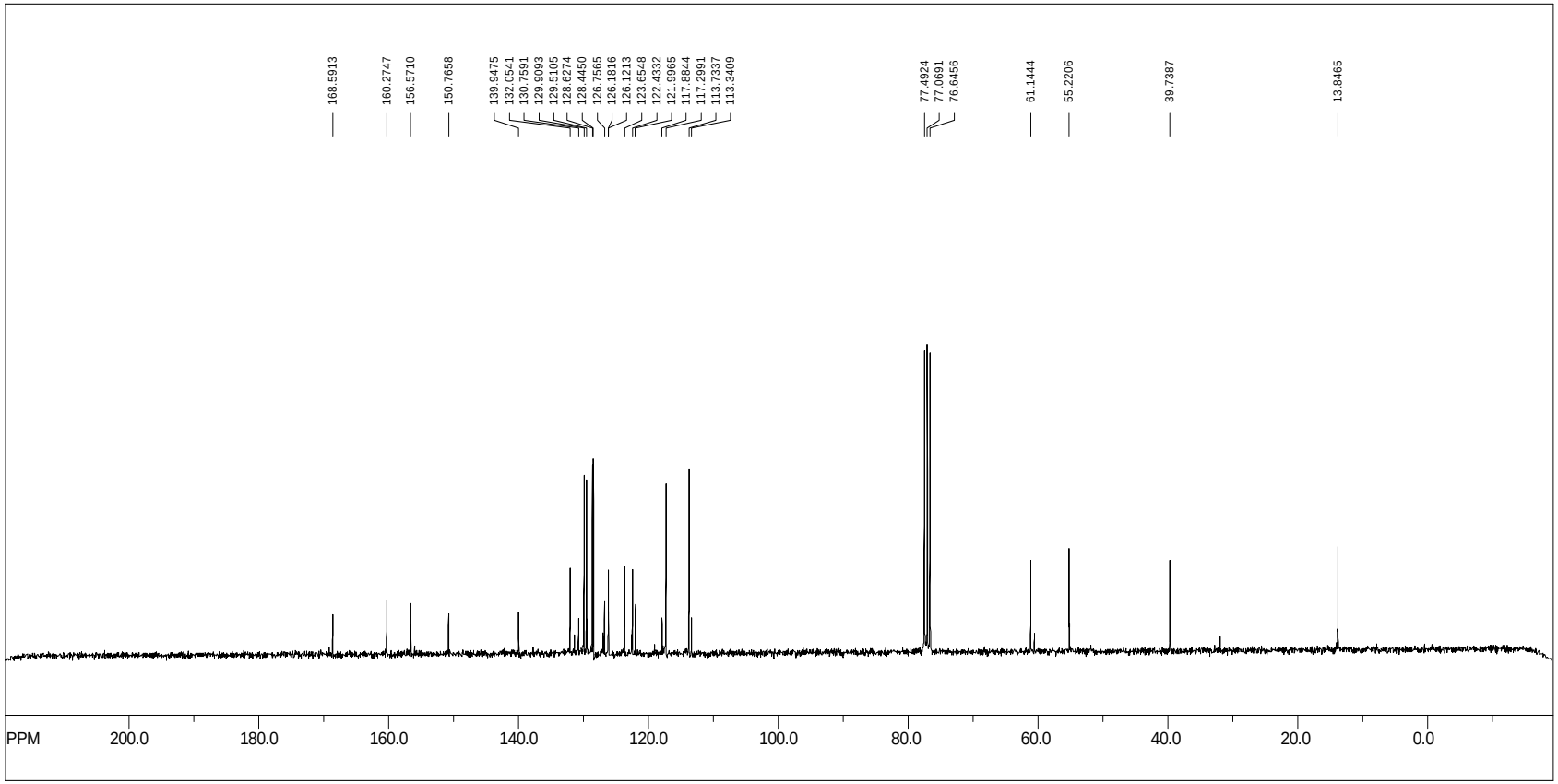
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



file: Z:\Laina\lmgxvi\lmgxvi_41a\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5

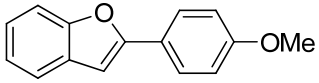


file: Z:\Laina\lmgxvi\lmgxvi_41a\4\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

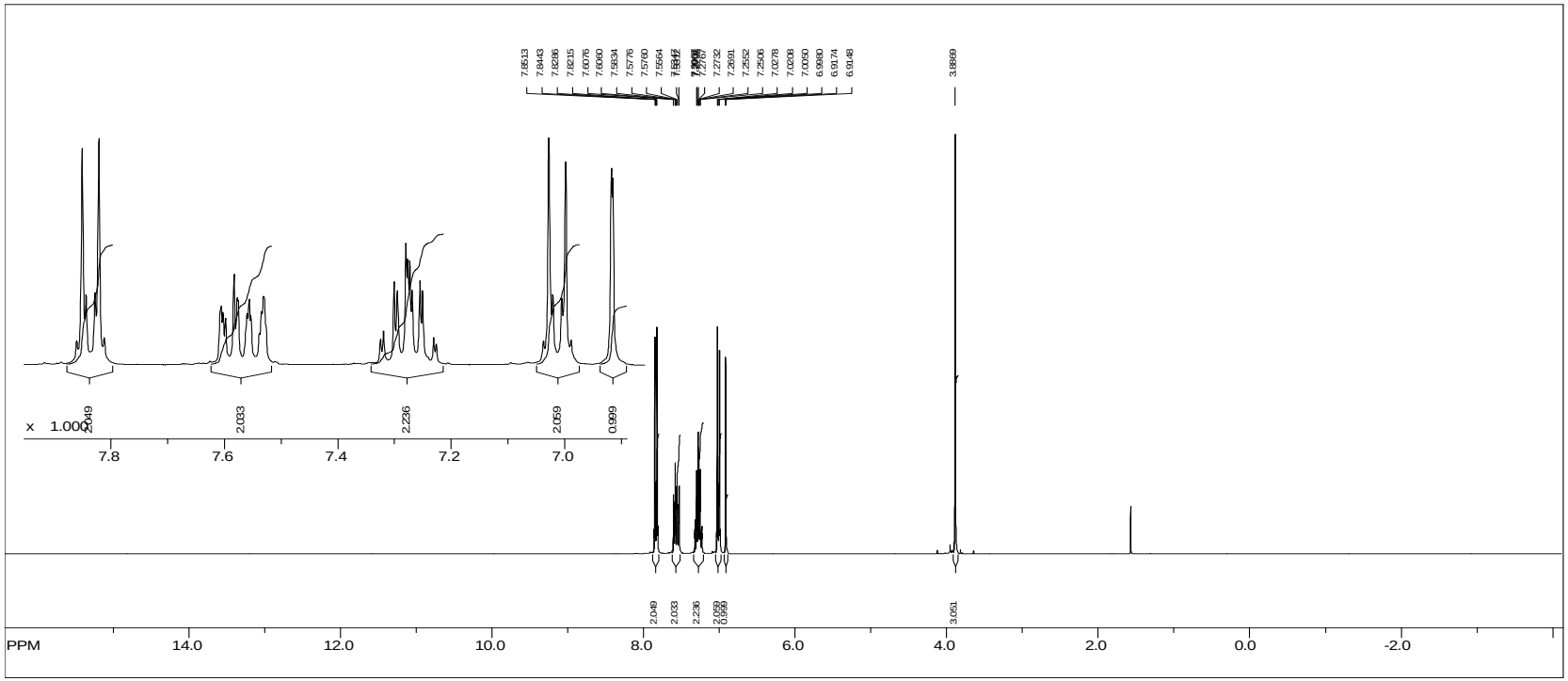
freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

6.5: Section 2.6 – Benzofurans

2-(4-Methoxyphenyl)-benzofuran (301)



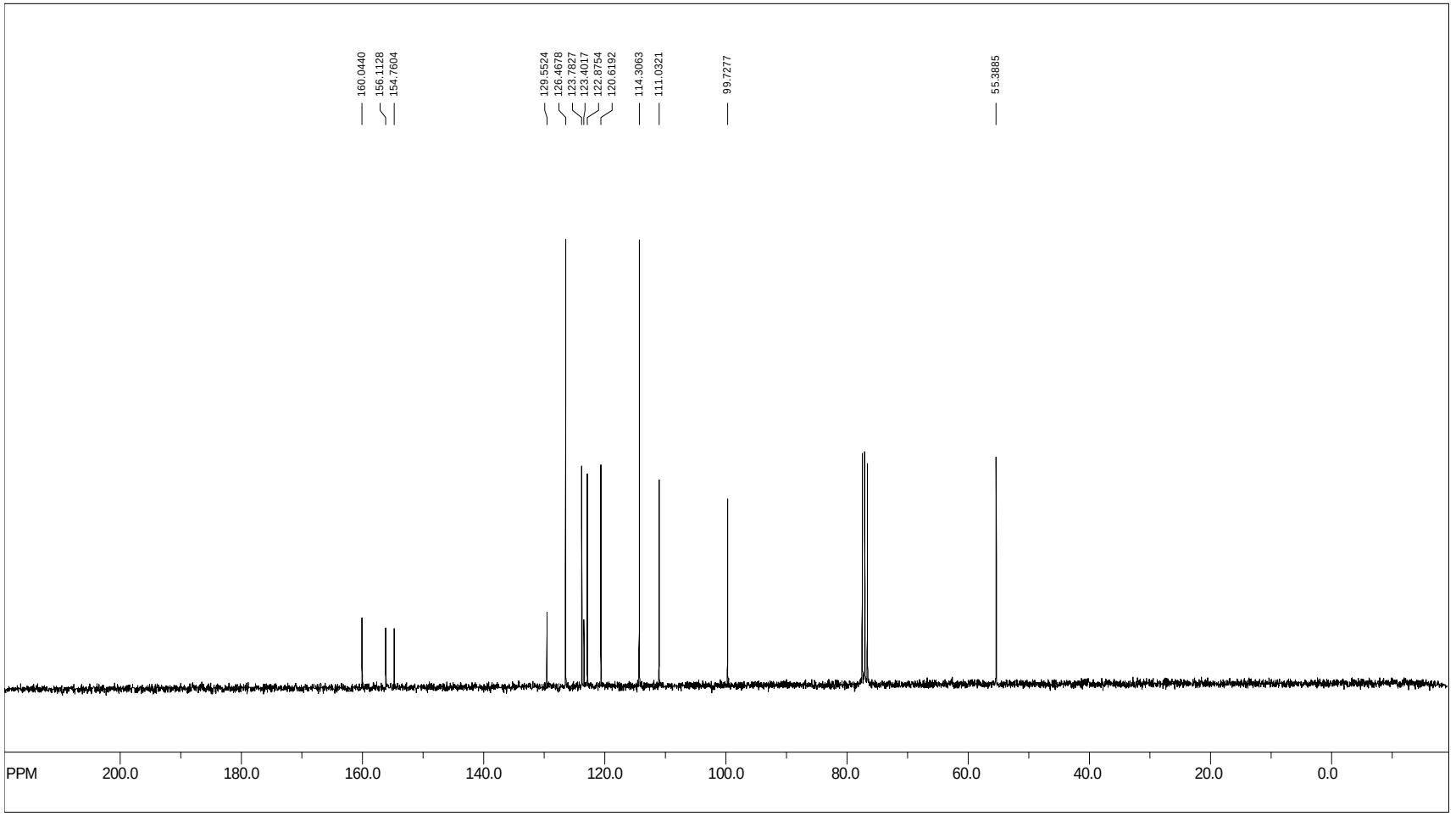
SpinWorks 2.5: 2-(4-methoxyphenyl)-benzo[b]furan



file: Z:\Laina\lmgviii\lmgviii_82a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 6

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

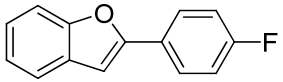
SpinWorks 2.5: 2-(4-methoxyphenyl)-benzo[b]furan



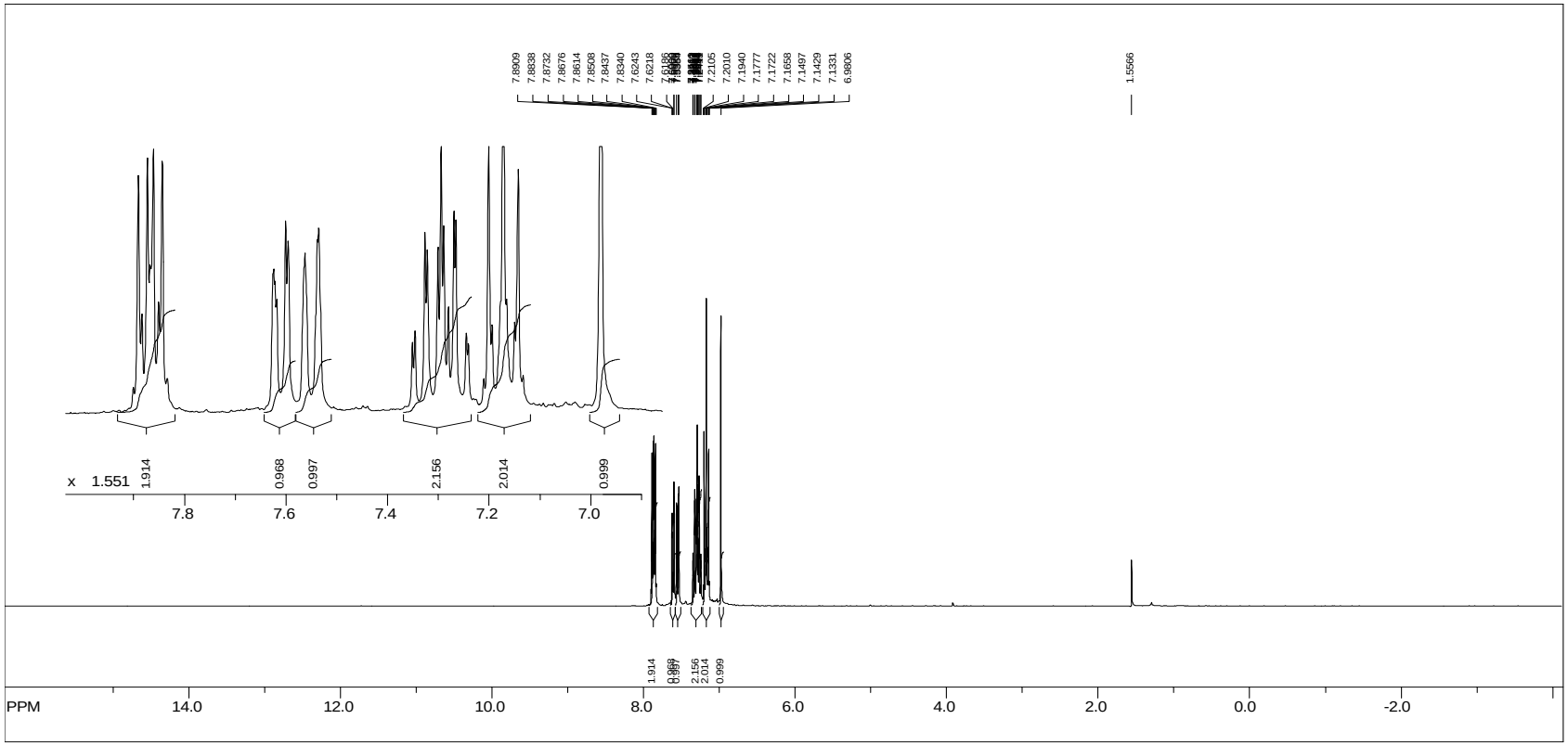
file: C:\Users\Laina\Documents\WORK\NMR\lmgviii\lmgviii_82a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 180

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Fluorophenyl)-benzofuran (302)



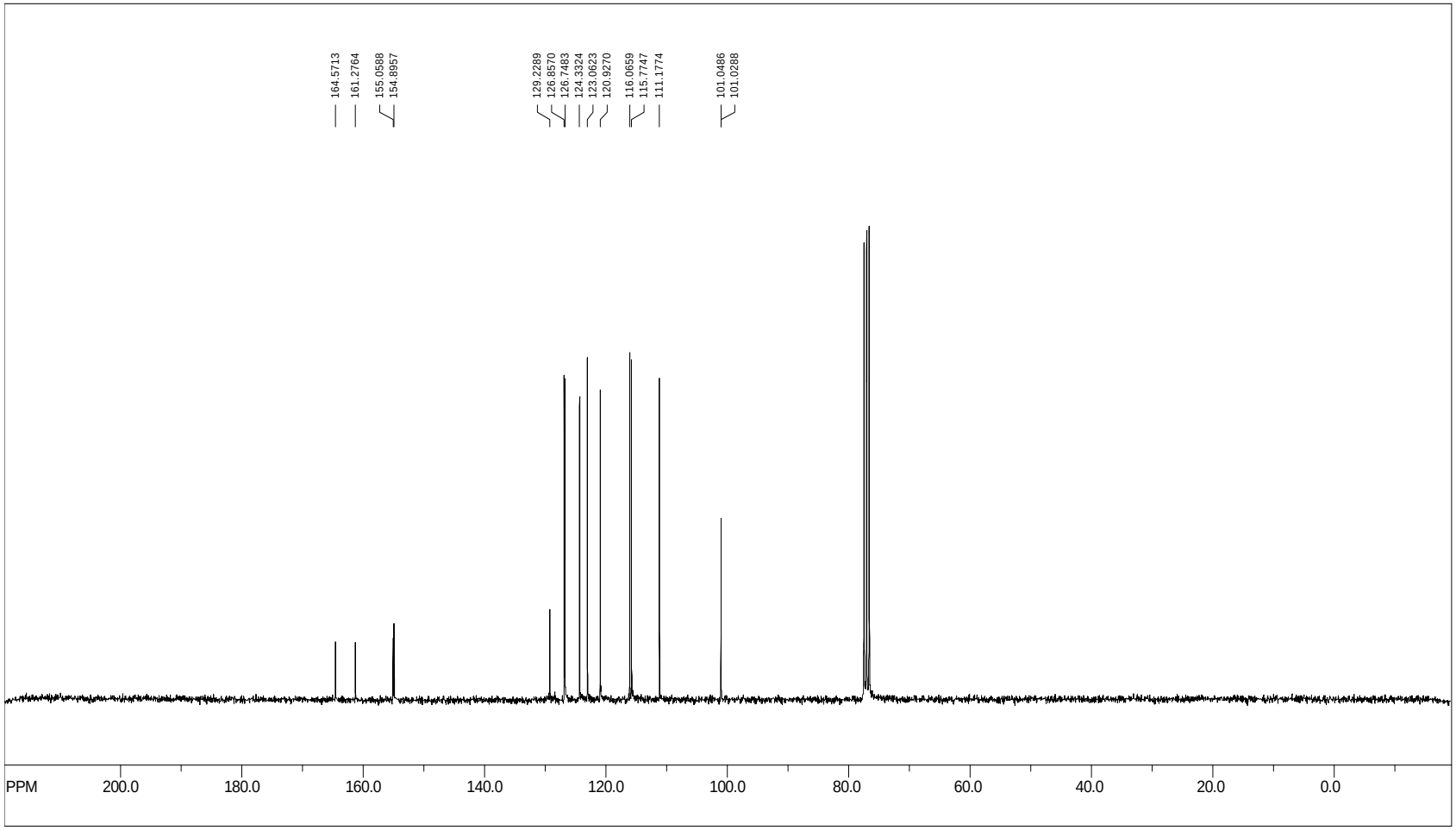
SpinWorks 2.5: 2-(4-fluorophenyl)-benzo[b]furan



file: Z:\Laina\lmgviii\lmgviii_77a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

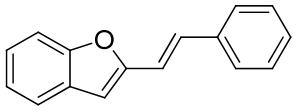
SpinWorks 2.5: 2-(4-fluorophenyl)-benzo[b]furan



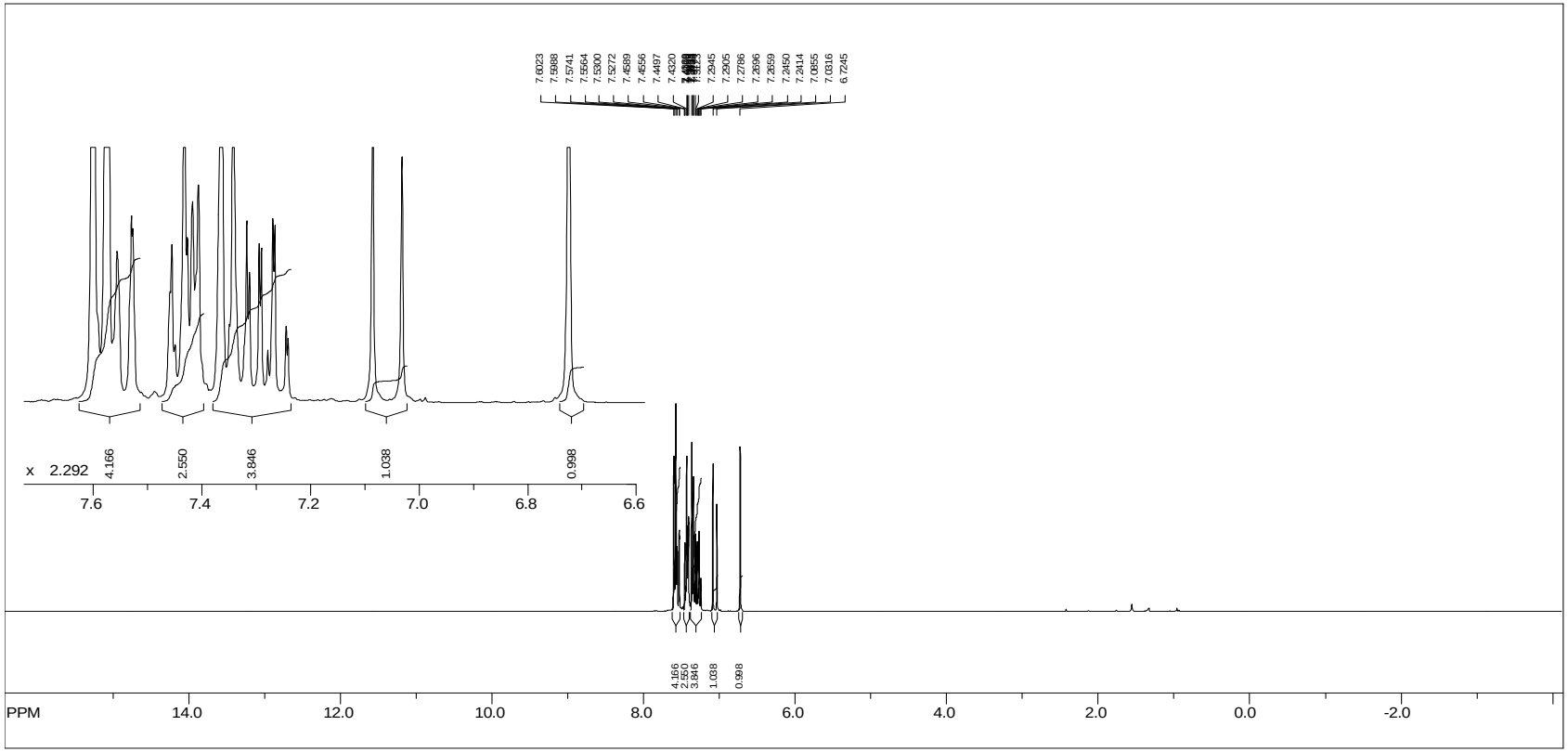
file: C:\Users\Laina\Documents\WORK\NMR\lmgviii\lmgviii_77a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(*trans*-2-Phenylethenyl)benzofuran (303)



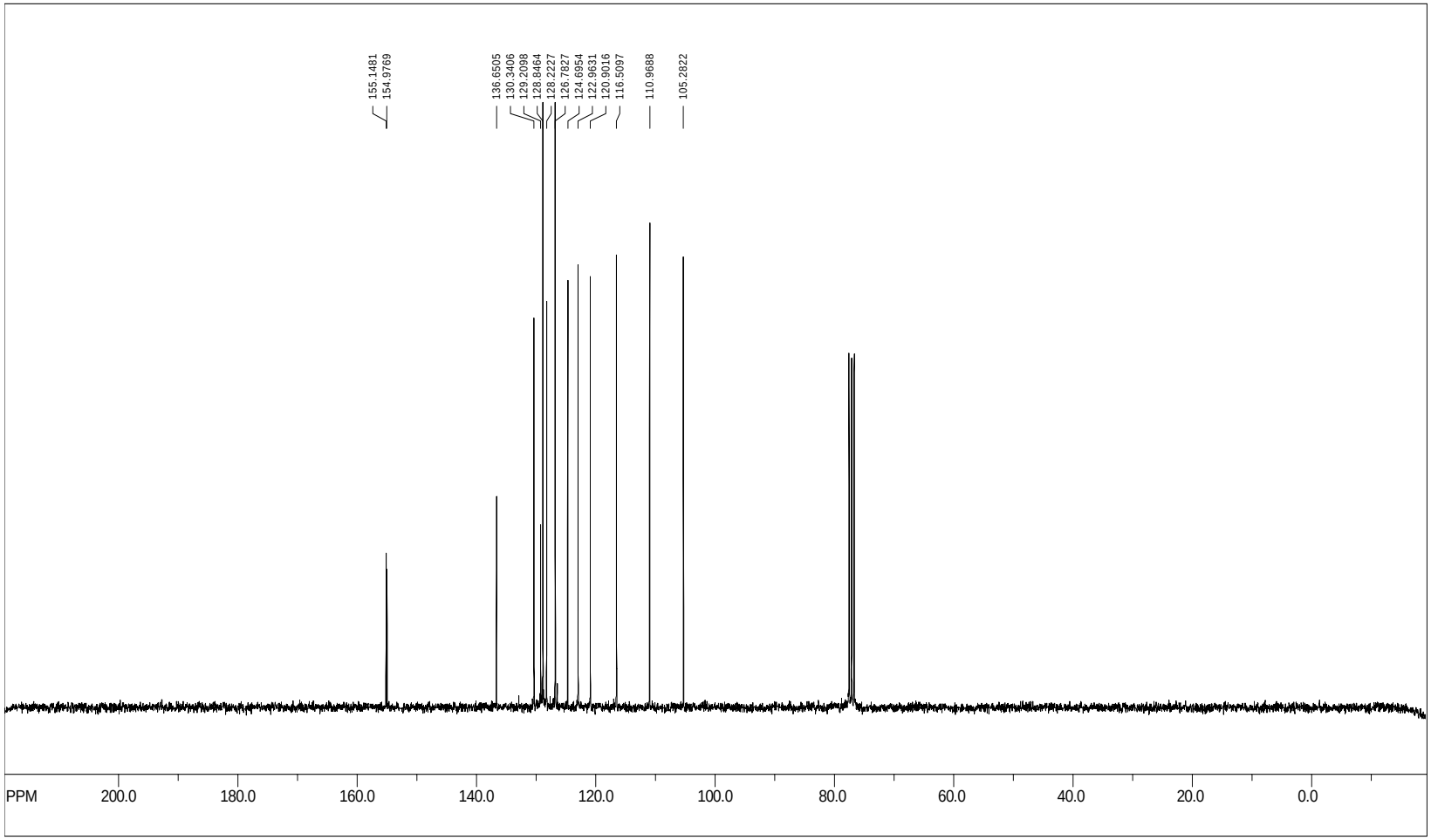
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



file: Z:\Laina\lmgxl\lmgxl_51a\1\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

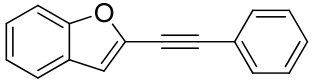
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



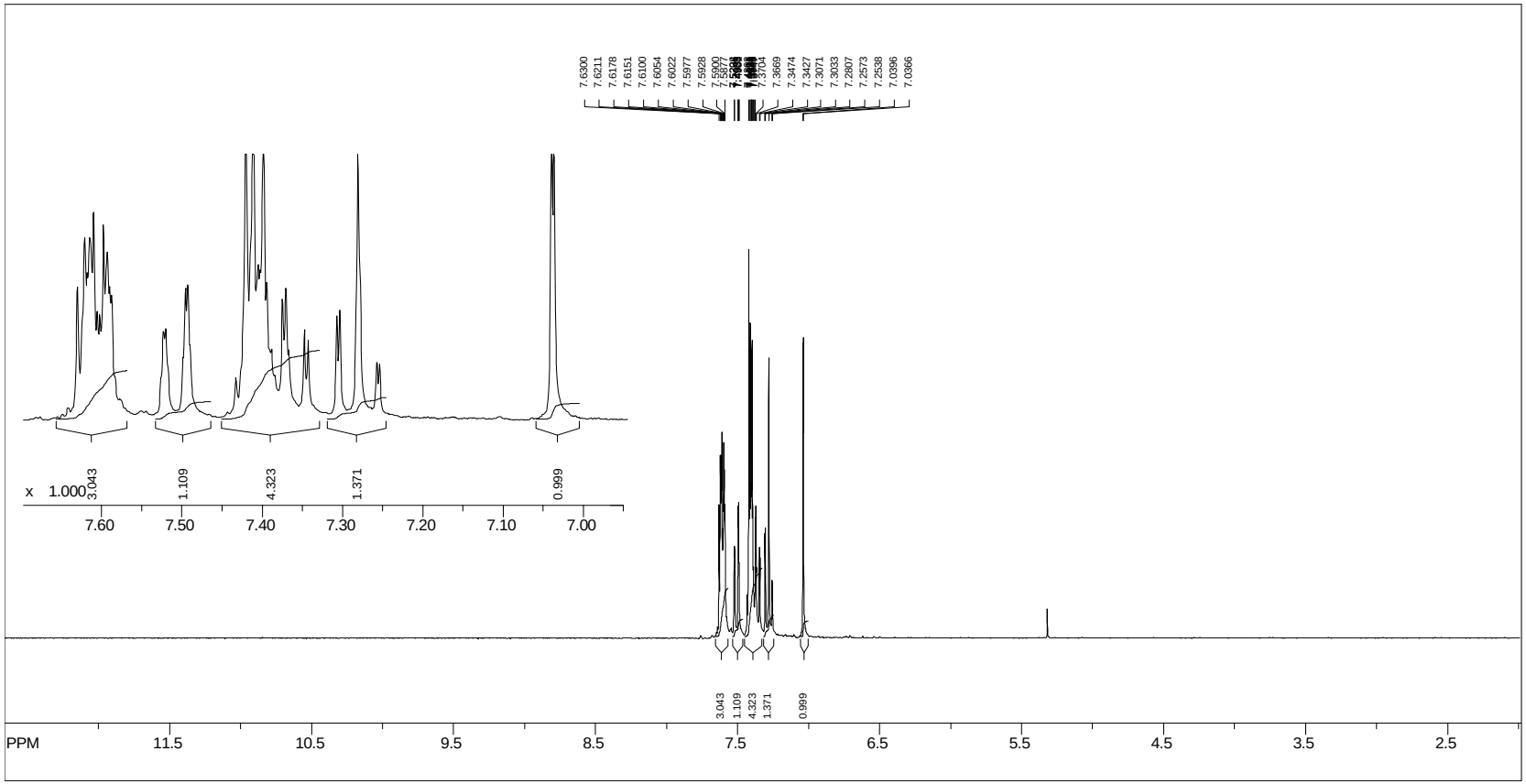
file: C:\Users\Laina\Documents\WORK\NMR\lmgxi\lmgxi_51a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(2-Phenylethynyl)benzofuran (304)



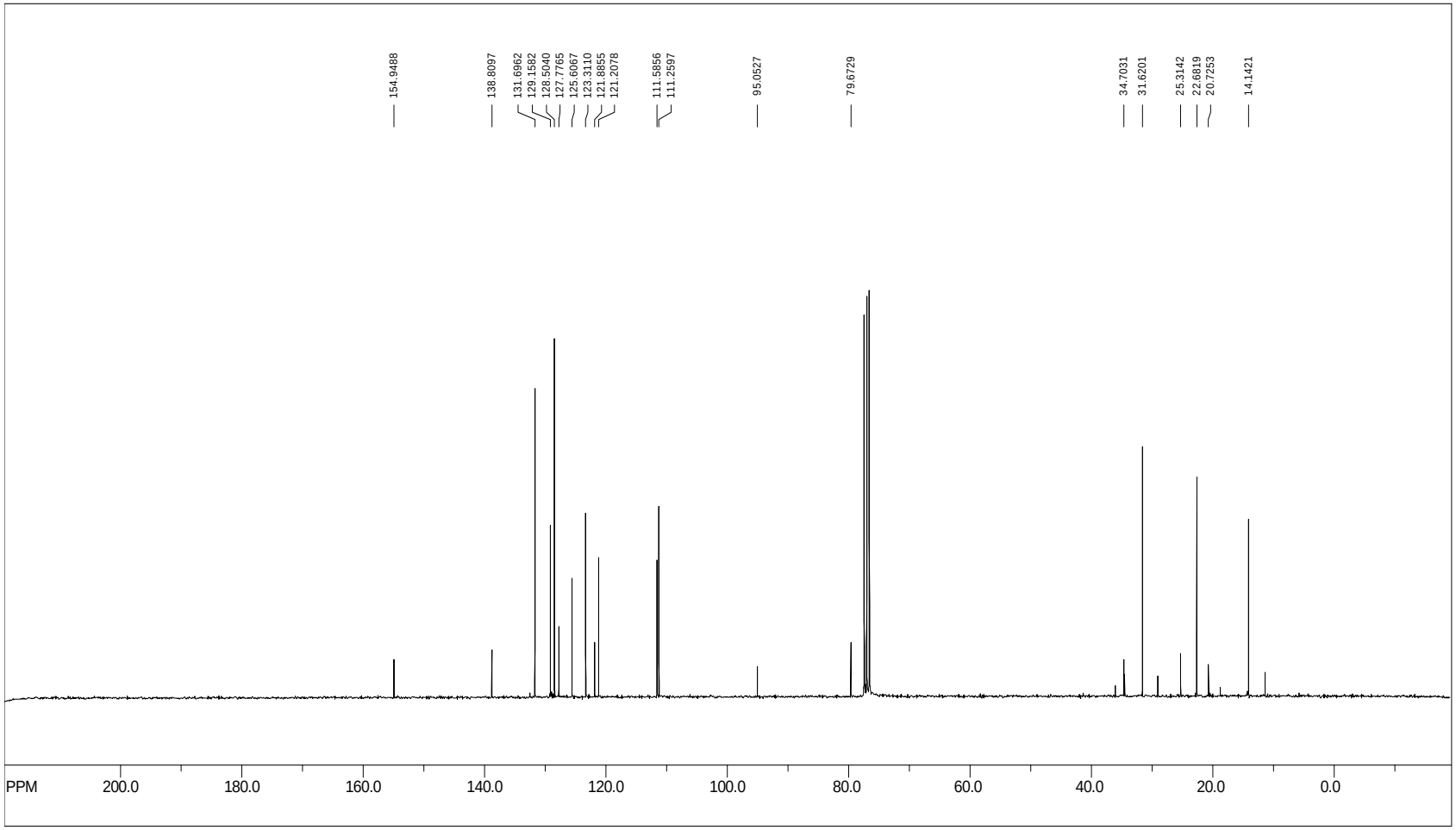
SpinWorks 2.5: cyclization of sonogashira adduct



file: Z:\Laina\lmgviii\lmgviii_95a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

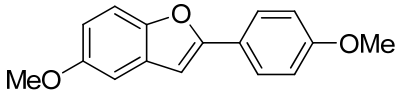
SpinWorks 2.5: 2-alkynylbenzofuran



file: Z:\Laina\lmgviii\lmgviii_95a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 8000

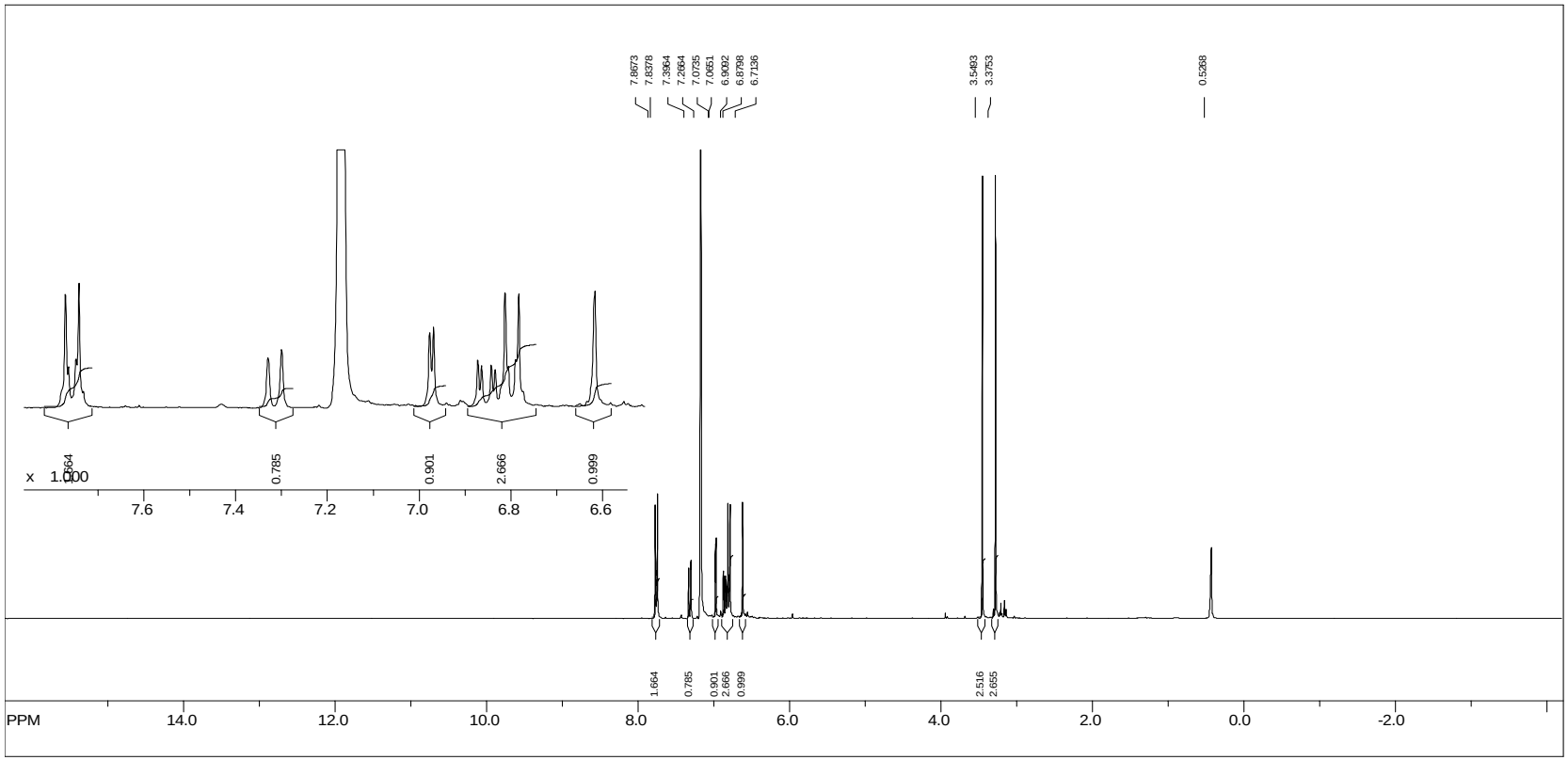
freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-5-methoxy-benzofuran (Corsifuran C) (305)



in C_6D_6

SpinWorks 2.5: in benzene d-6!

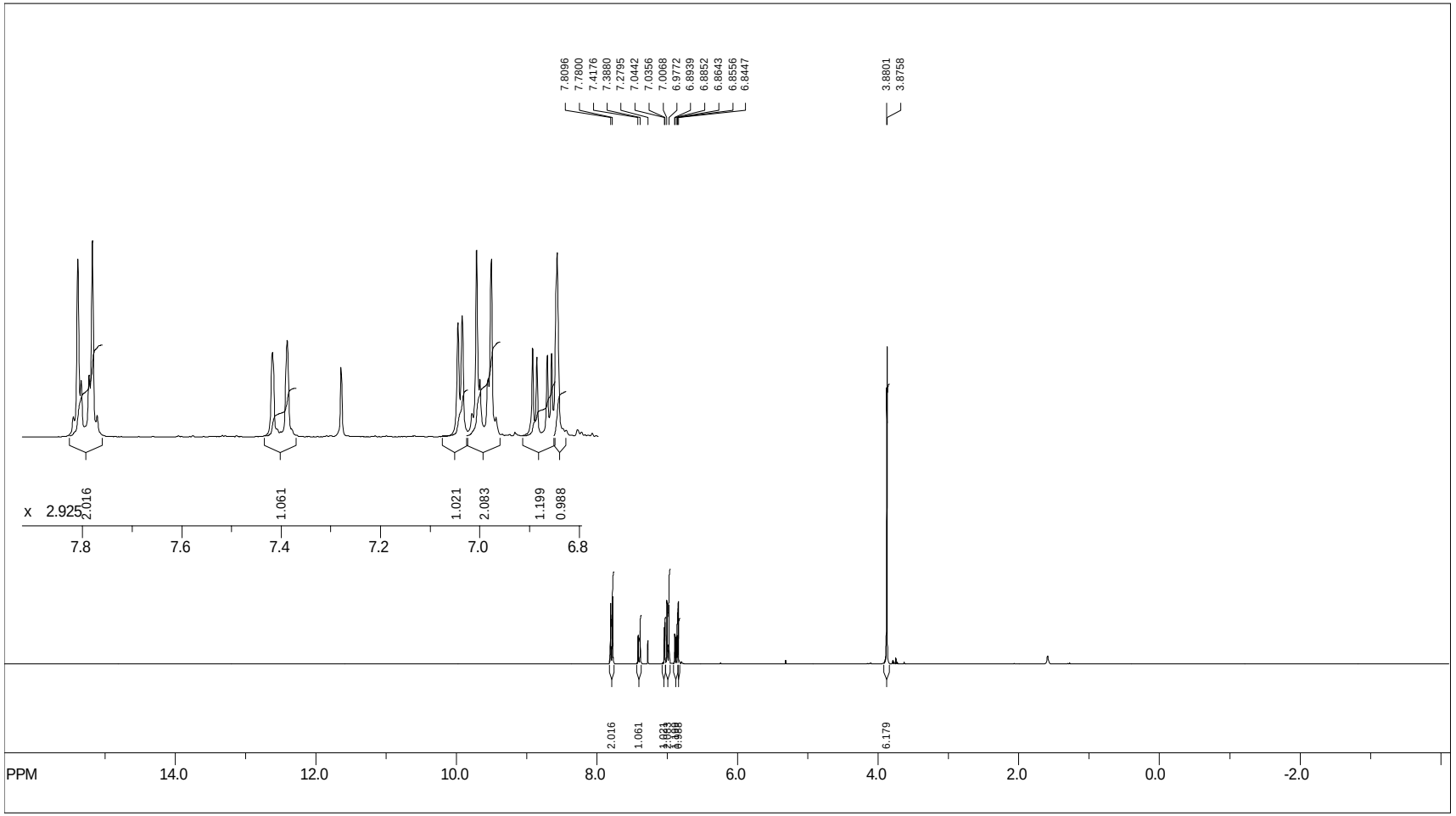


file: Z:\Laina\lmgxi\lmgxi_19ci\6\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 6

freq. of 0 ppm: 300.130029 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

In $CDCl_3$

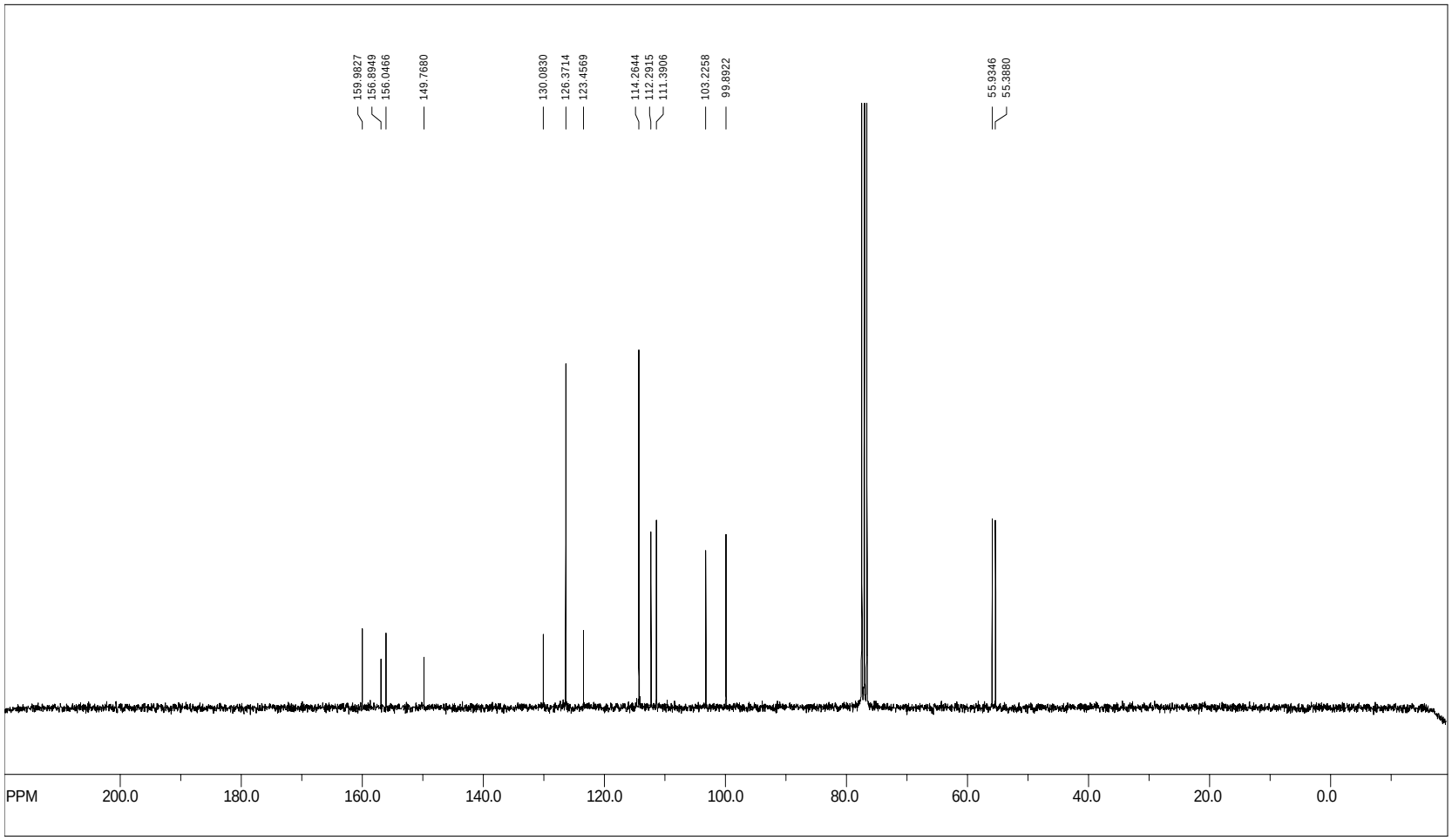
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 15



file: Z:\Laina\lmgxi\lmgxi_19ci\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 6

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

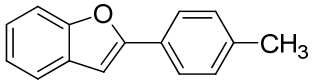
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 15



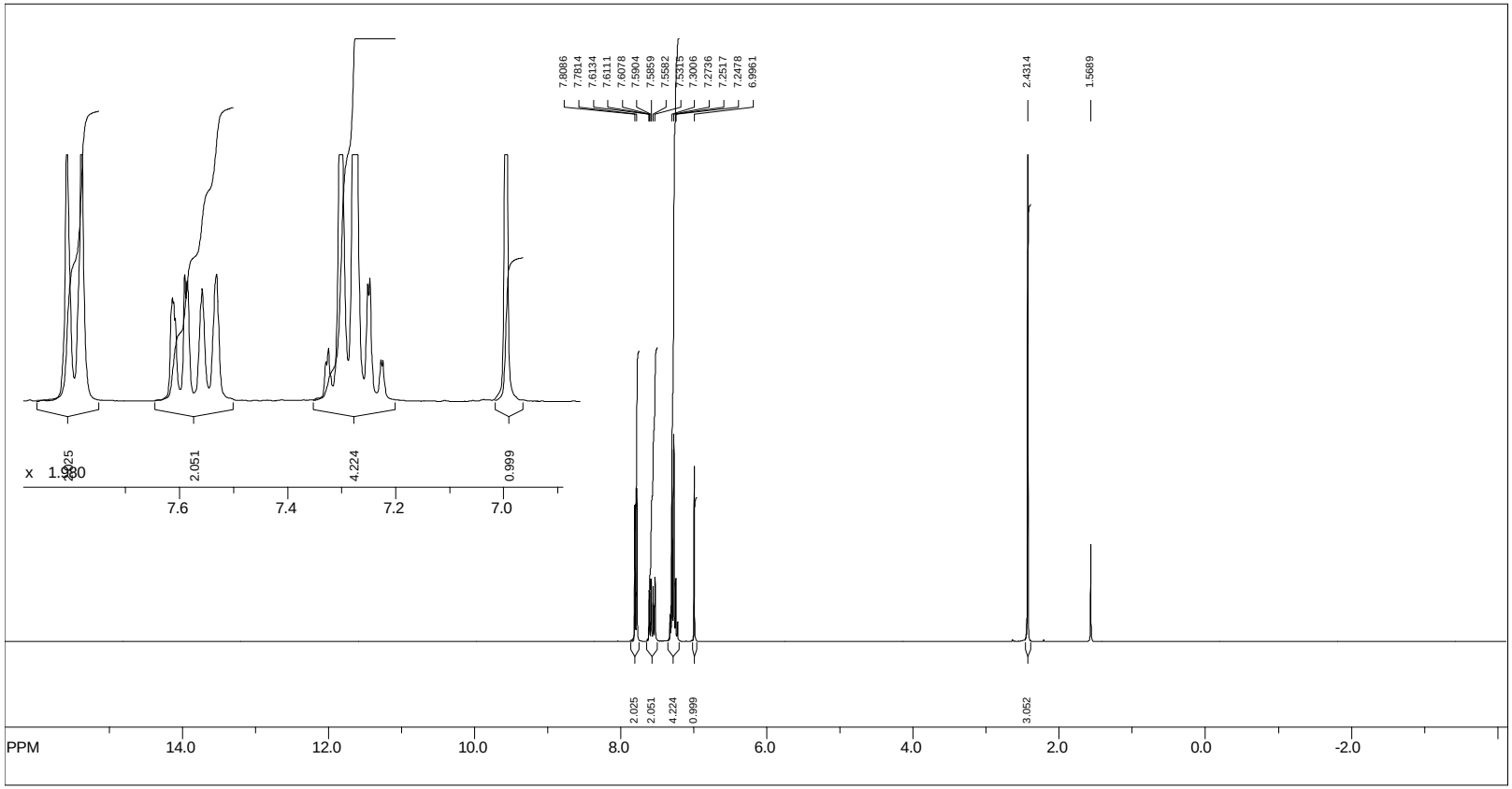
file: C:\Users\Laina\Documents\WORK\NMR\lmgxi\lmgxi_19ci\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methylphenyl)benzofuran (306)



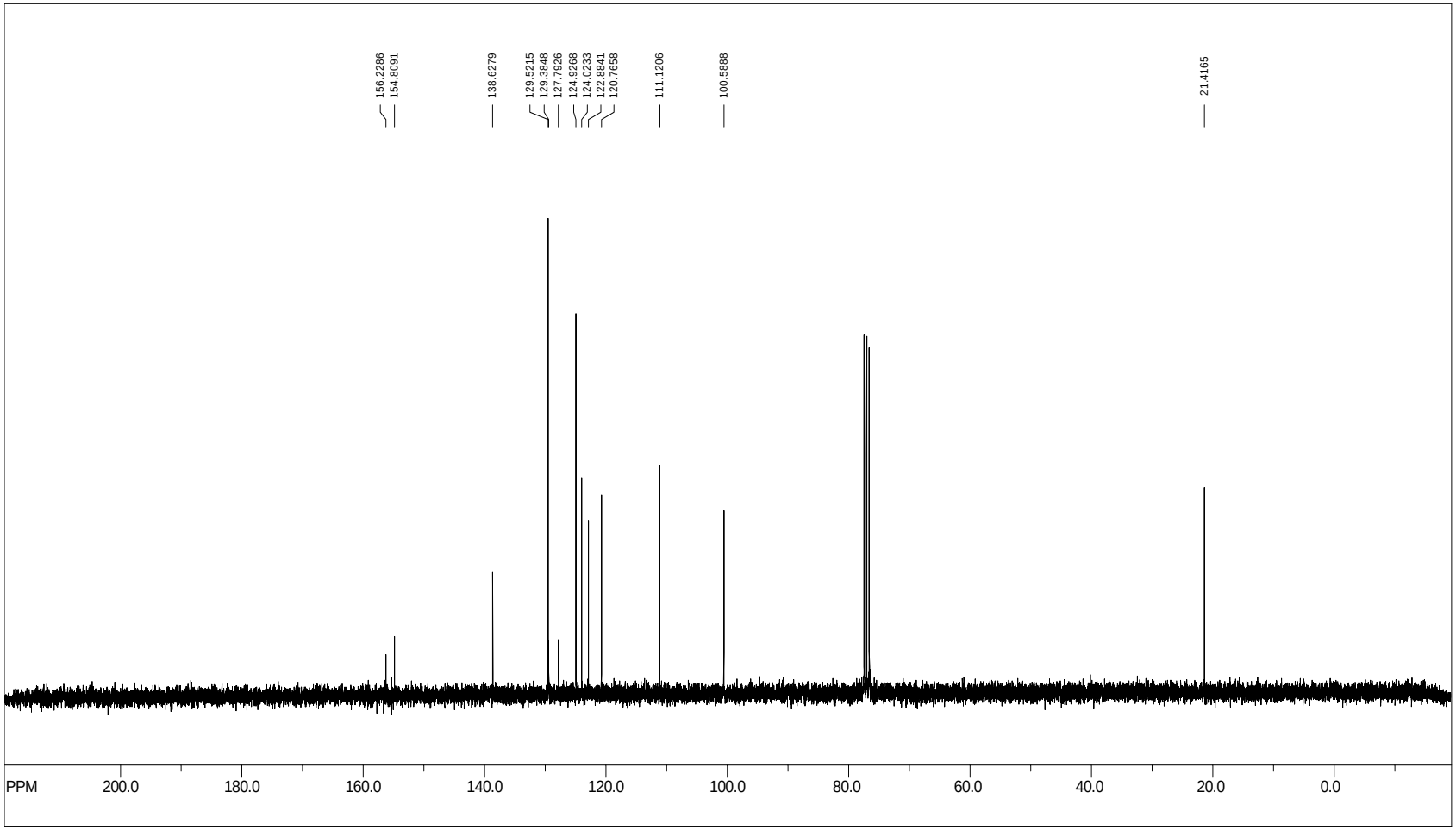
SpinWorks 2.5: SCA-P71-1



file: Z:\Stephanie\SCA-P71-1\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

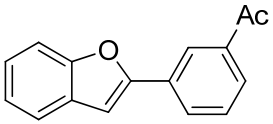
SpinWorks 2.5: SCA-P71-1



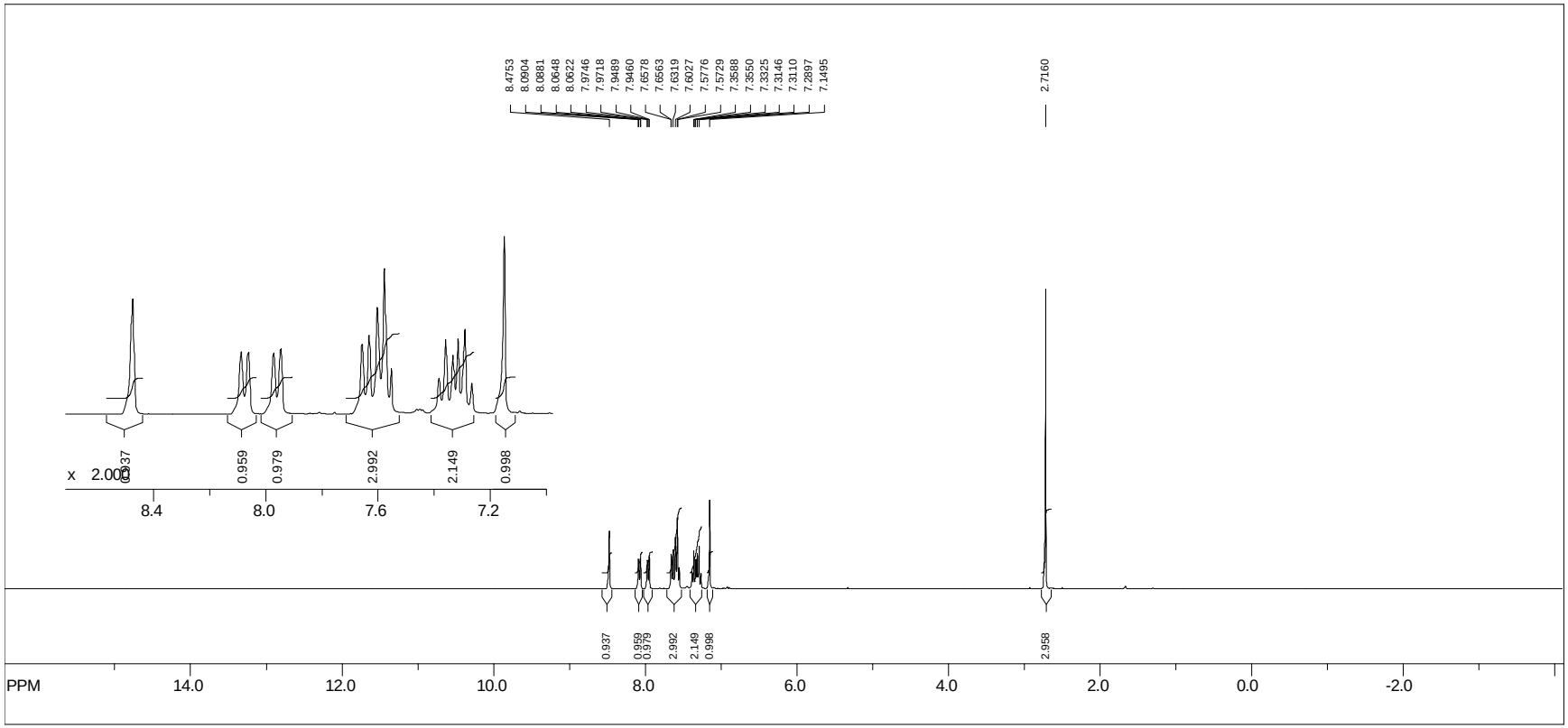
file: Z:\Stephanie\SCA-P71-1\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 128

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(3-Acetylphenyl)benzofuran (311)



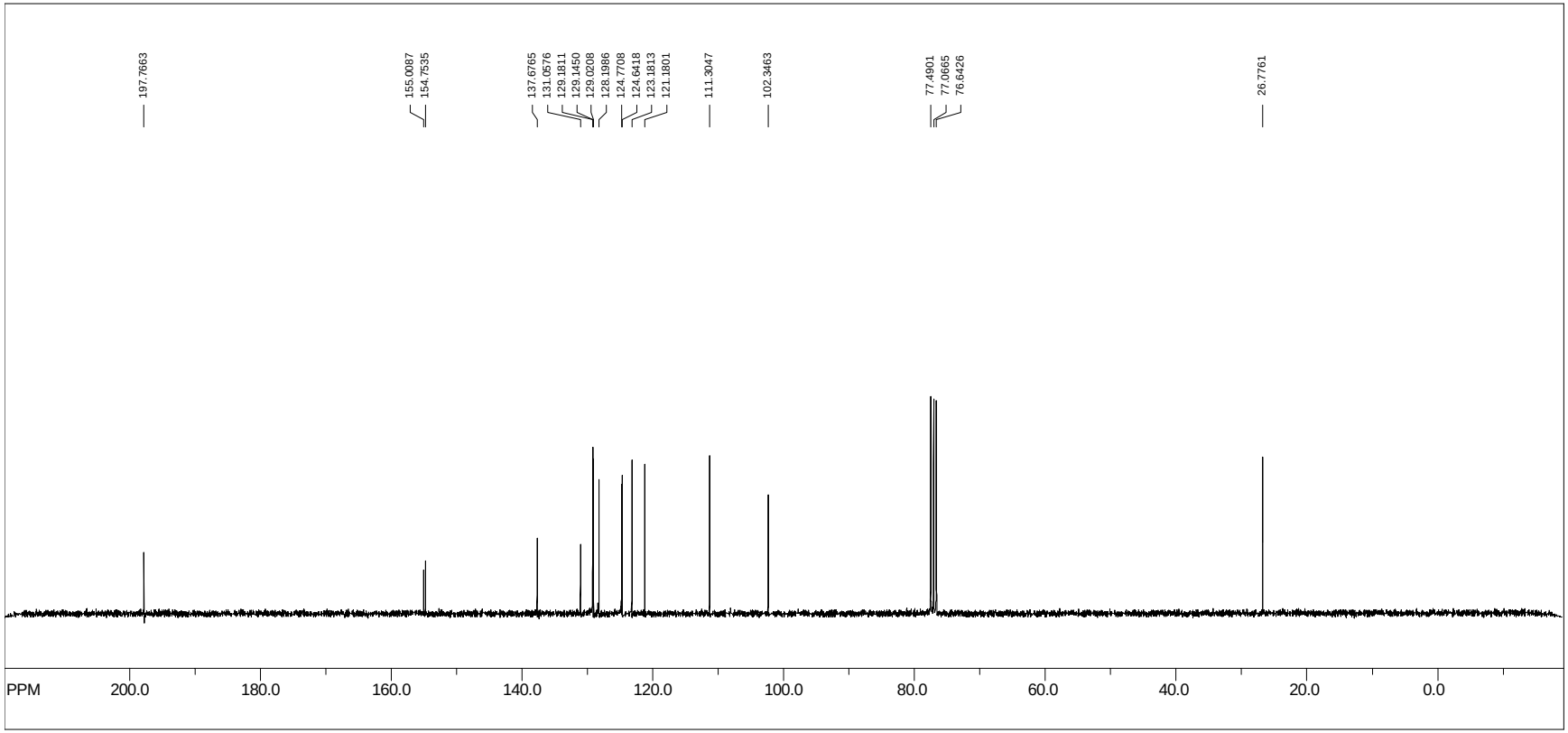
SpinWorks 2.5: 2-(3-acetylphenyl)benzofuran



file: Z:\Laina\lmgxvi\lmgxvi_07d\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

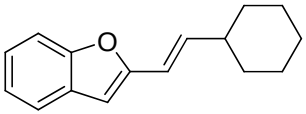
SpinWorks 2.5: 2-(3-acetylphenyl)benzofuran



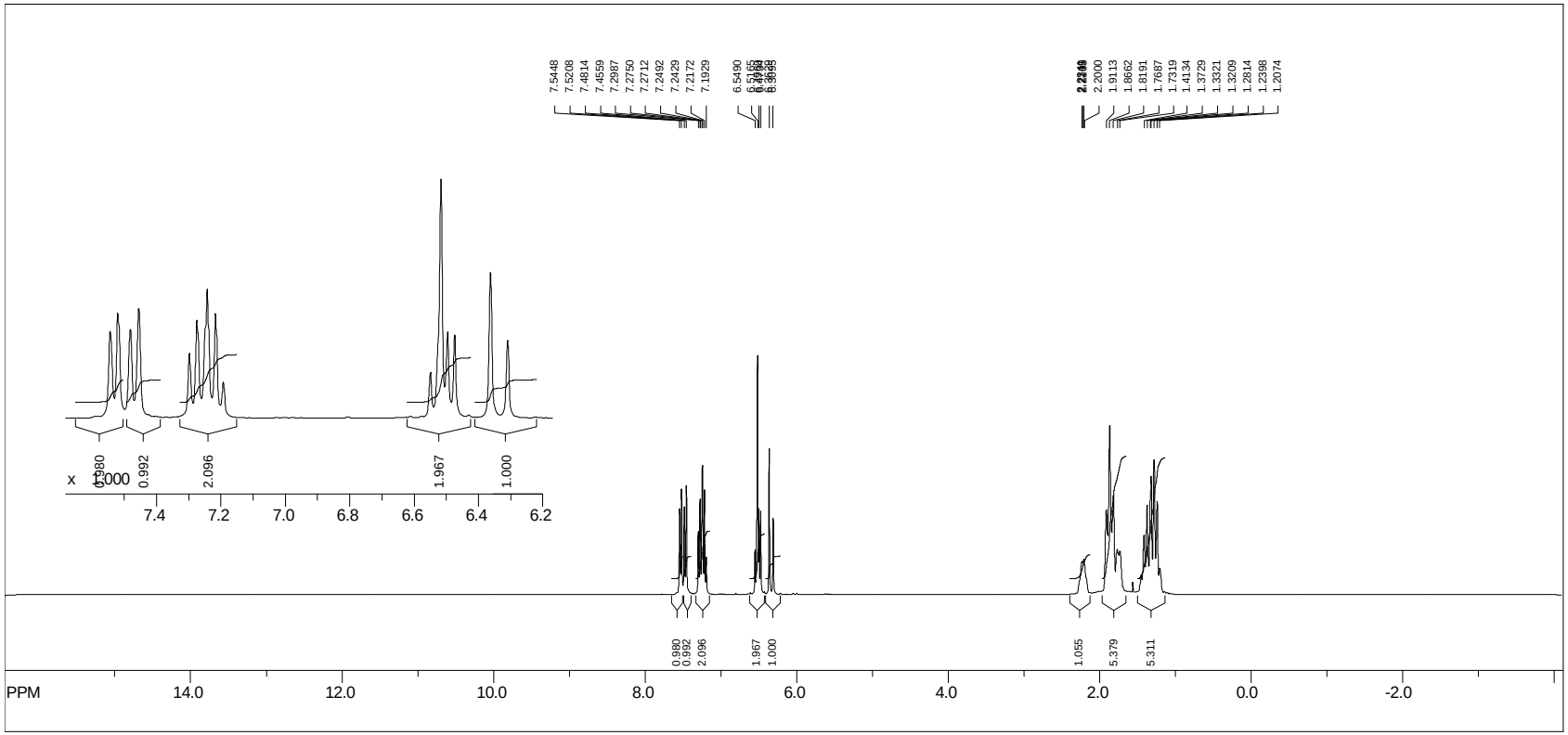
file: Z:\Laina\lmgwi\lmgwi_07cl2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-2-(2-Cyclohexylvinyl)benzofuran (312)



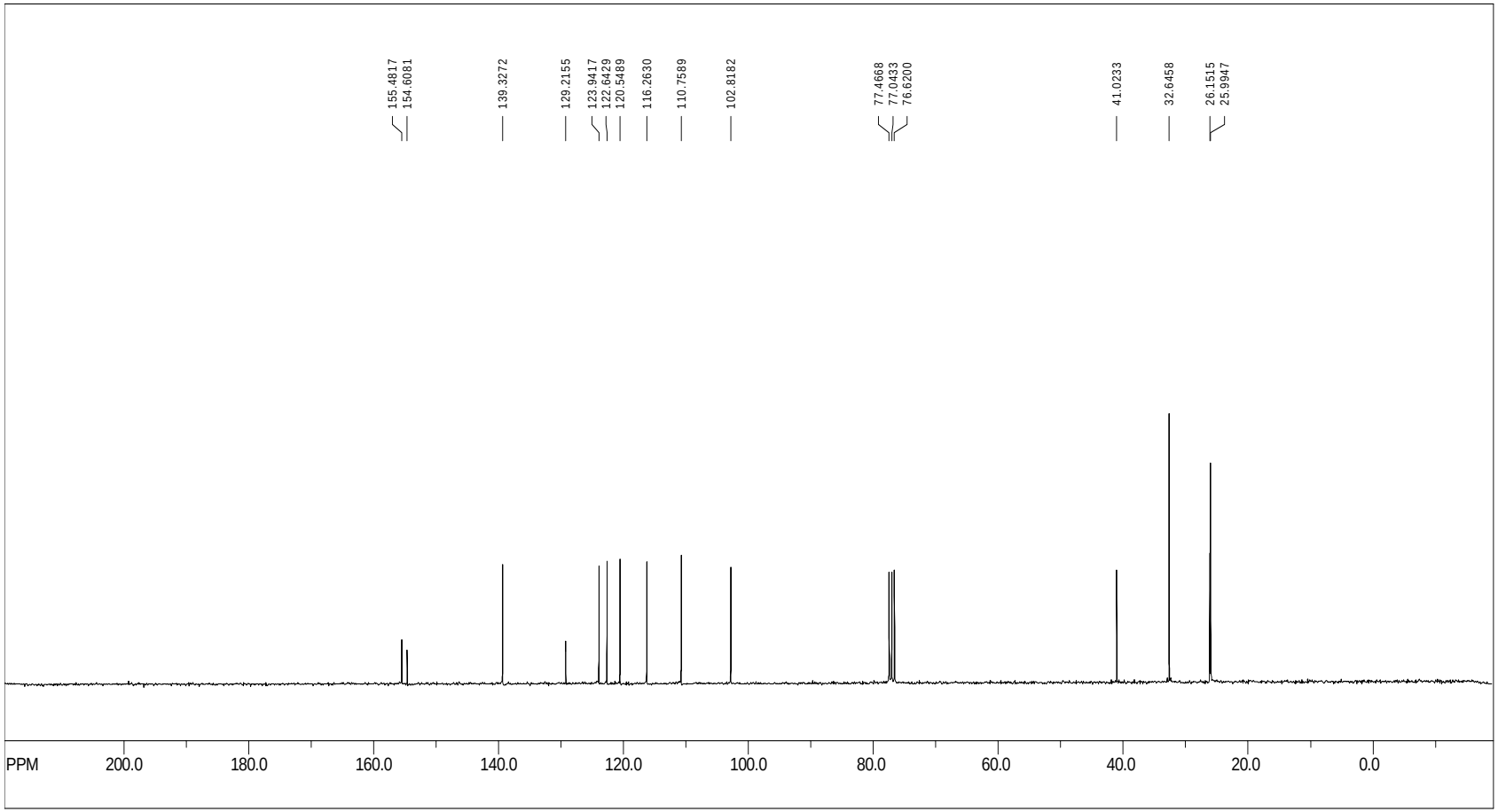
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



file: Z:\Laina\lmgxv\lmgxv_76a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

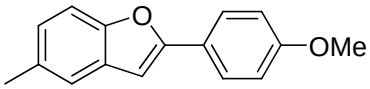
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



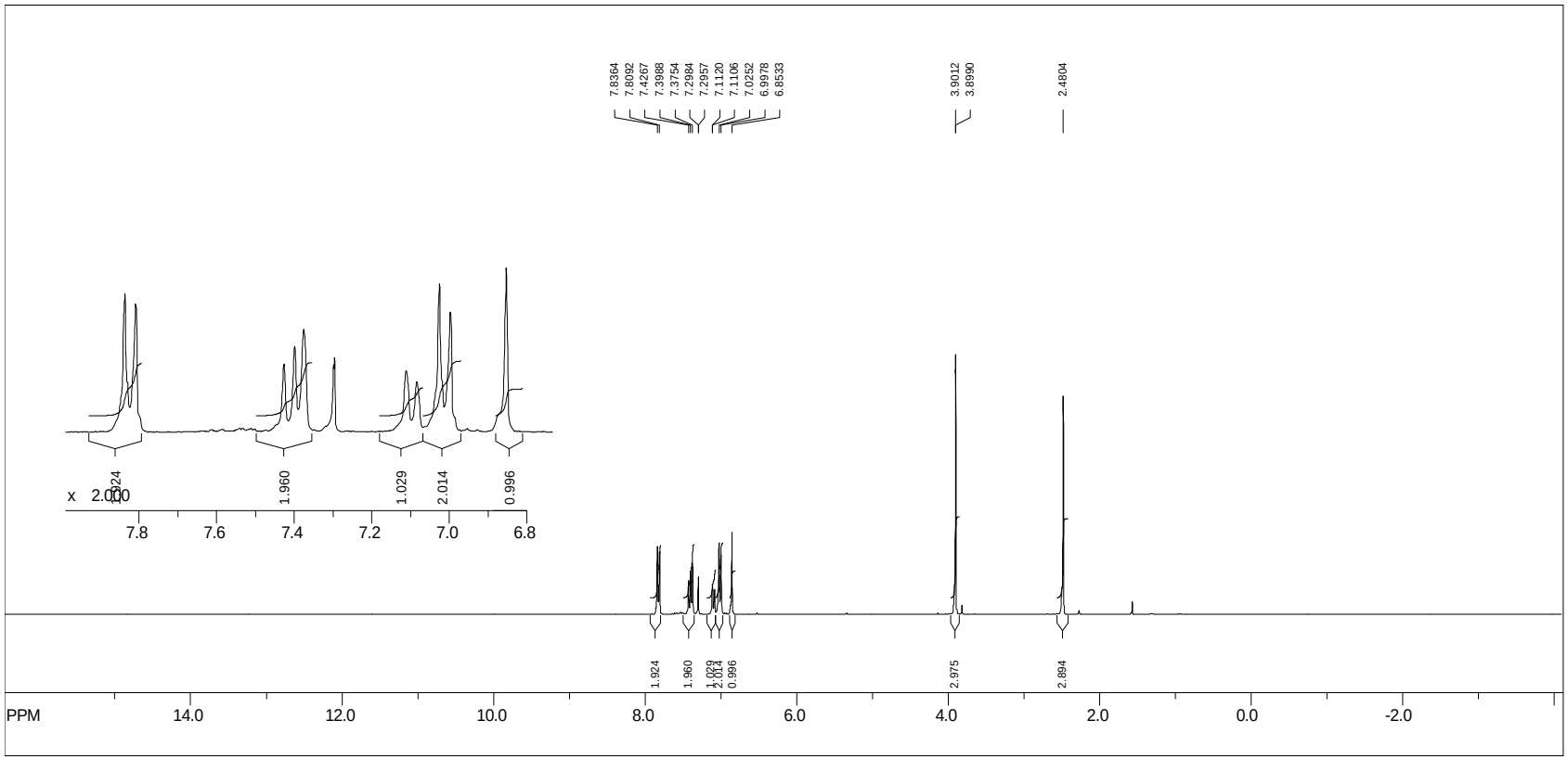
file: Z:\Laina\lmgxv\lmgxv_76a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 471

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(4-Methoxyphenyl)-5-methylbenzofuran (313)



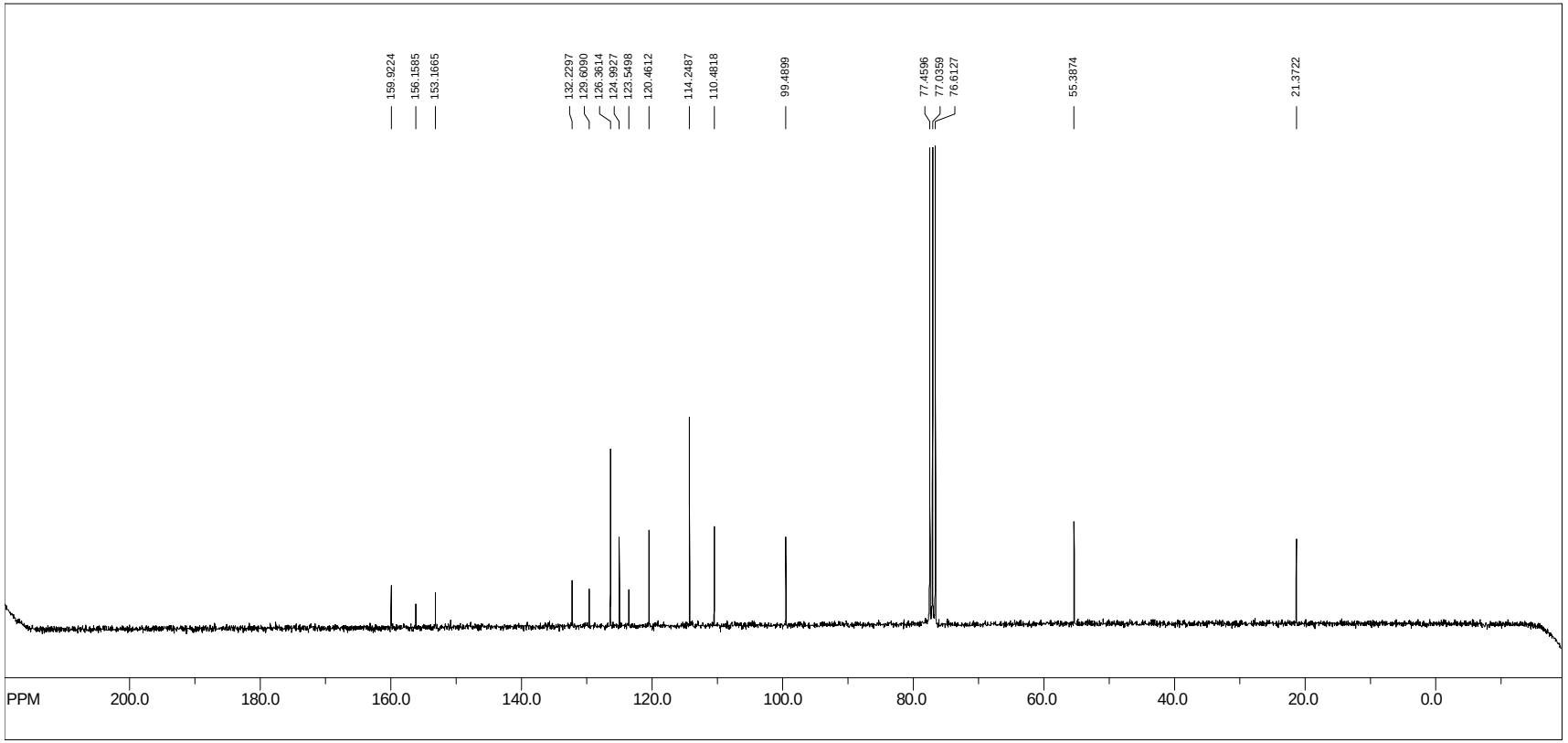
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



file: Z:\Laina\lmgxiv\lmgxiv_40b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

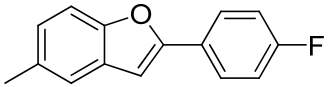
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



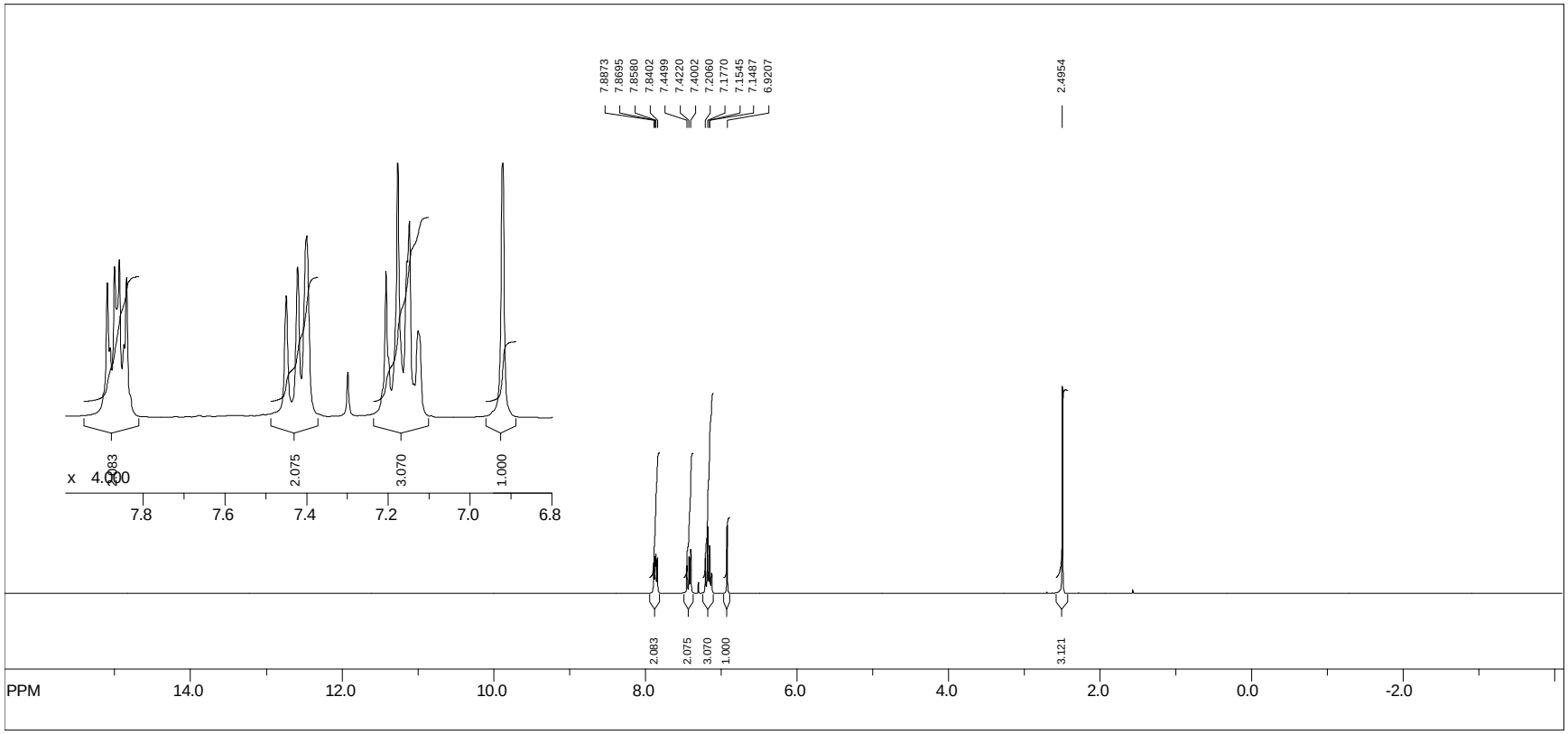
file: Z:\Laina\lmgxiv\lmgxiv_40b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 925

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(4-Fluorophenyl)-5-methylbenzofuran (314)



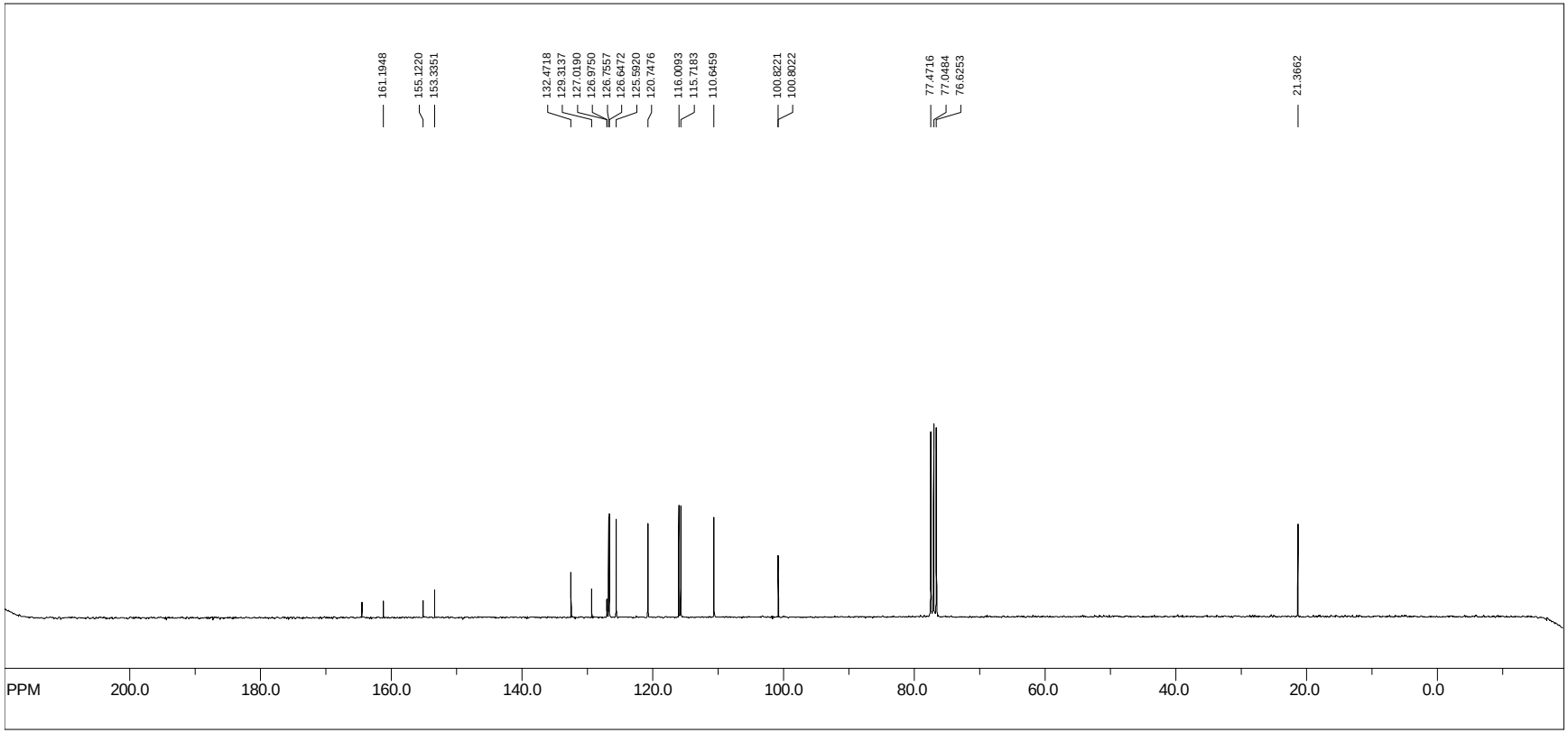
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



file: Z:\Laina\lmgxiv\lmgxiv_40-1a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

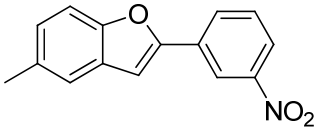
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



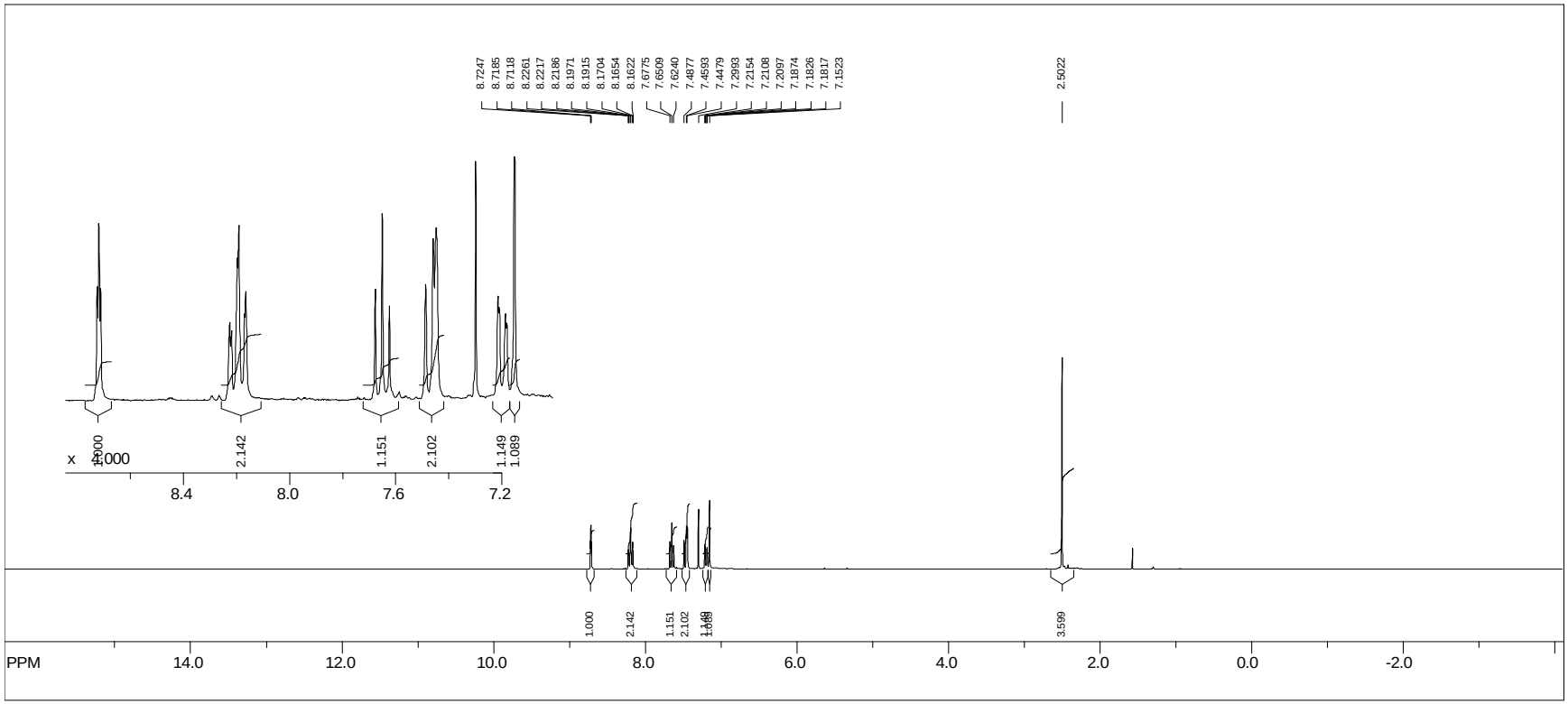
file: Z:\Laina\lmgxiv\lmgxiv_40-1a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(3-Nitrophenyl)-5-methylbenzofuran (315)



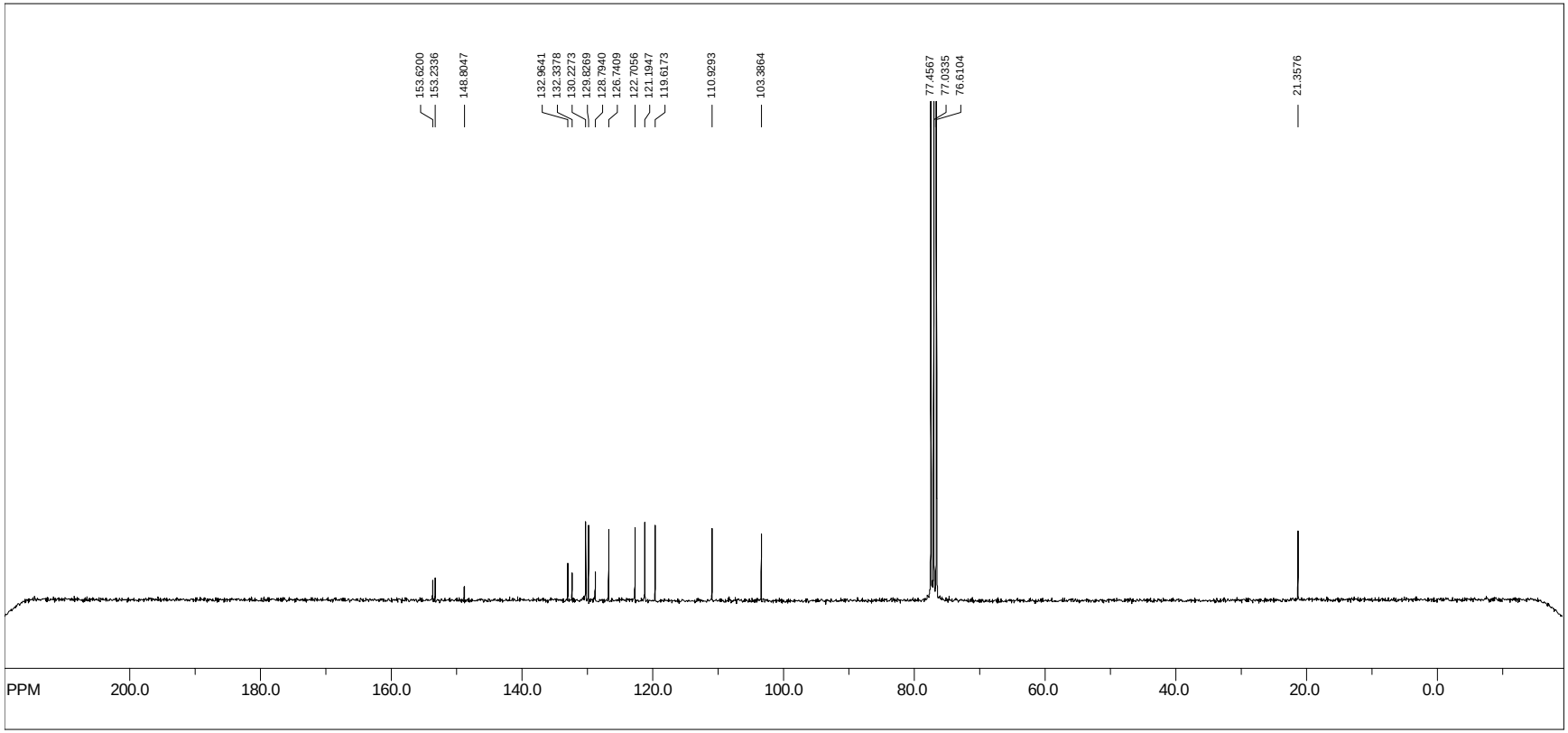
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 14



file: Z:\Laina\lmgxiv\lmgxiv_41b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

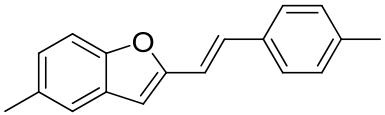
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



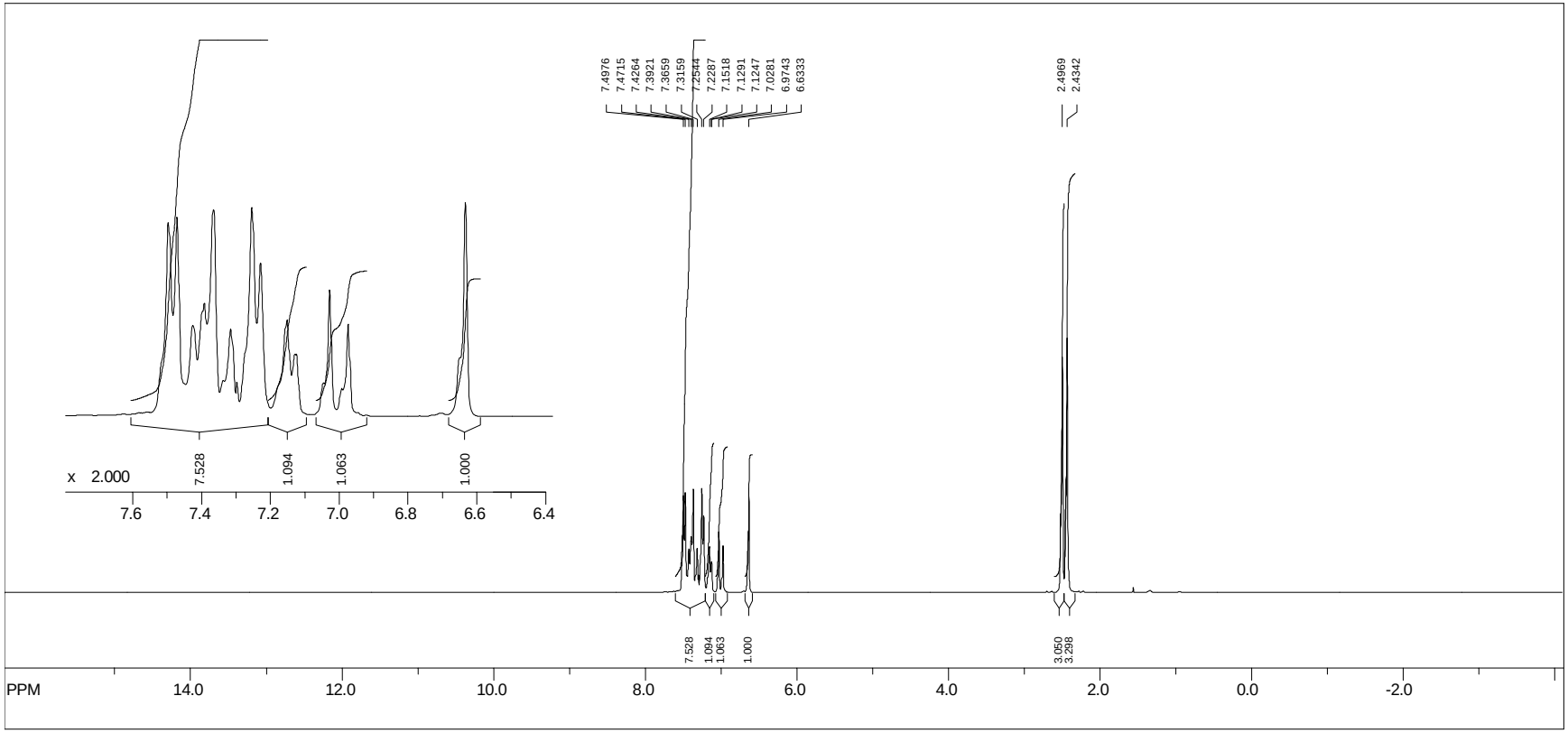
file: Z:\Laina\lmgxiv\lmgxiv_41b\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4096

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(2-*trans*-(4-Methylphenyl)ethenyl)-5-methylbenzofuran (316)



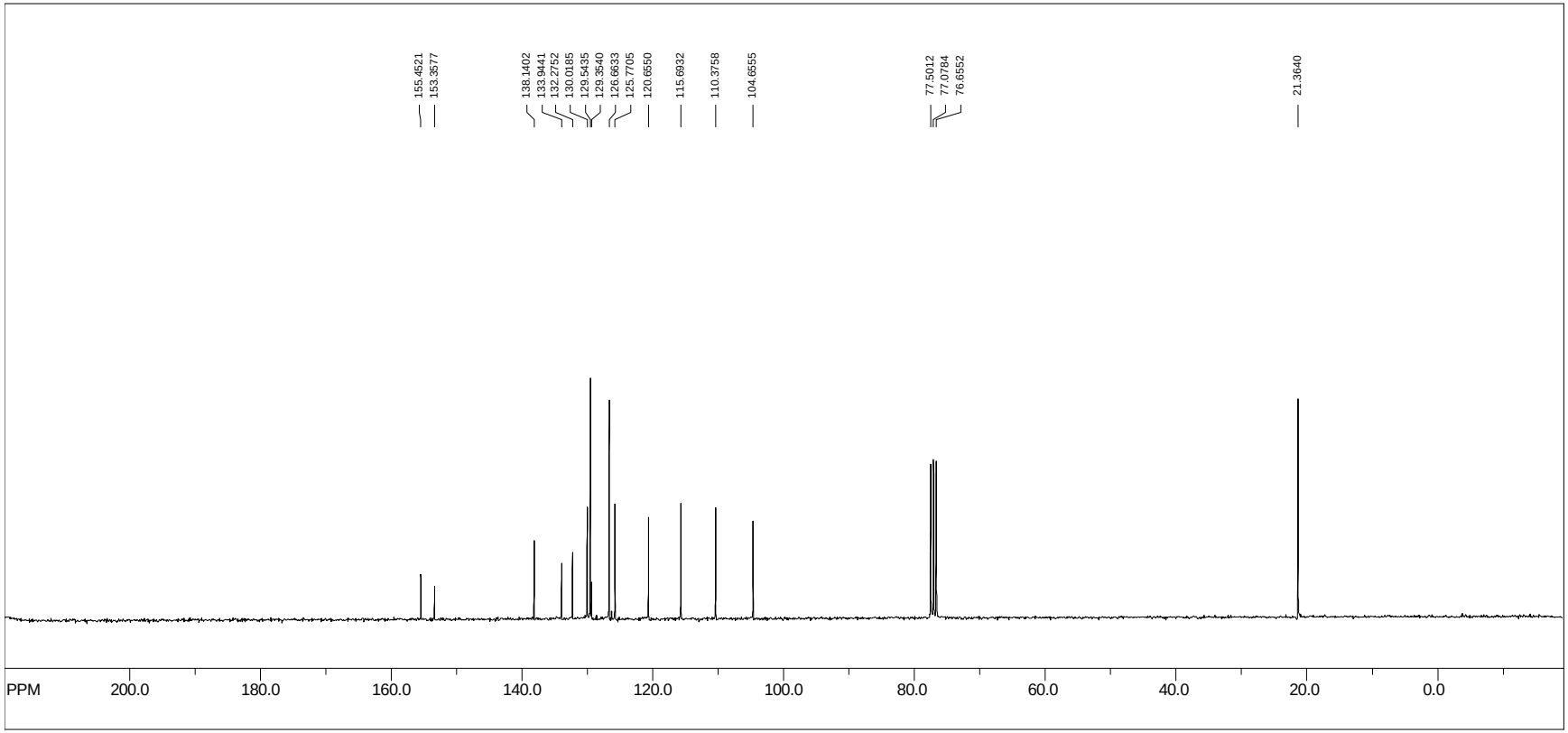
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 12



file: Z:\Laina\lmgxiv\lmgxiv_43bi\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

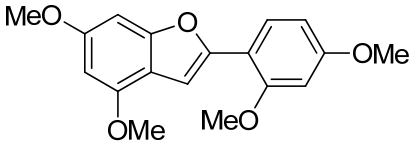
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 12



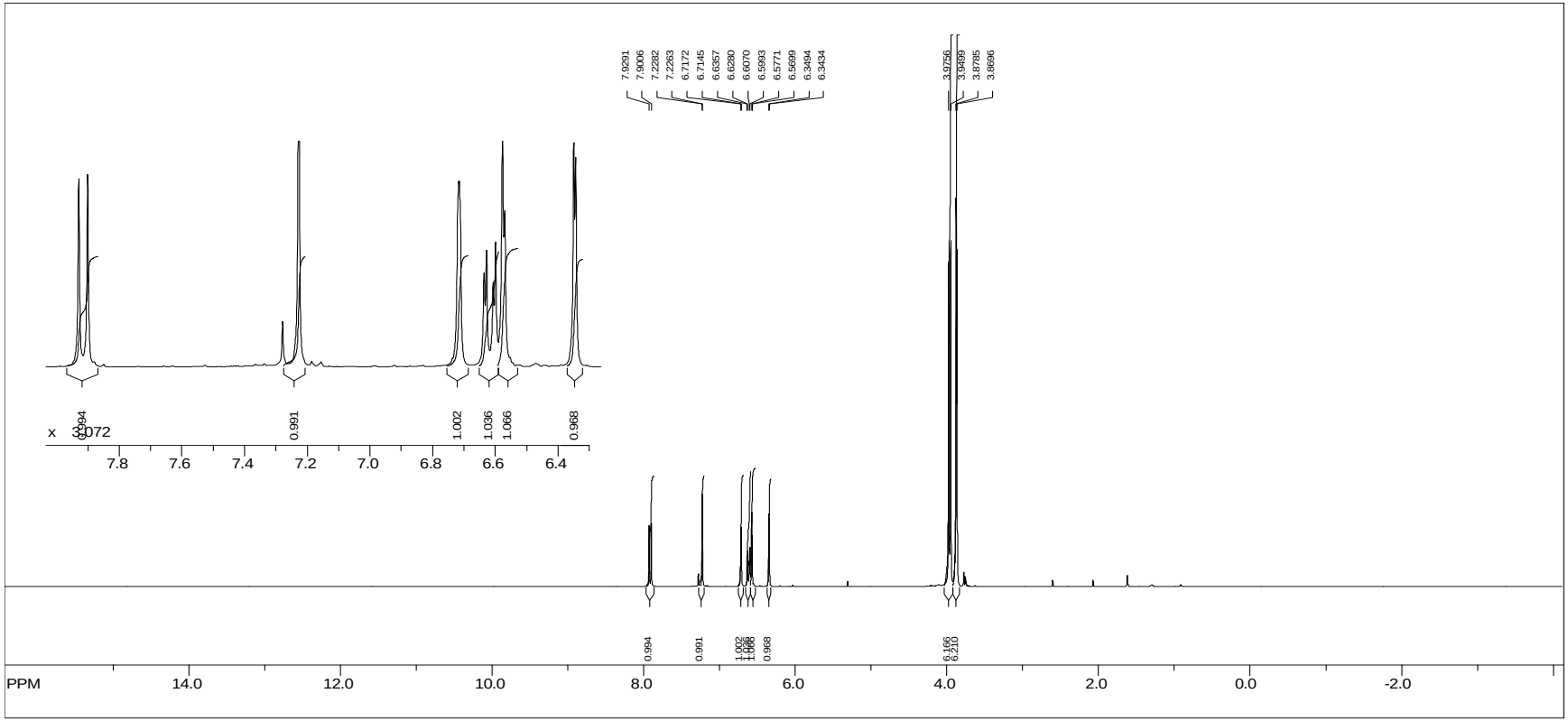
file: Z:\Laina\lmgxiv\lmgxiv_43bi\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 844

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(2,4-Dimethoxyphenyl)-4,6-dimethoxy-benzofuran (317)



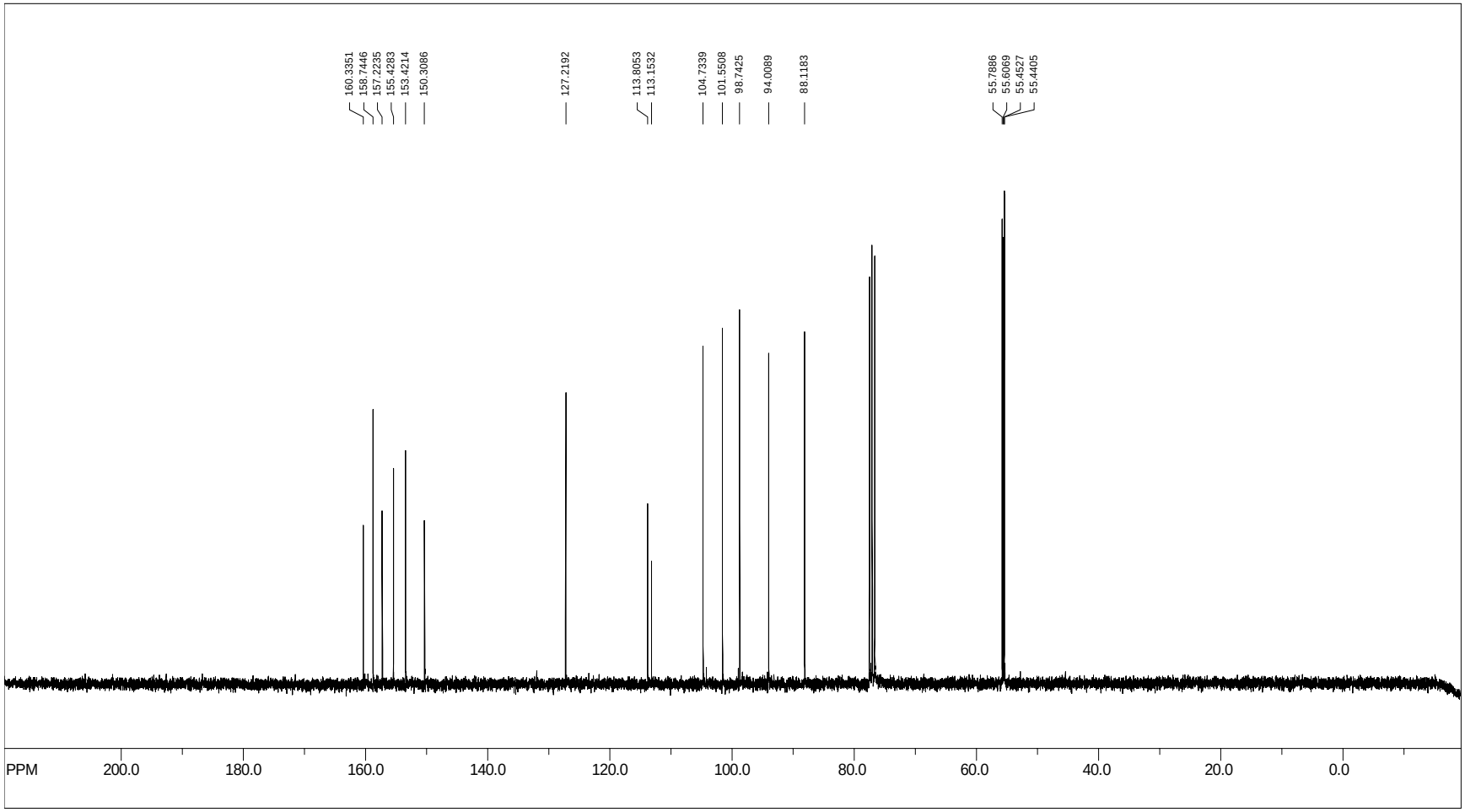
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgx\lmgx_06b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

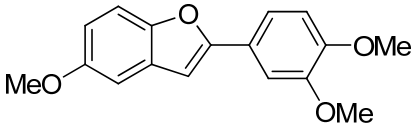
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



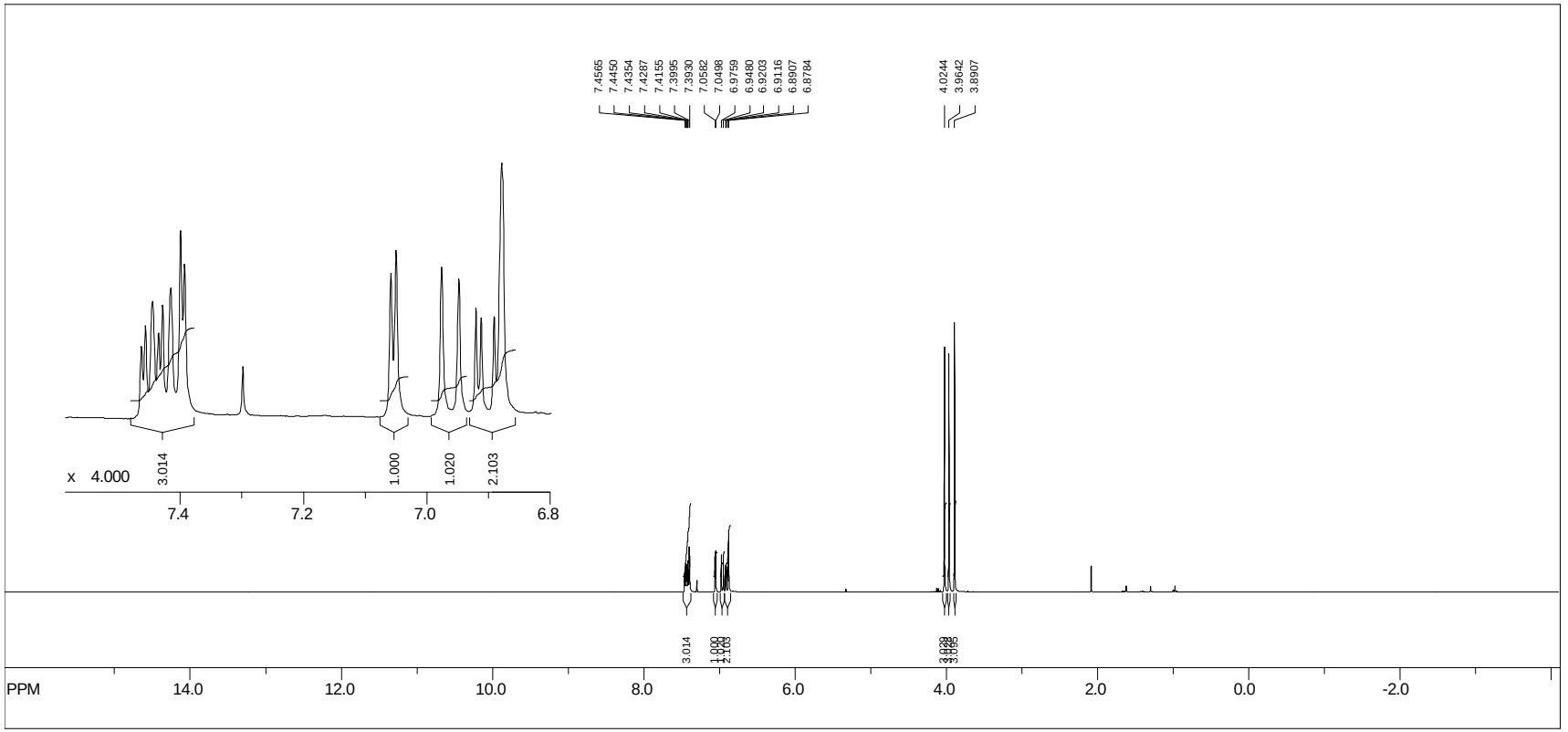
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_06b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 396

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(3,4-Dimethoxyphenyl)-5-methoxybenzofuran (318)



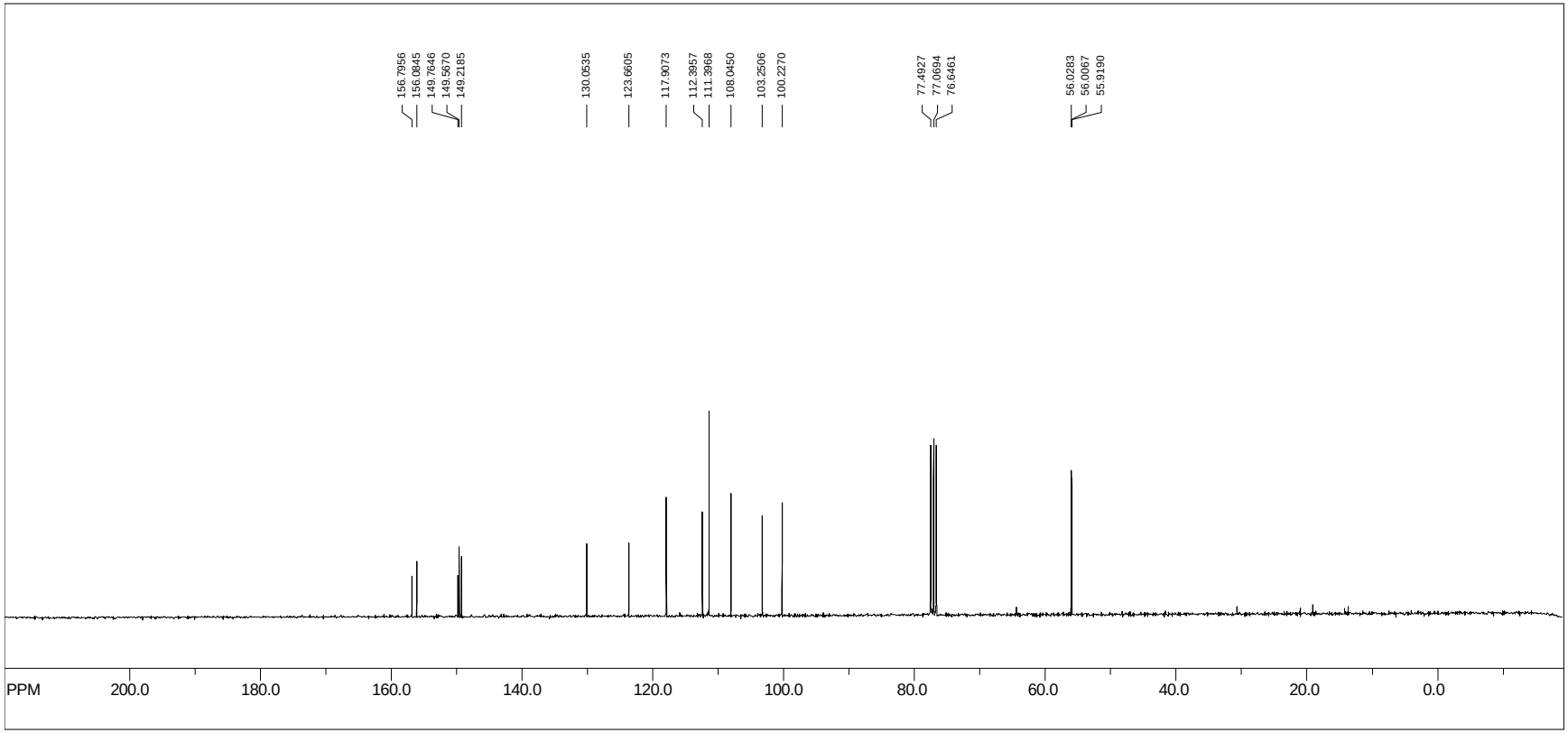
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 17



file: Z:\Laina\lmgxiv\lmgxiv_78b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

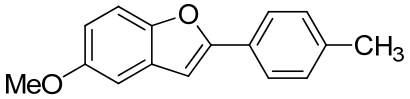
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



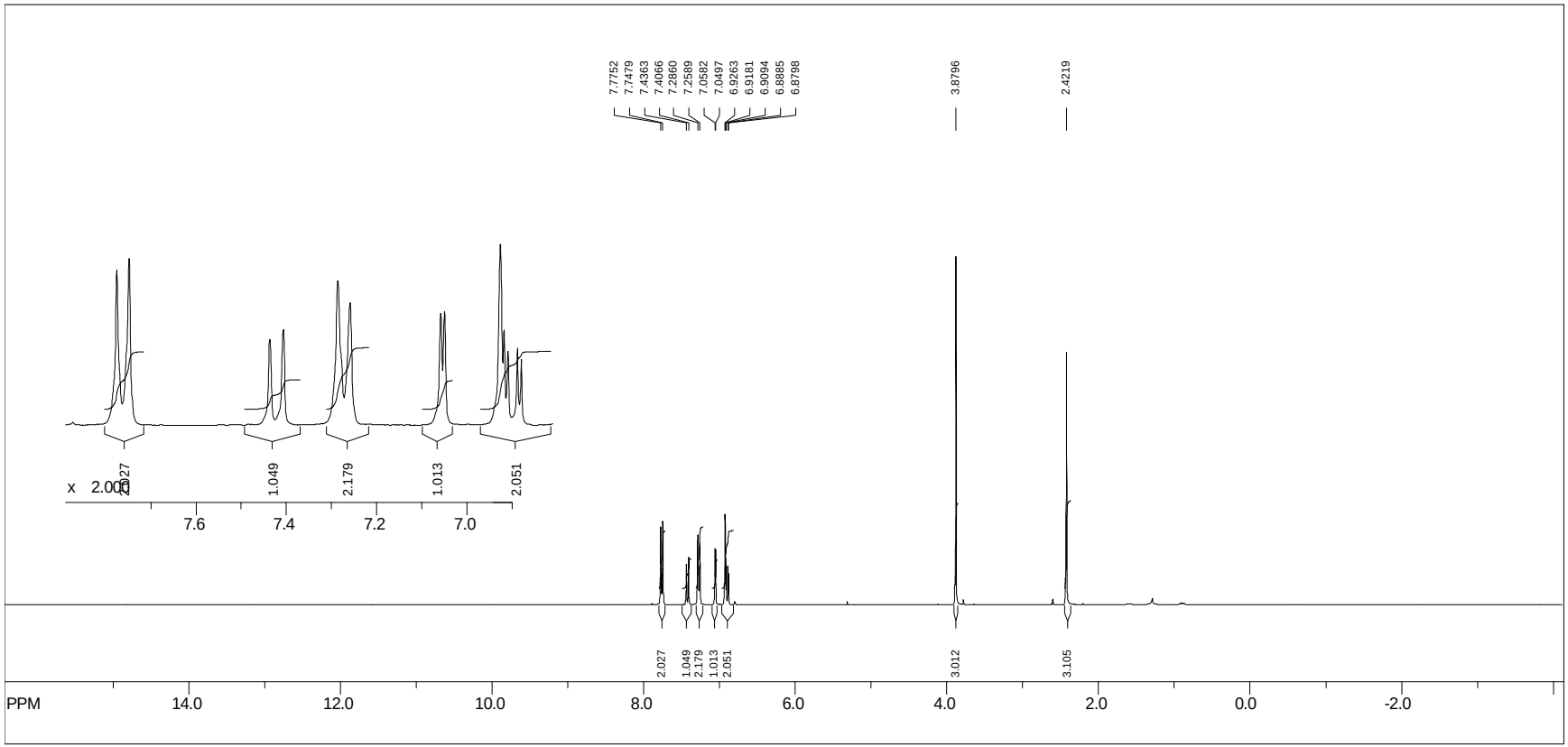
file: Z:\Laina\lmgxiv\lmgxiv_78b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 779

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methylphenyl)-5-methoxybenzofuran (319)



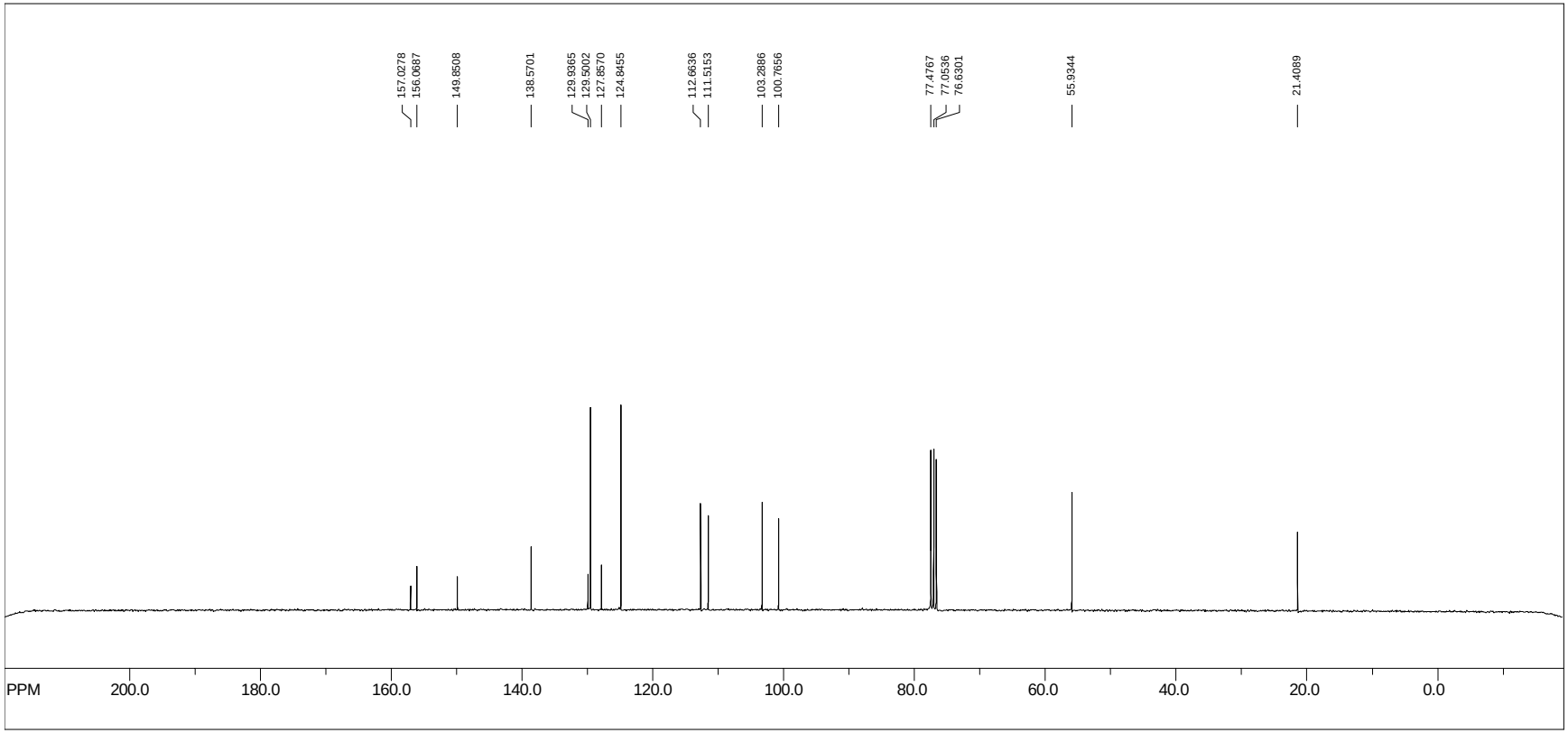
SpinWorks 2.5: 5-methoxy-2-(4-methylphenyl)benzofuran



file: Z:\Laina\lmgxiii\lmgxiii_06a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

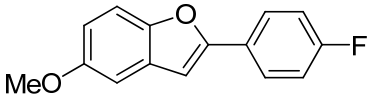
SpinWorks 2.5: 5-methoxy-2-(4-methylphenyl)benzofuran



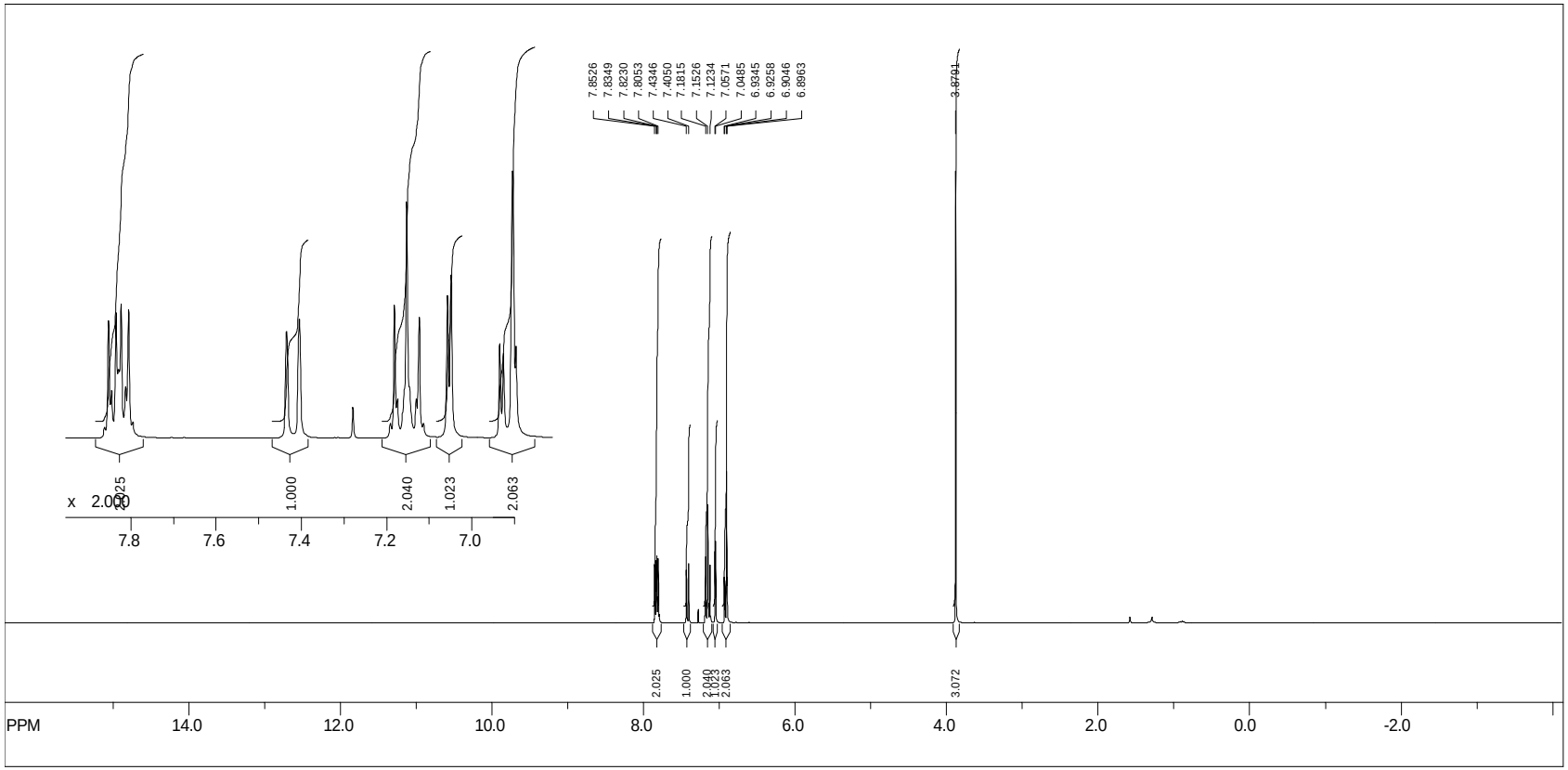
file: Z:\Laina\lmgxiii\lmgxiii_06a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 2048

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Fluorophenyl)-5-methoxybenzofuran (320)



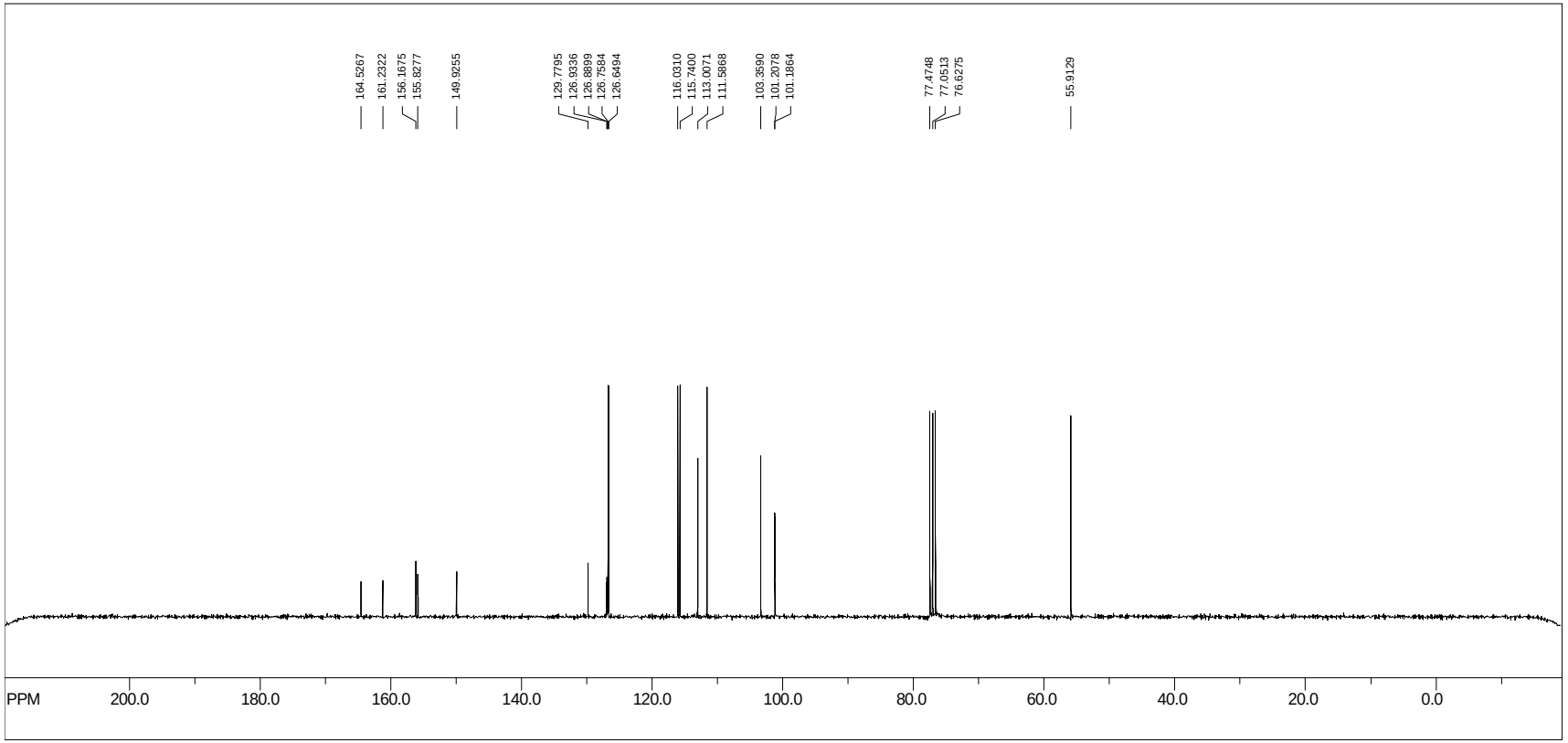
SpinWorks 2.5: 5-methoxy-2-(4-fluorophenyl)benzofuran



file: Z:\Laina\lmgxii\lmgxii_99ai\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

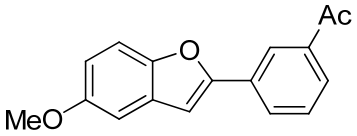
SpinWorks 2.5: 5-methoxy-2-(4-fluorophenyl)benzofuran



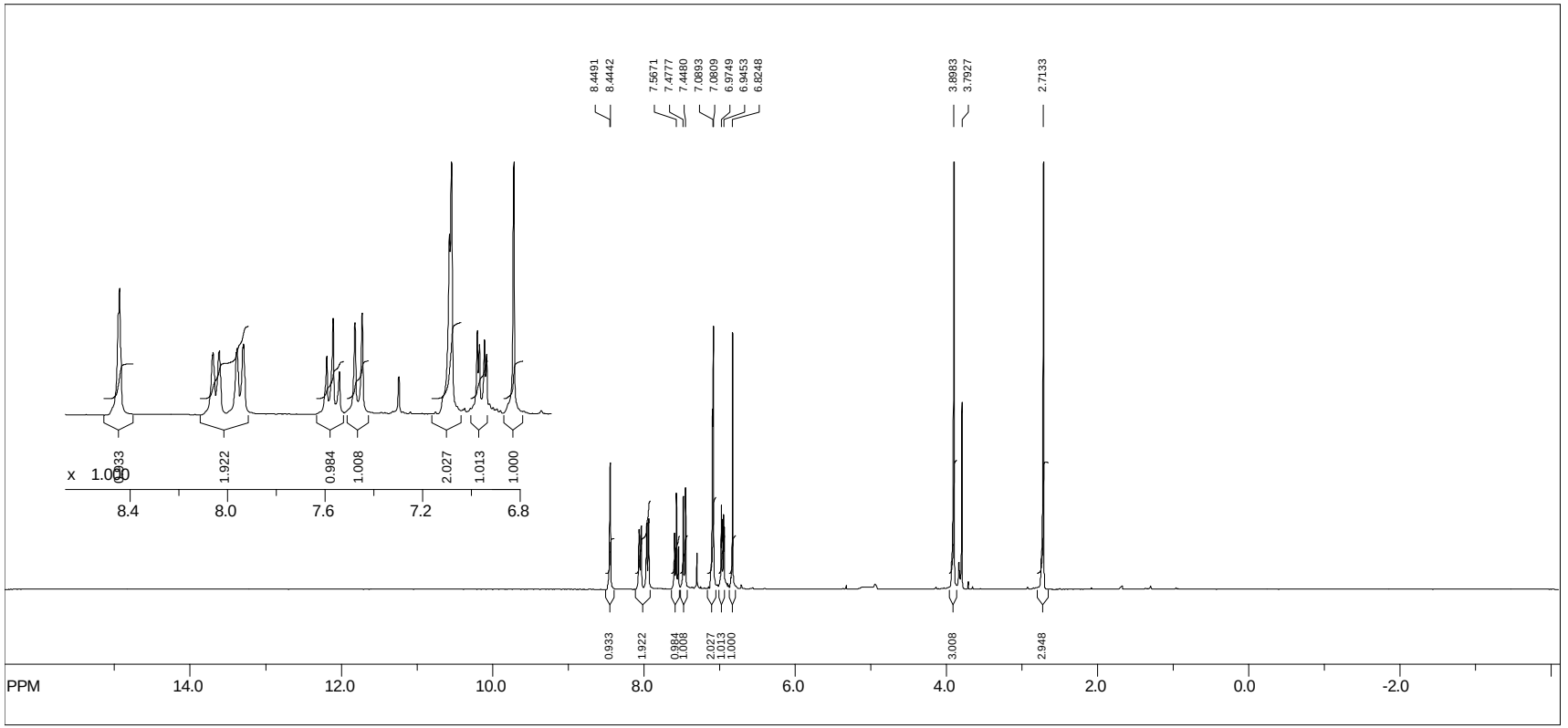
file: Z:\Laina\lmgxii\lmgxii_99aii\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(3-Acetylphenyl)-5-methoxybenzofuran (321)



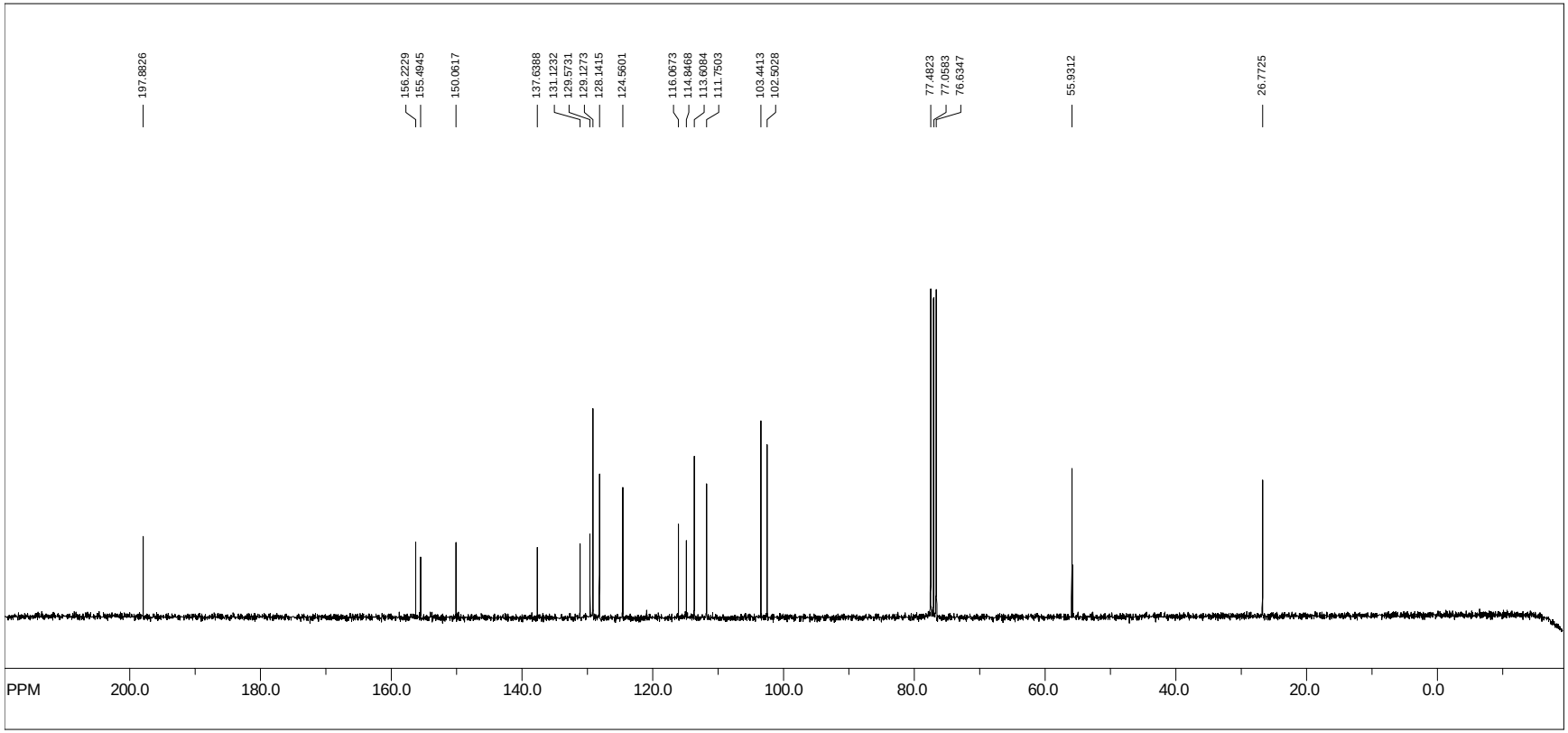
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 15



file: Z:\Laina\lmgxiv\lmgxiv_76a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

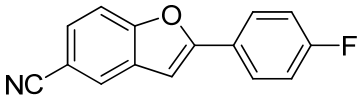
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



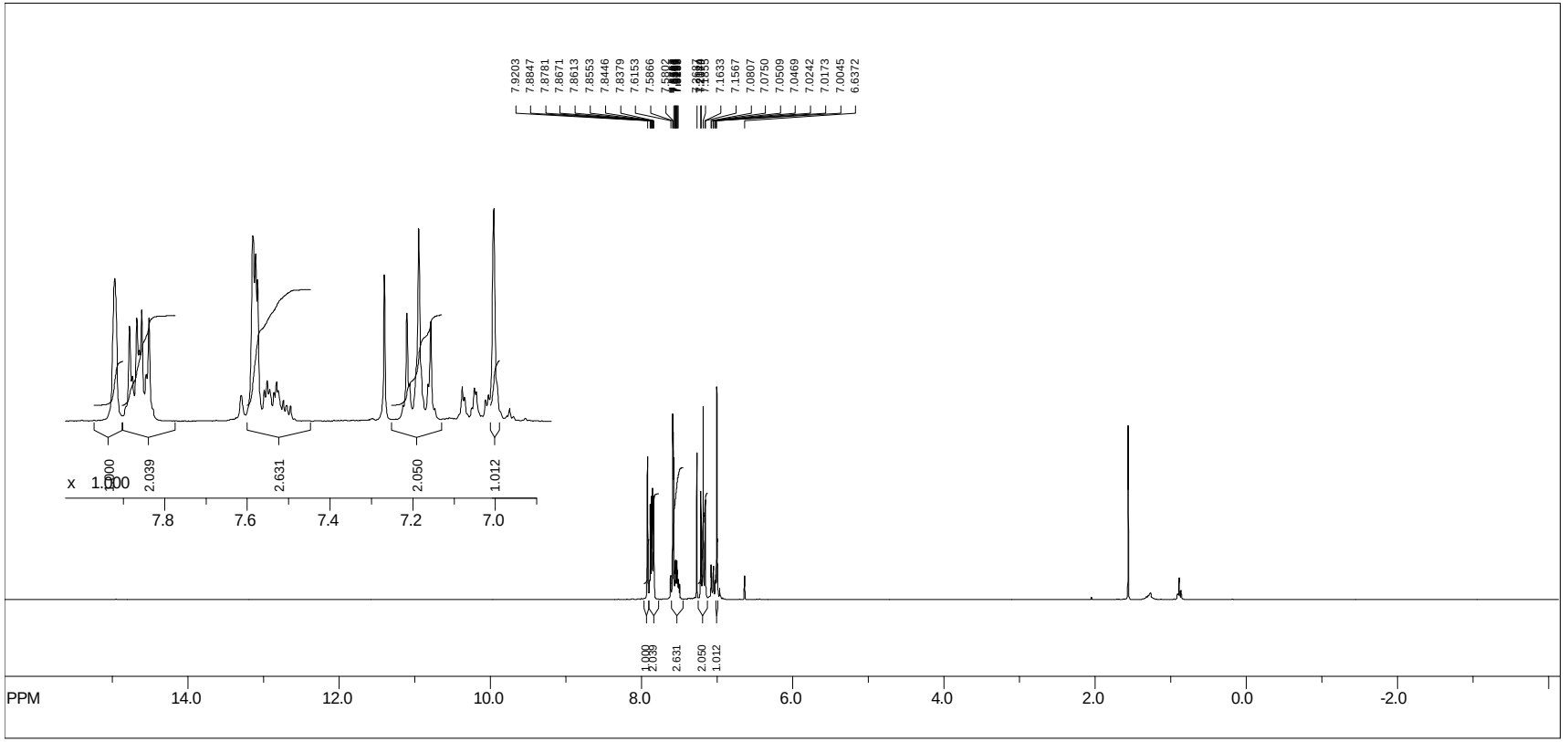
file: Z:\Laina\lmgxiv\lmgxiv_76a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 867

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Fluorophenyl)-5-cyanobenzofuran (322)



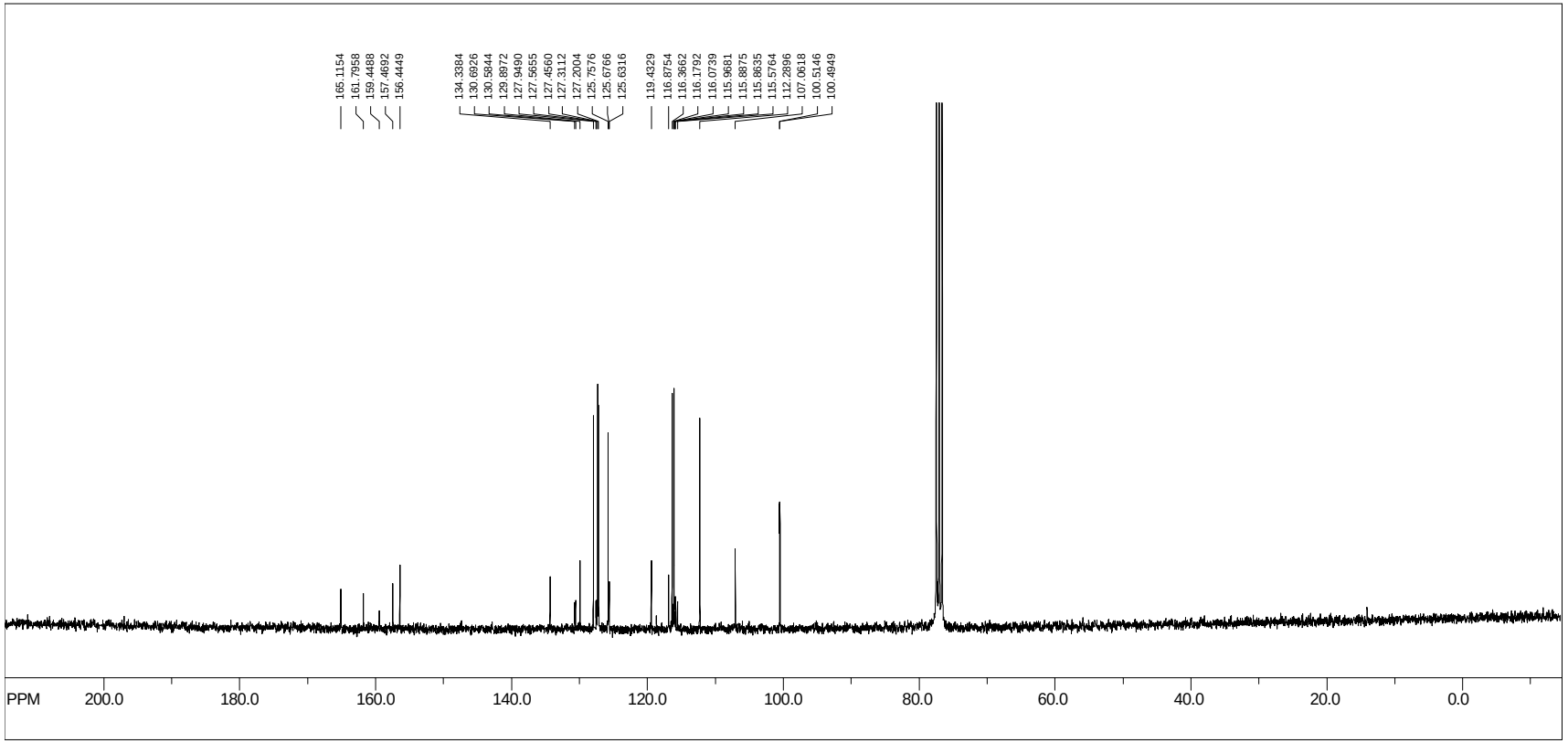
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgxiii\lmgxiii_61bii\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130009 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

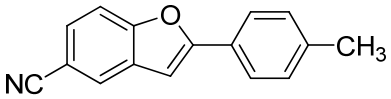
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



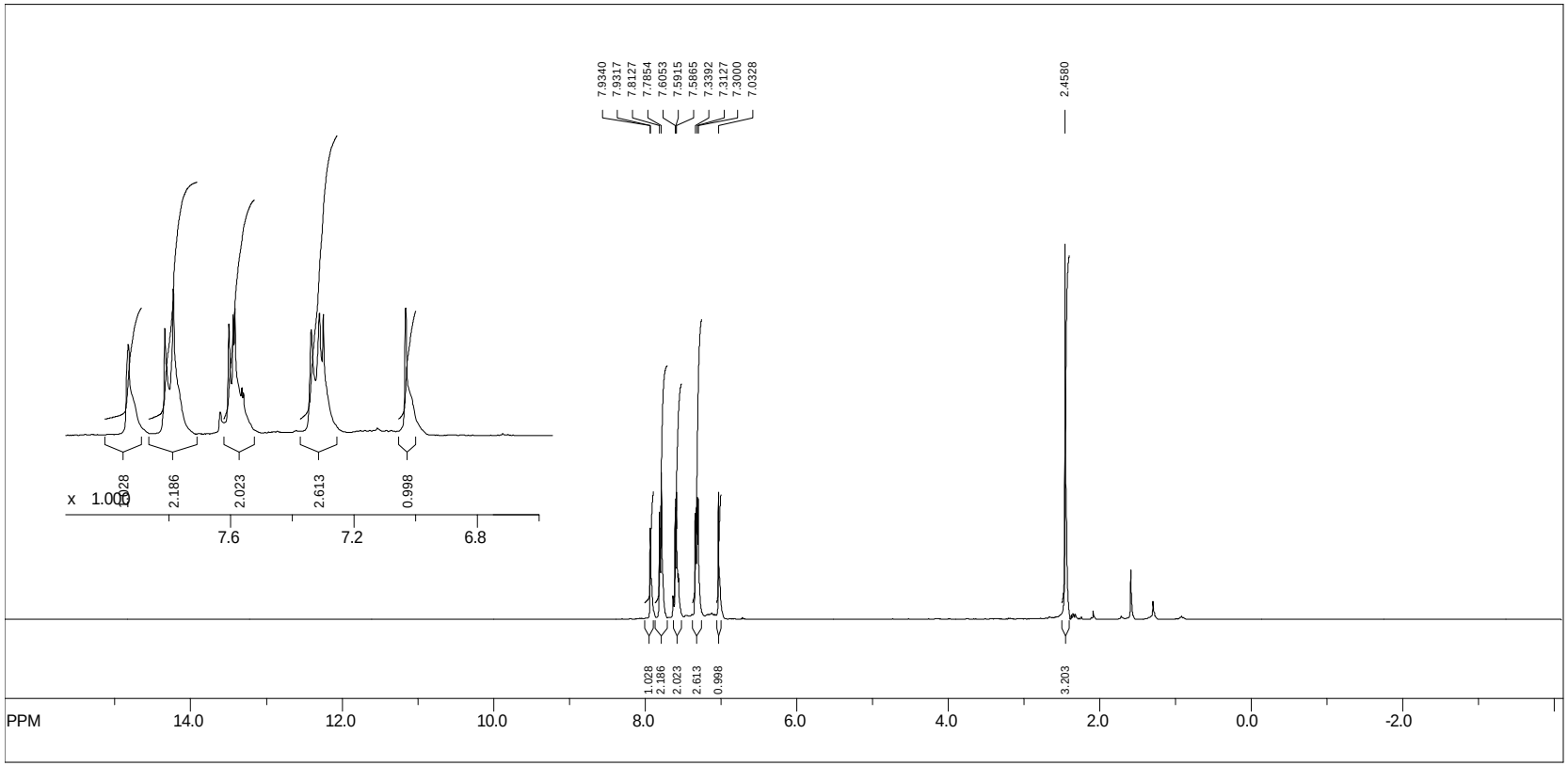
file: Z:\Laina\lmgxiii\lmgxiii_61bii\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 2540

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(4-Methylphenyl)-5-cyanobenzofuran (323)



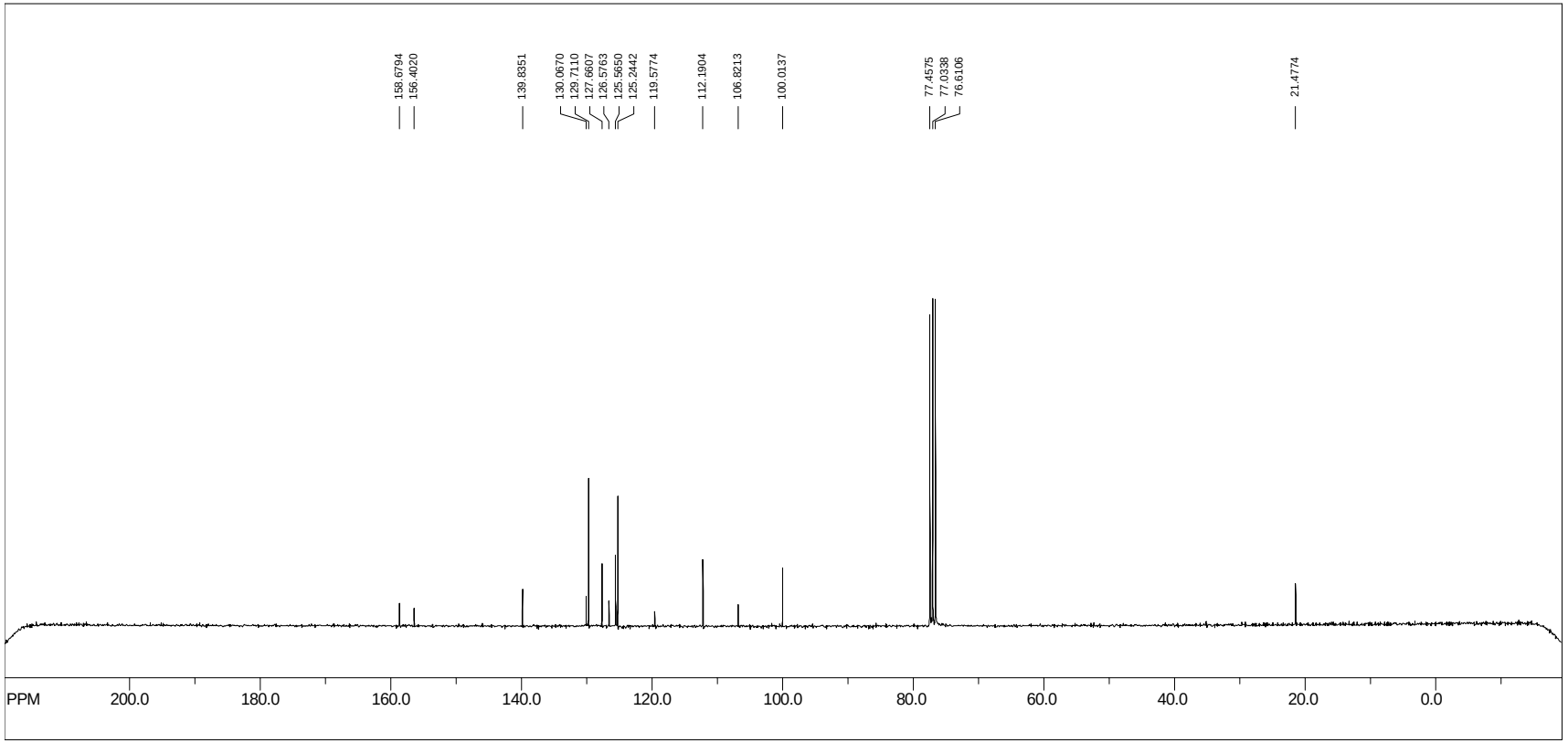
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 15



file: Z:\Laina\lmgxiii\lmgxiii_53aii\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

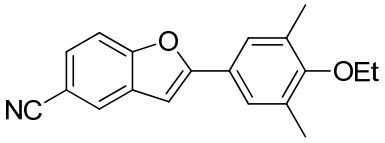
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 15



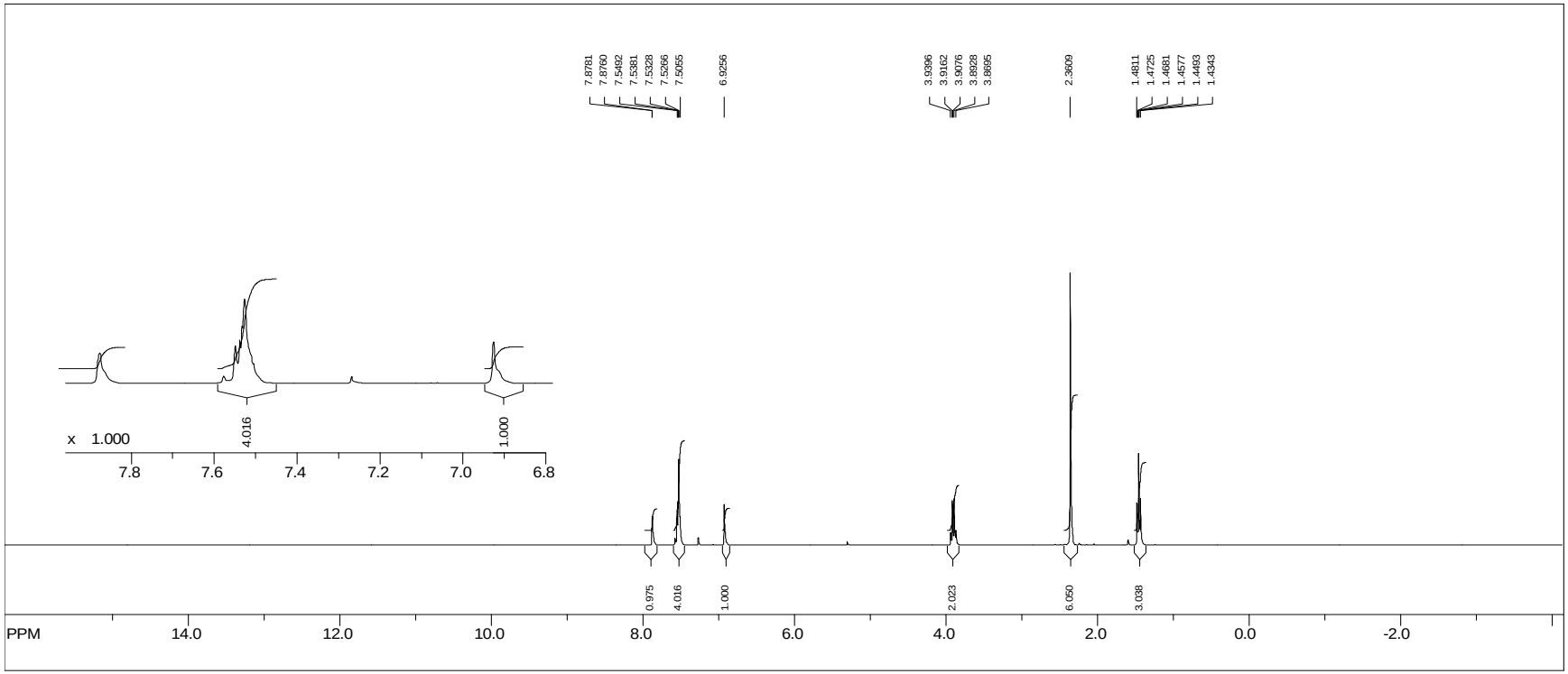
file: Z:\Laina\lmgxiii\lmgxiii_53aii\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4196

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(3,5-Dimethyl-4-ethoxyphenyl)-5-cyanobenzofuran (324)



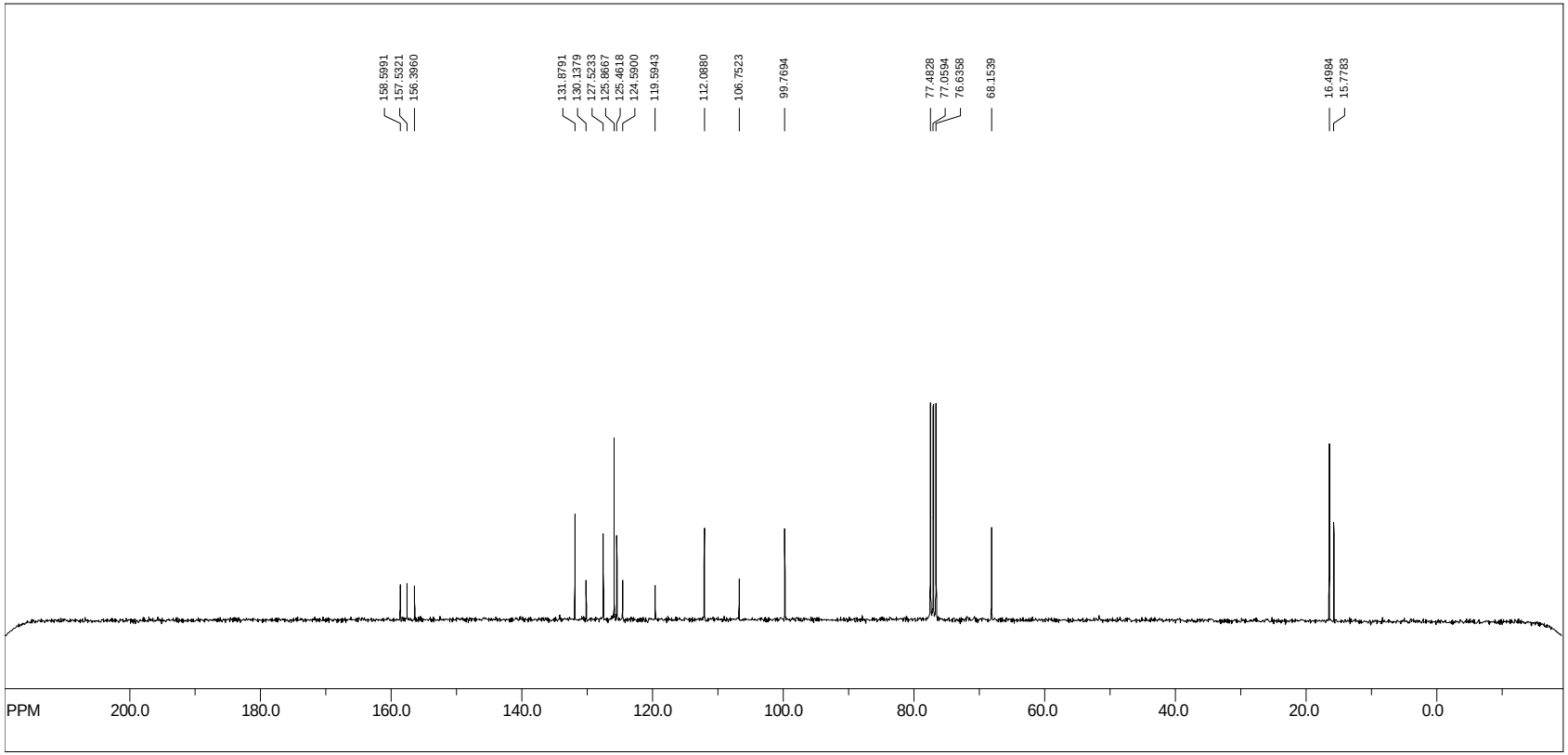
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxiii\lmgxiii_71a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130009 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

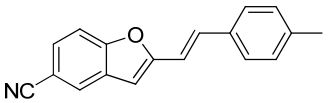
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



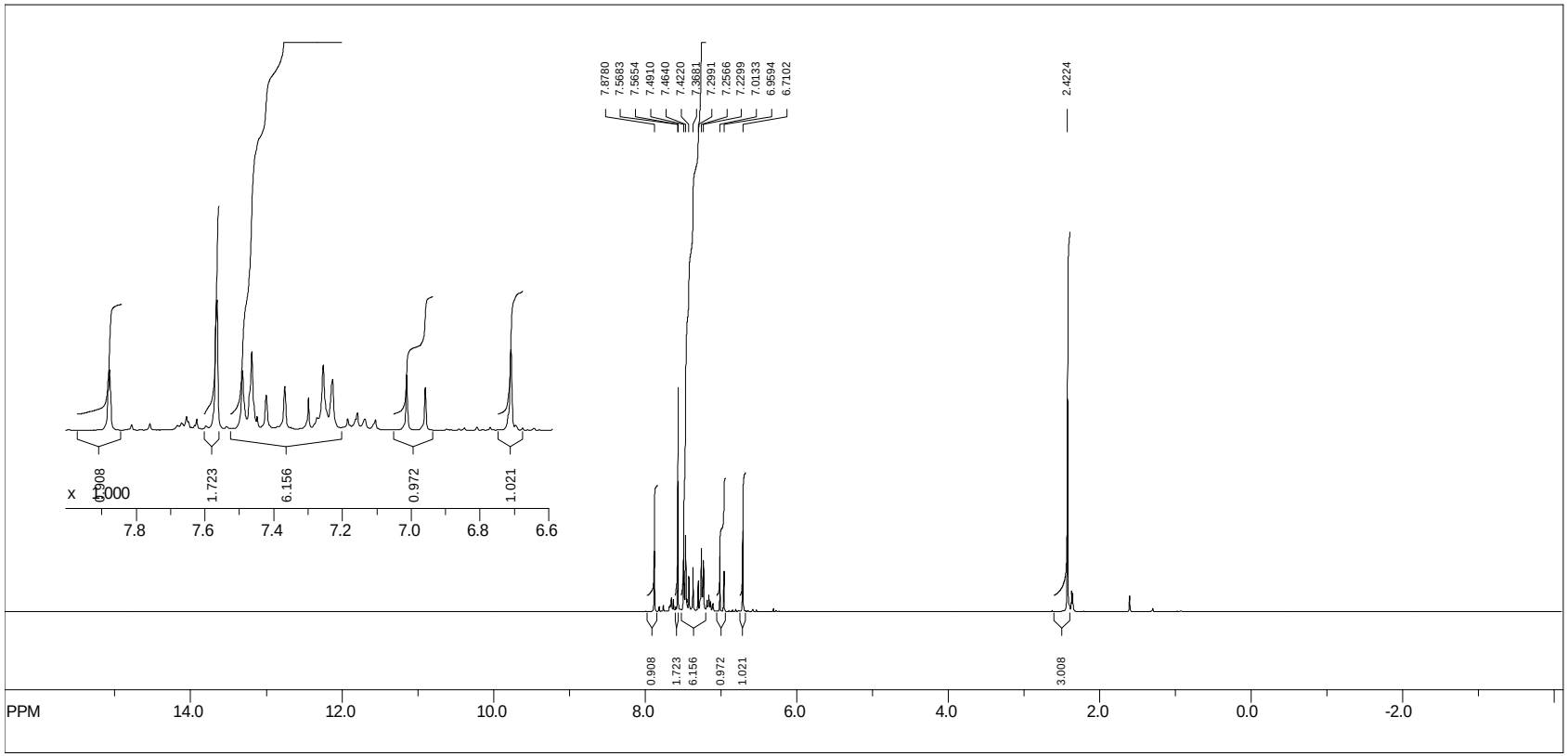
file: Z:\Laina\lmgxiii\lmgxiii_71a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(2-*trans*-(4-Methylphenyl)ethenyl)-5-cyanobenzofuran (325)



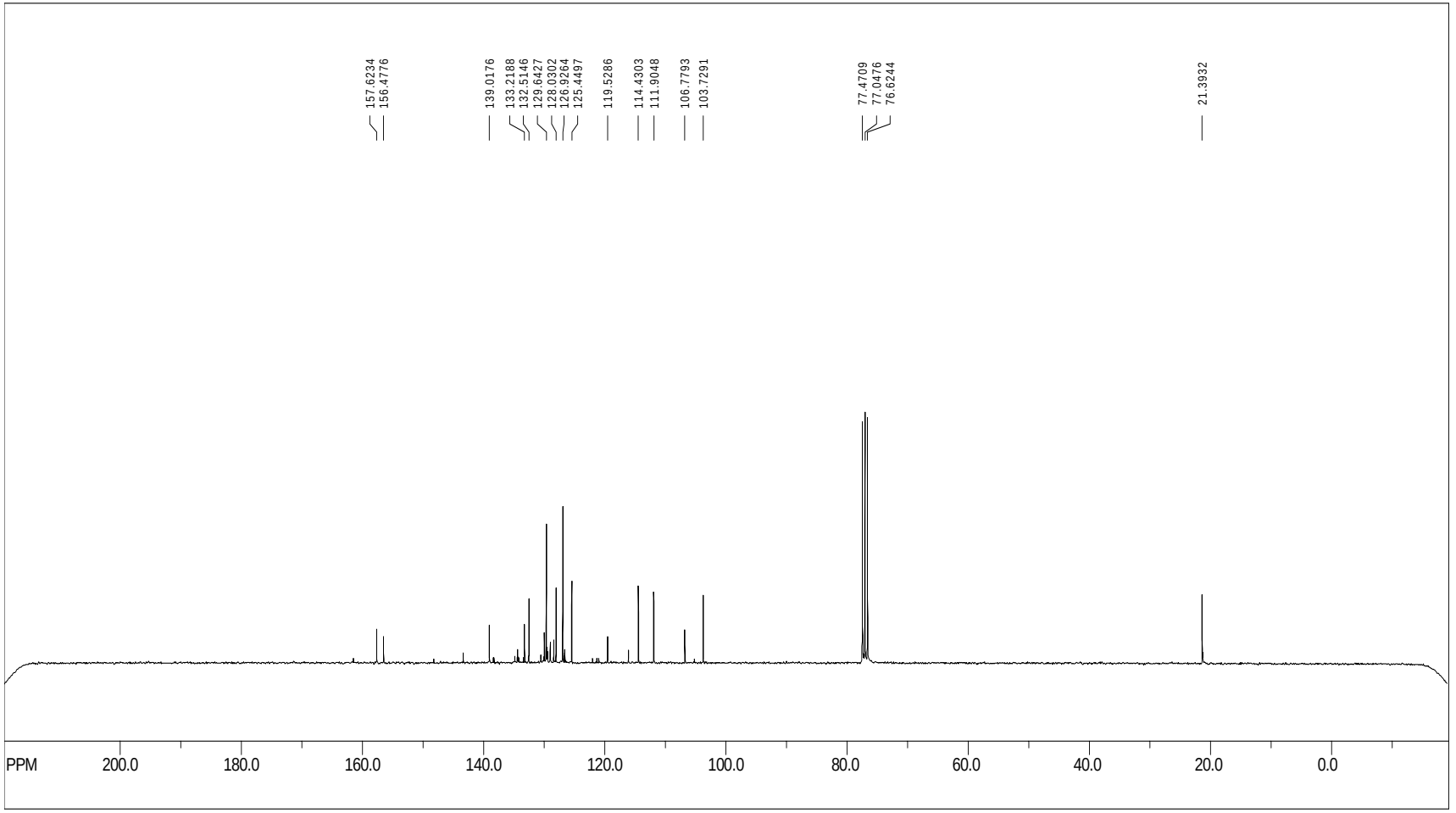
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxiii\lmgxiii_63b\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

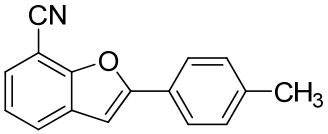
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



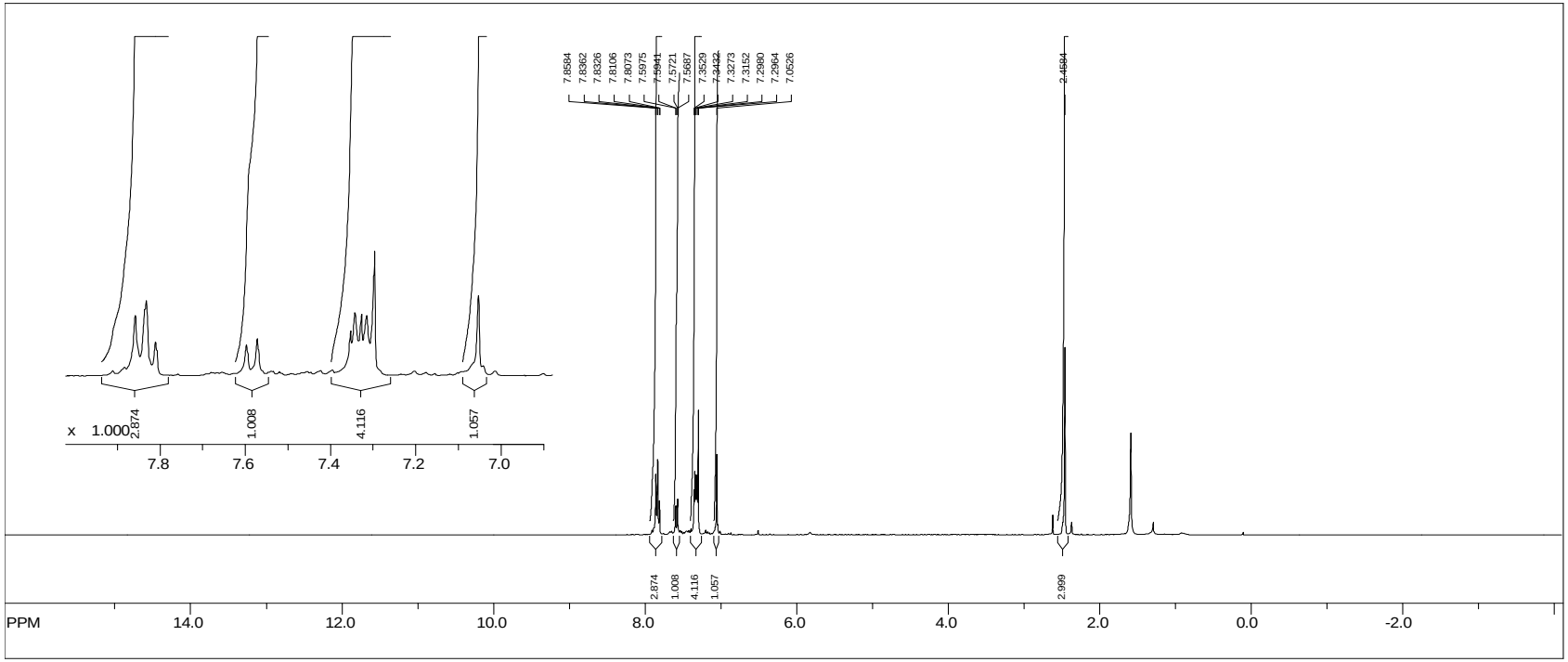
file: Z:\Laina\lmgxiii\lmgxiii_63b\4\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 3500

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(4-Methylphenyl)-7-cyanobenzofuran (328)



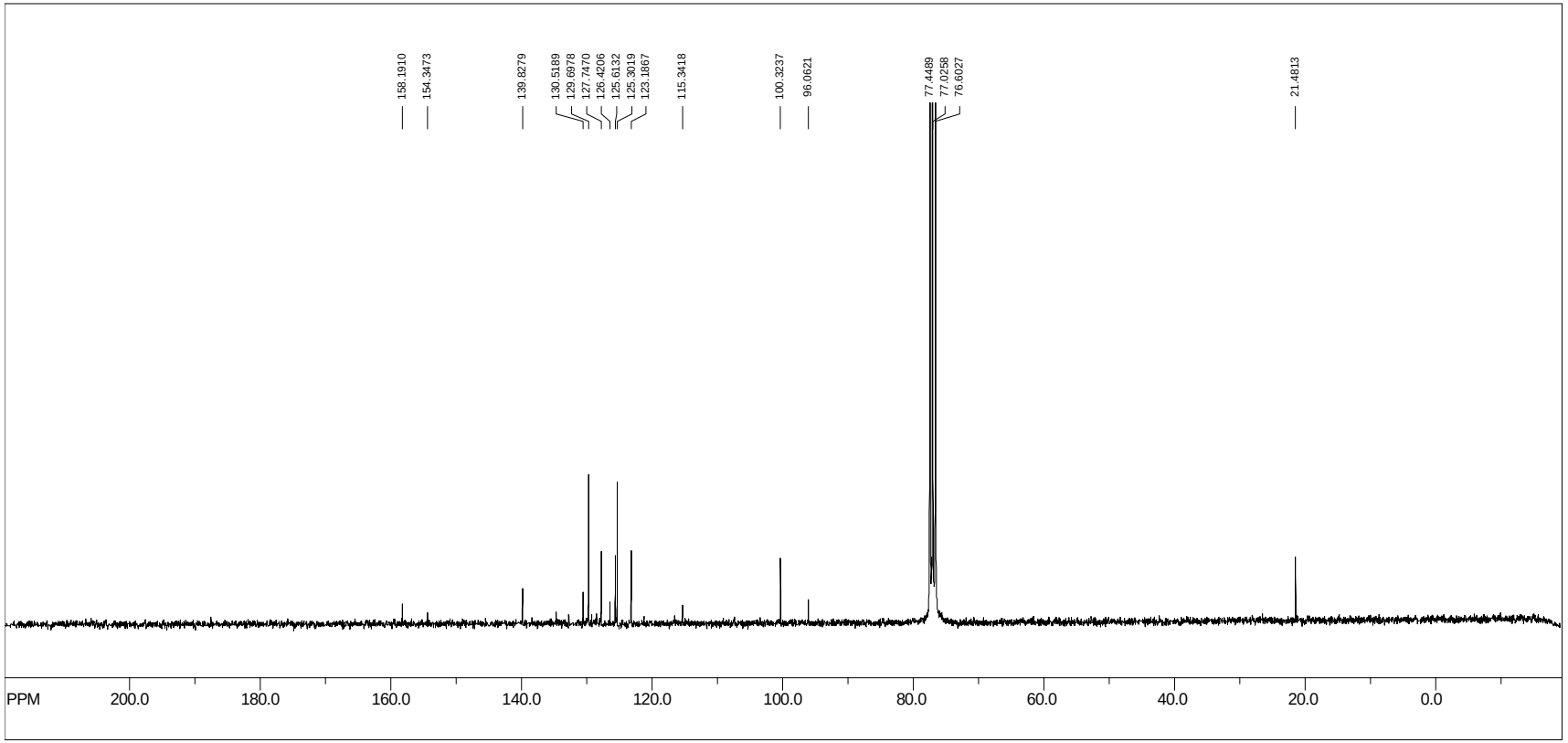
SpinWorks 2.5: PROTON128 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxvi\lmgxvi_53a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 128

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

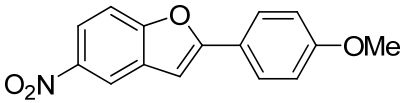
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



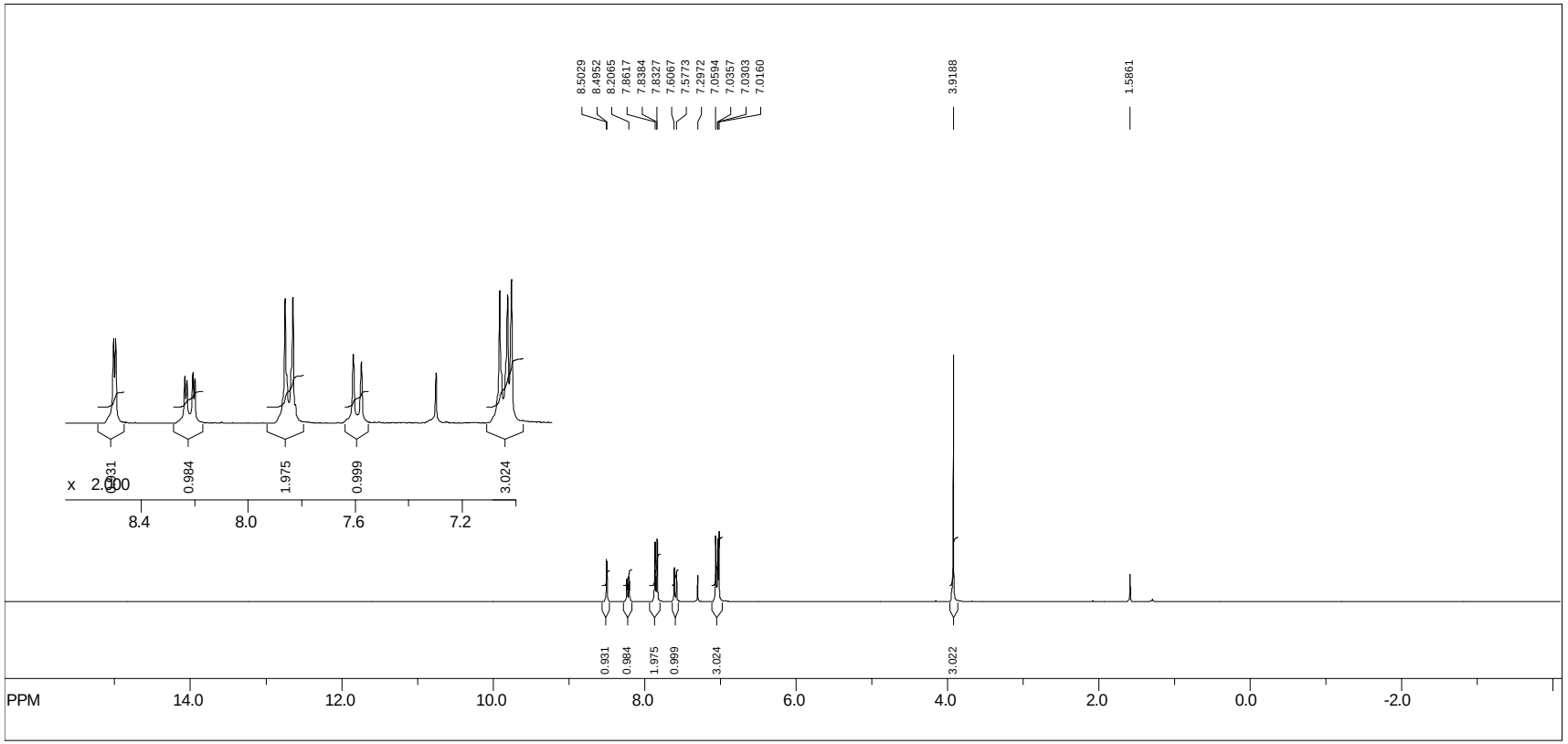
file: Z:\Laina\lmgxvi\lmgxvi_53a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 14000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(4-Methoxyphenyl)-5-nitrobenzofuran (330)



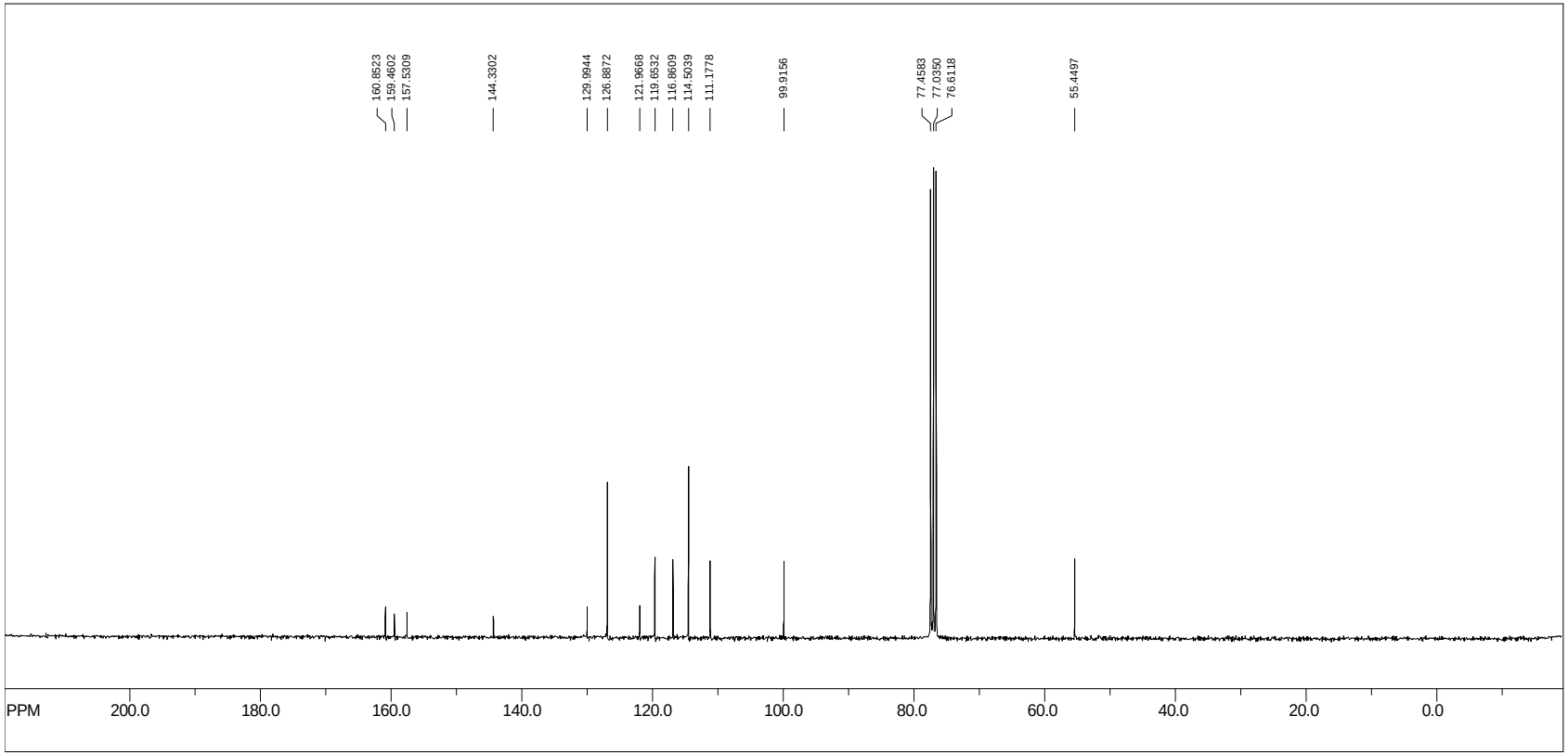
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxvi\lmgxvi_52b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

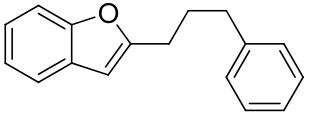
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



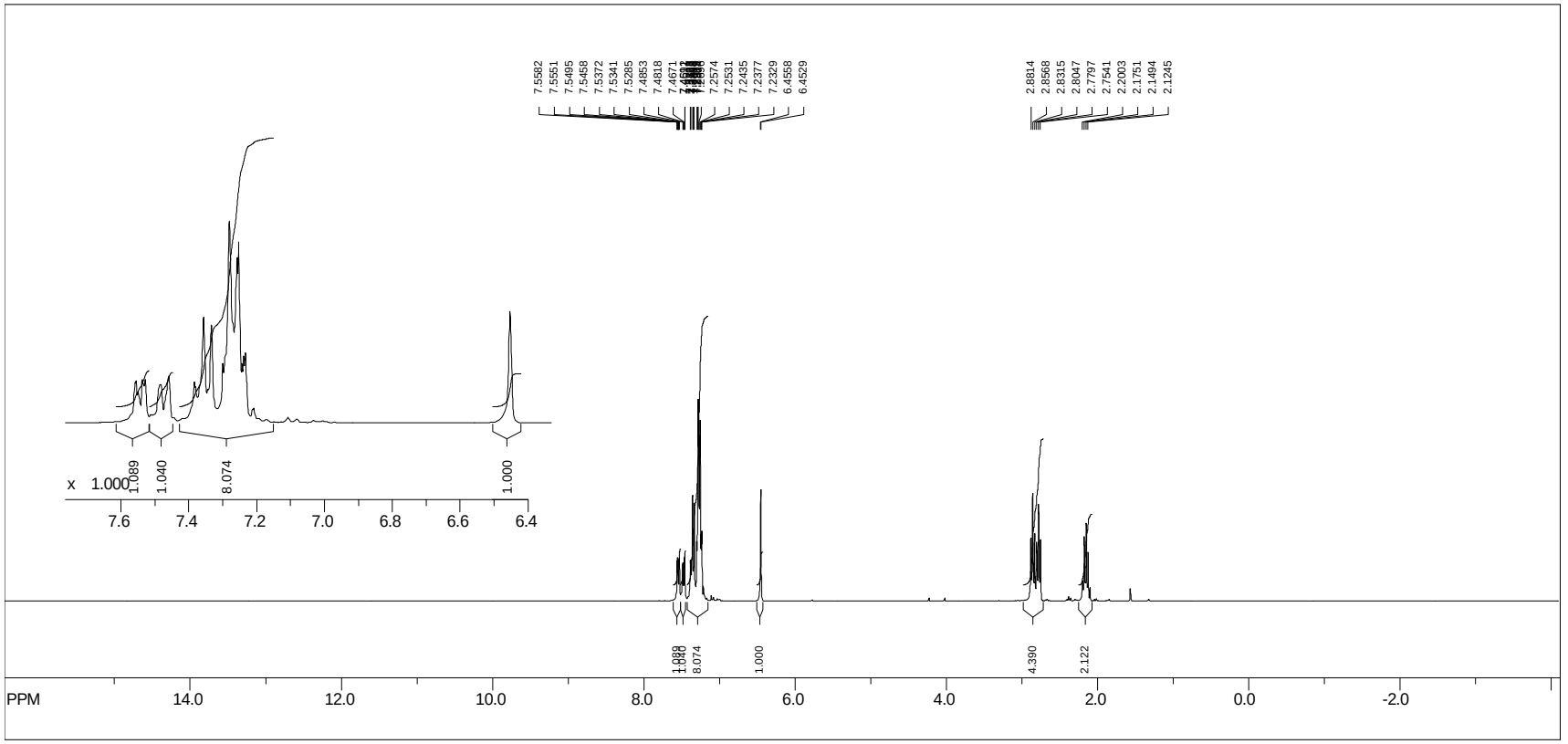
file: Z:\Laina\lmgxvi\lmgxvi_52b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 2166

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(3-Phenylpropyl)benzofuran (333)



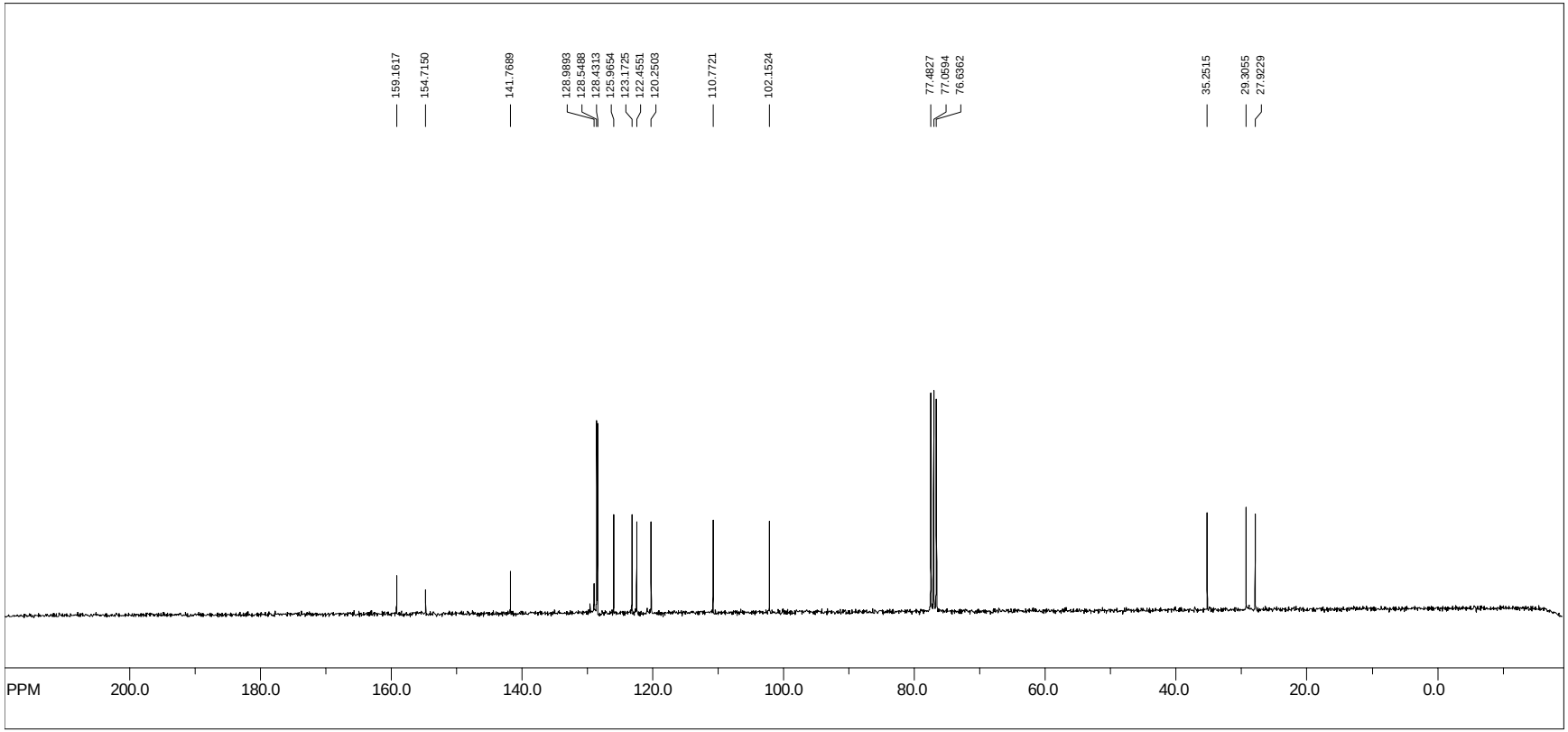
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 9



file: Z:\Laina\lmgxv\lmgxv_50a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

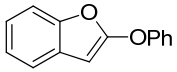
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 23



file: Z:\Laina\lmgxv\lmgxv_50a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

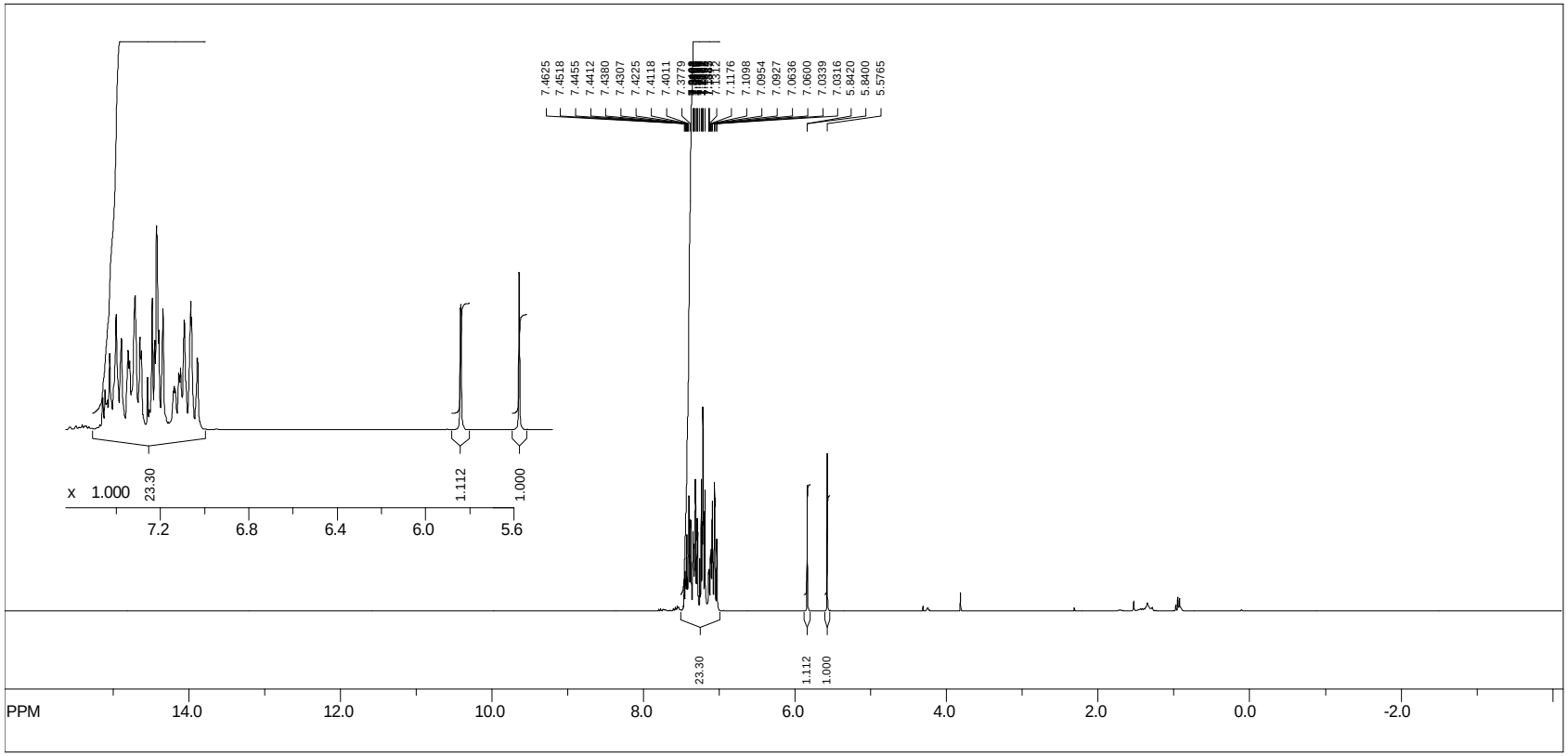
freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-Phenoxybenzofuran (334**)**



(contains equal amount of ketene acetal 81).

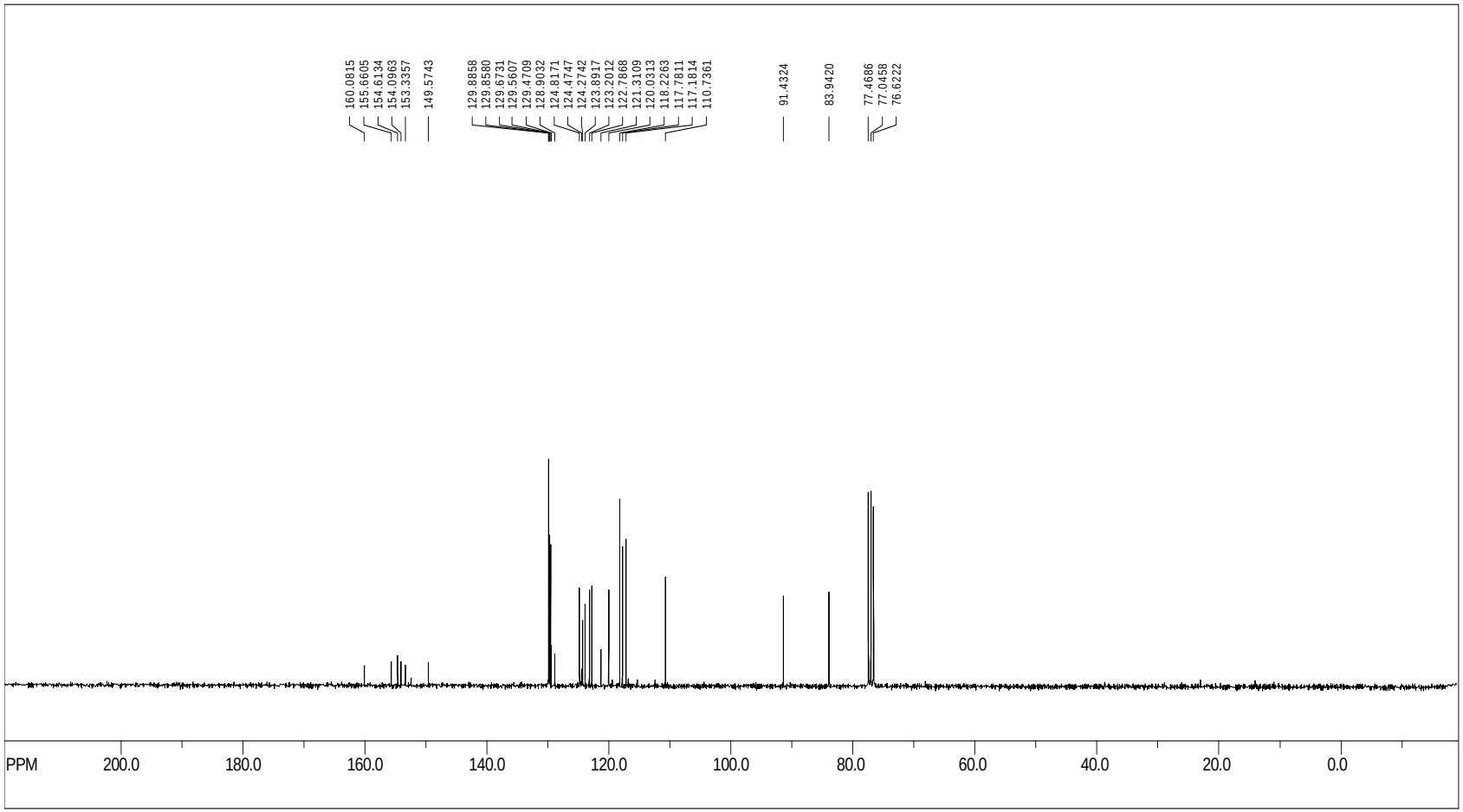
SpinWorks 2.5: attempted oxidative coupling of diphenol ether



file: Z:\Laina\lmgvii\lmgvii_45a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

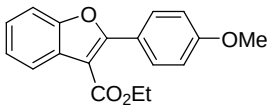
SpinWorks 2.5: attempted oxidative coupling of diphenol ether



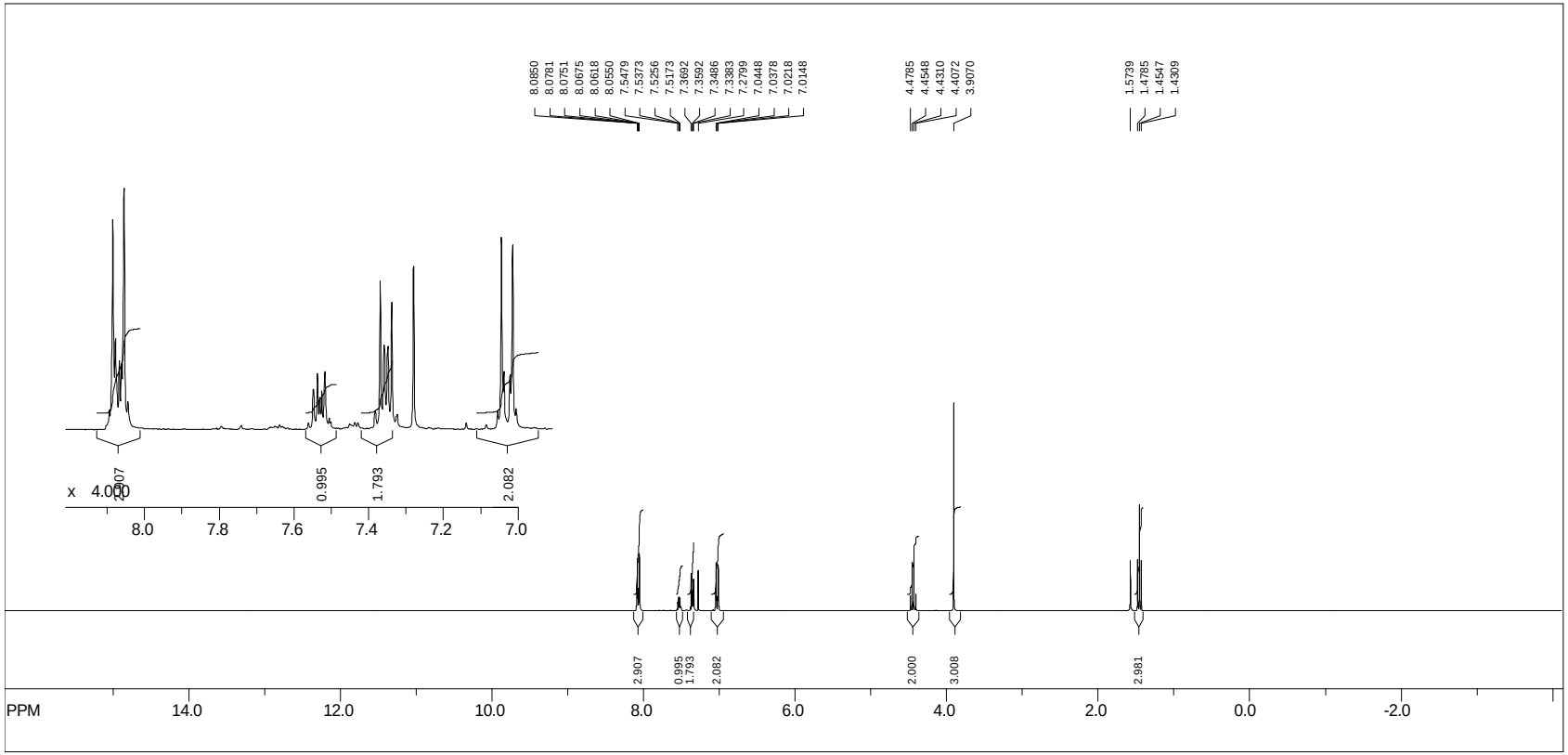
file: Z:\Laina\lmgvii\lmgvii_45a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 461

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

Ethyl 2-(4-methoxyphenyl)benzofuran-3-carboxylate (336)



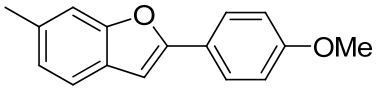
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



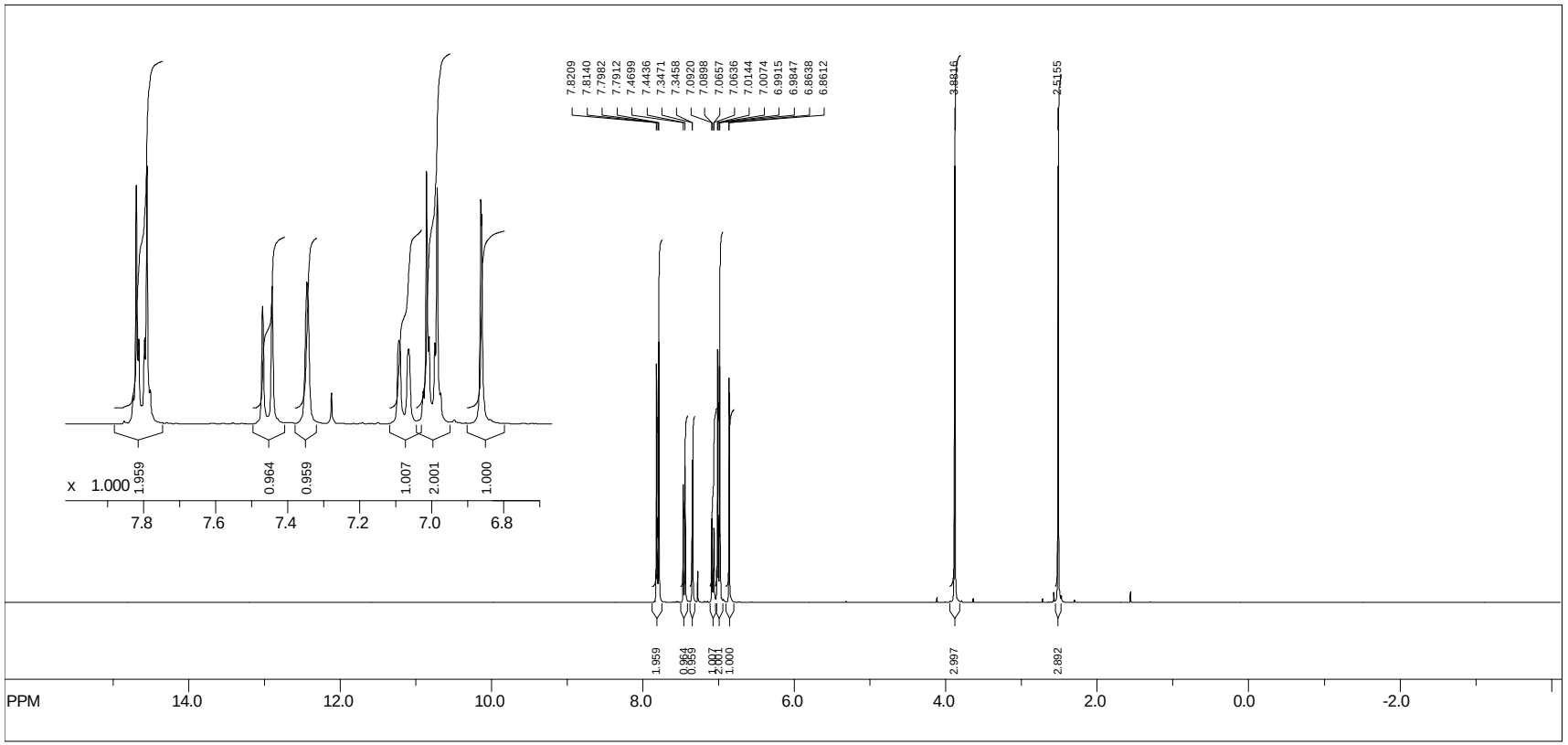
file: Z:\Laina\lmgxi\lmgxi_18a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 5

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-6-methylbenzofuran (343)



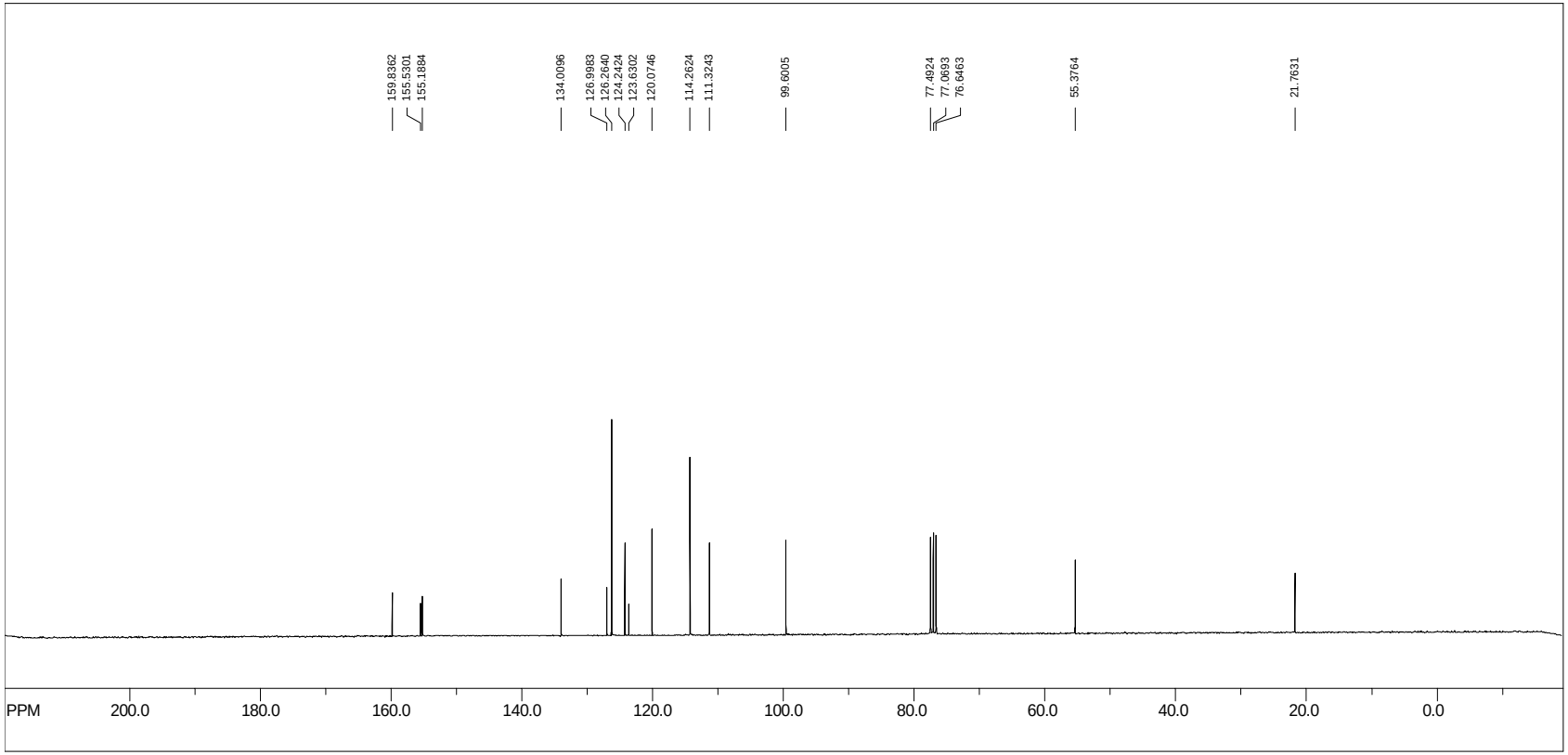
SpinWorks 2.5: 2-(4-methoxyphenyl)-4(6)-methylbenzo[b]furan



file: Z:\Laina\lmgxiv\lmgxiv_35a\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

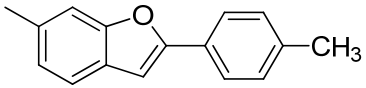
SpinWorks 2.5: 2-(4-methoxyphenyl)-4(6)-methylbenzo[b]furan



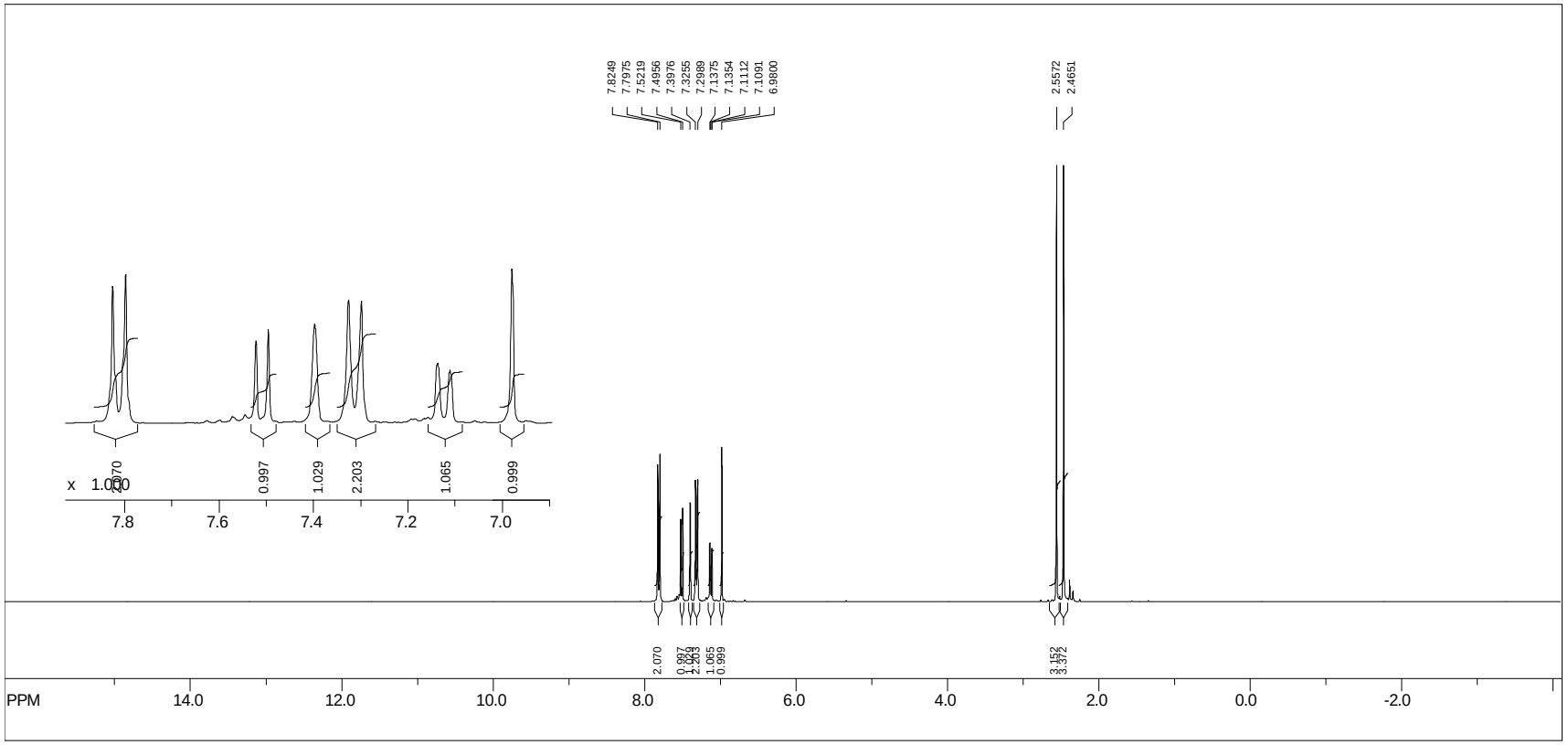
file: Z:\Laina\lmgxiv\lmgxiv_35a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methylphenyl)-6-methylbenzofuran (344)



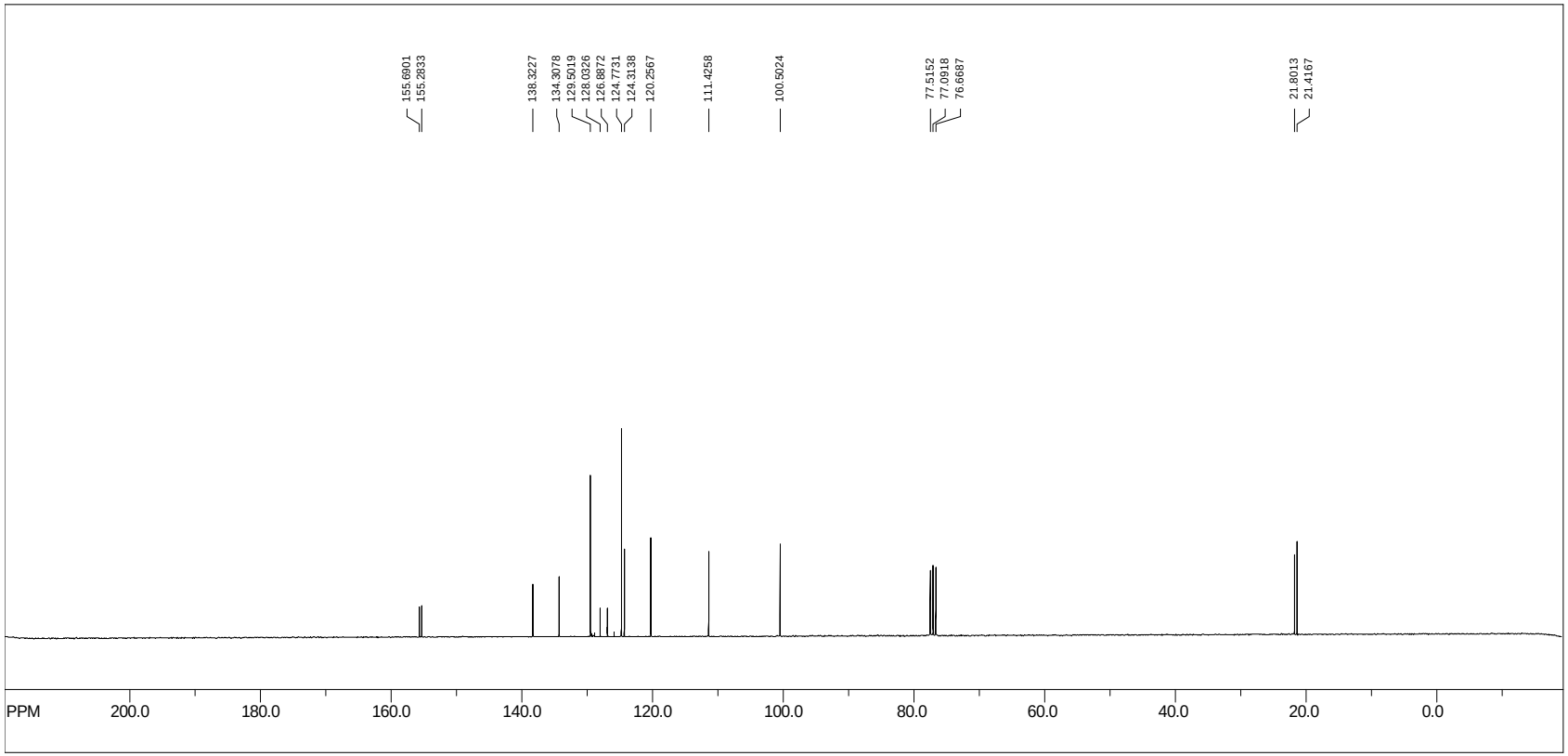
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



file: Z:\Laina\lmgxiv\lmgxiv_36a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

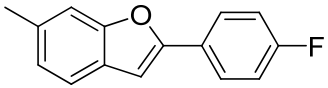
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



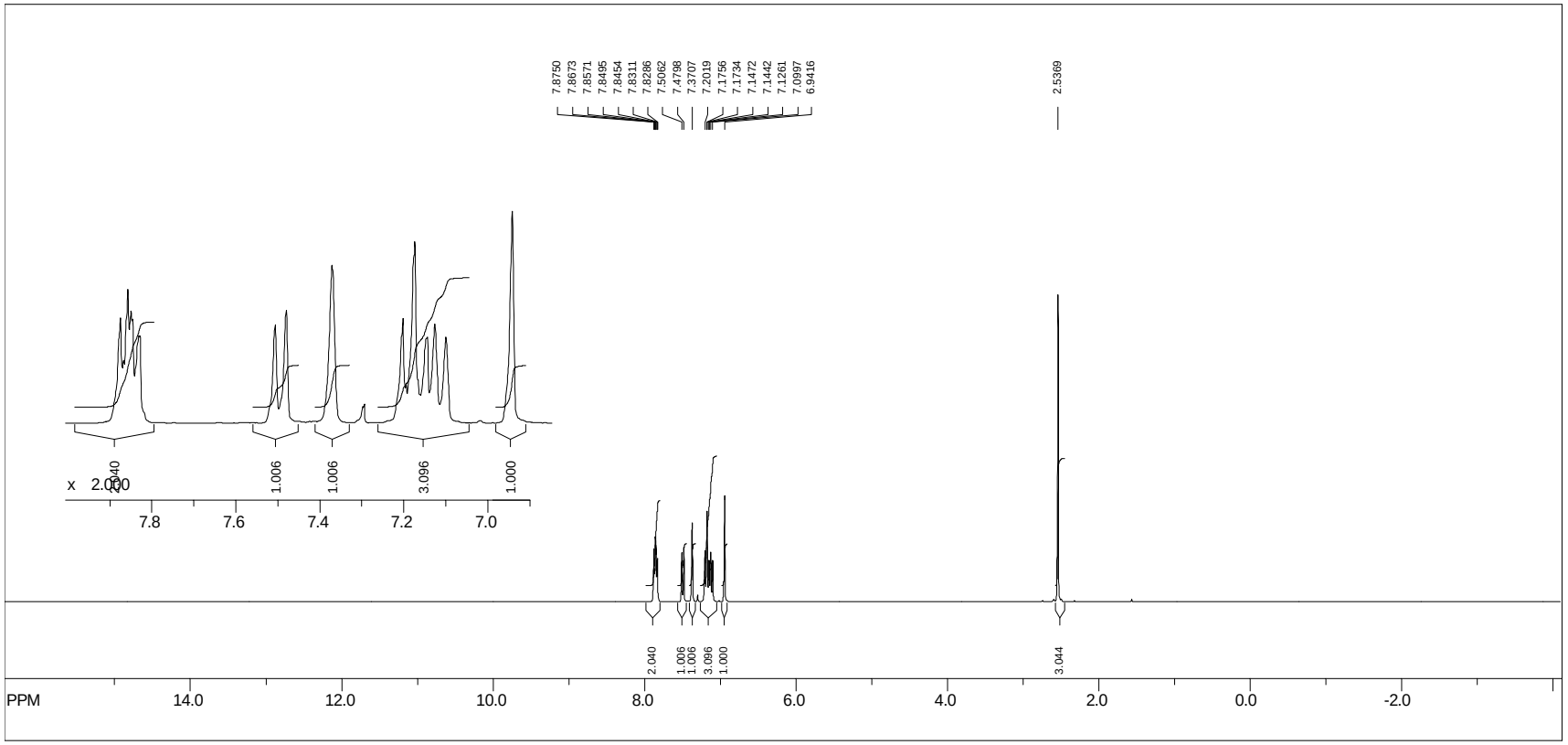
file: Z:\Laina\lmgxiv\lmgxiv_36a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 978

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Fluorophenyl)-6-methylbenzofuran (345)



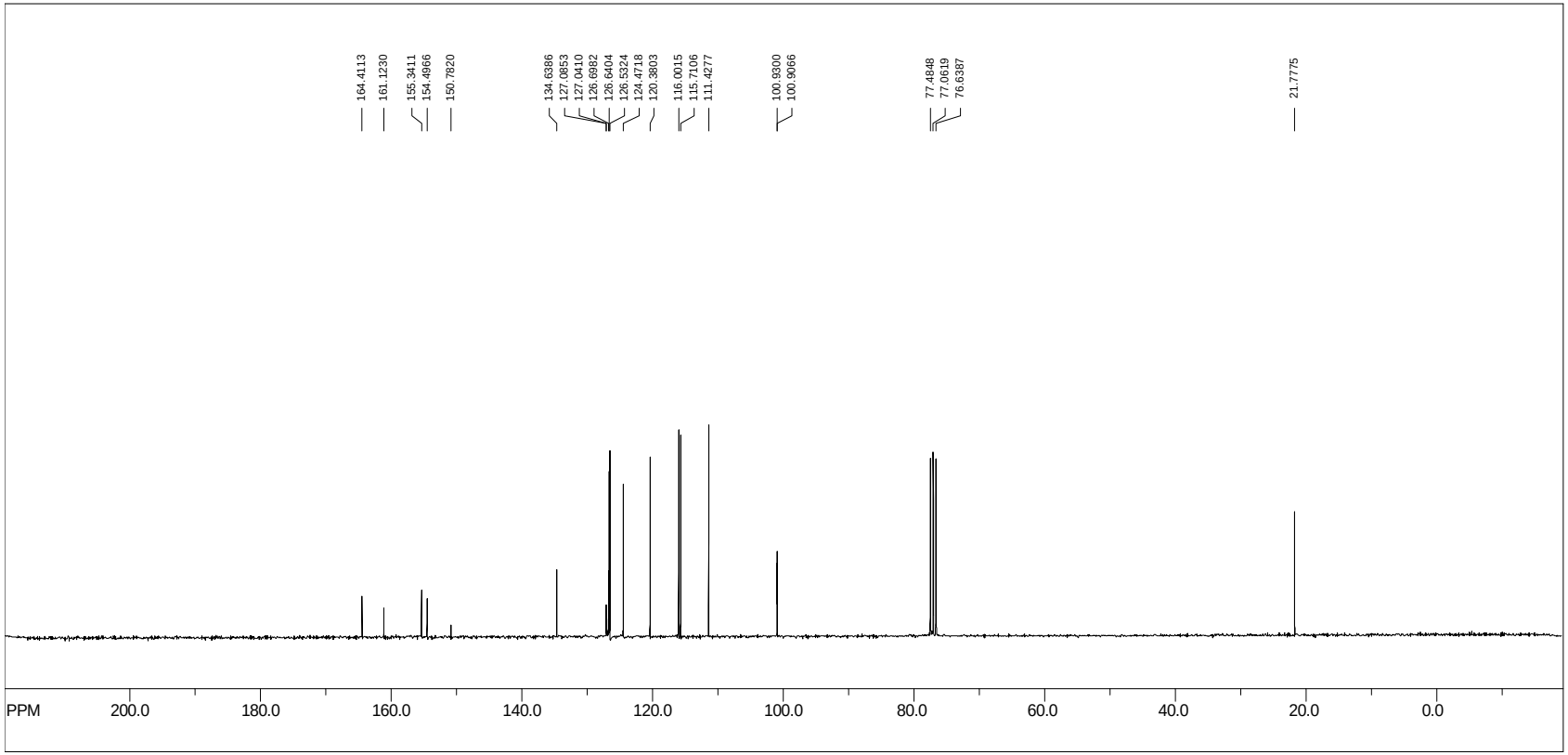
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



file: Z:\Laina\lmgxiv\lmgxiv_37a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

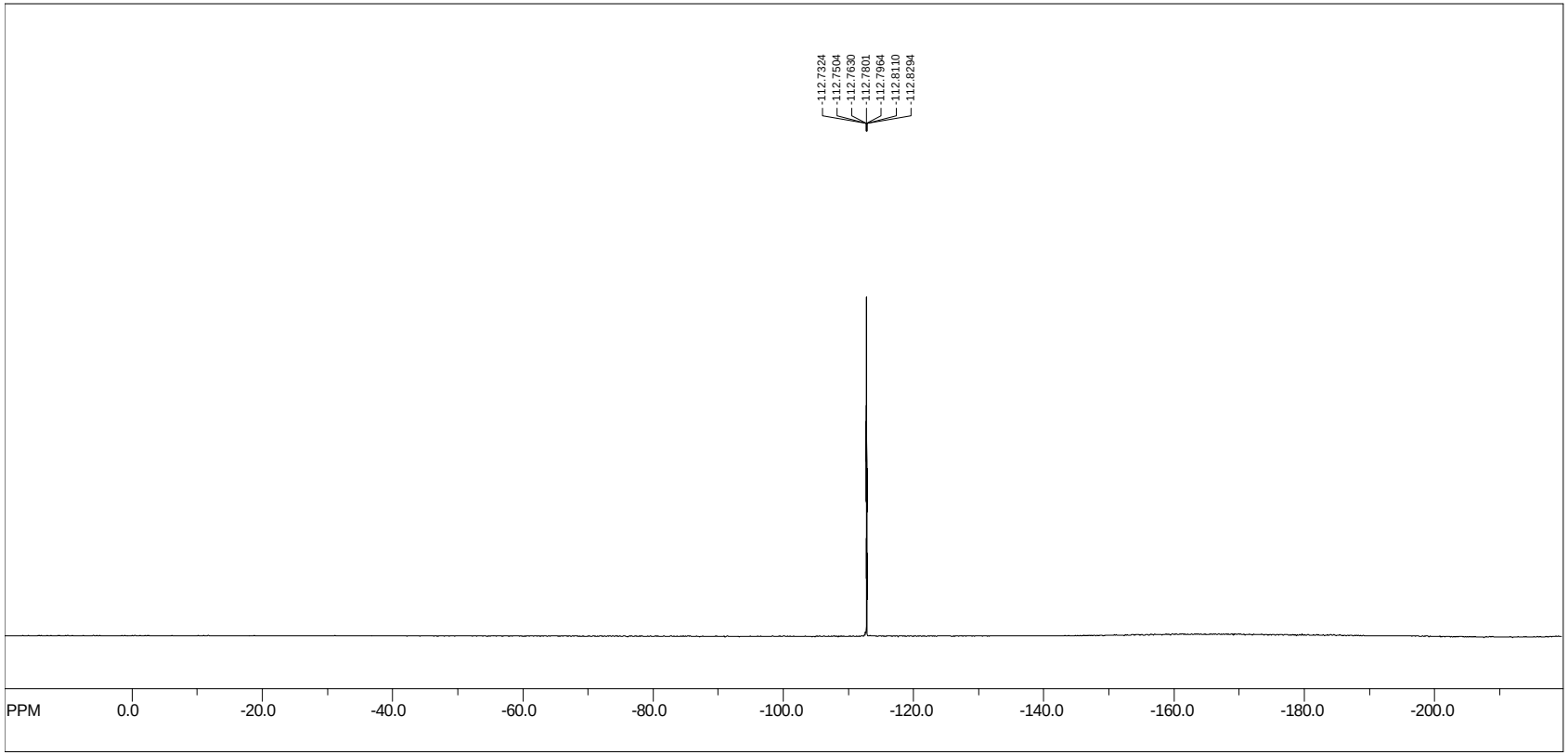
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxiv\lmgxiv_37a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 801

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

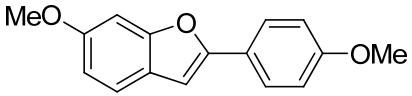
SpinWorks 2.5: F19 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



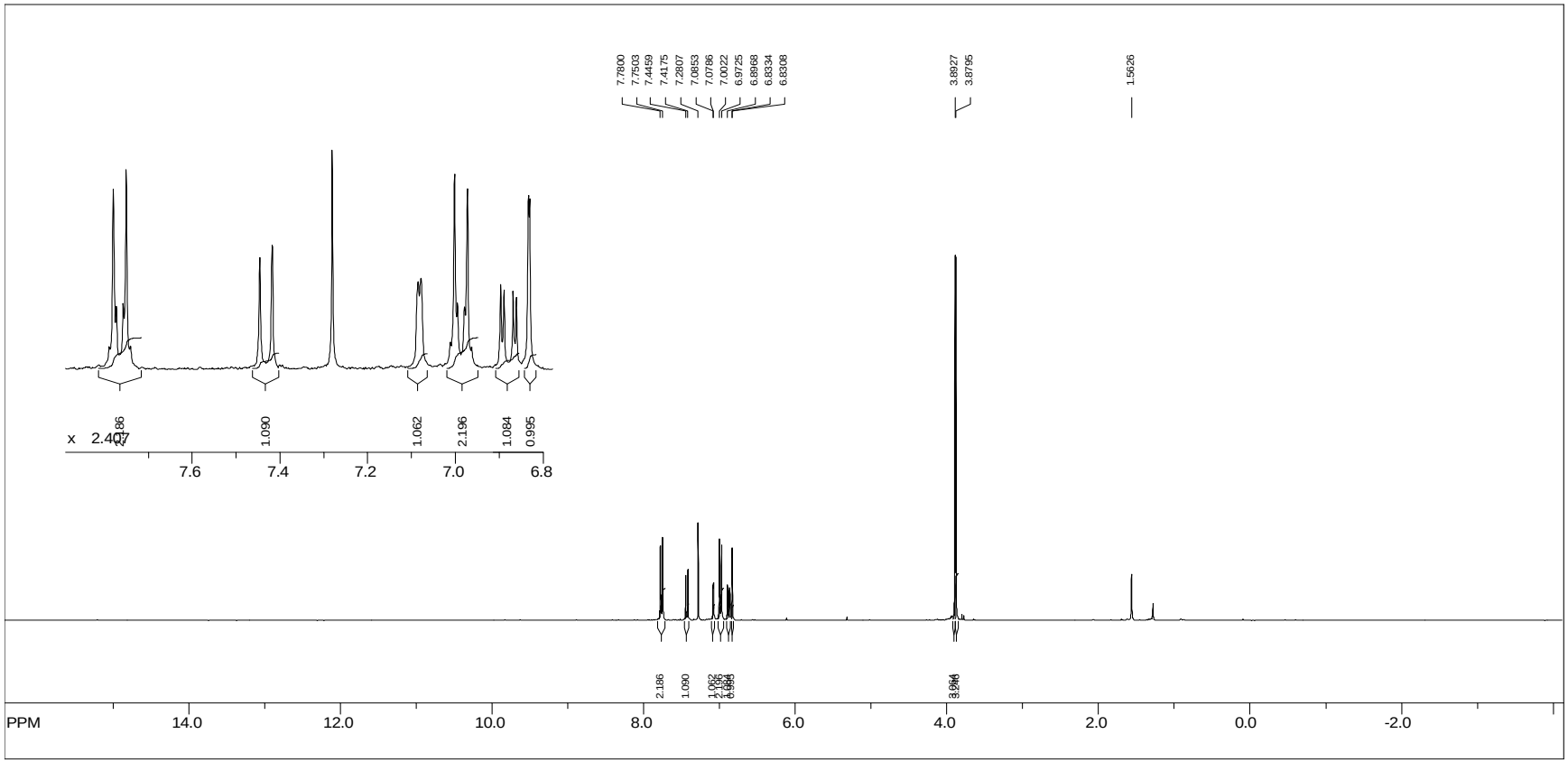
file: Z:\Laina\lmgxiv\lmgxiv_37a\2\fid expt: <zgflqn>
transmitter freq.: 282.376115 MHz
time domain size: 131072 points
width: 67567.57 Hz = 239.282163 ppm = 0.515500 Hz/pt
number of scans: 16

freq. of 0 ppm: 282.404355 MHz
processed size: 65536 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-6-methoxybenzofuran (346)



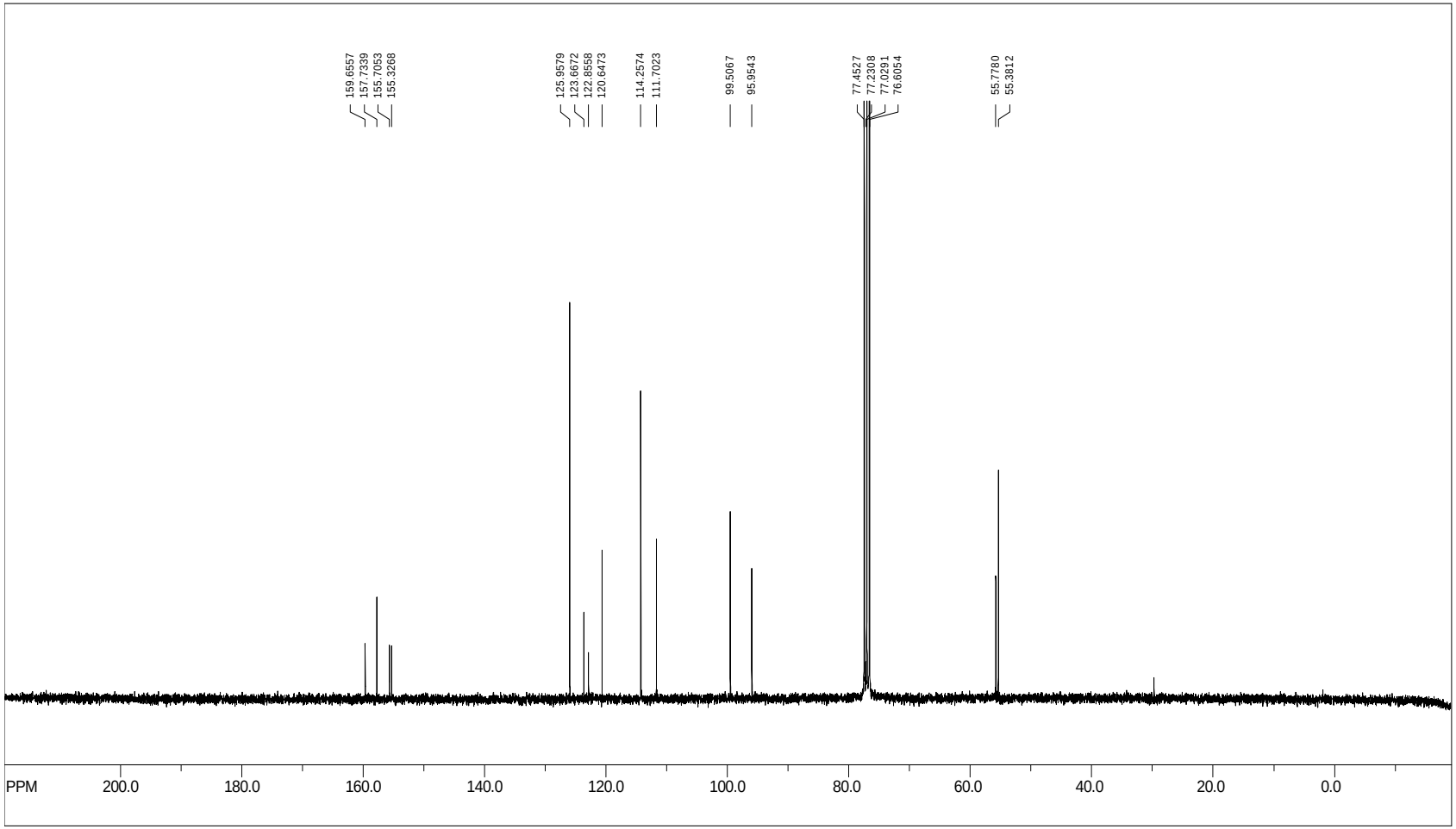
SpinWorks 2.5: fractions 14-18



file: Z:\Laina\lmgix\lmgix_45d\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

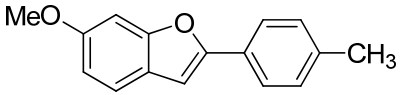
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



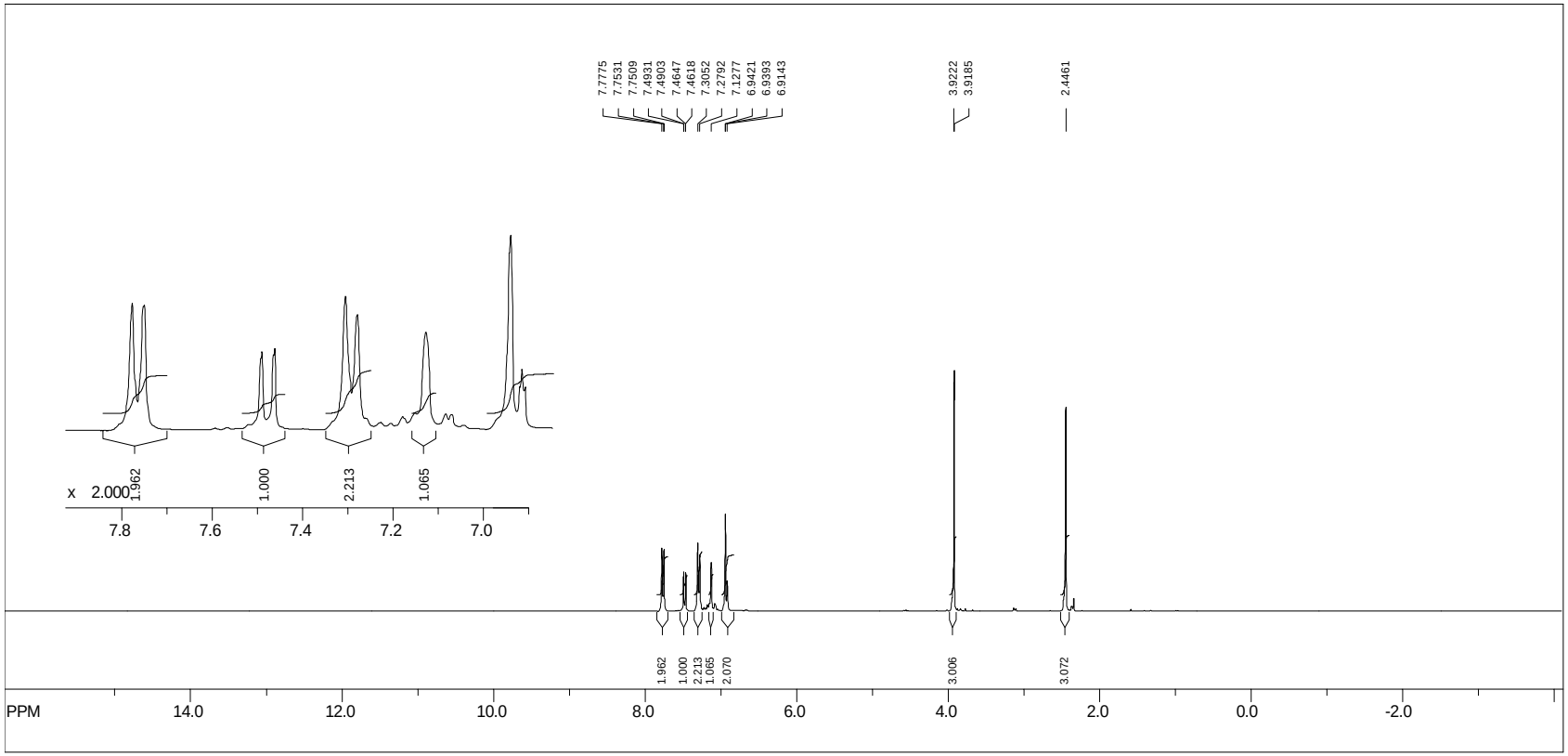
file: Z:\Laina\lmgix\lmgix_45d\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4096

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methylphenyl)-6-methoxybenzofuran (347)



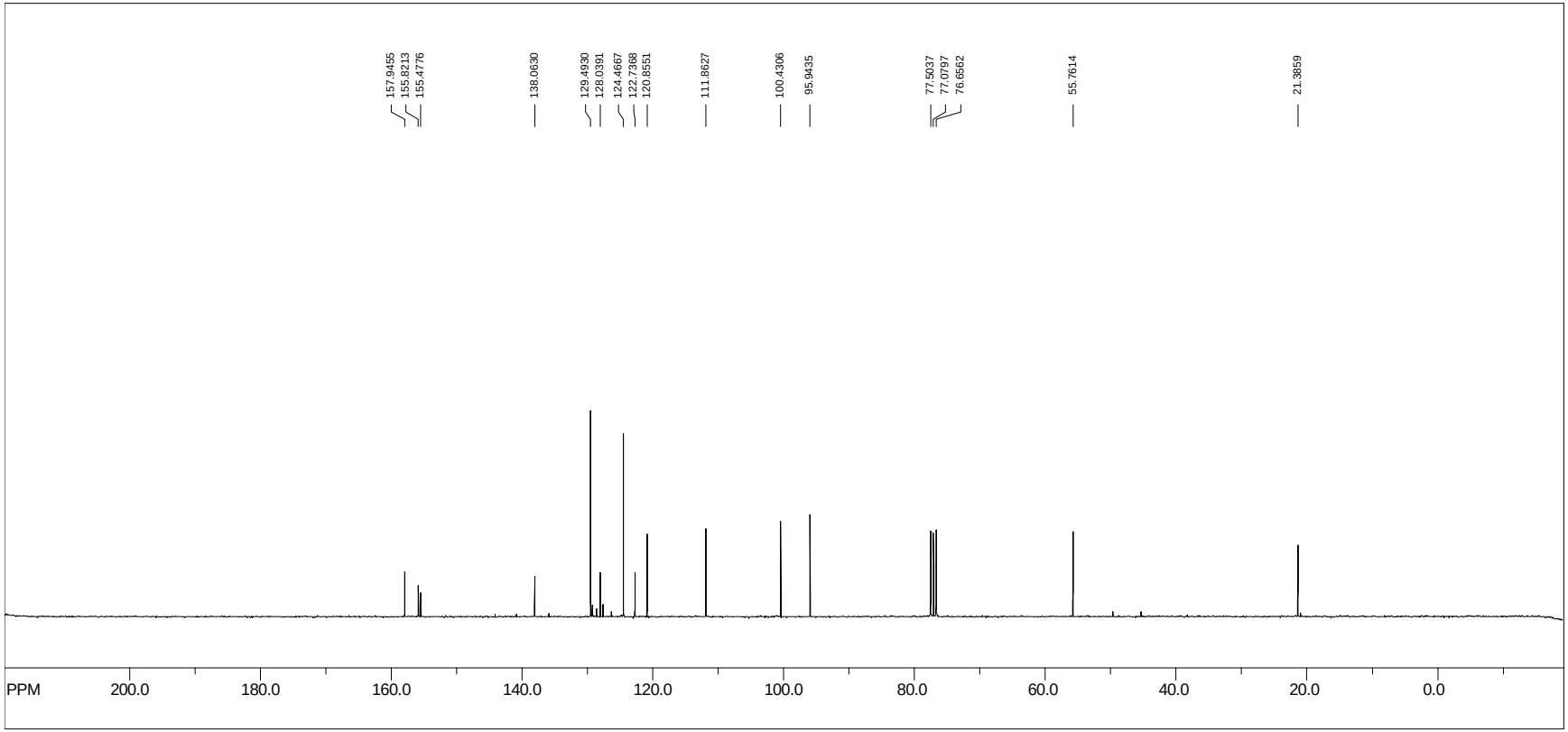
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxiv\lmgxiv_52b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

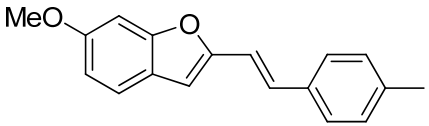
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



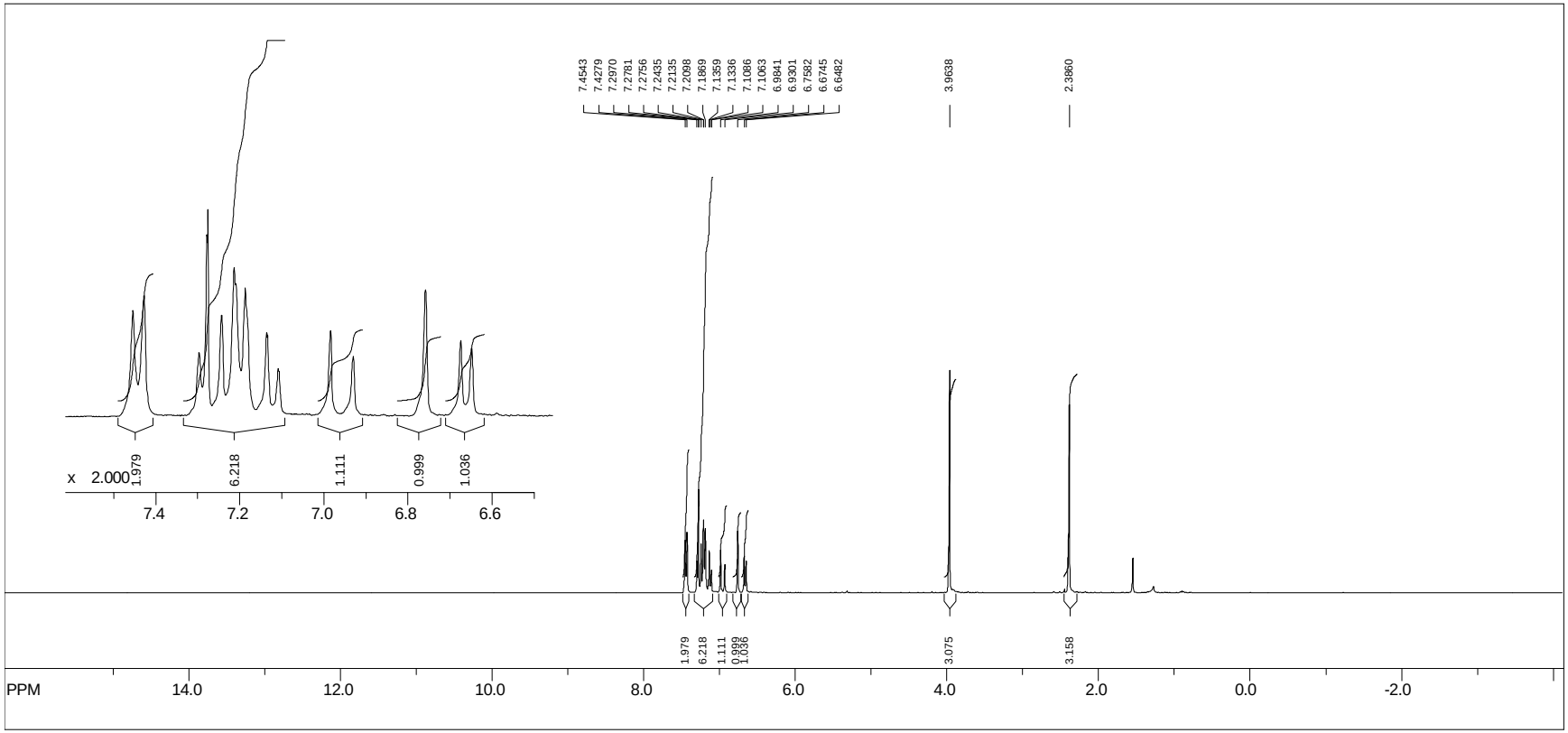
file: Z:\Laina\lmgxiv\lmgxiv_52b\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(2-*trans*-(4-Methylphenyl)ethenyl)-6-methylbenzofuran (348)



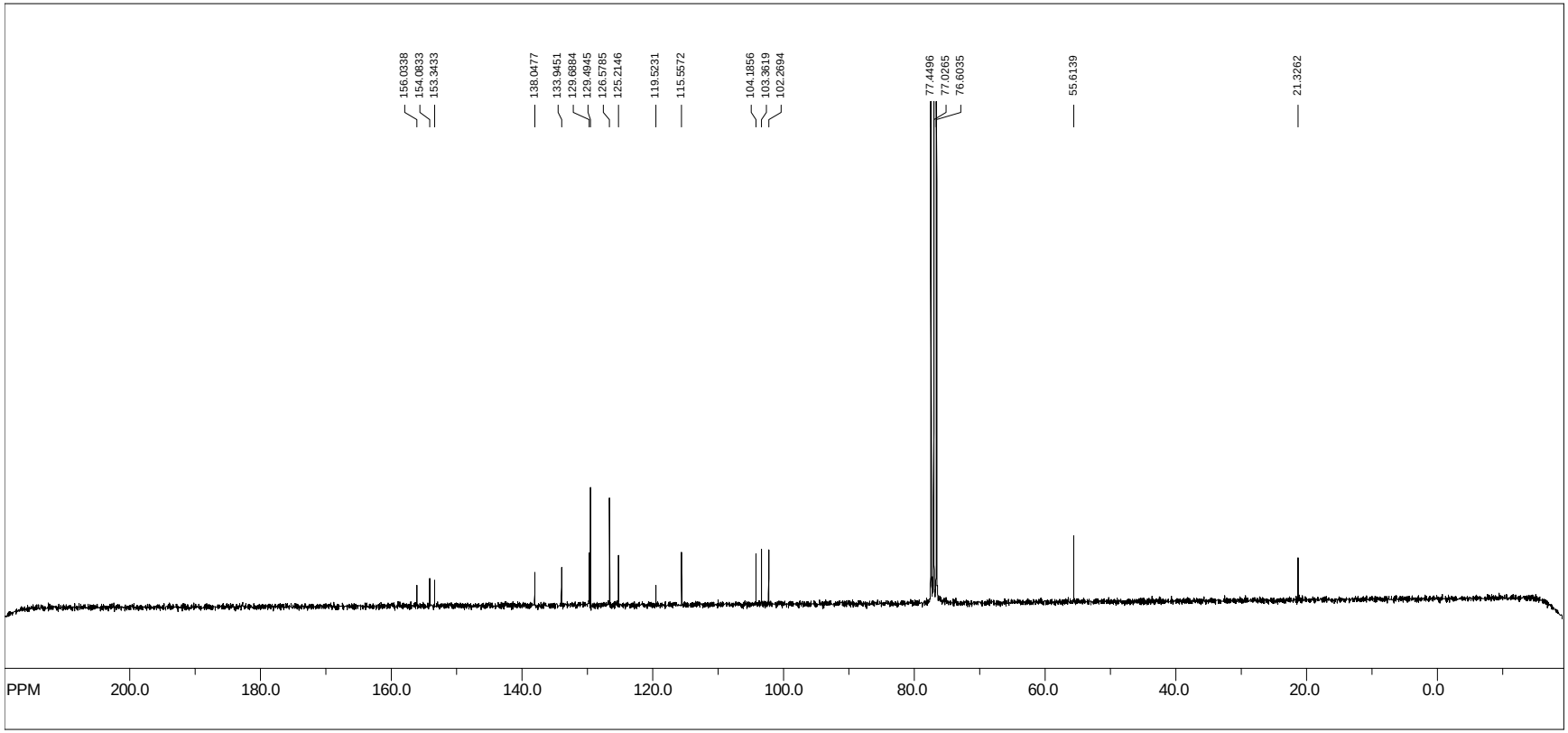
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgxiv\lmgxiv_55a\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

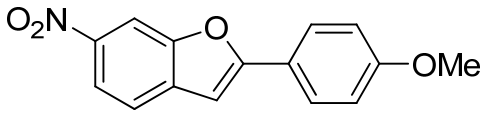
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



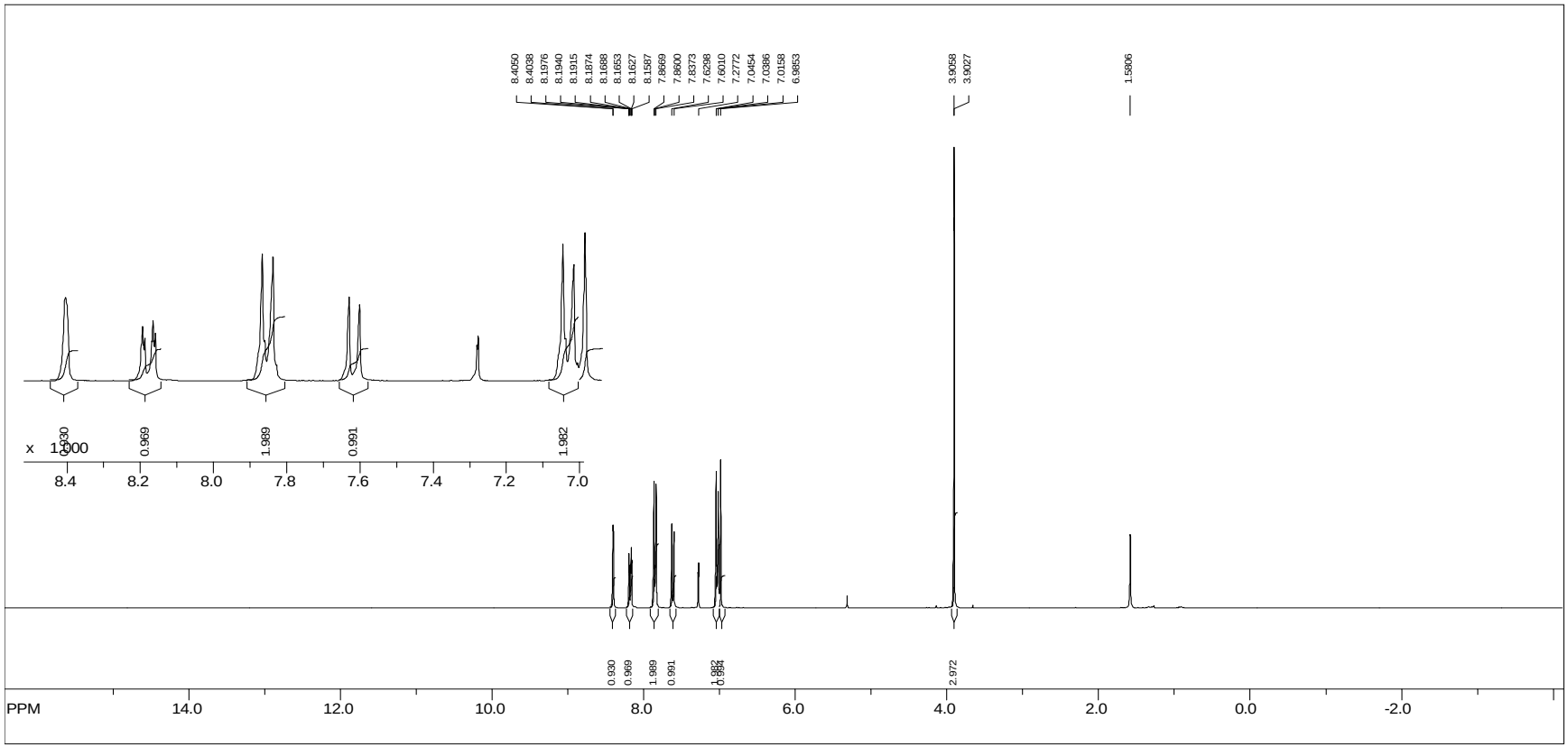
file: Z:\Laina\lmgxiv\lmgxiv_55a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 10000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-6-nitro-benzofuran (349)



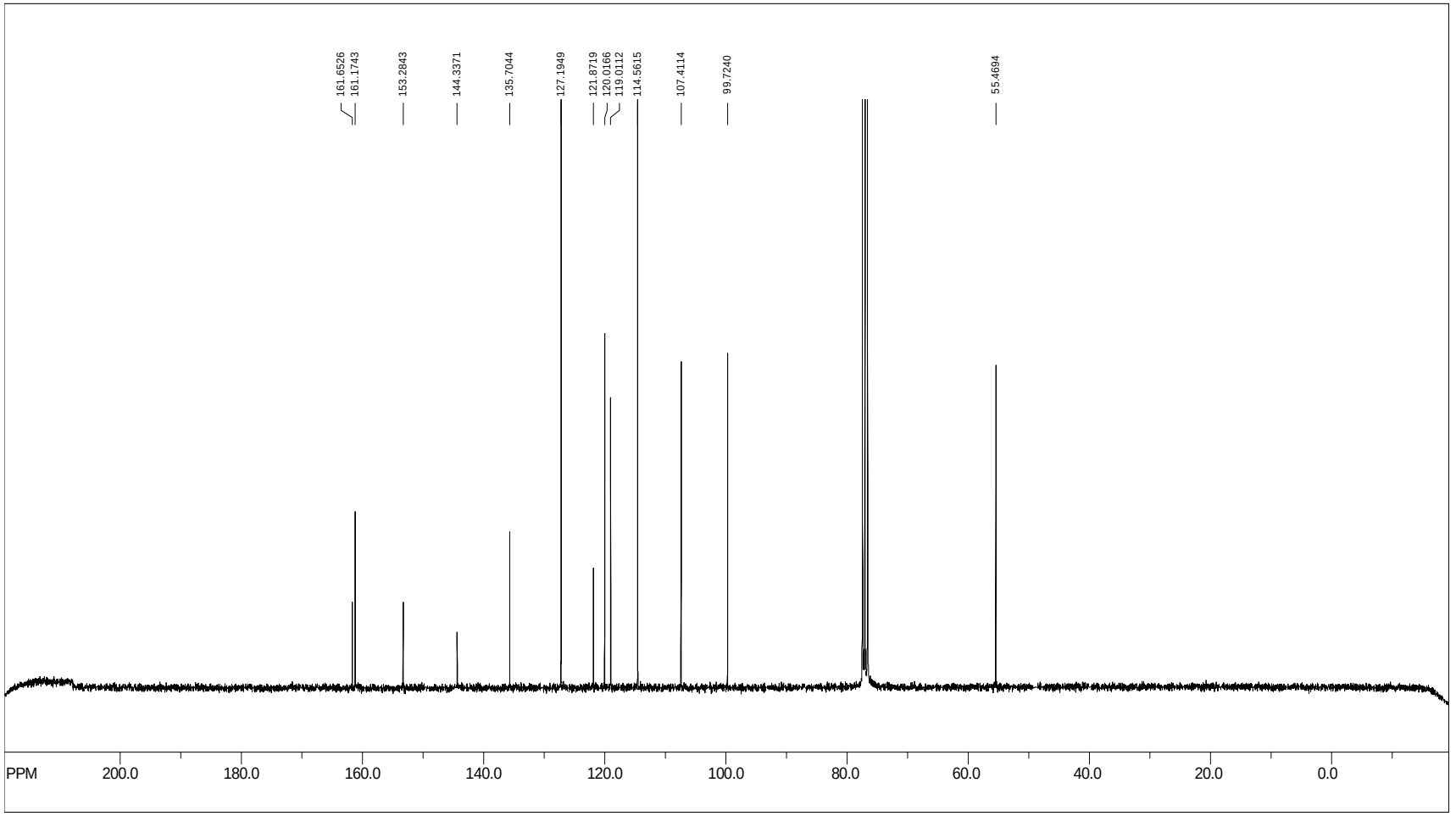
SpinWorks 2.5: major component



file: Z:\Laina\lmgx\lmgx_44b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

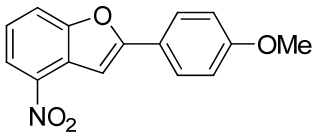
SpinWorks 2.5: benzofuran from m-nitrophenol and p-methoxyboronic acid



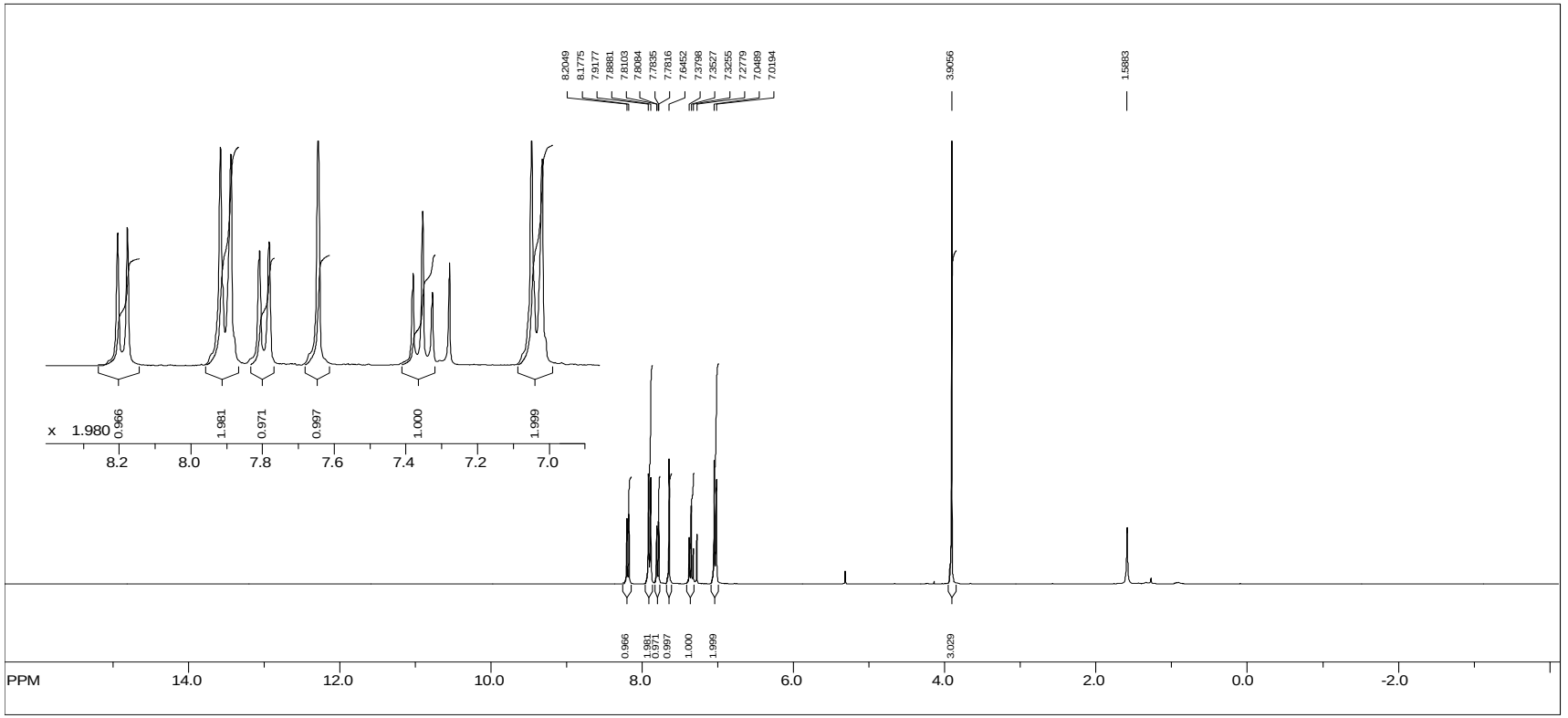
file: C:\Users\Laina\Documents\WORK\NMR\lmgix\lmgix_46d\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 9148

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-4-nitro-benzofuran (350)



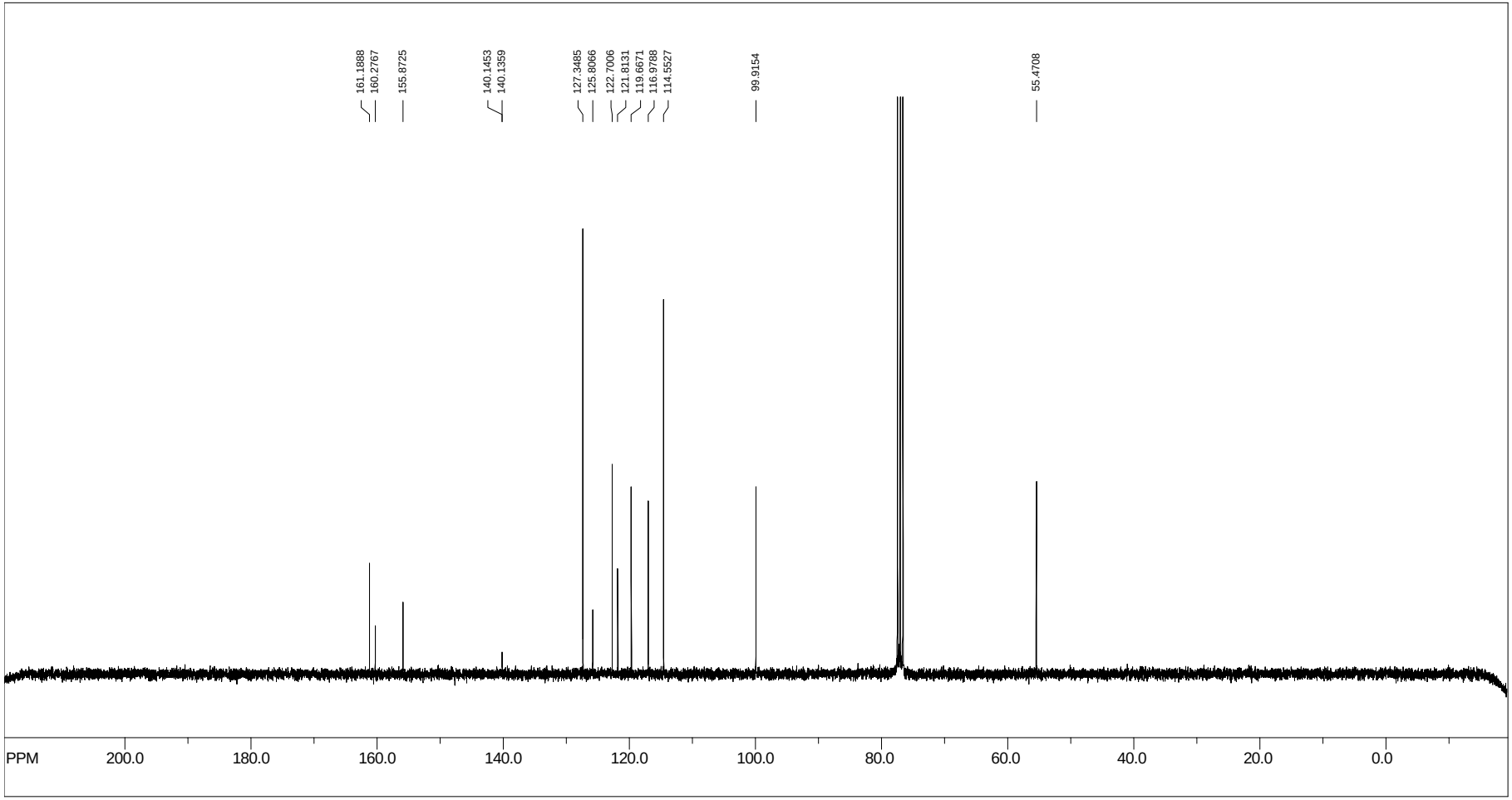
SpinWorks 2.5: minor component



file: Z:\Laina\lmgx\lmgx_44a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

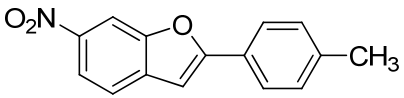
SpinWorks 2.5: minor component



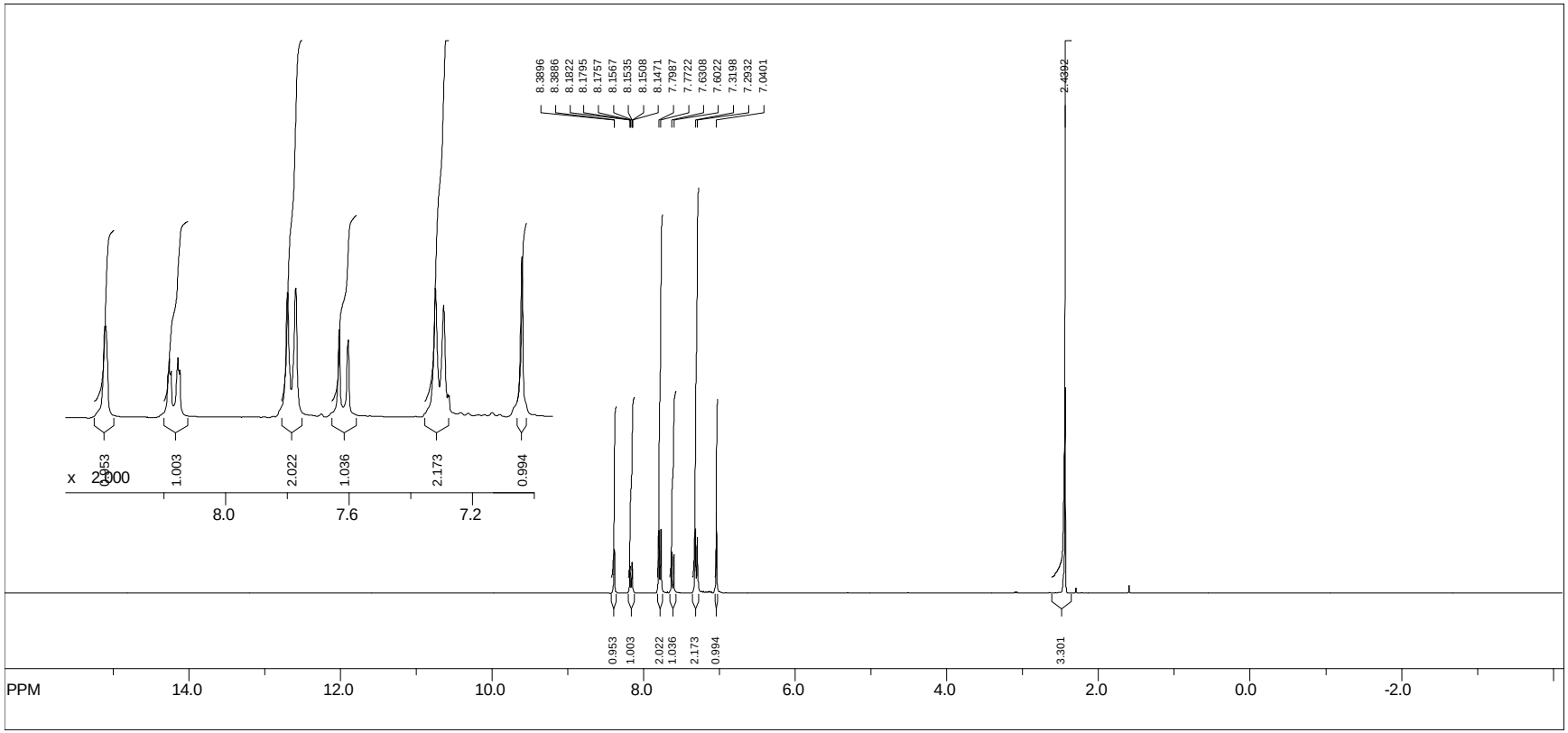
file: C:\Users\Laina\Documents\WORK\NMR\lmgx\lmgx_44a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 2048

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methylphenyl)-6-nitro-benzofuran (351)



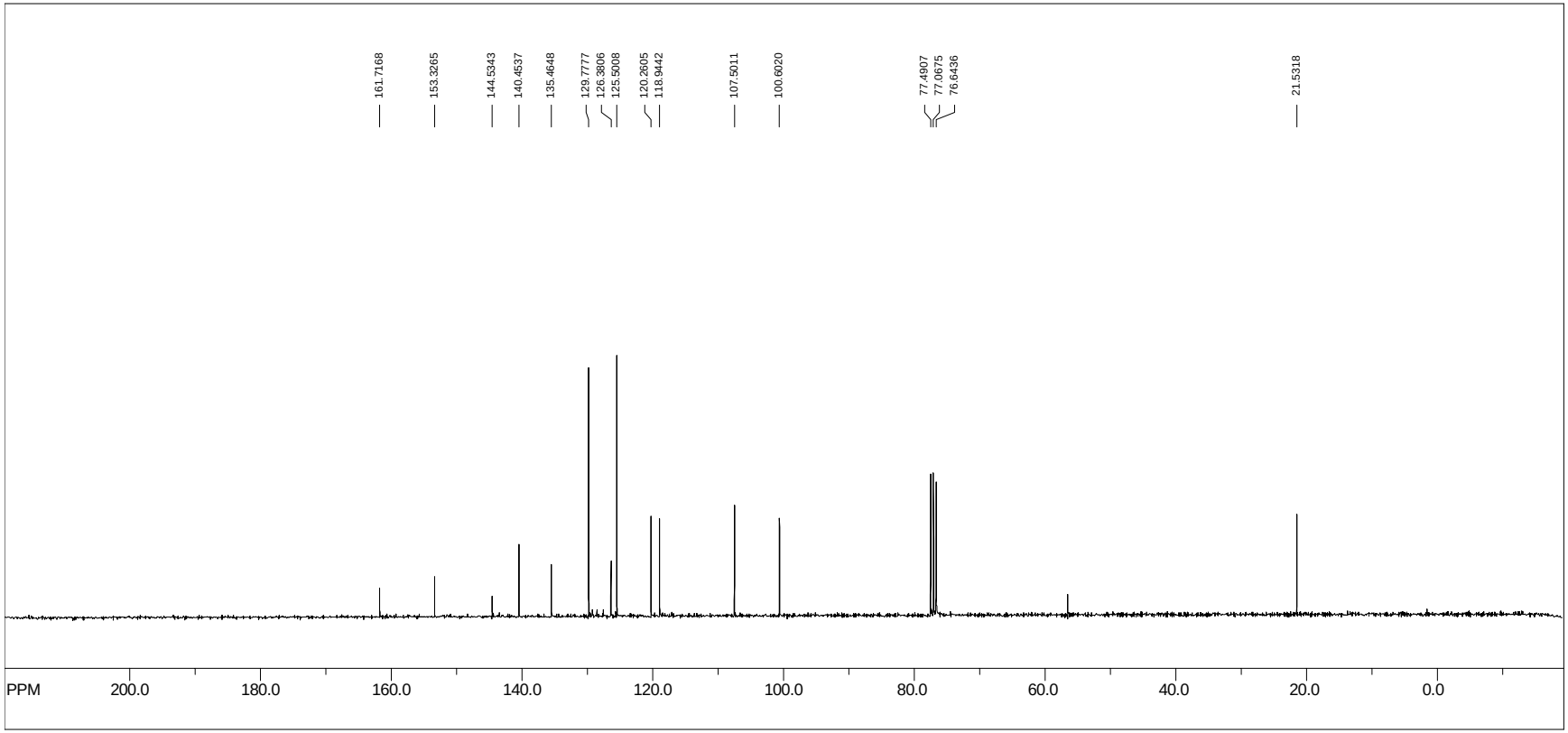
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



file: Z:\Laina\lmgxiii\lmgxiii_94b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

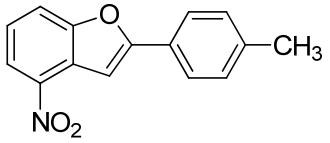
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



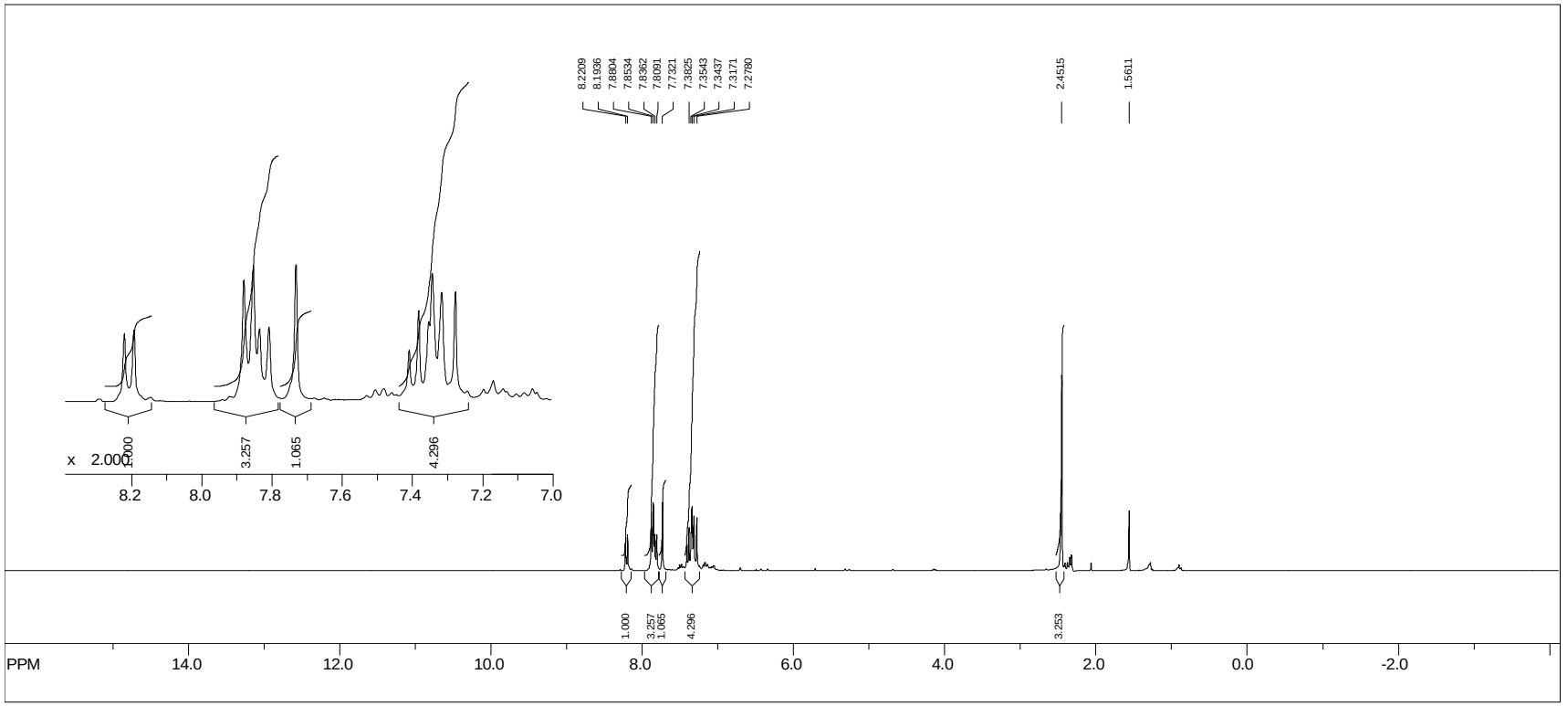
file: Z:\Laina\lmgxiii\lmgxiii_94b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methylphenyl)-4-nitro-benzofuran (352)



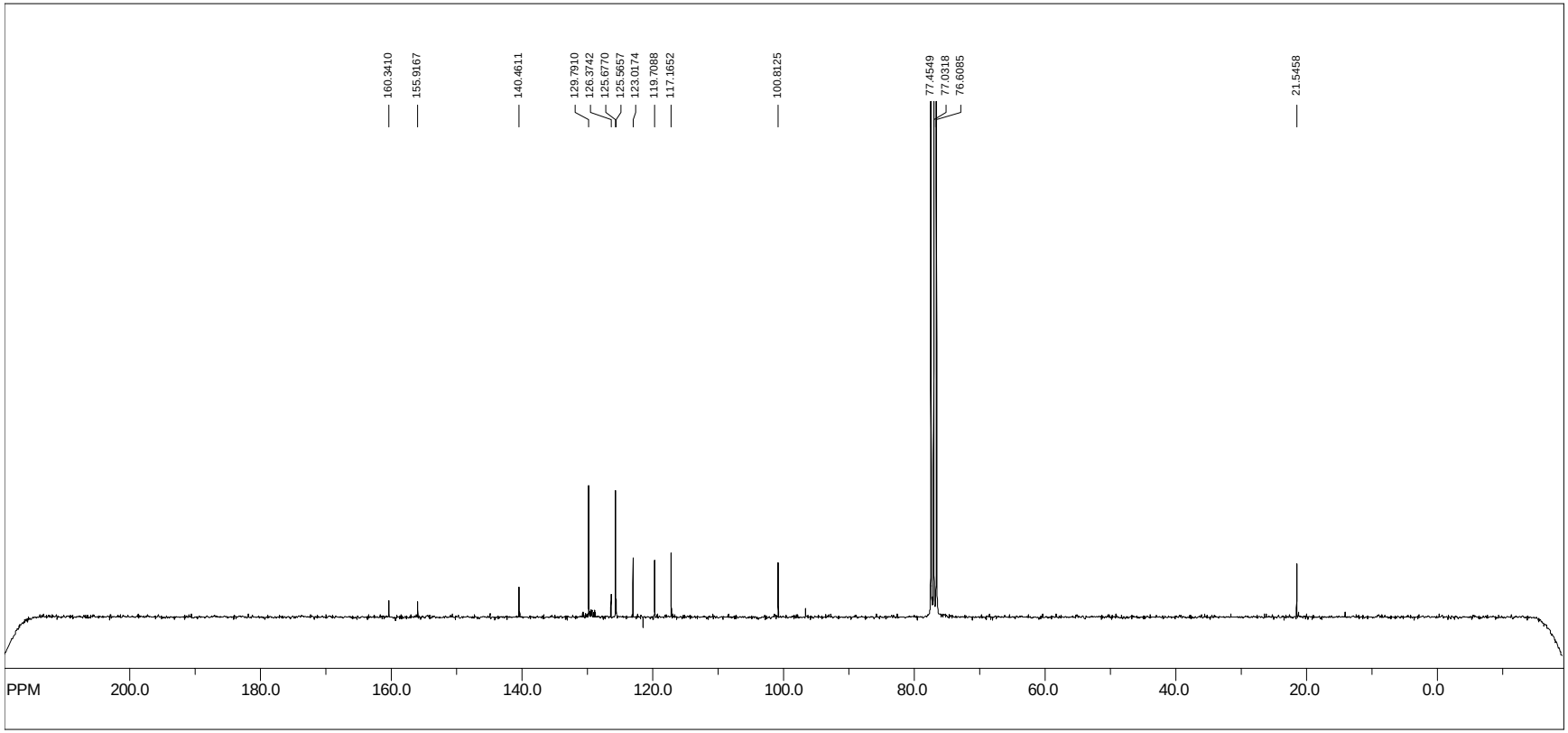
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 12



file: Z:\Laina\lmgxiii\lmgxiii_94a\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

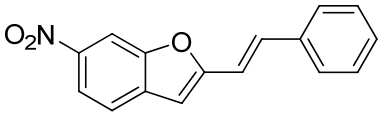
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 12



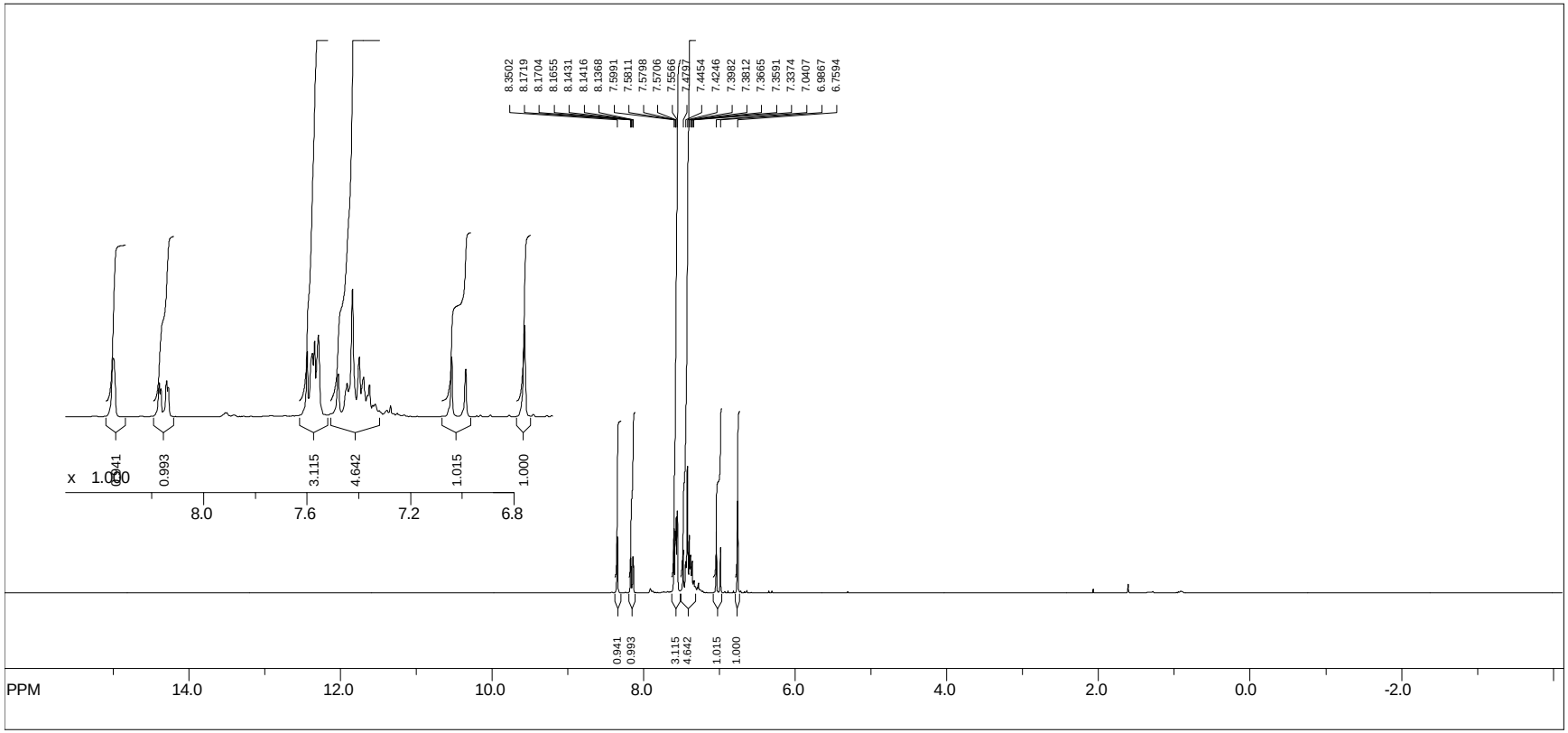
file: Z:\Laina\lmgxiii\lmgxiii_94a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4096

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(trans-Phenylethenyl)-6-nitro-benzofuran (353)



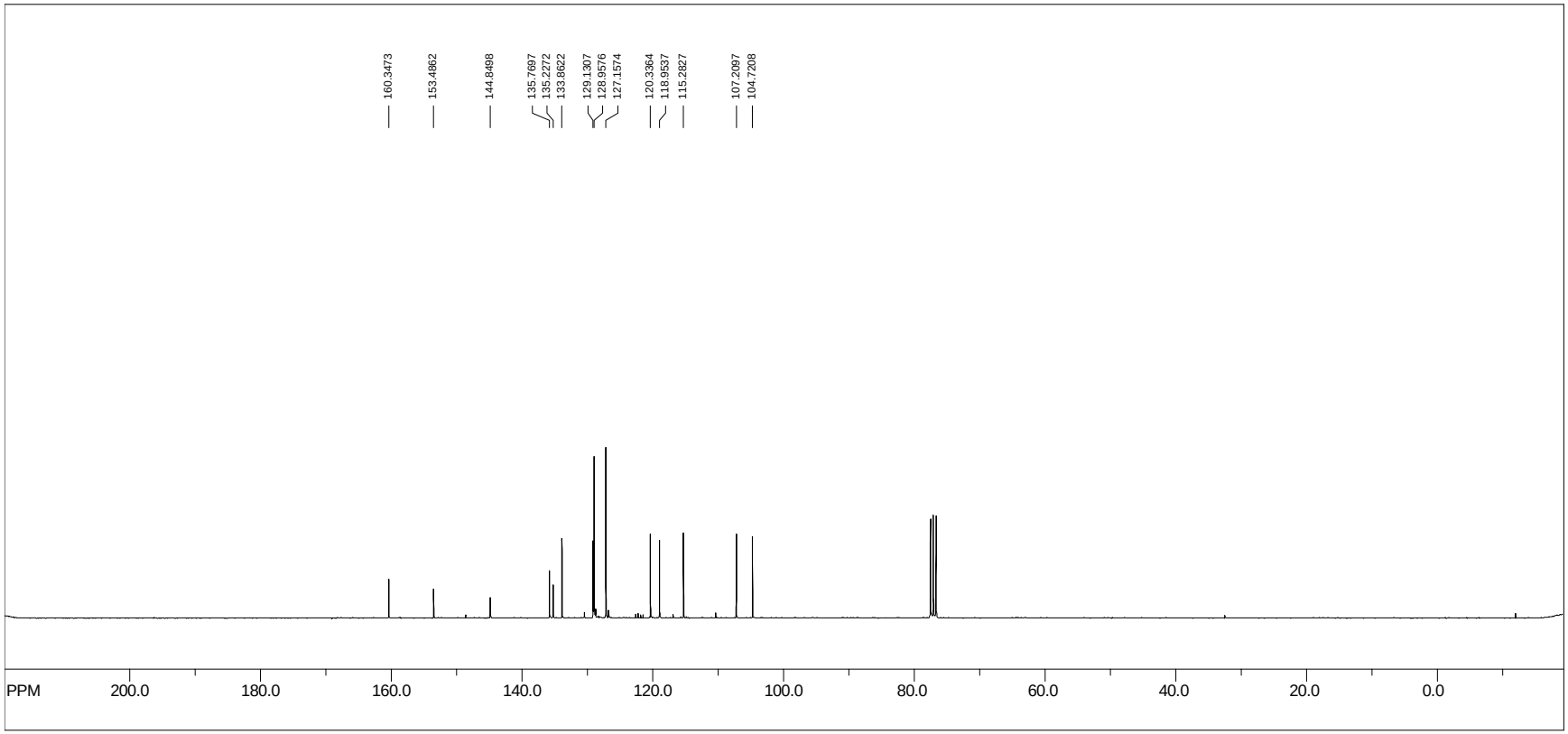
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgxiii\lmgxiii_97c\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

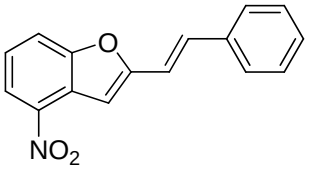
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



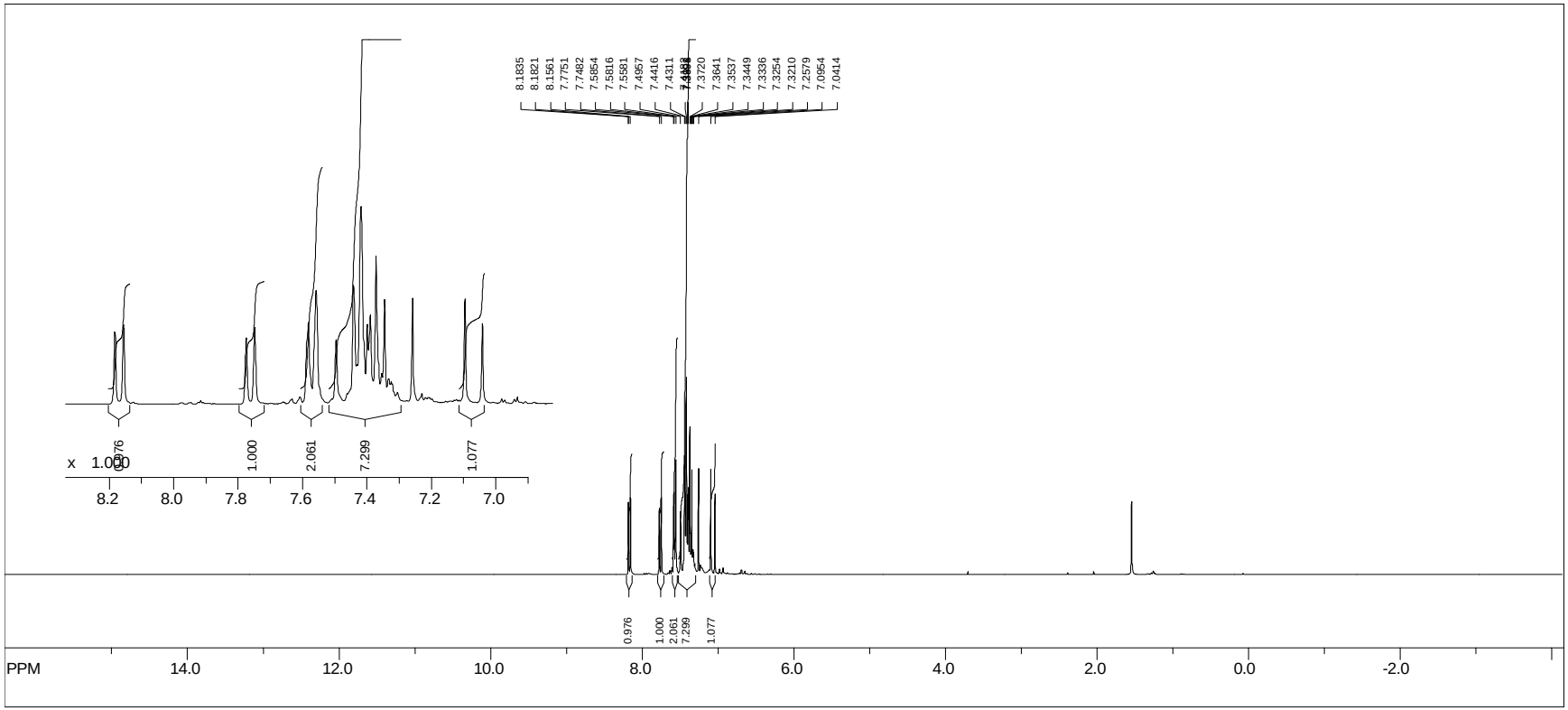
file: Z:\Laina\lmgxiii\lmgxiii_97c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(trans-Phenylethenyl)-4-nitro-benzofuran (354)



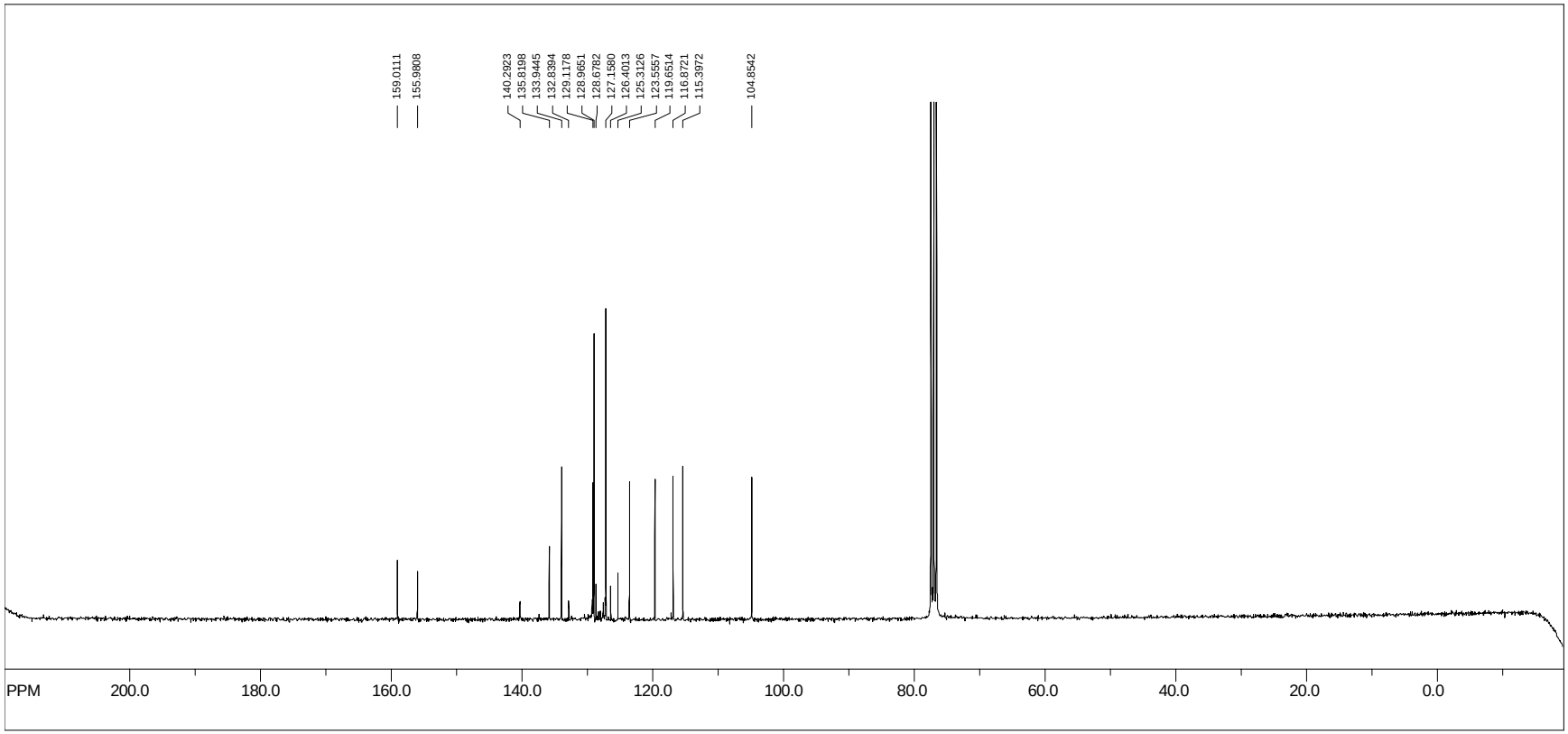
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



file: Z:\Laina\lmgxiii\lmgxiii_97ai\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

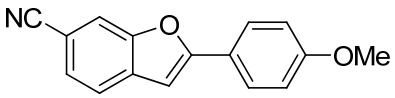
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



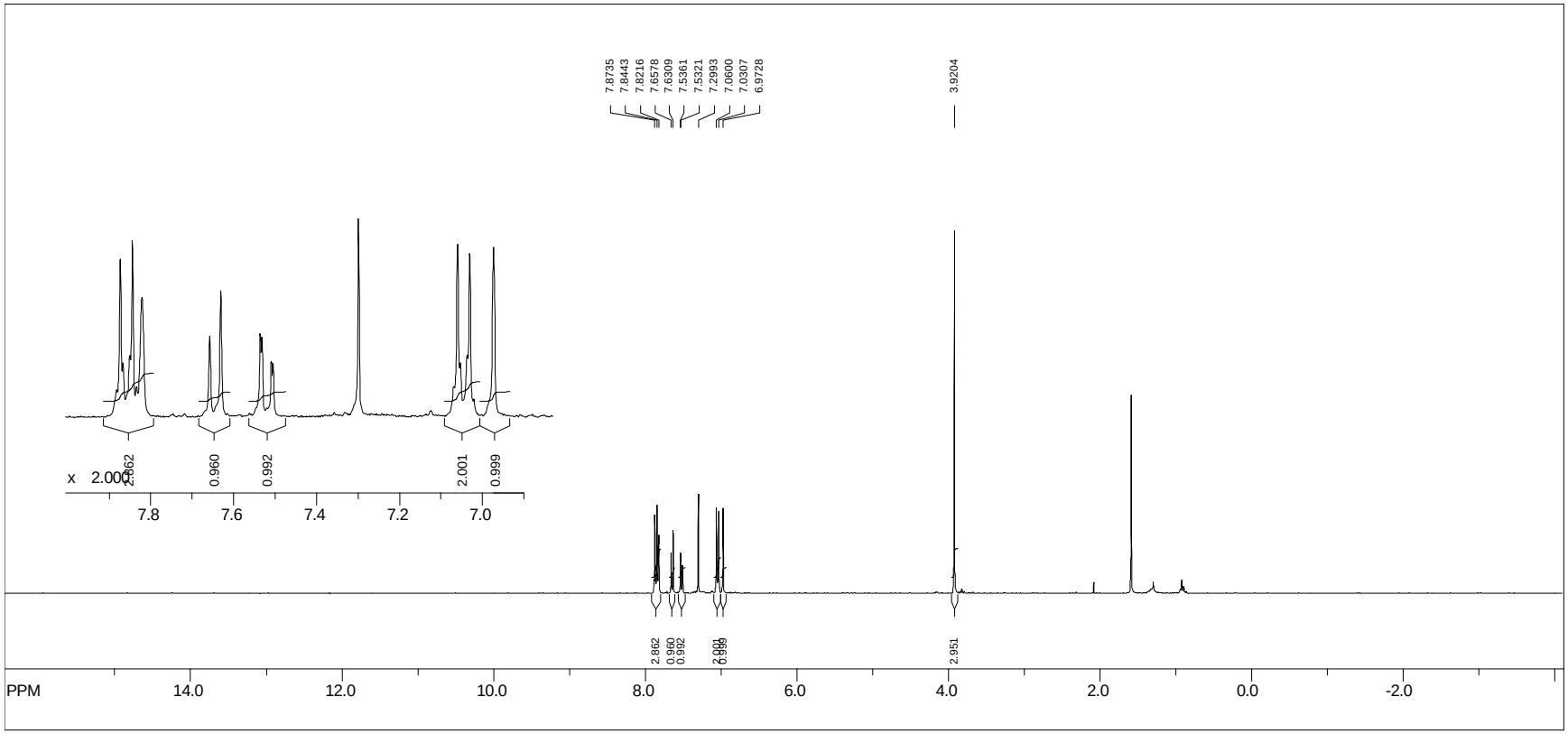
file: Z:\Laina\lmgxiii\lmgxiii_97ai\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 10000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(4-Methoxyphenyl)-6-cyano-benzofuran (355)



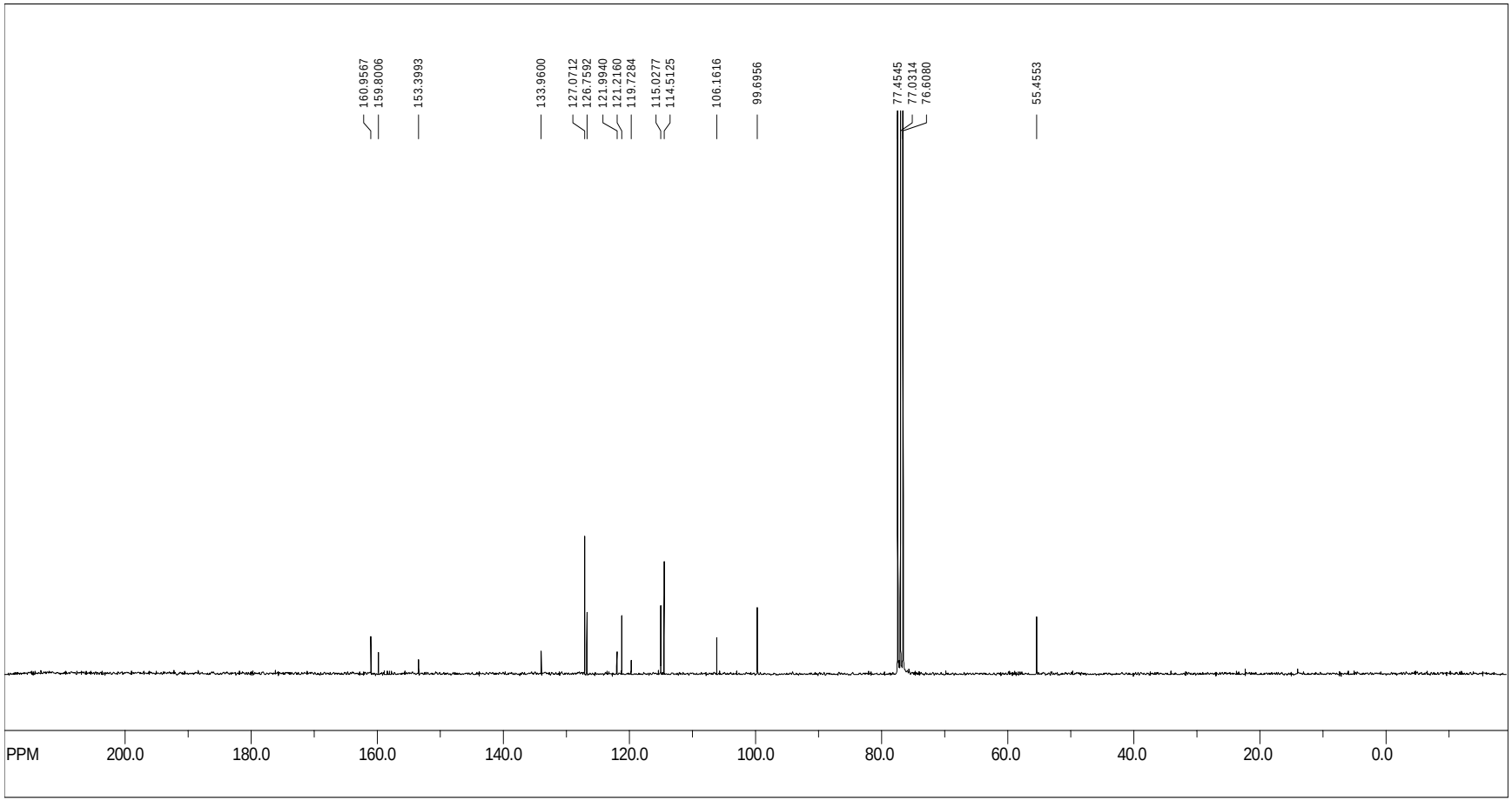
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgx\lmgxv_46bii\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

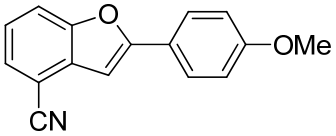
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



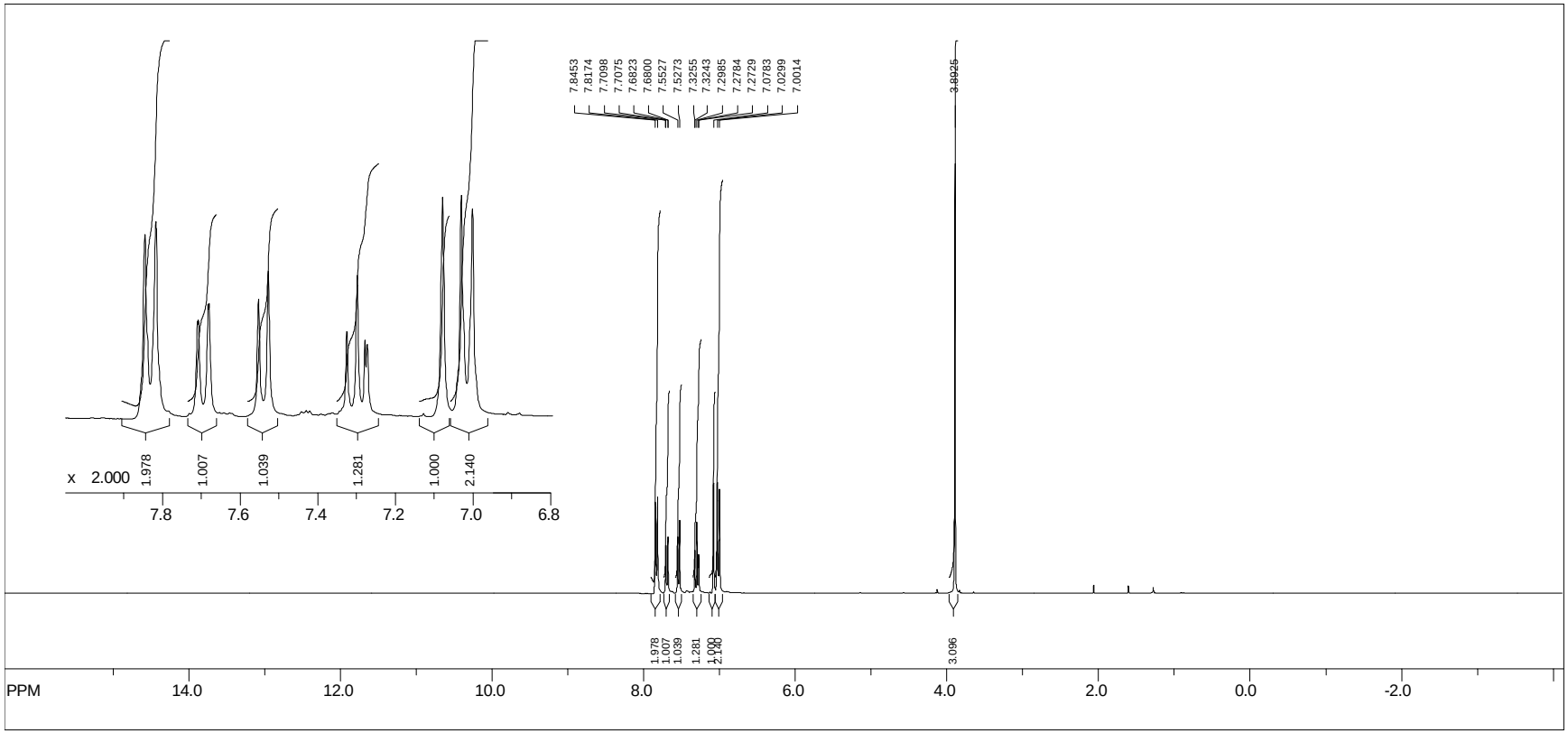
file: Z:\Laina\lmgw\lmgw_46bii\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 8000

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-4-cyano-benzofuran (356)



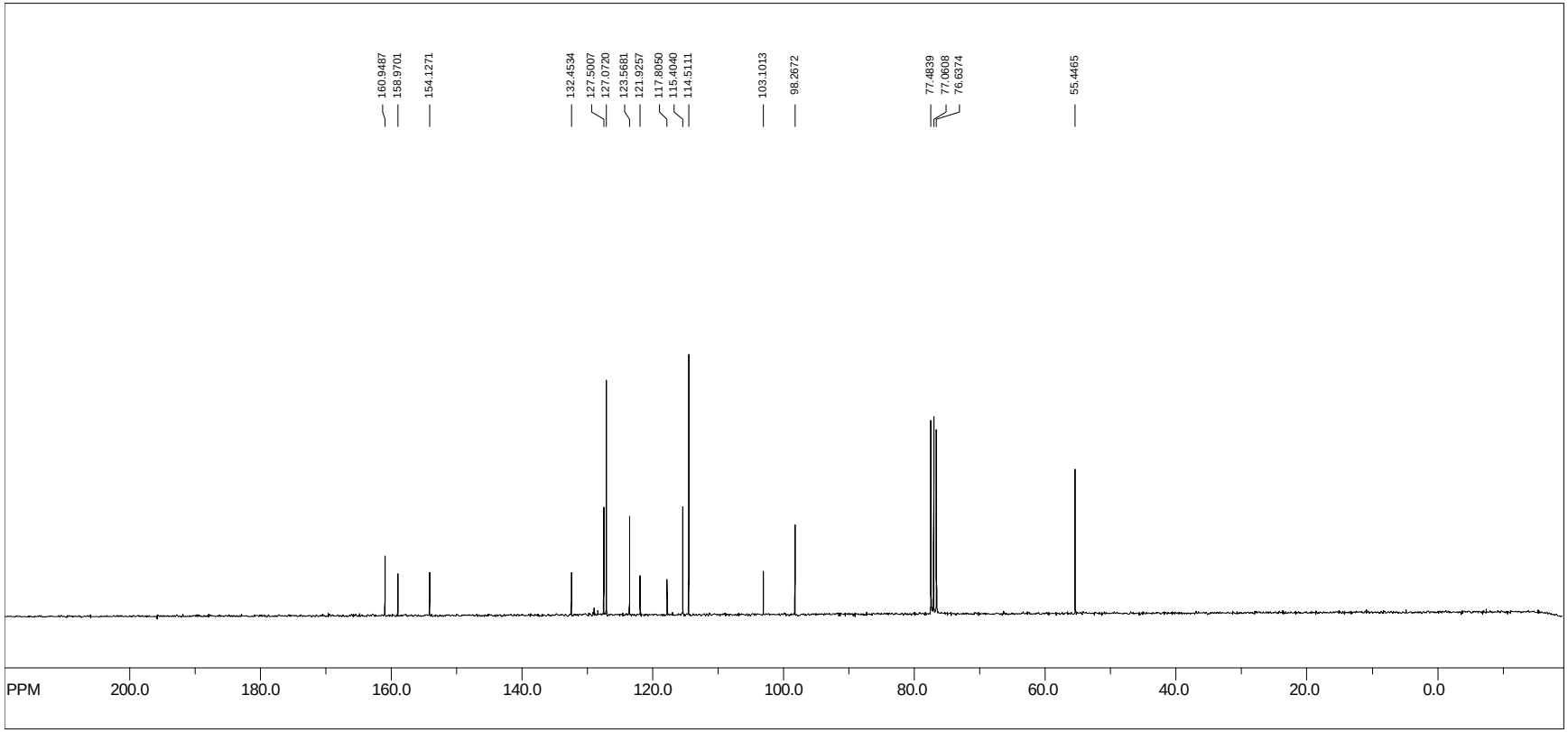
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxv\lmgxv_46a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

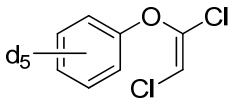
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



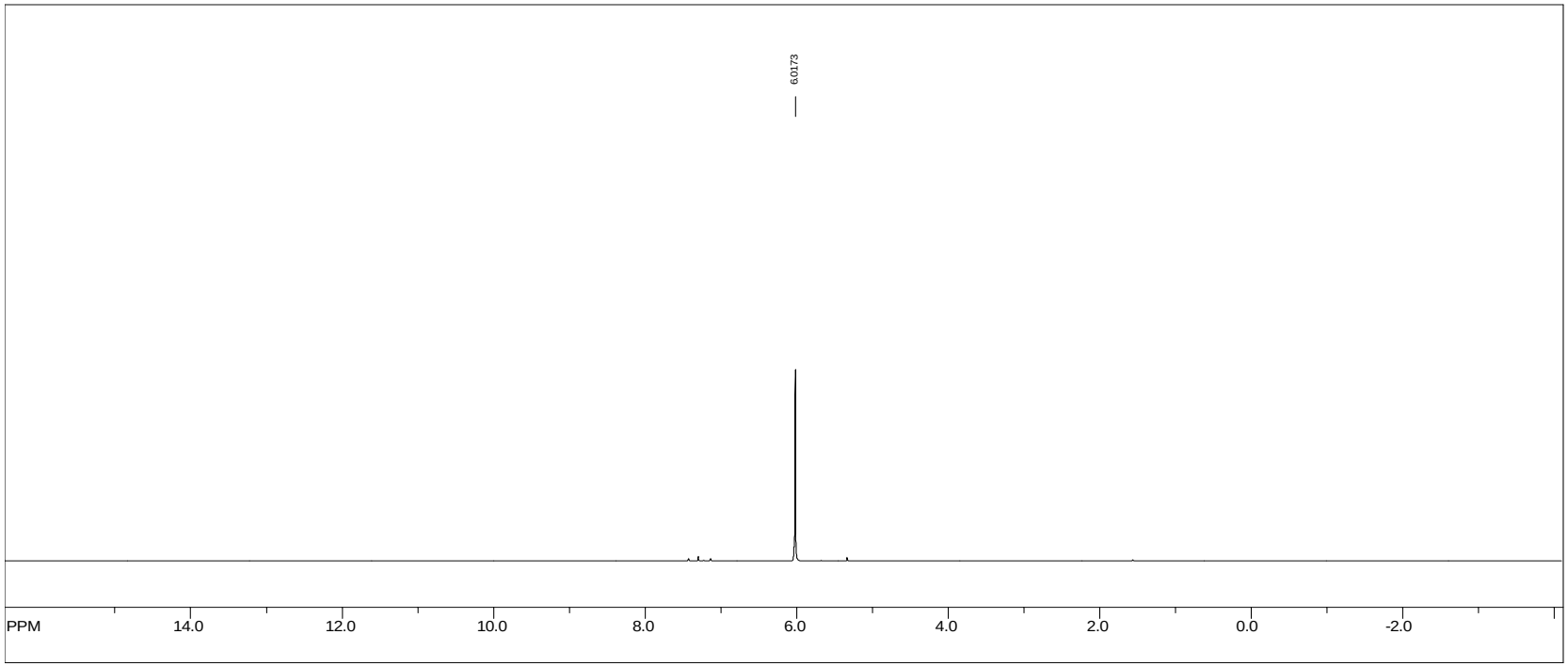
file: Z:\Laina\lmgxv\lmgxv_46a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1500

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(E)-(1,2-Dichlorovinyloxy)pentadeuterobenzene (93-d_5)



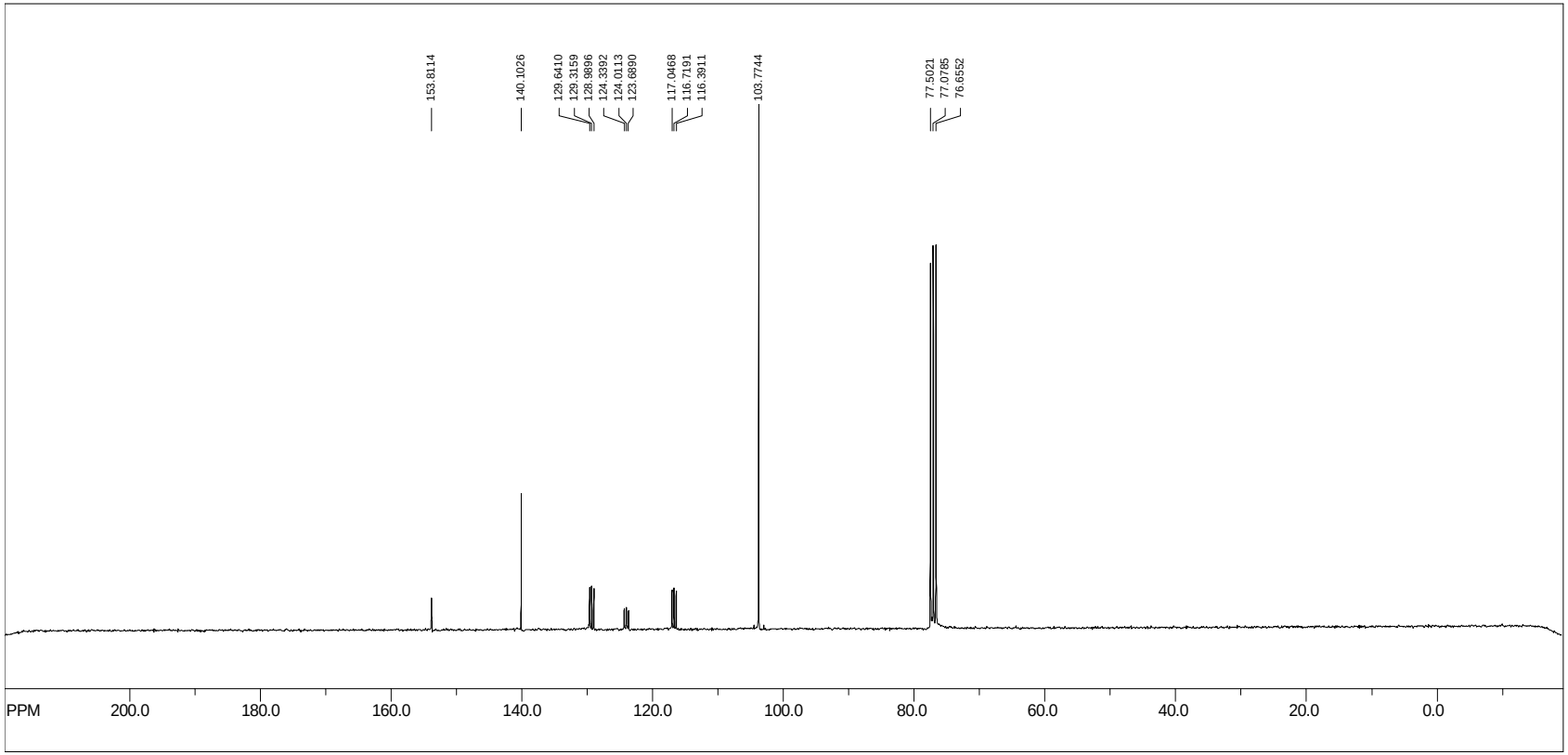
SpinWorks 2.5: perdeuterated-1,2-dichlorophenol ether



file: Z:\Laina\lmgxiv\lmgxiv_74a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

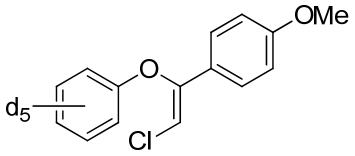
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



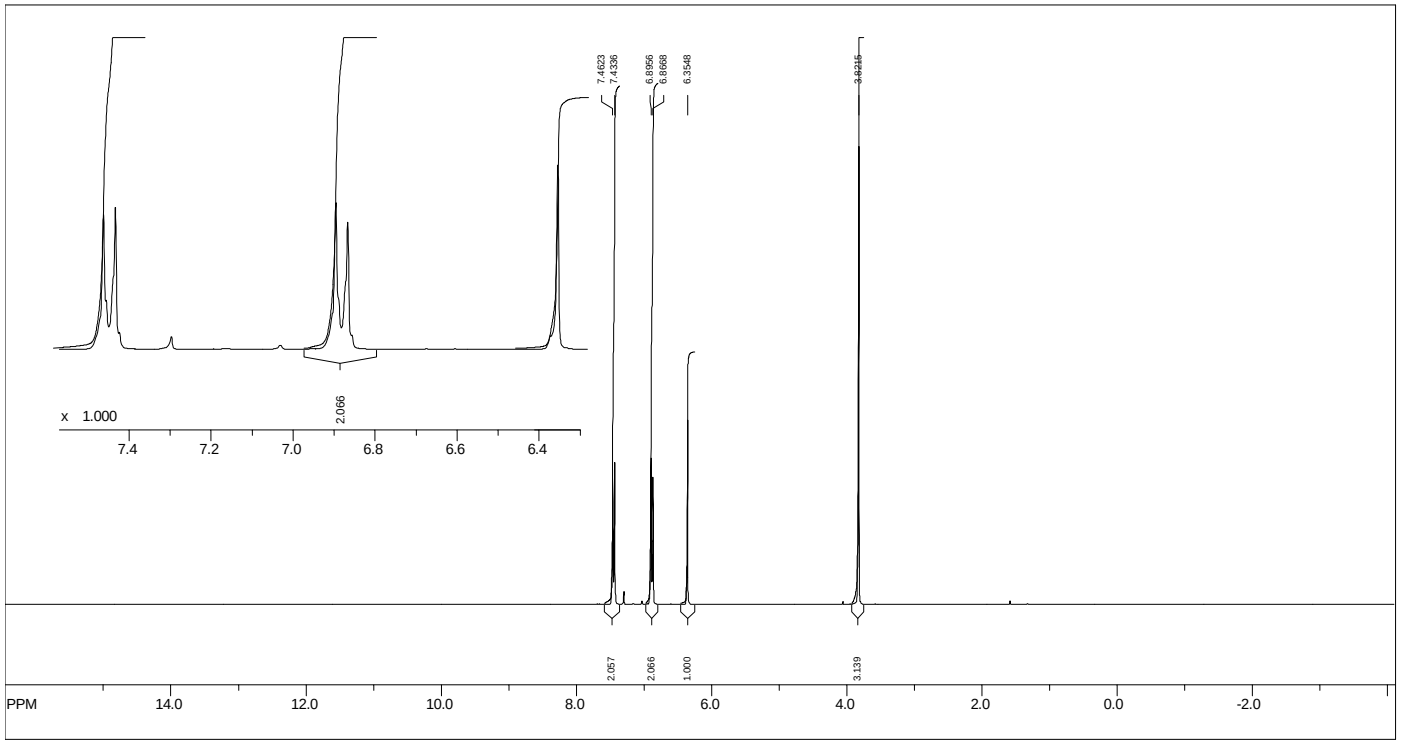
file: Z:\Laina\lmgxiv\lmgxiv_74a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 4196

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(Z)-1-(2-Chloro-1-(4-methoxyphenyl)vinyloxy)-2,3,4,5,6-pentadeuterobenzene (173-d_5)



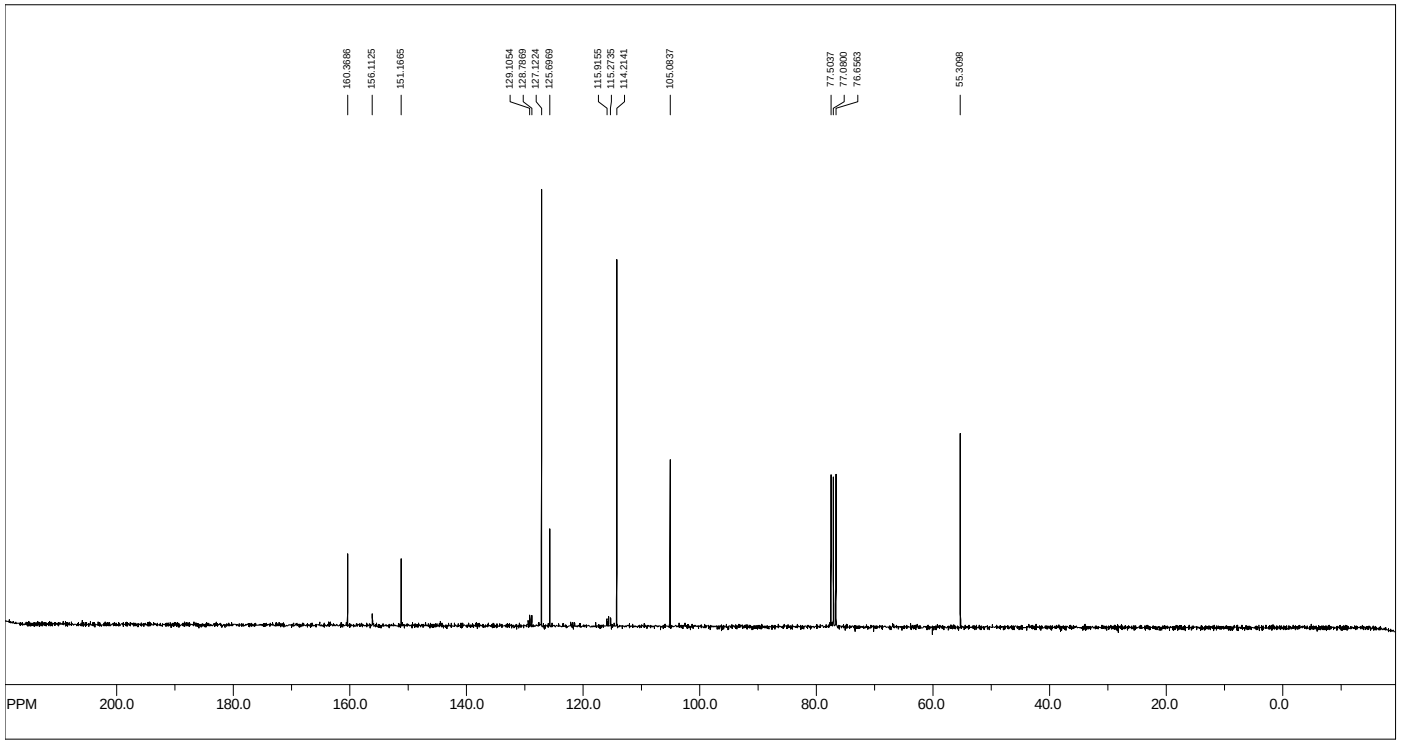
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



file: Z:\Laina\lmgw\lmgwv_10a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

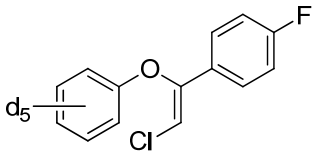
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 7



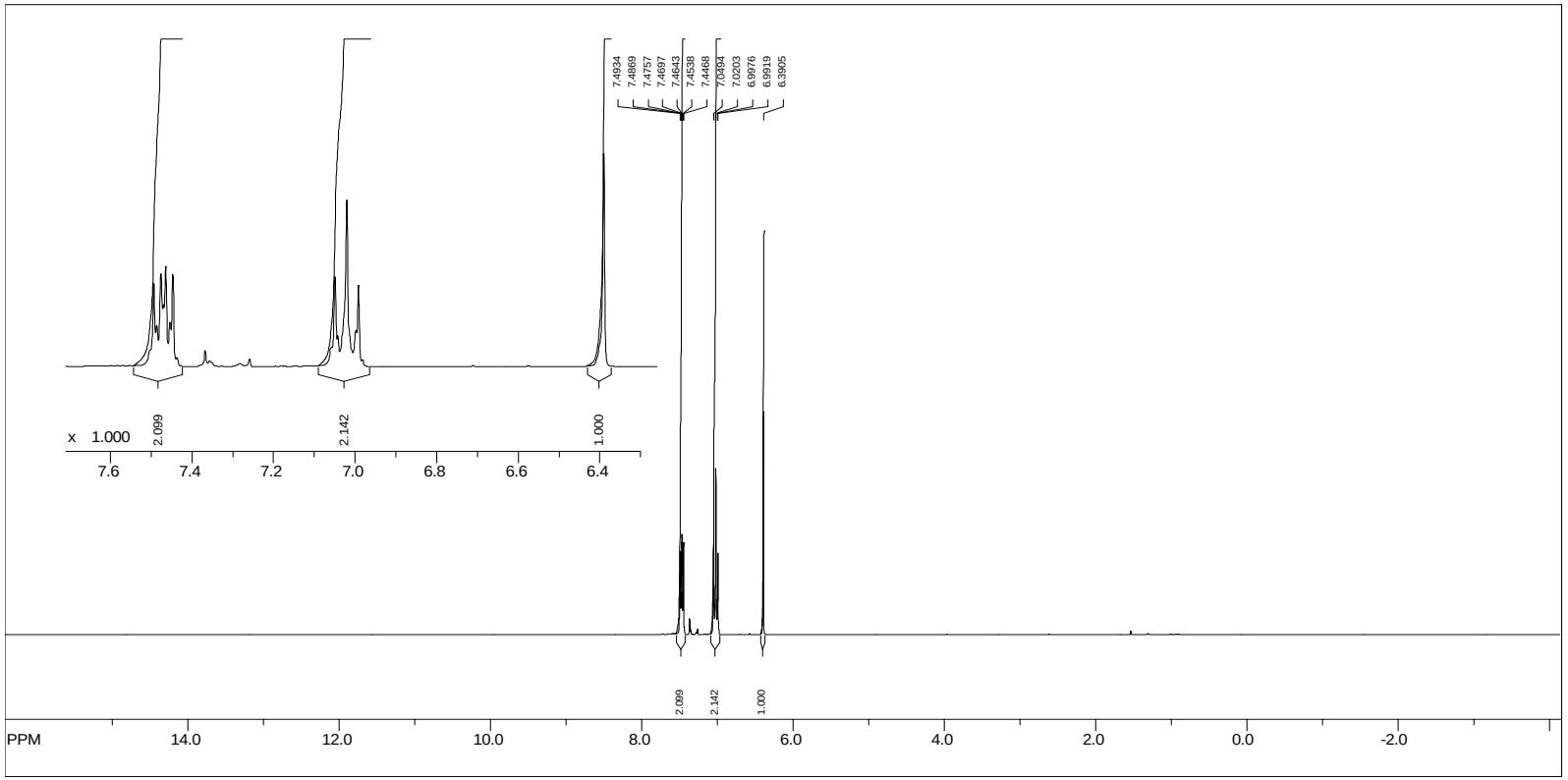
file: Z:\Laina\lmgw\lmgw_10a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 485

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(Z)-1-(2-Chloro-1-(4-fluorophenyl)vinyloxy)-2,3,4,5,6-pentadeuterobenzene



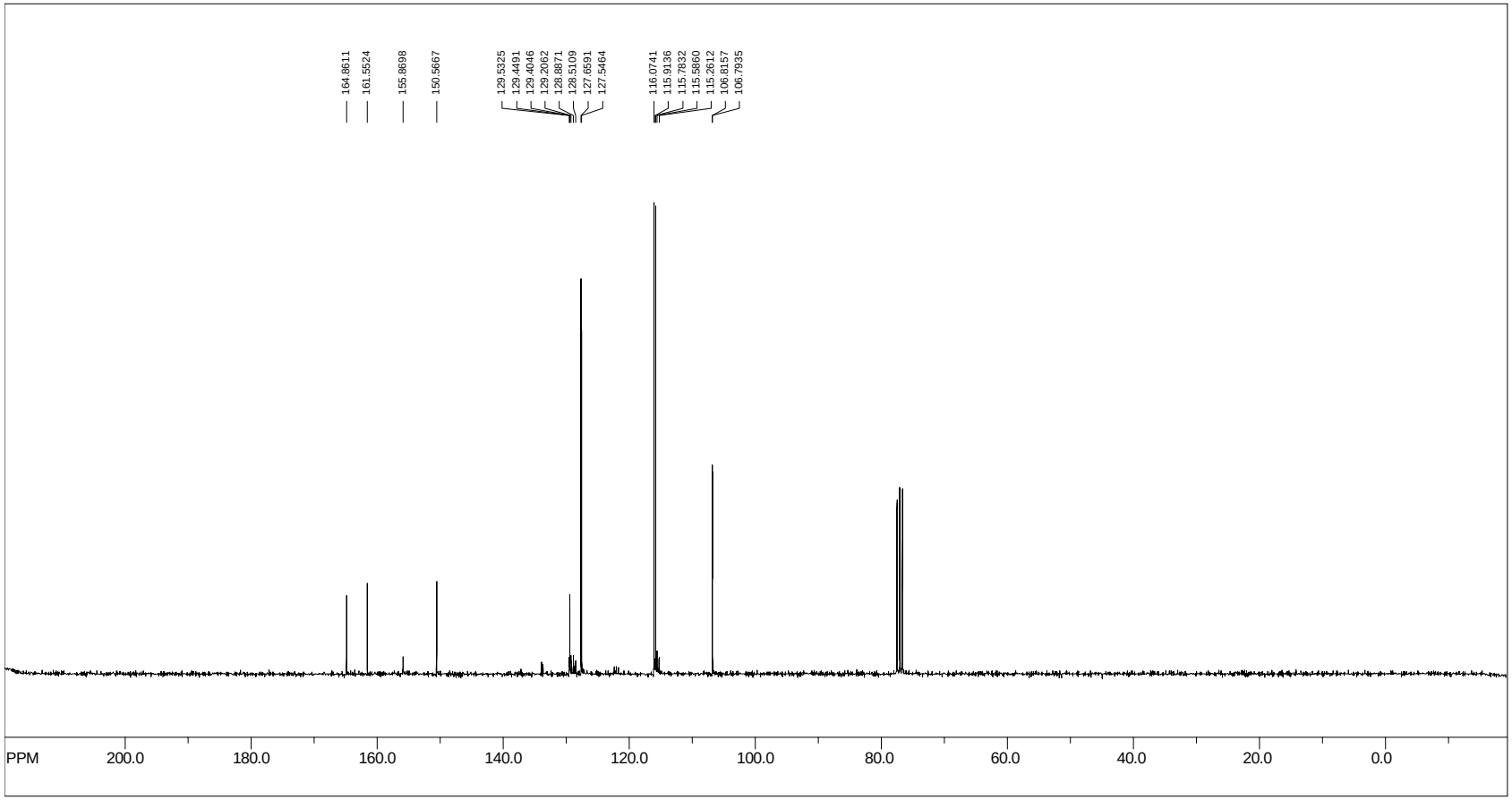
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



file: Z:\Laina\lmgxv\lmgxv_12a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

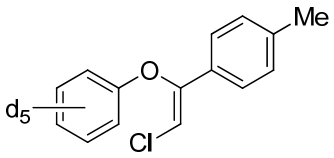
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 11



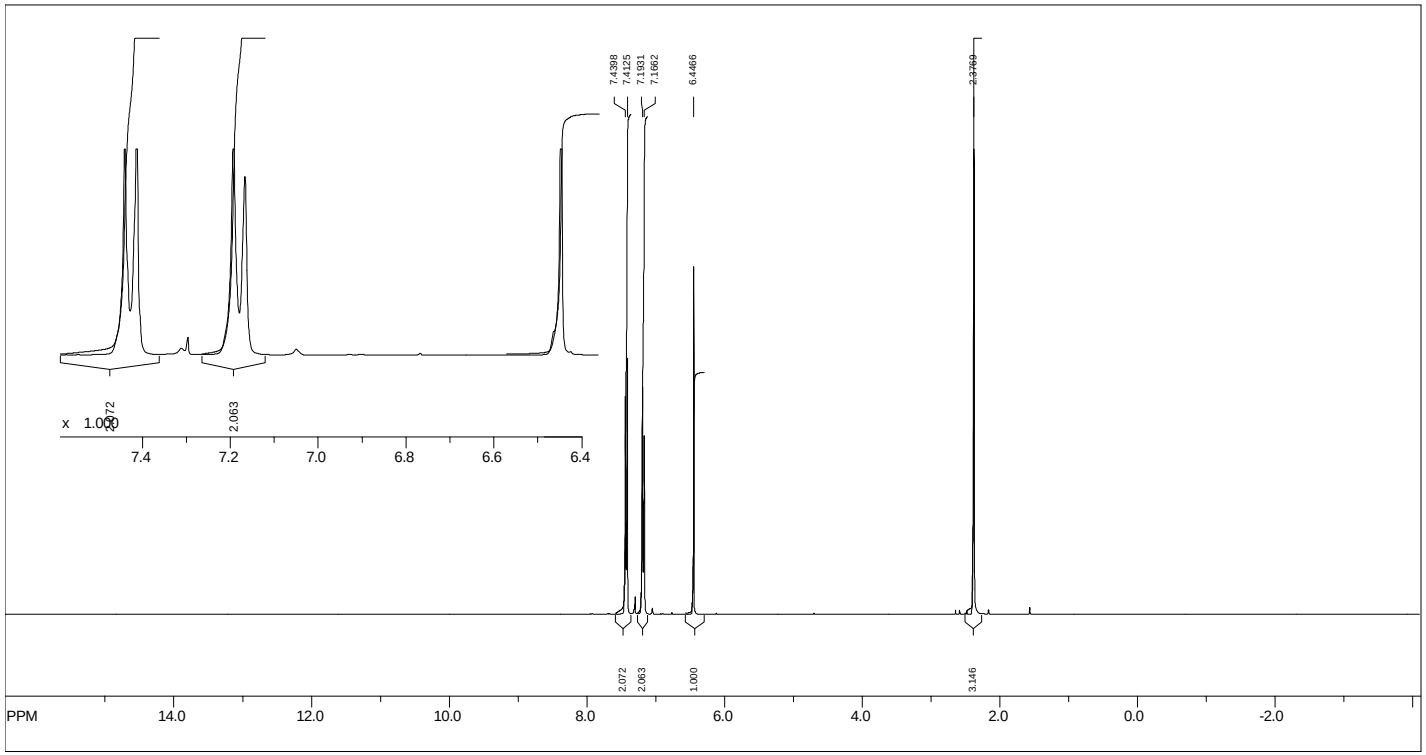
file: Z:\Laina\lmgxv\lmgxv_12a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(Z)-1-(2-Chloro-1-(4-methylphenyl)vinyloxy)-2,3,4,5,6-pentadeuterobenzene (194-d_5)



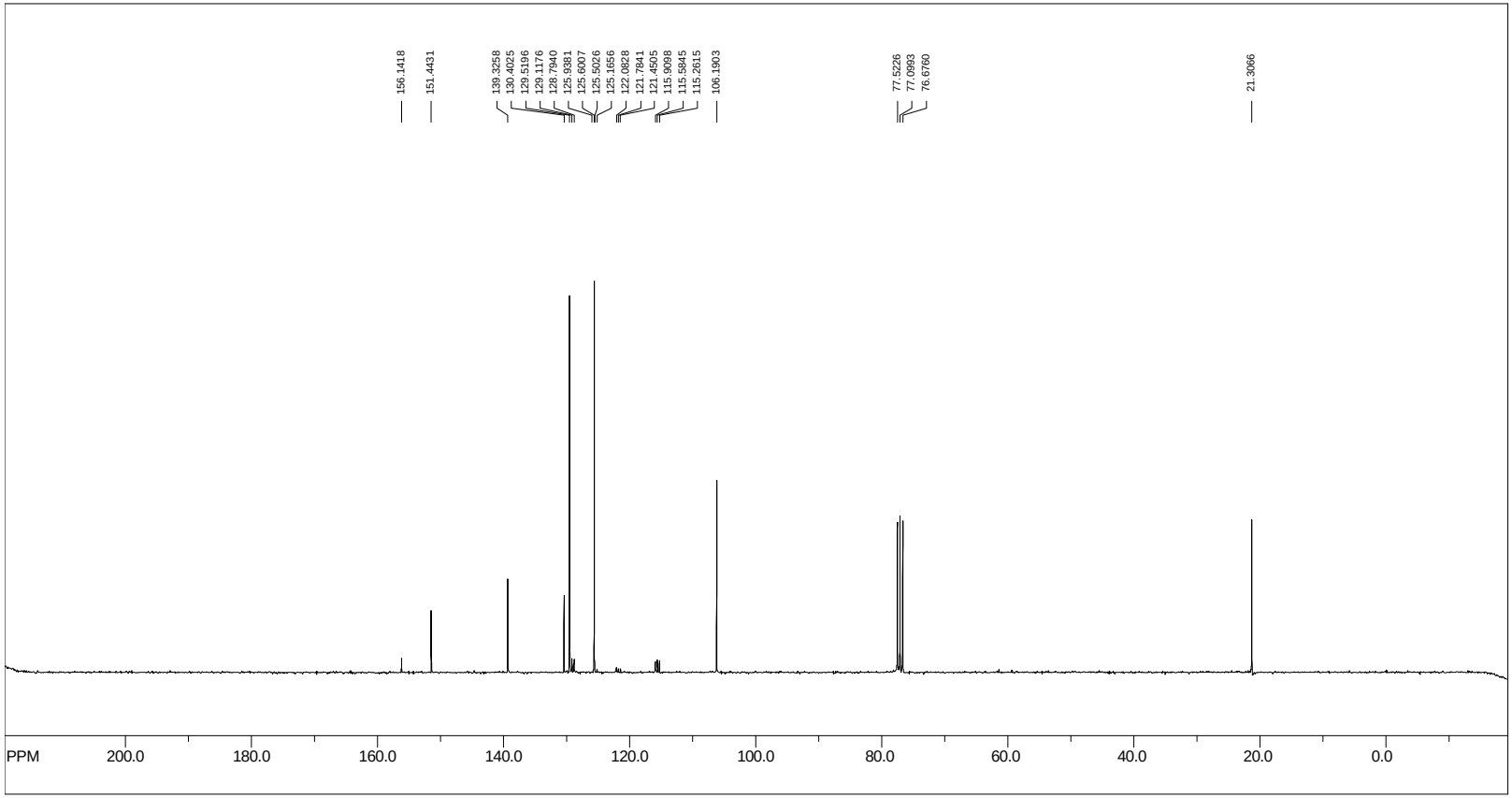
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



file: Z:\Laina\lmgw\lmgw_11a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

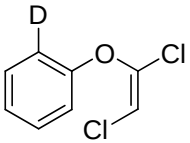
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



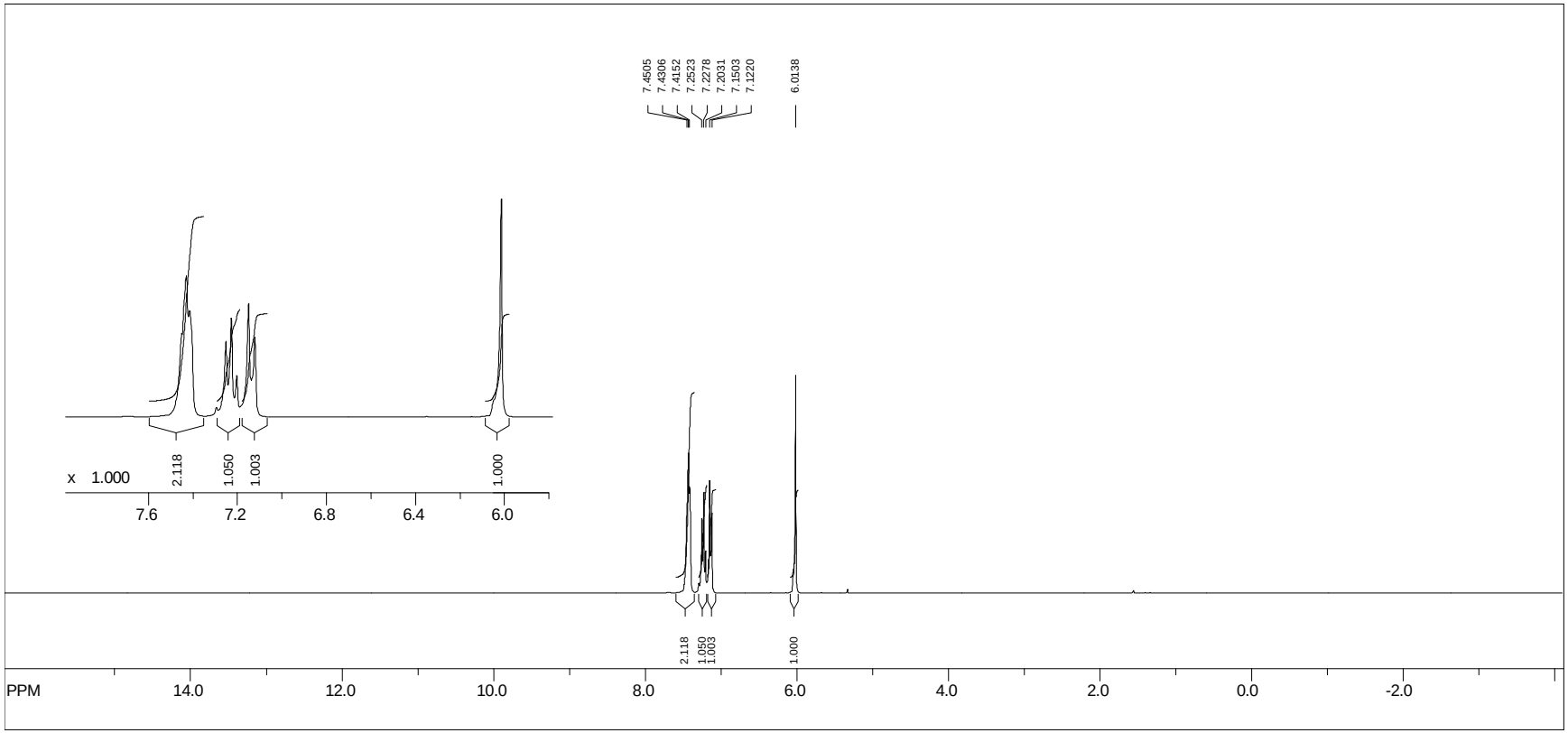
file: Z:\Laina\lmgx\lmgxv_11a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

(E)-(1,2-Dichlorovinyloxy)-2-deuteriobenzene (93-d)



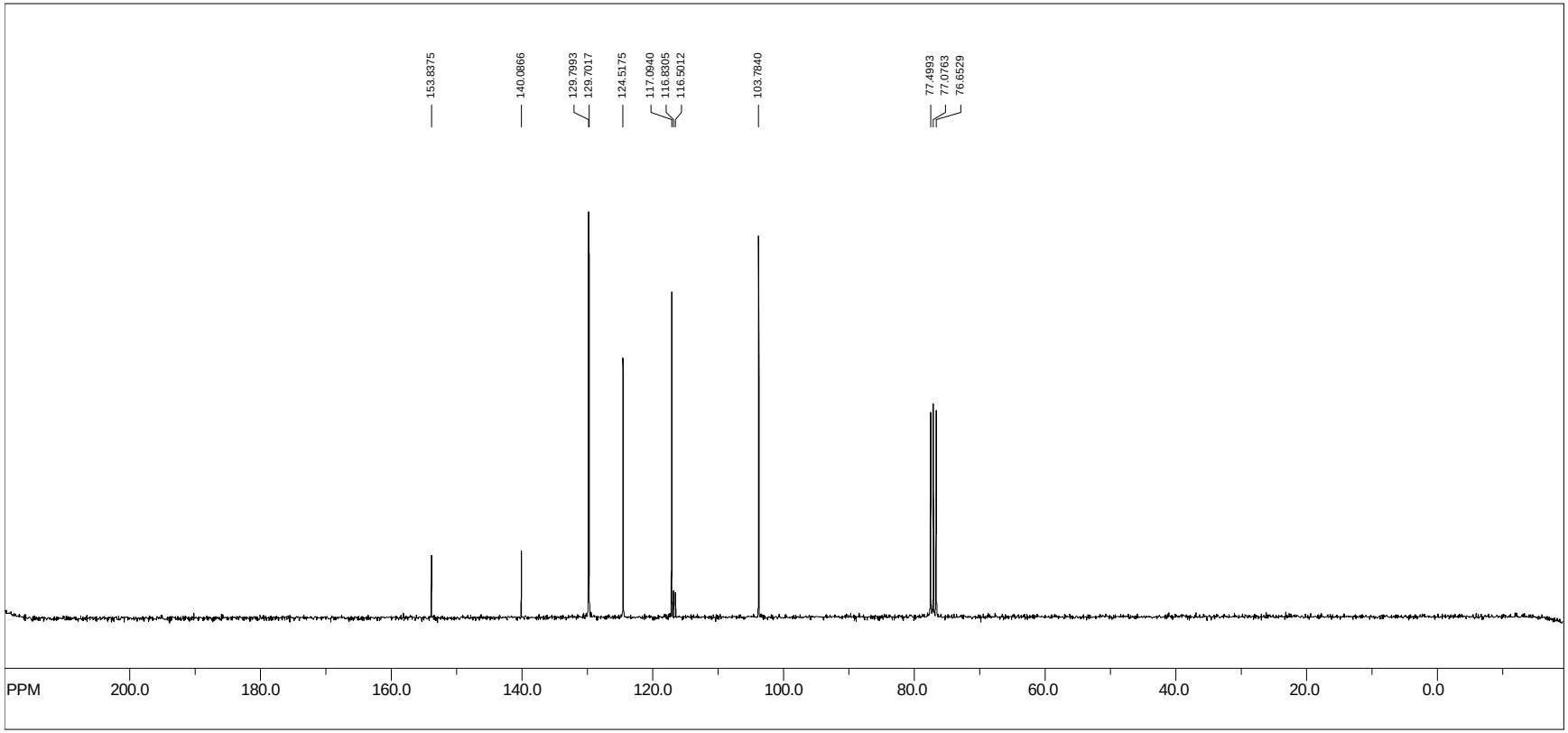
SpinWorks 2.5: o-D-1,2-dichlorophenol ether



file: Z:\Laina\lmgxiv\lmgxiv_73a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

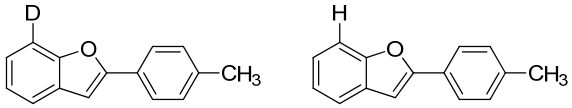
SpinWorks 2.5: o-D-1,2-dichlorophenol ether



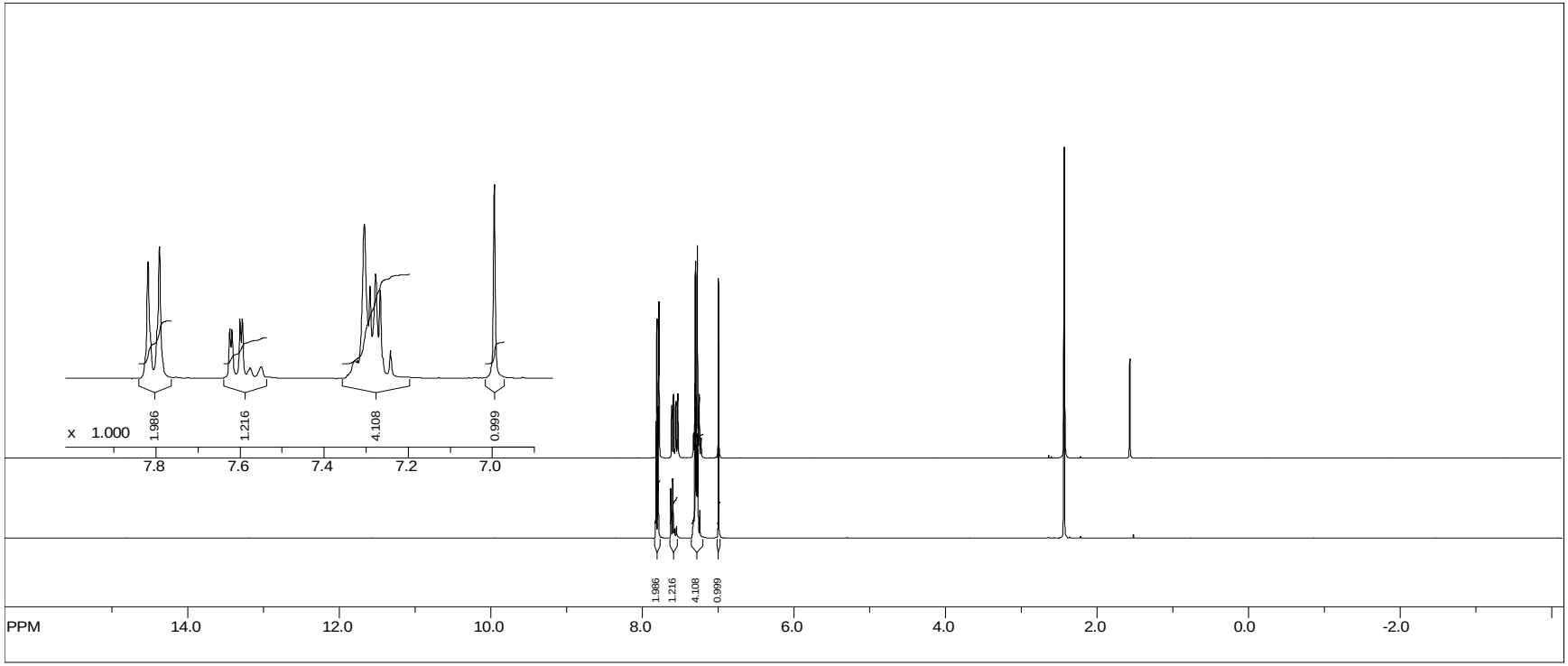
file: Z:\Laina\lmgxiv\lmgxiv_73a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 420

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(4-Methylphenyl)benzofuran (306) and 2-(4-Methylphenyl)-7-deuteriobenzofuran (306-d)



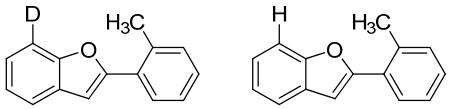
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



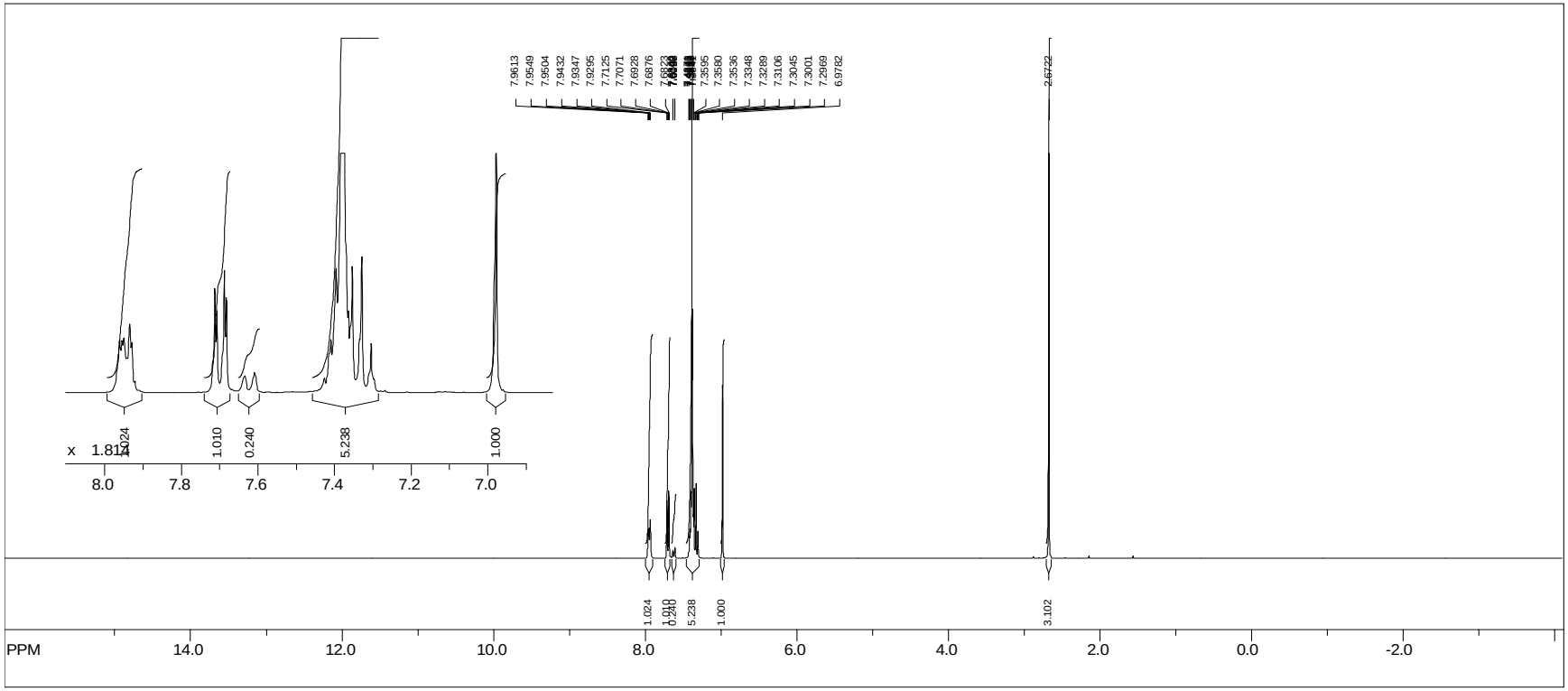
file: Z:\Laina\lmgpiv\lmgpiv_83a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130012 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(2-Methylphenyl)benzofuran (359) and 2-(2-Methylphenyl)-7-deuteriobenzofuran (359-d)



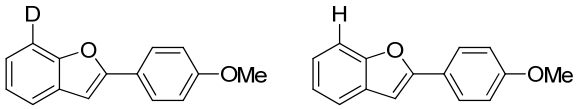
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 3



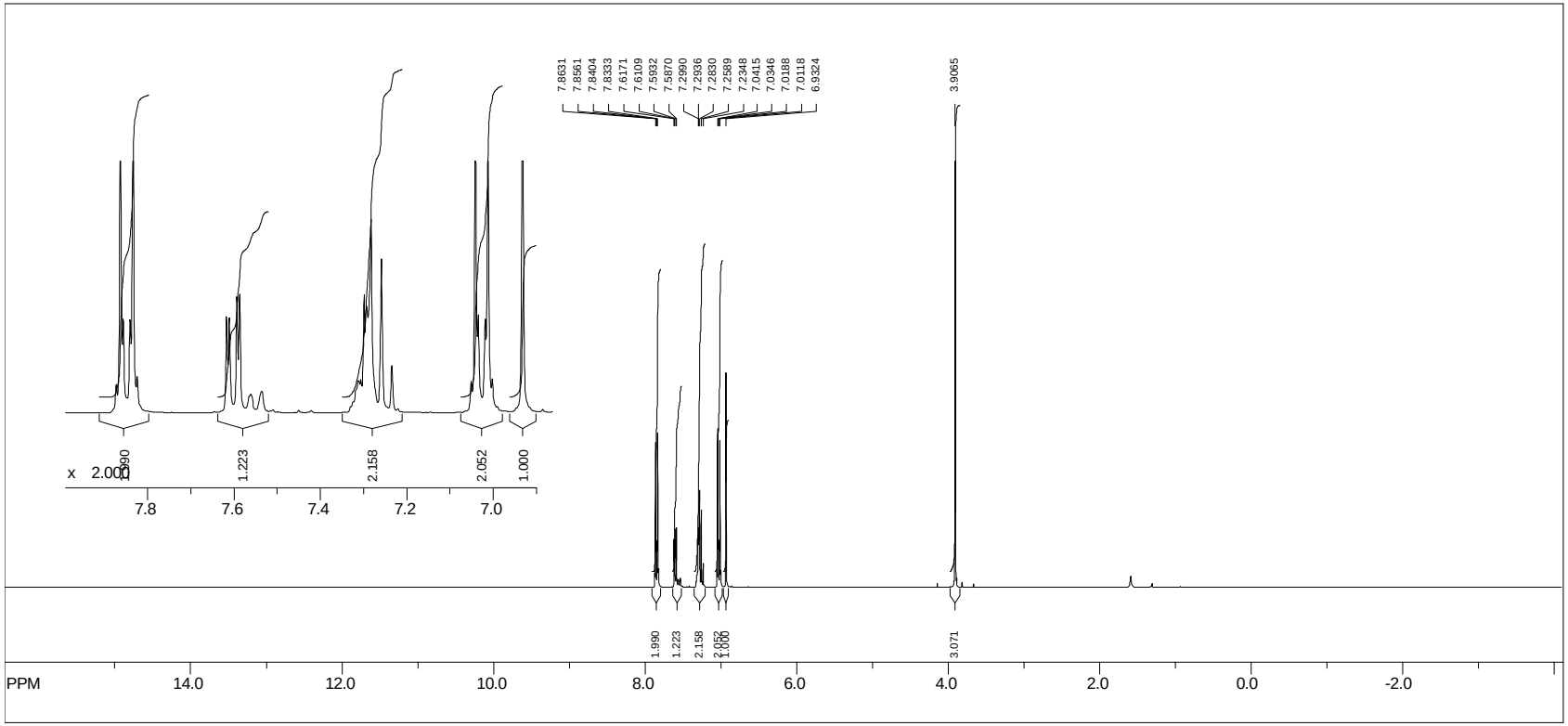
file: Z:\Laina\lmgxiv\lmgxiv_84a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)benzofuran (301) and 2-(4-methoxyphenyl)-7-deuteriobenzofuran (301-d)



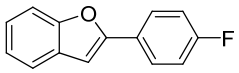
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2

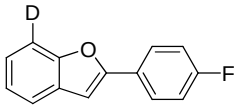


file: Z:\Laina\lmgxvi\lmgxvi_54a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

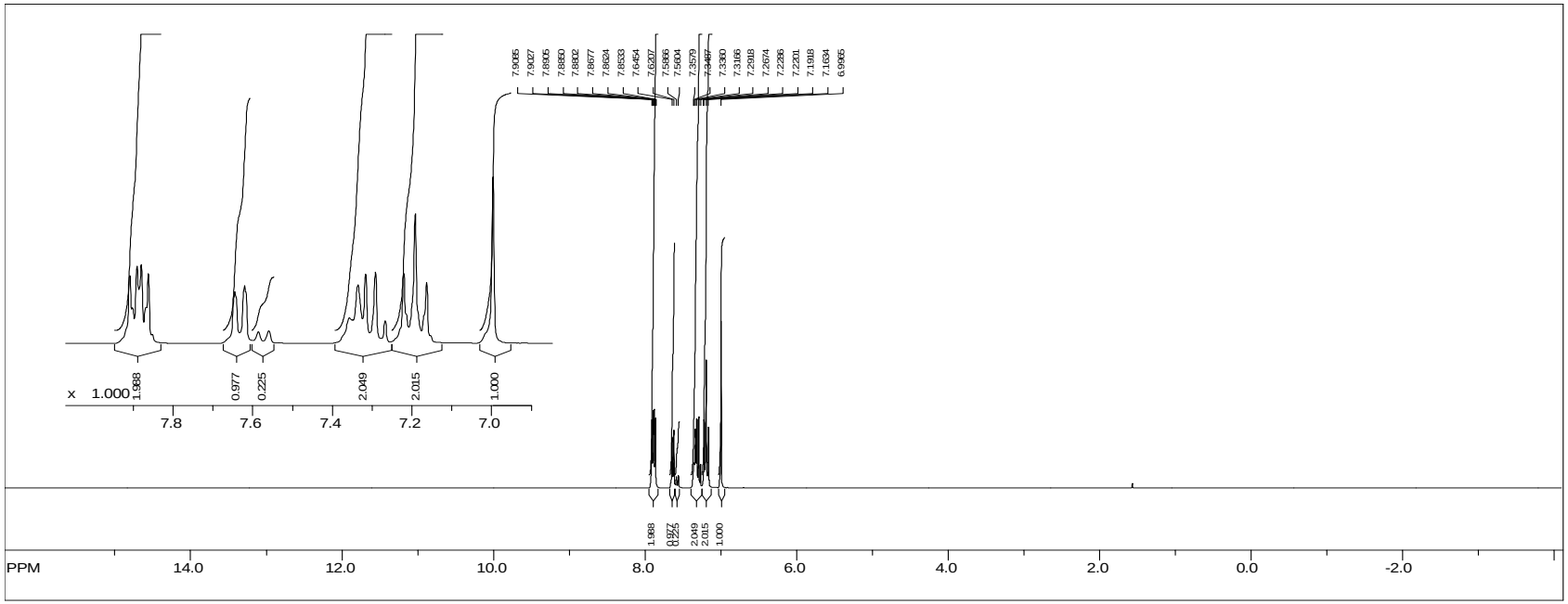
freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Fluorophenyl)benzofuran (302) and 2-(4-fluorophenyl)-7-deuteriobenzofuran (302-d)





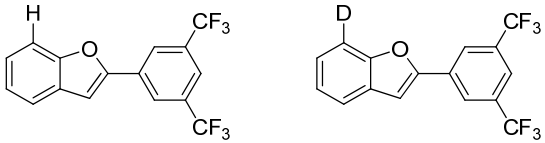
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5



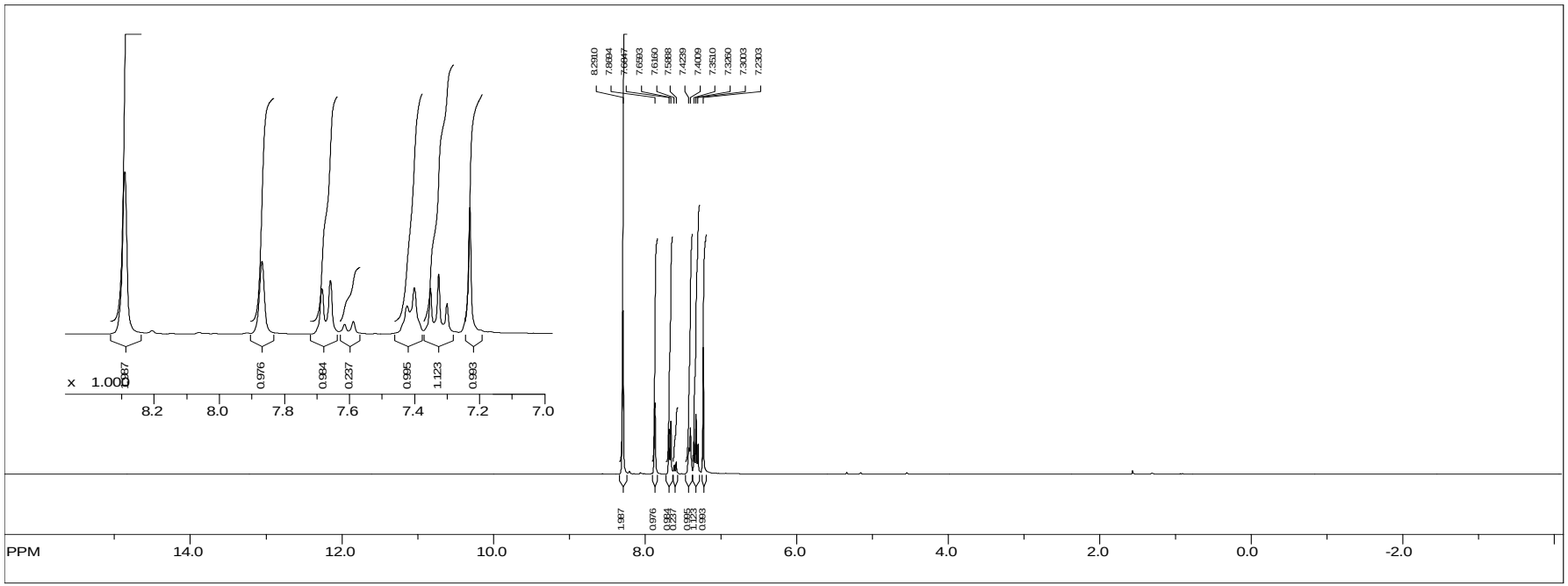
file: Z:\Laina\lmgxiv\lmgxiv_86a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-[3,5-Bis(trifluoromethyl)phenyl]benzofuran (360) and 2-[3,5-bis(trifluoromethyl)phenyl]-7-deuteriobenzofuran (360-d)



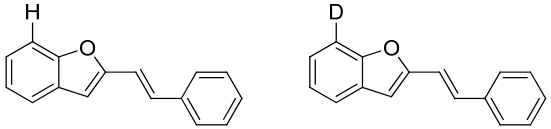
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 8



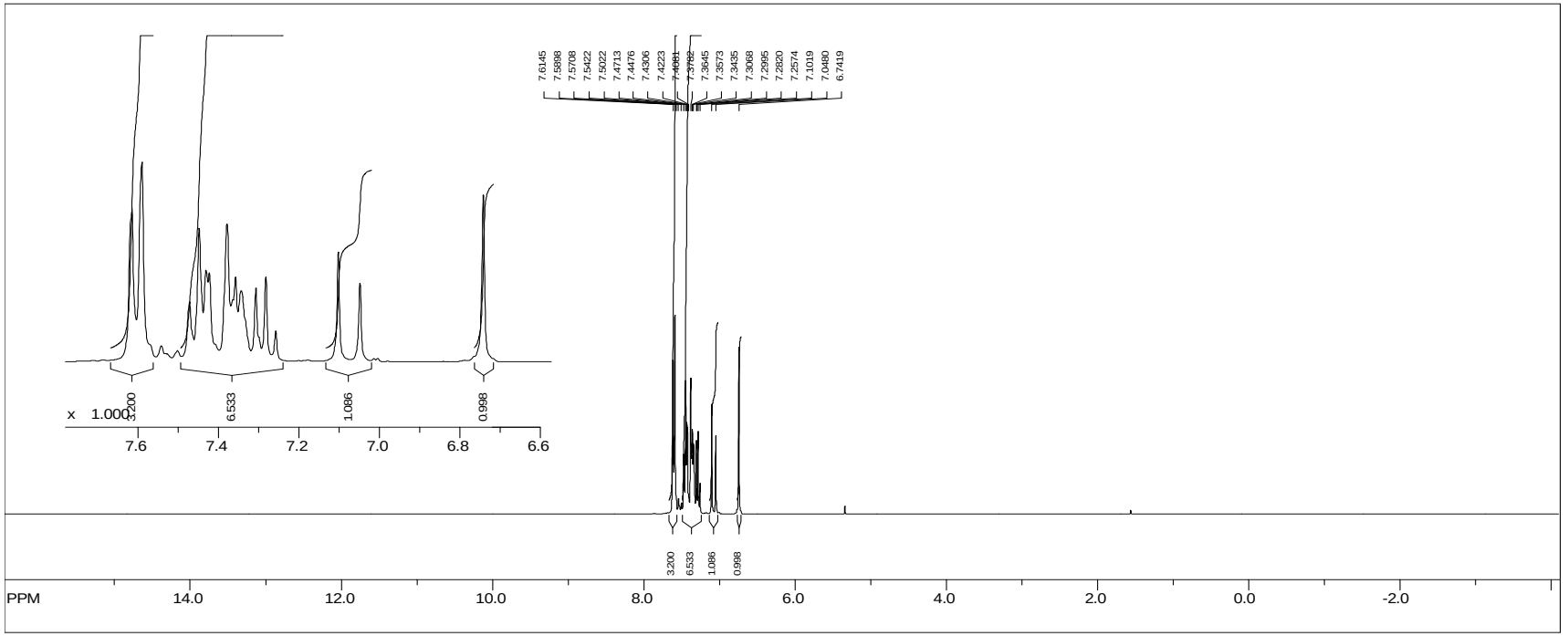
file: Z:\Laina\lmgxiv\lmgxiv_87c\1\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(trans-2-Phenylethenyl)benzo[b]furan (303) and 2-(trans-2-Phenylethenyl)-7-deuteriobenzo[b]furan (303-d)



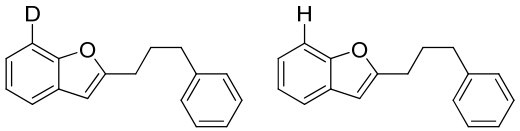
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



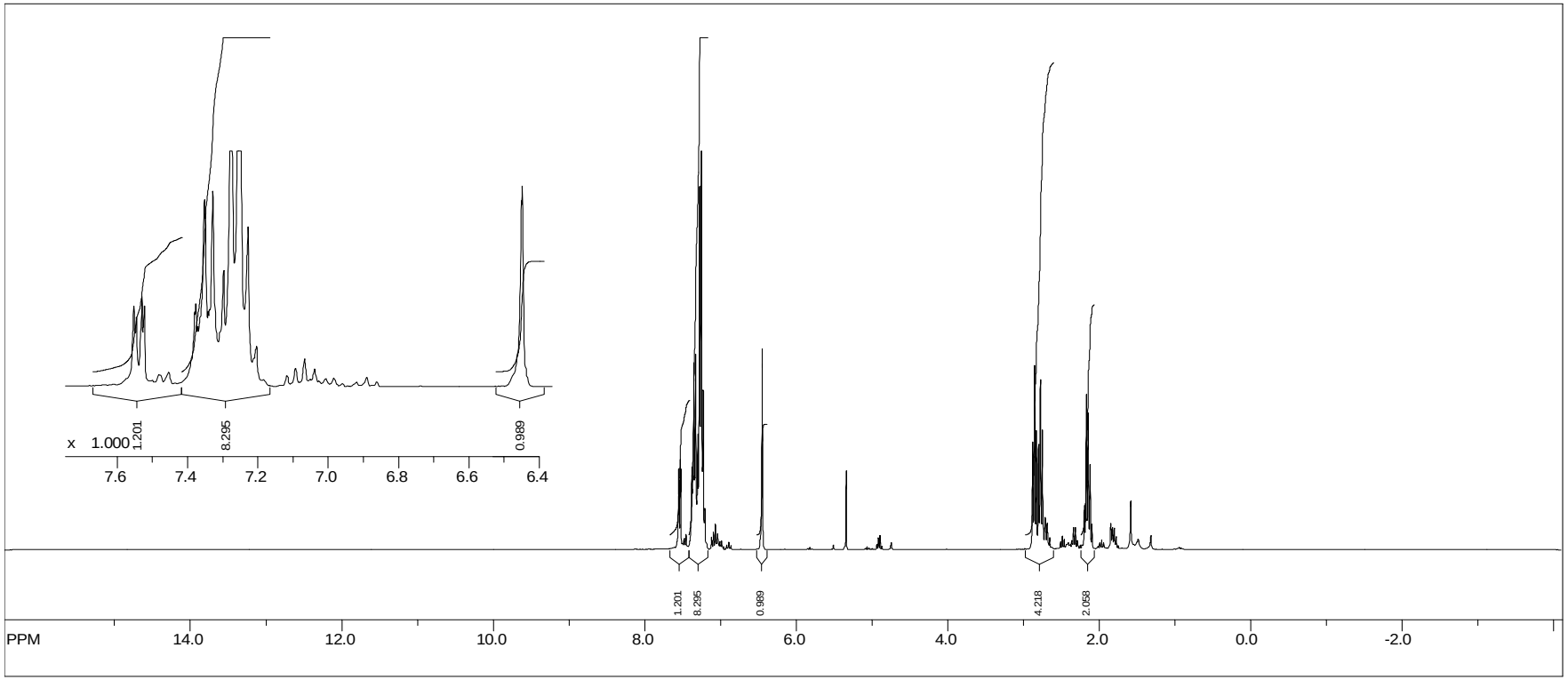
file: Z:\Laina\lmgxiv\lmgxiv_85a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

2-(3-Phenylpropane)benzofuran (333) and 2-(3-Phenylpropane)-7-deuteriobenzofuran (333-d)



SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1

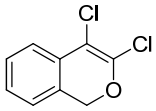


file: Z:\Laina\lmgxvi\lmgxvi_18b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

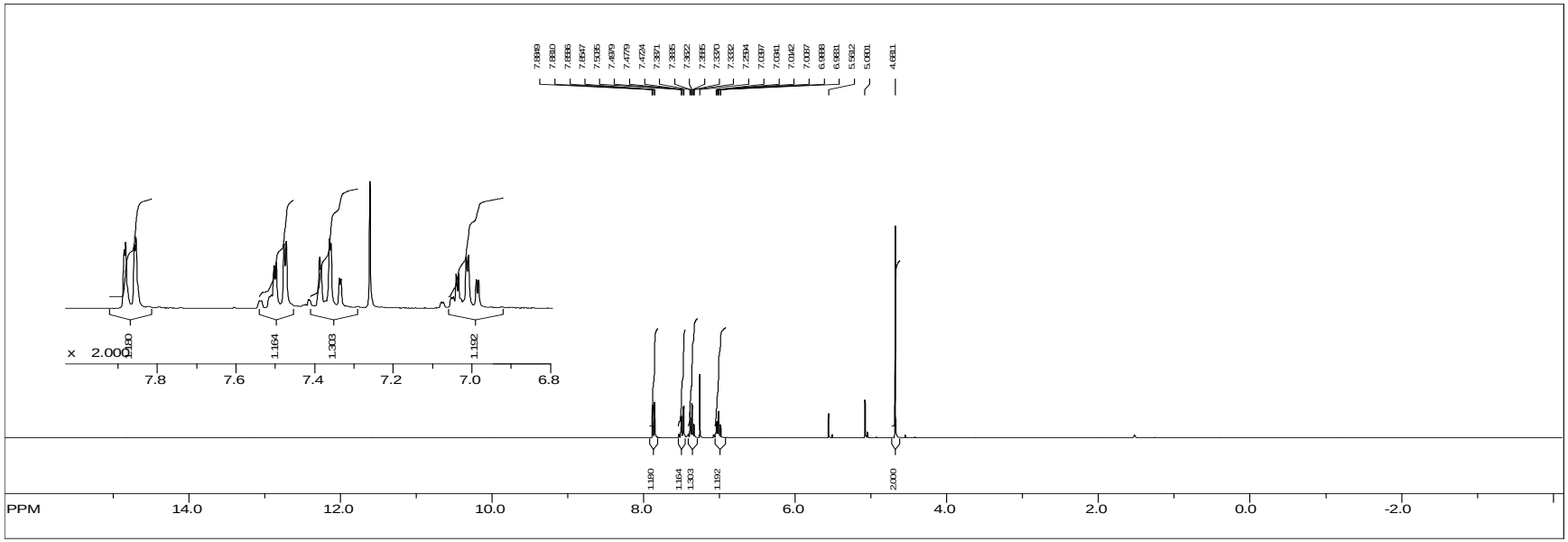
freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

6.6: Section 2.7 – Other Heterocycles

3,4-Dichloro-1*H*-isochromene (365)



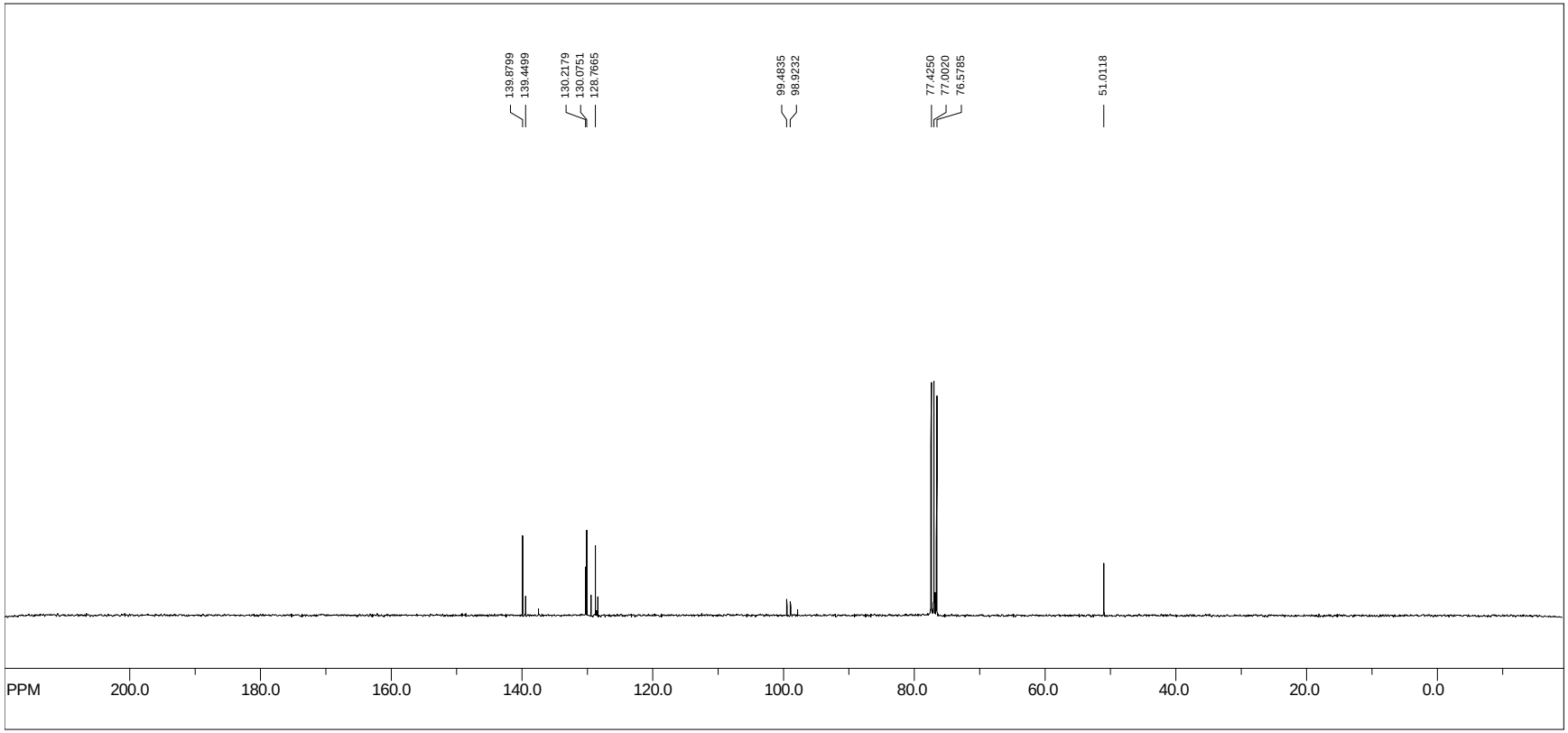
SpinWorks 2.5: intramol heck? fraction 6



file: Z:\Laina\lmgvi\lmgvi_77b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 8

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

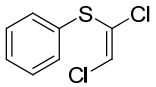
SpinWorks 2.5: intramol heck? fraction 6



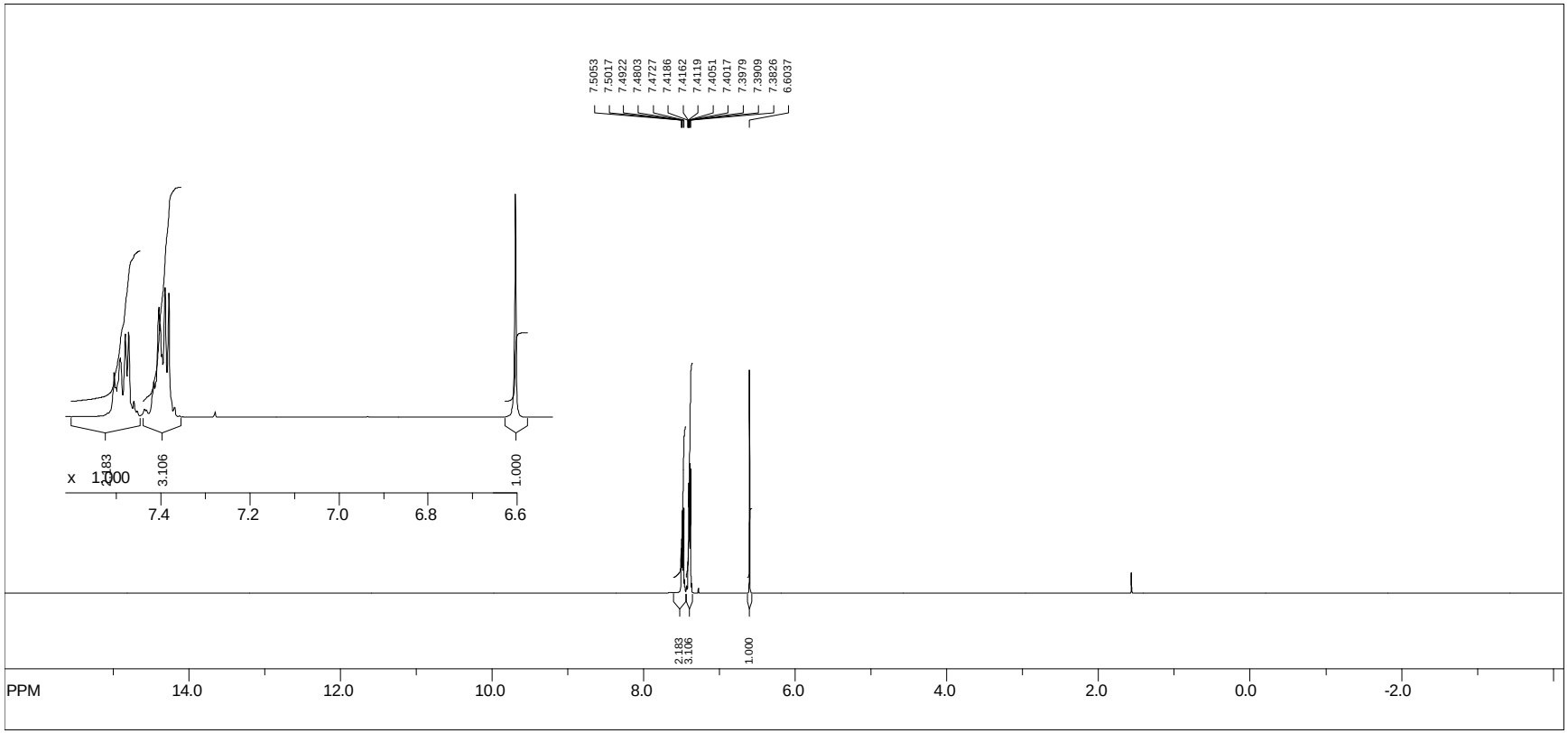
file: Z:\Laina\lmgvii\lmgvii_77b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 3612

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*E*)-(1,2-Dichlorovinyl)(phenyl)sulfane (367)



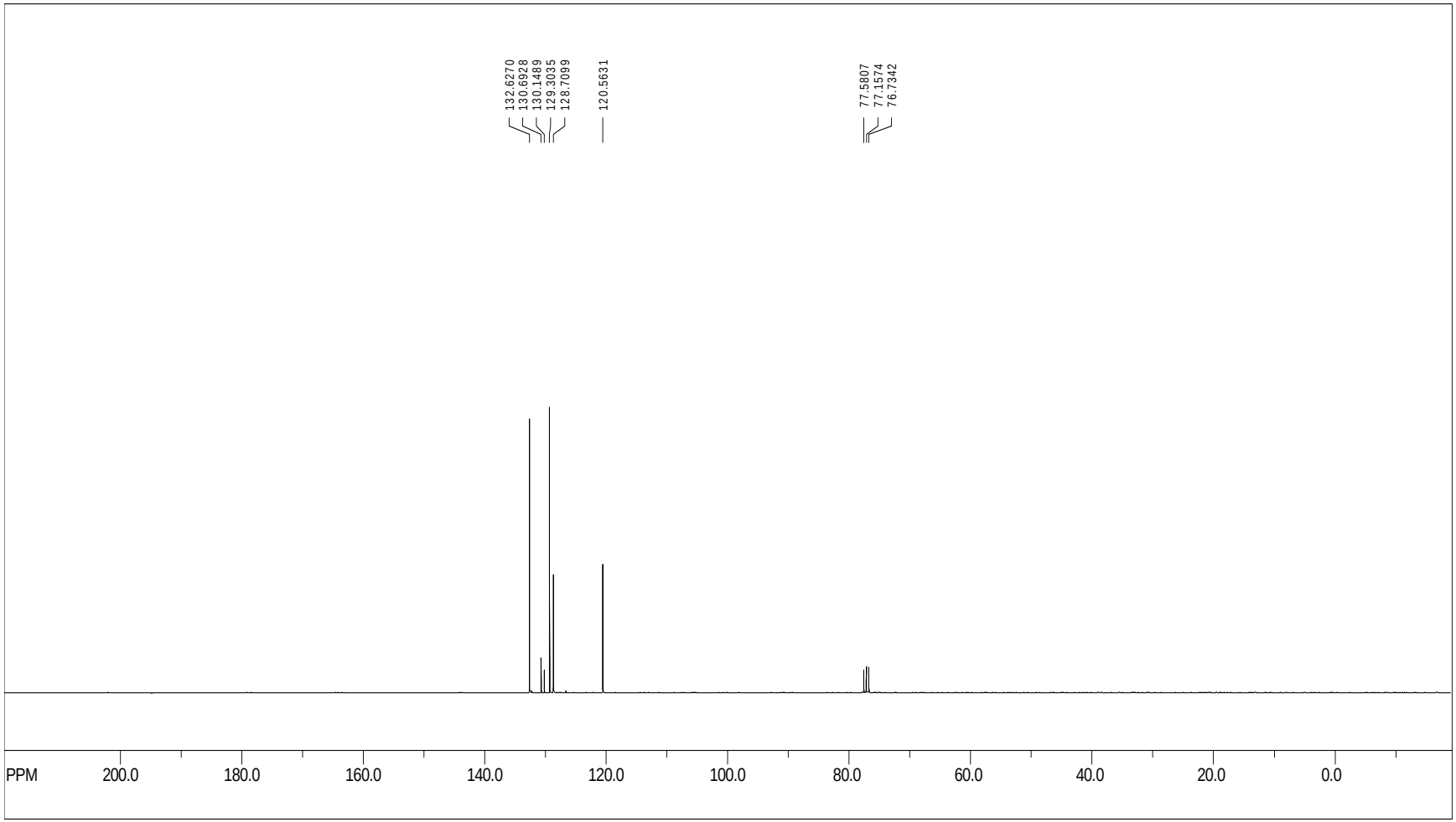
SpinWorks 2.5: thiophenol addition to TCE



file: Z:\Laina\lmgxii\lmgxii_11a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

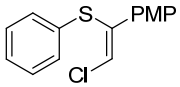
SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



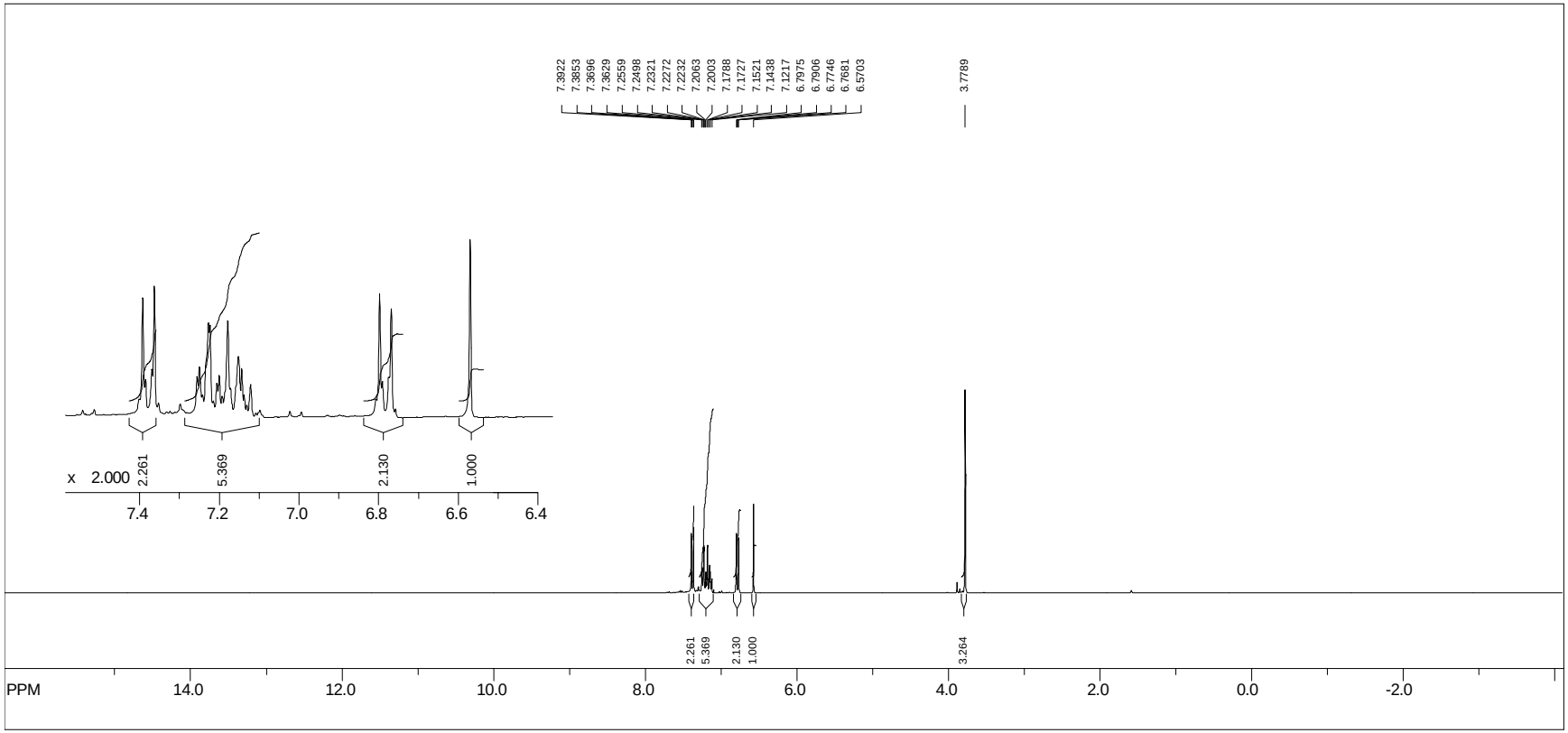
file: Z:\Laina\lmgxii\lmgxii_11a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 256

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

(*Z*)-(2-Chloro-1-(4-methoxyphenyl)vinyl)(phenyl)sulfane (368)



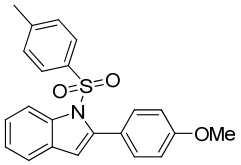
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



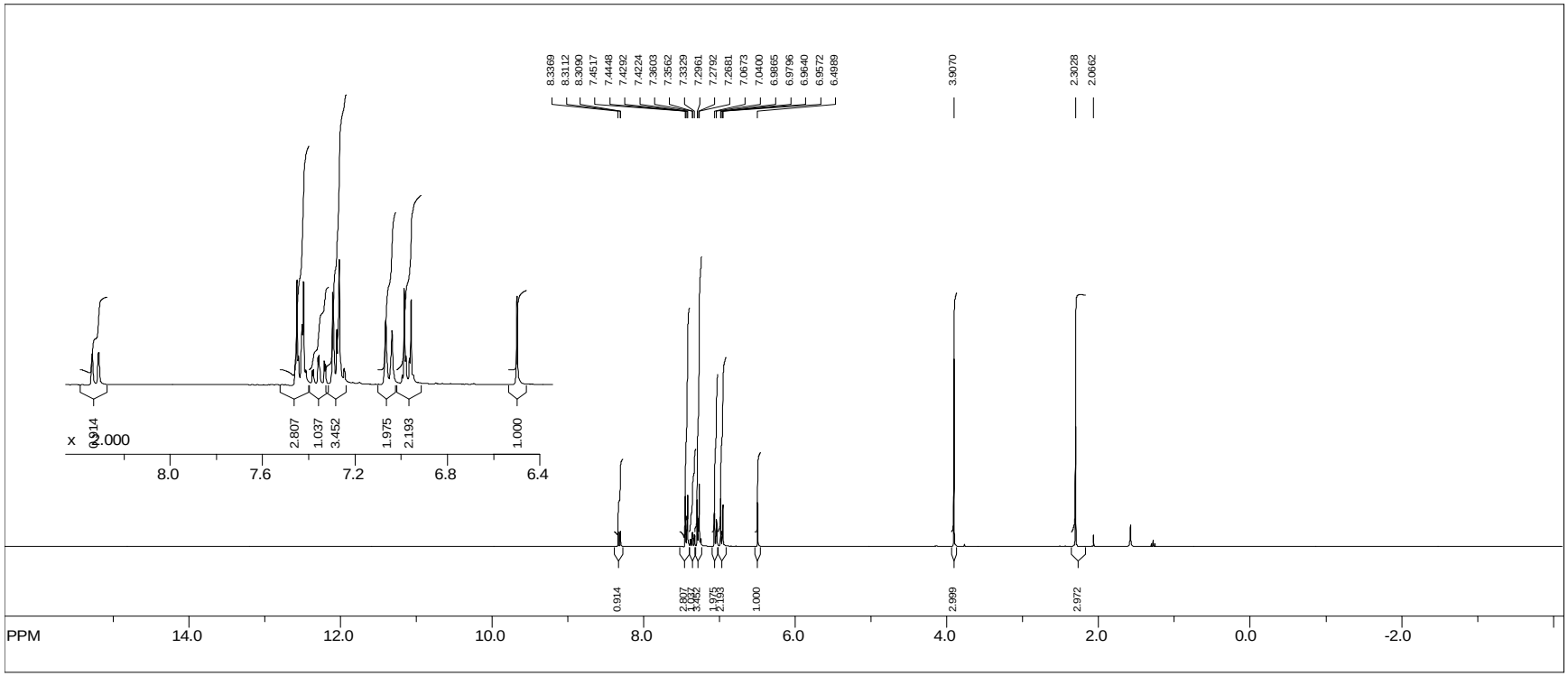
file: Z:\Laina\lmgxii\lmgxii_61a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-1-Tosyl-1*H*-indole (370)



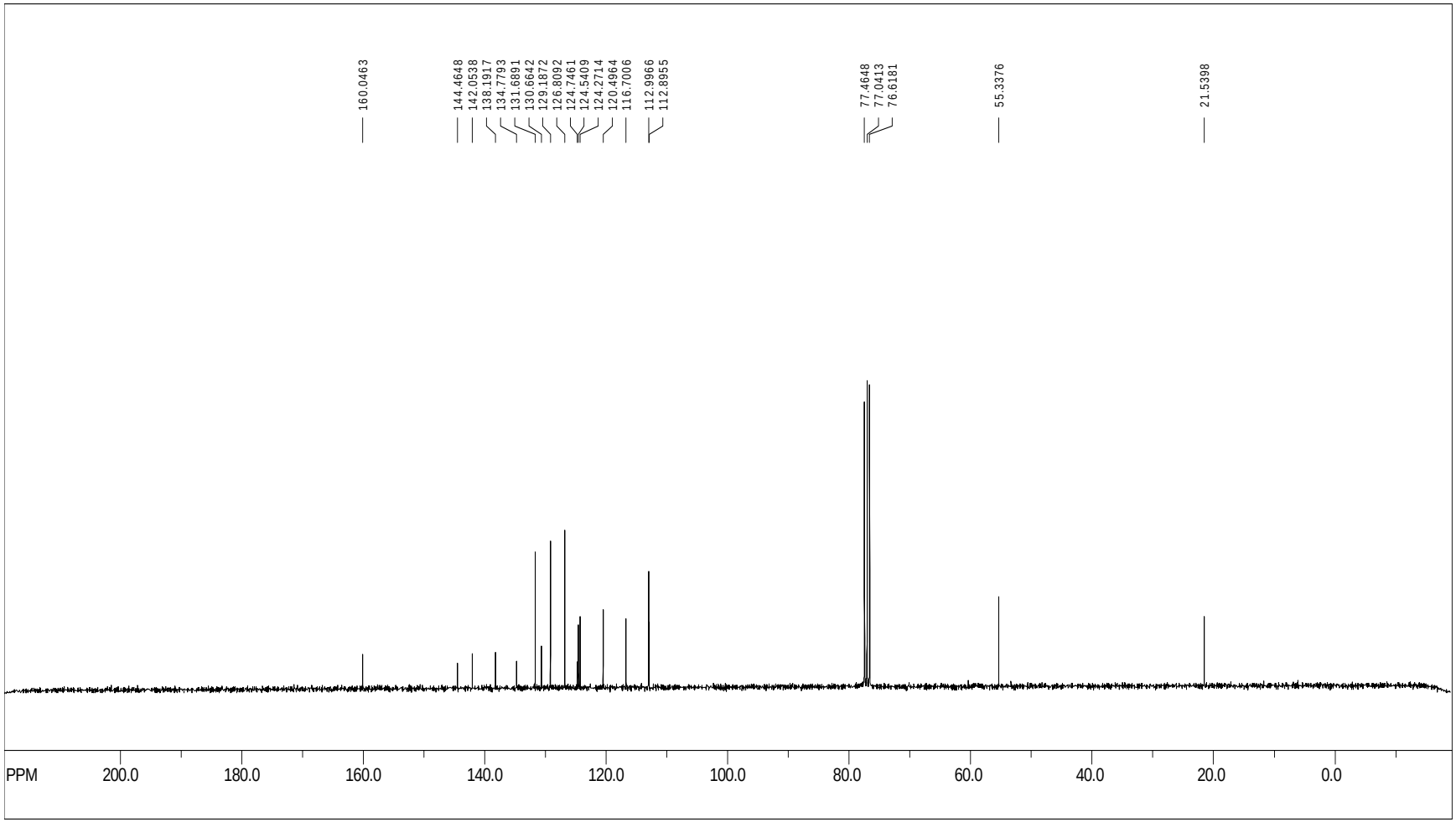
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



file: Z:\Laina\lmgxi\lmgxi_56b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

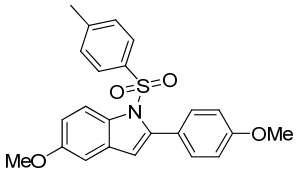
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 6



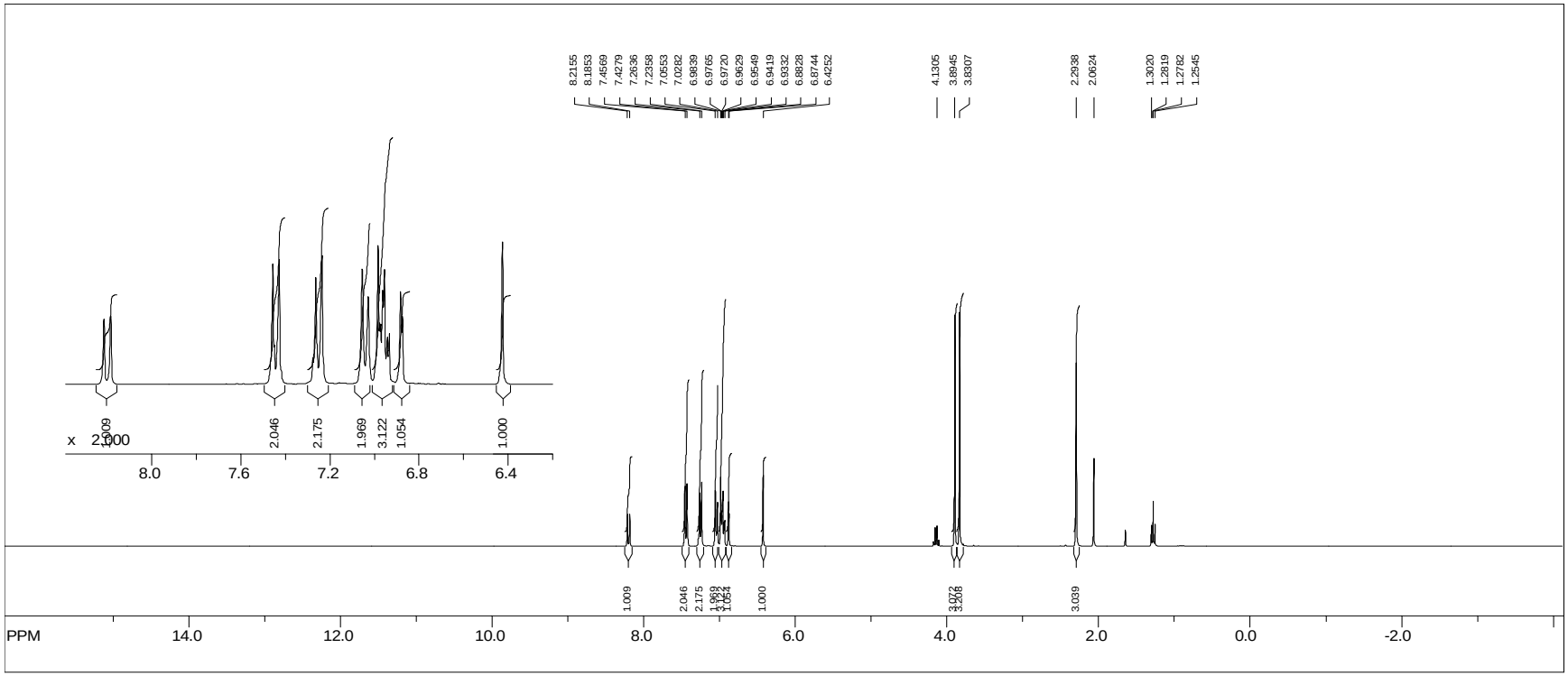
file: Z:\Laina\lmgxi\lmgxi_56b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 986

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

5-Methoxy-2-(4-methoxyphenyl)-1-tosyl-1*H*-indole (371)



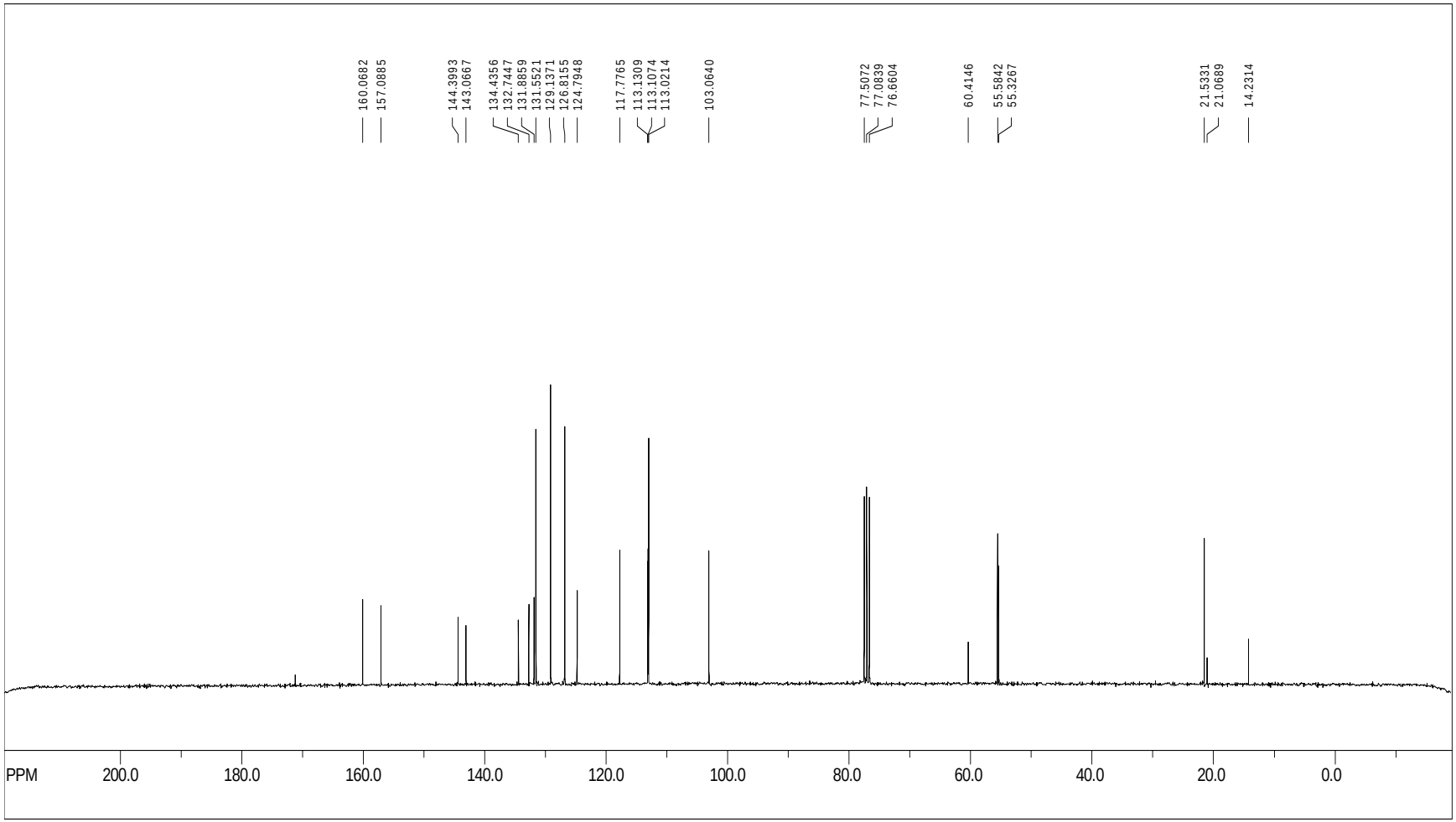
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



file: Z:\Laina\lmgxi\lmgxi_57a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

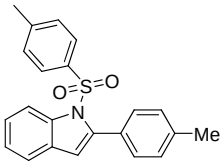
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 10



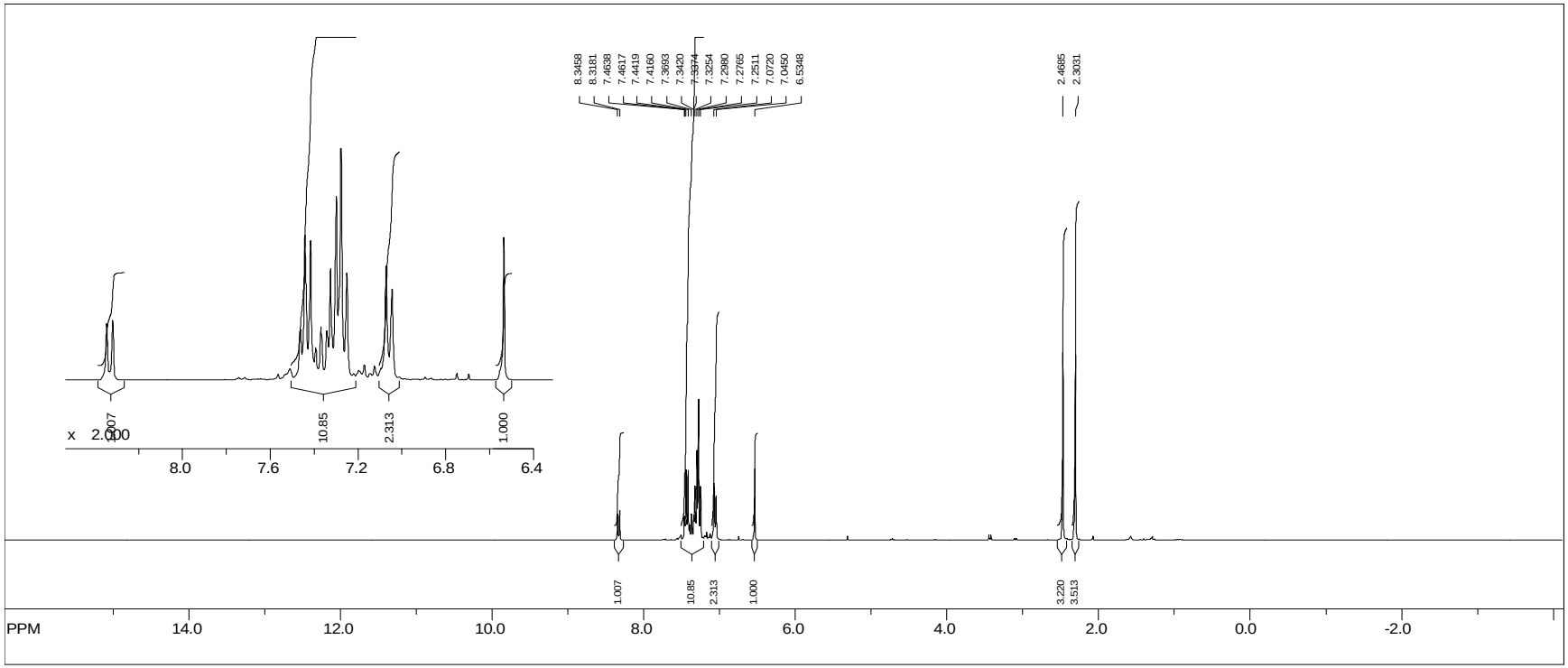
file: Z:\Laina\lmgxi\lmgxi_57a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 999

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-*p*-Tolyl-1-tosyl-1*H*-indole (372)



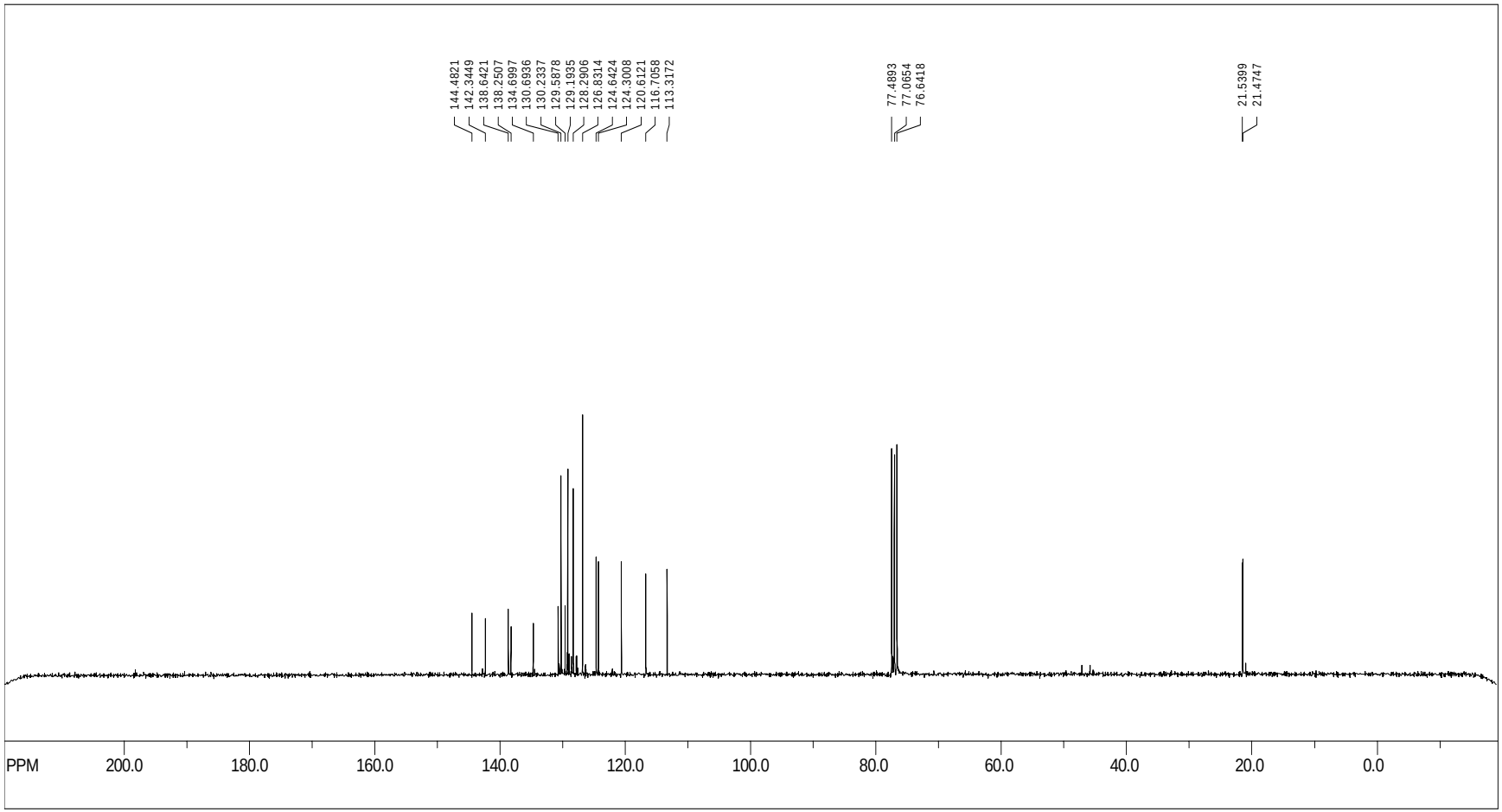
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 9



file: Z:\Laina\lmgxii\lmgxii_92b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

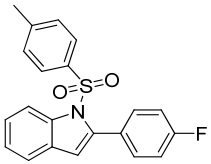
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 9



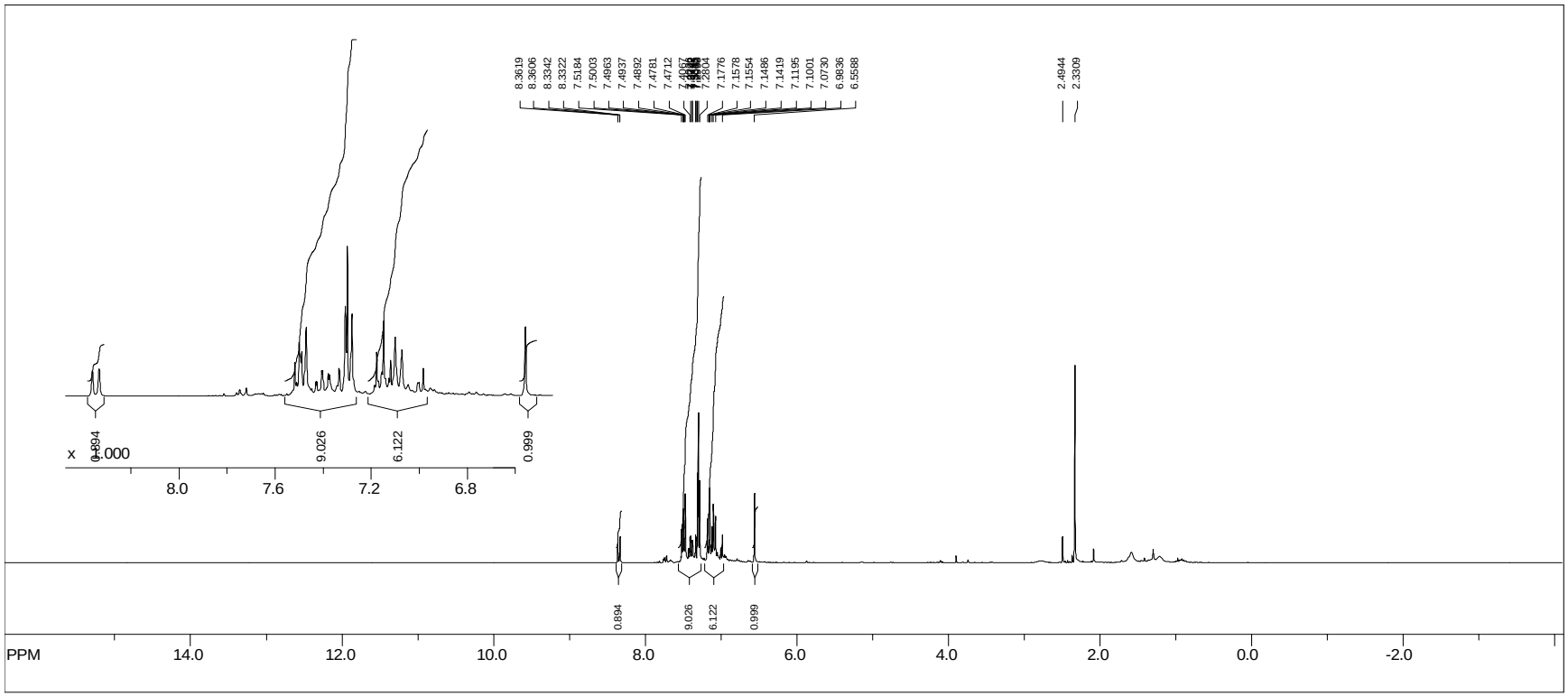
file: Z:\Laina\lmgxii\lmgxii_92b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Fuorophenyl)-1-tosyl-1*H*-indole (373)



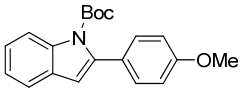
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



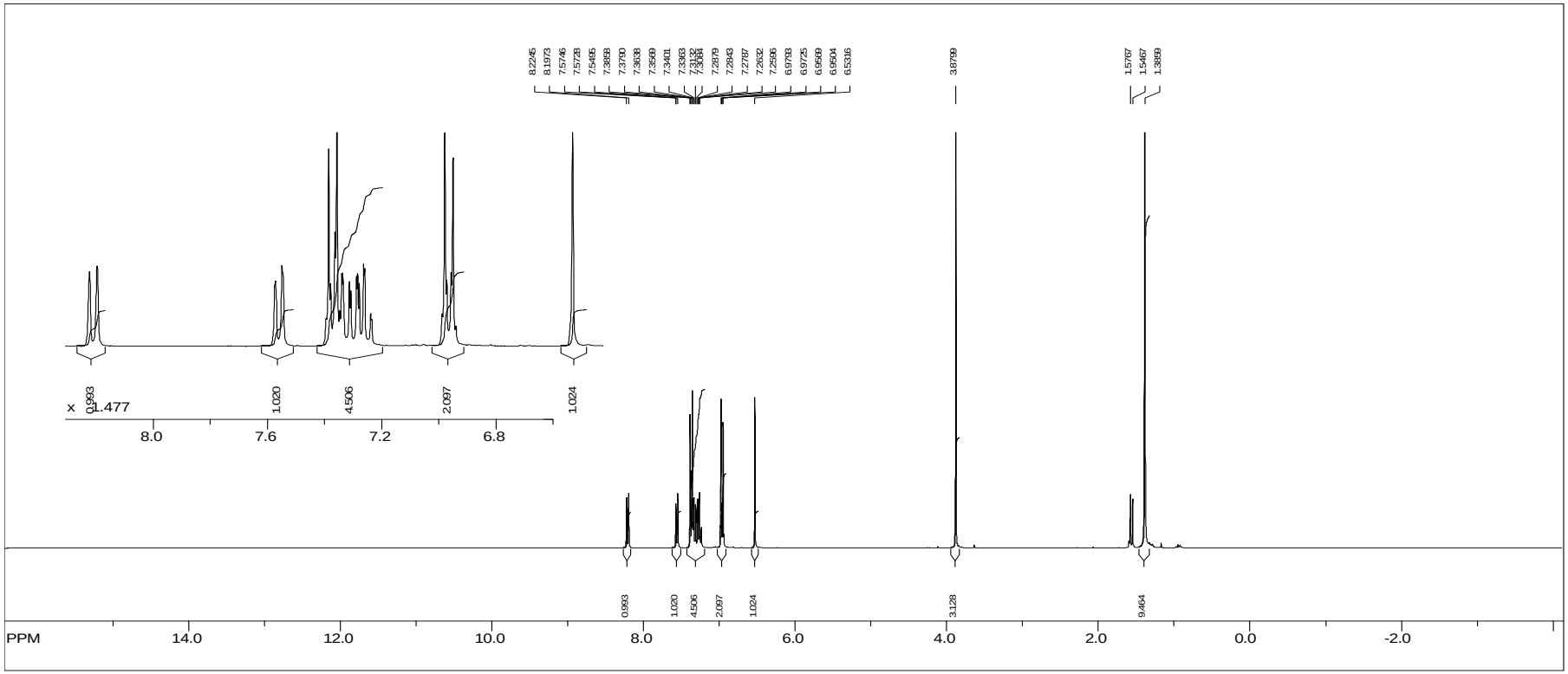
file: Z:\Laina\lmgxii\lmgxii_94b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

tert-Butyl 2-(4-methoxyphenyl)-1*H*-indole-1-carboxylate (374)



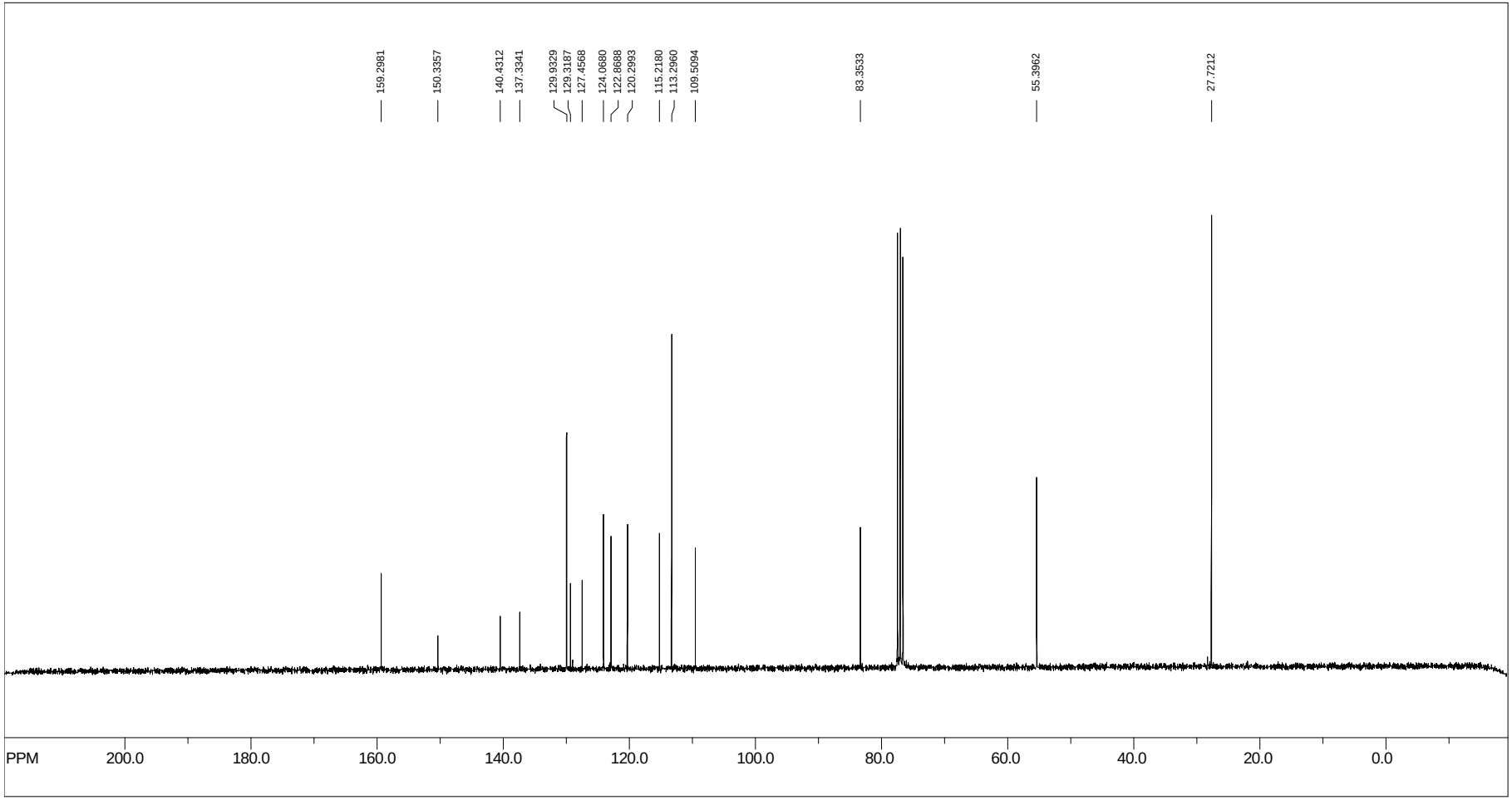
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxi\lmgxi_65a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 7

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

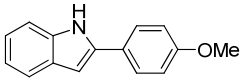
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



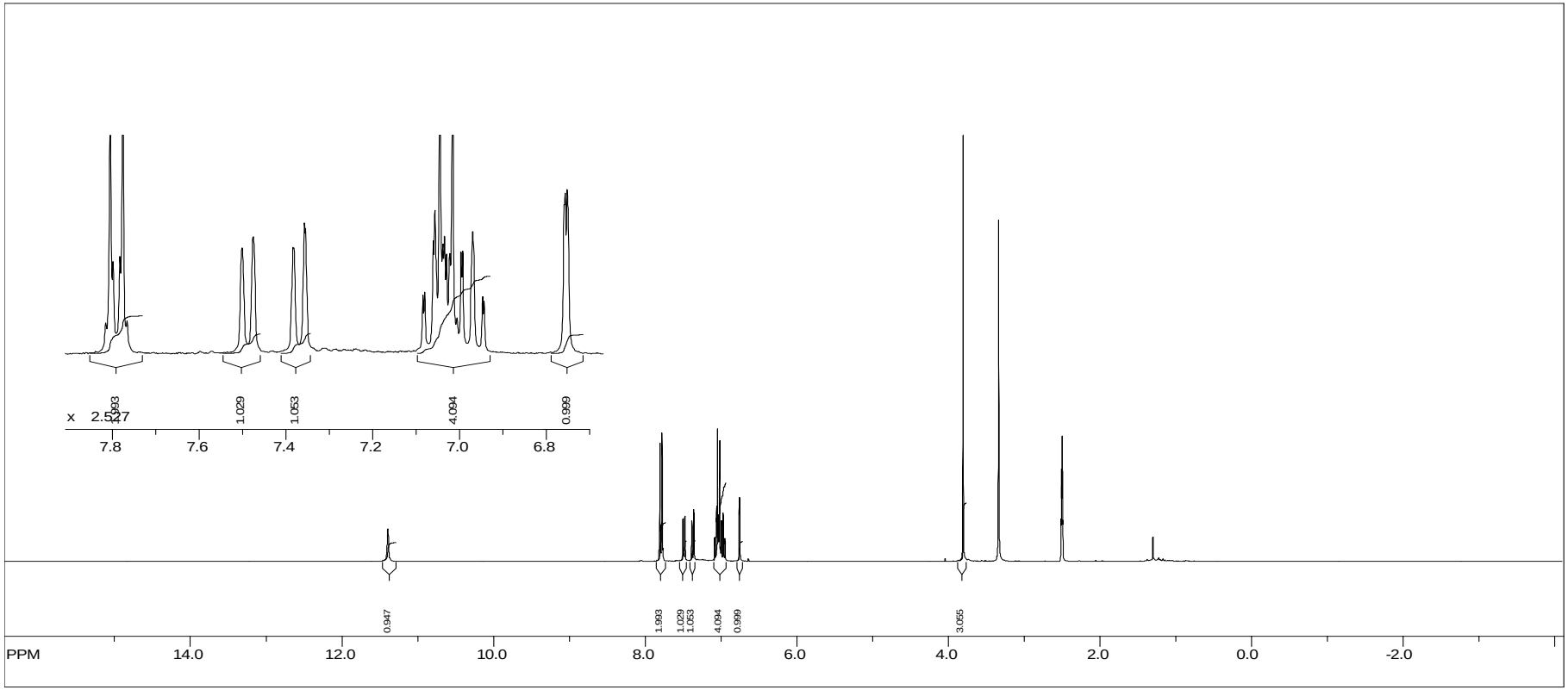
file: Z:\Laina\lmgxi\lmgxi_65a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 2048

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-1*H*-indole (375)



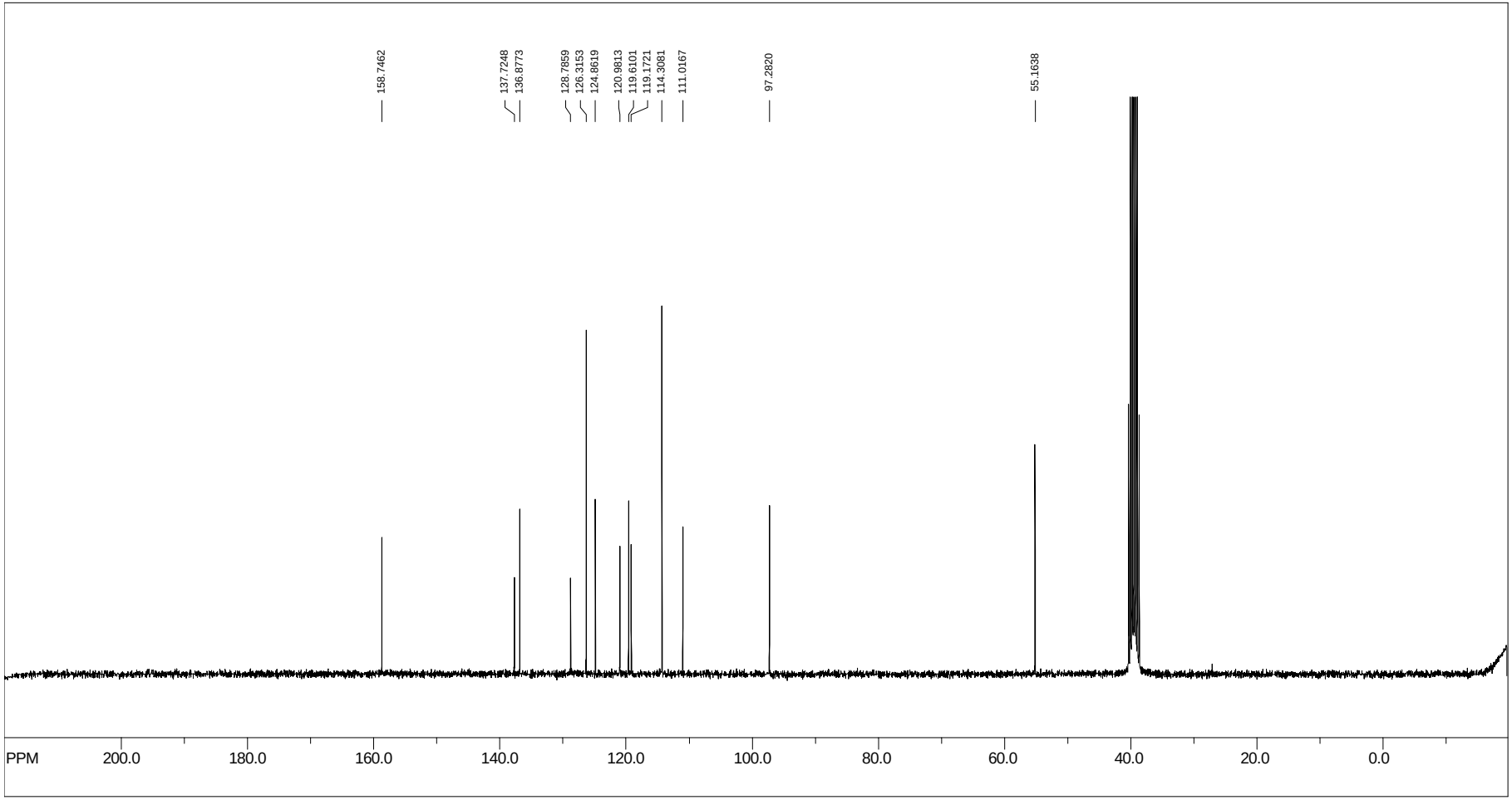
SpinWorks 2.5: PROTON DMSO {C:\Bruker\TOPSPIN1.3} hultin 5



file: Z:\Laina\lmgx\lmgxi_65c\3\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 4

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

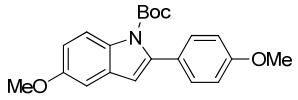
SpinWorks 2.5: C13CPD DMSO {C:\Bruker\TOPSPIN1.3} hultin 3



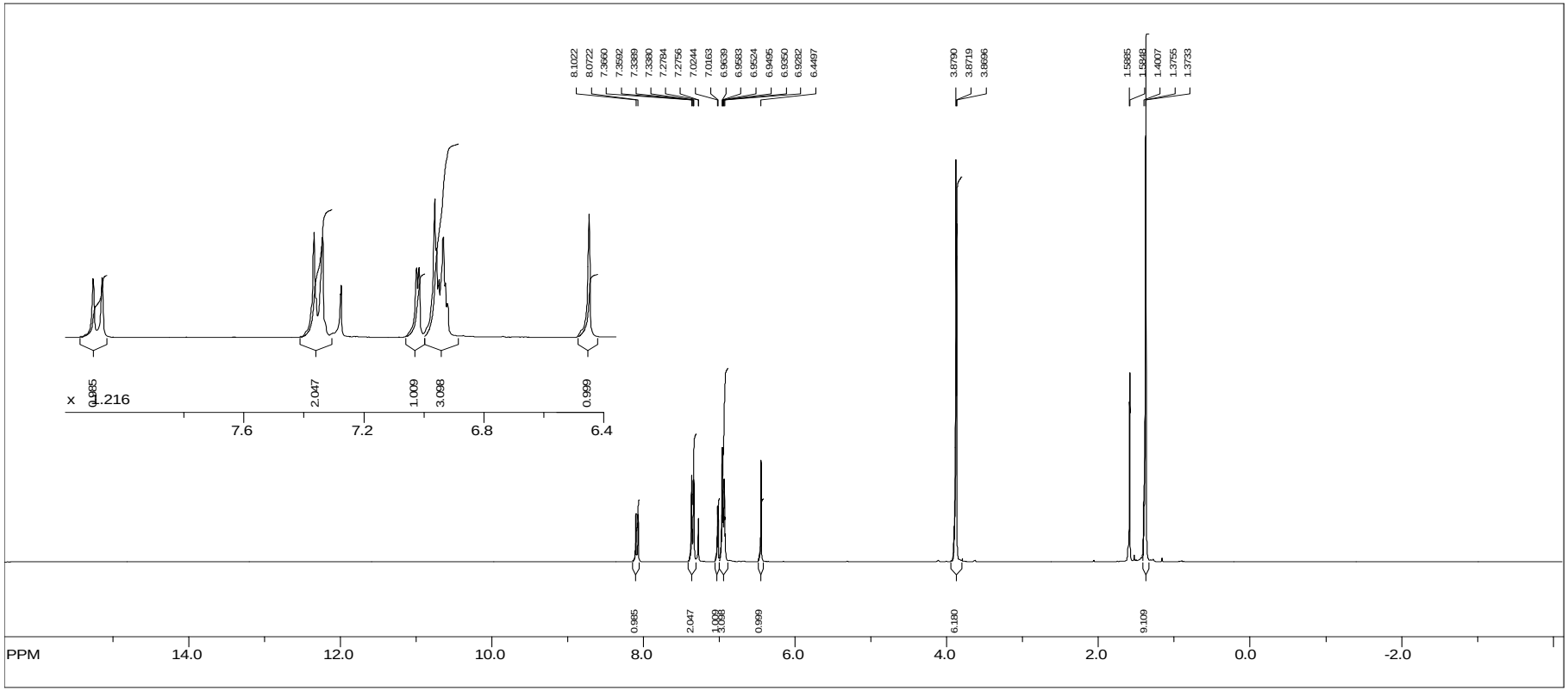
file: Z:\Laina\lmgxi\lmgxi_65c\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 8000

freq. of 0 ppm: 75.467787 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

tert-Butyl 5-methoxy-2-(4-methoxyphenyl)-1*H*-indole-1-carboxylate (376)



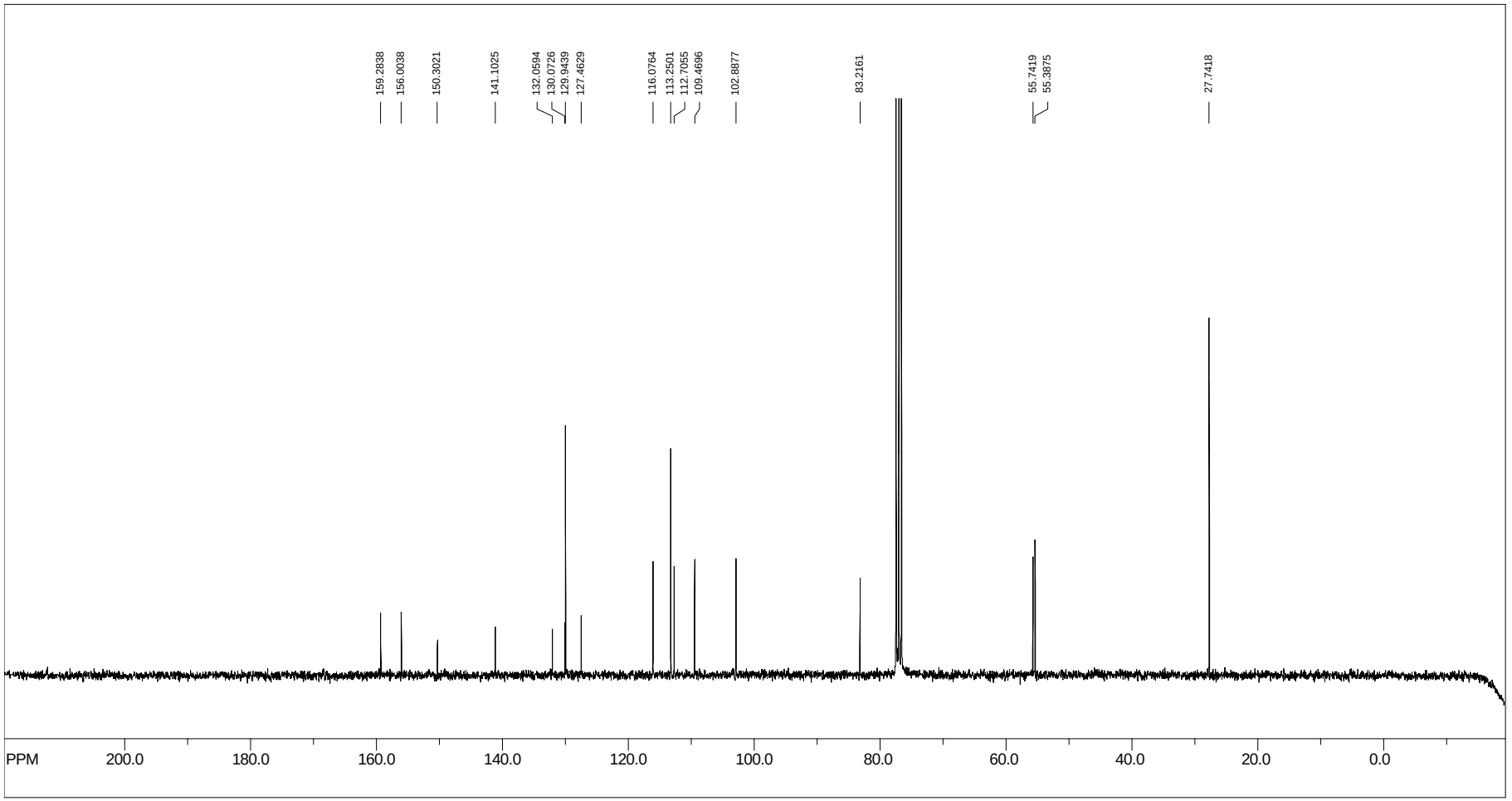
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxl\lmgxi_66a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

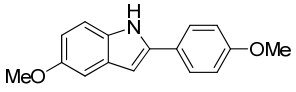
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxi\lmgxi_66a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1208

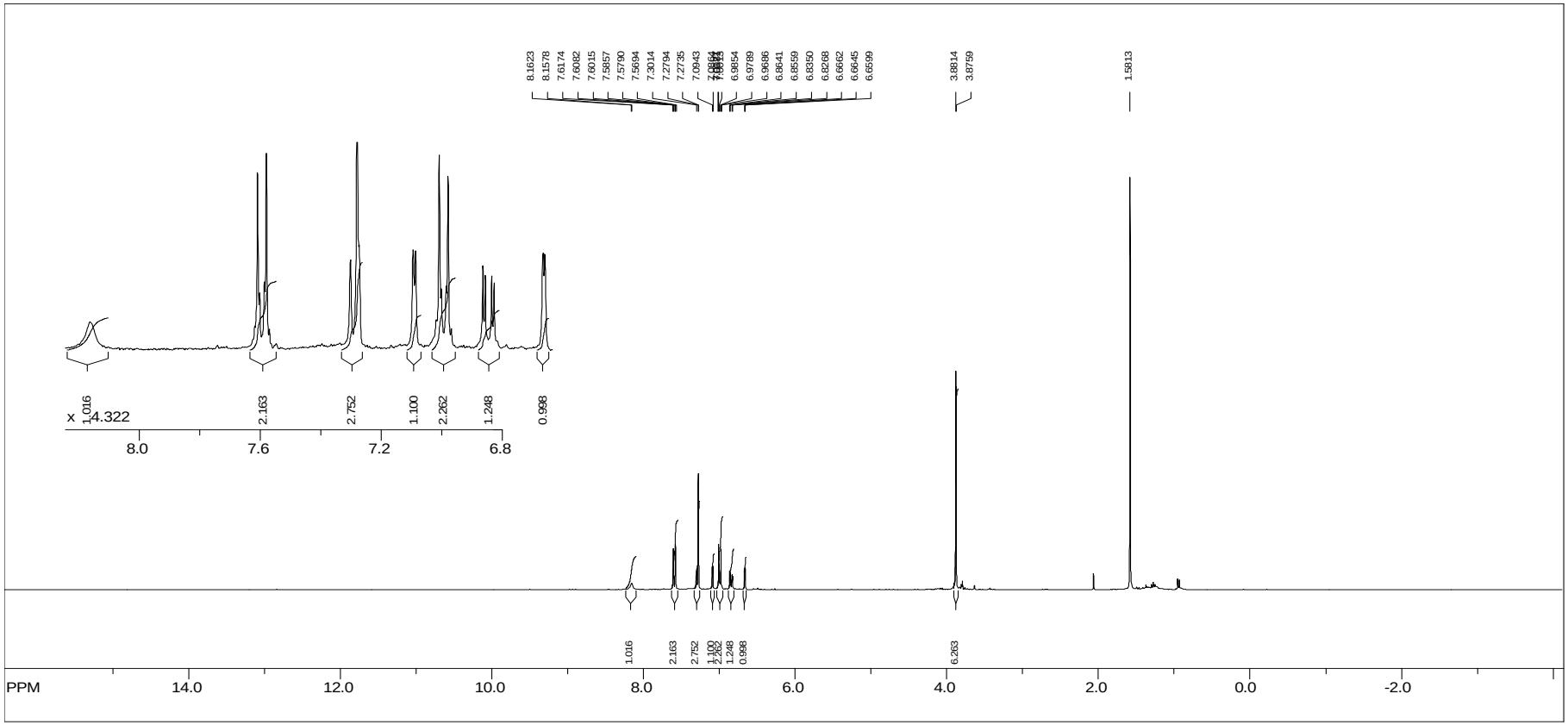
freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000

5-Methoxy-2-(4-methoxyphenyl)-1*H*-indole (377)



In $CDCl_3$

SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 5

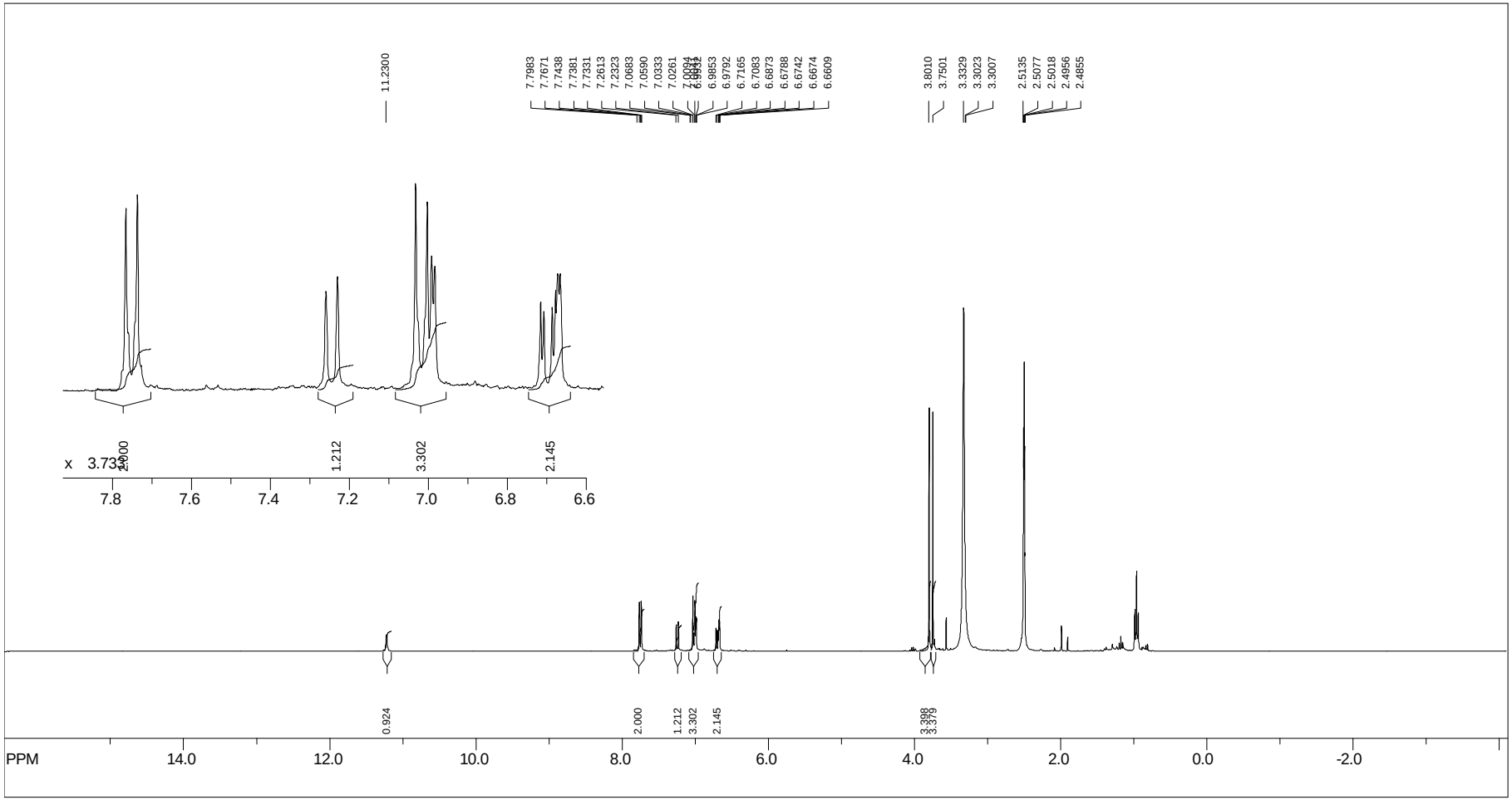


file: Z:\Laina\lmgxi\lmgxi_66cf\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

In DMSO-d_6

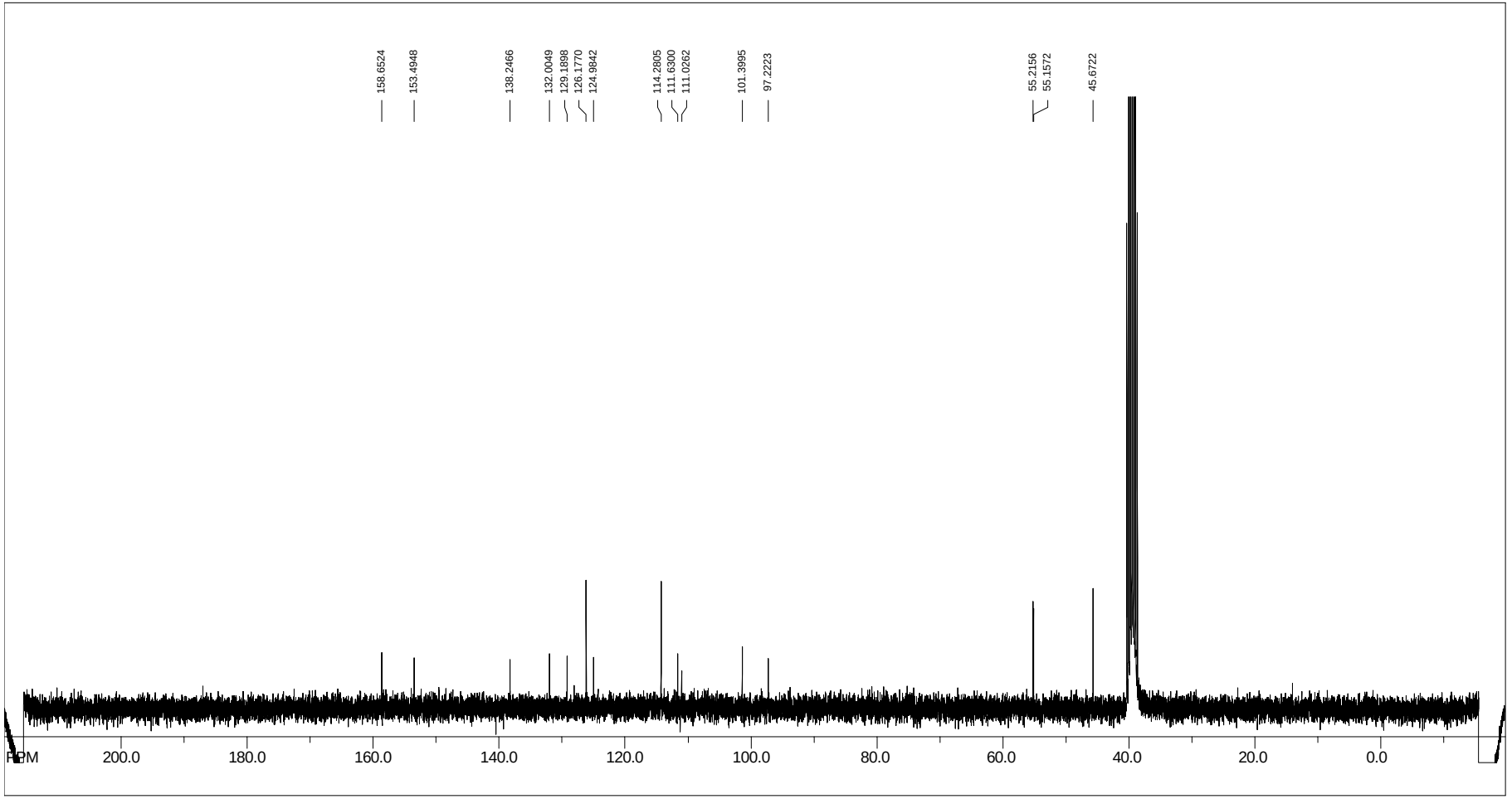
SpinWorks 2.5: PROTON DMSO {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxi\lmgxi_66d\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

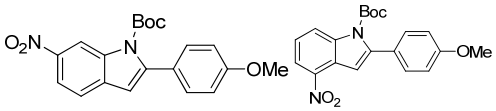
SpinWorks 2.5: C13CPD DMSO {C:\Bruker\TOPSPIN1.3} hultin 1



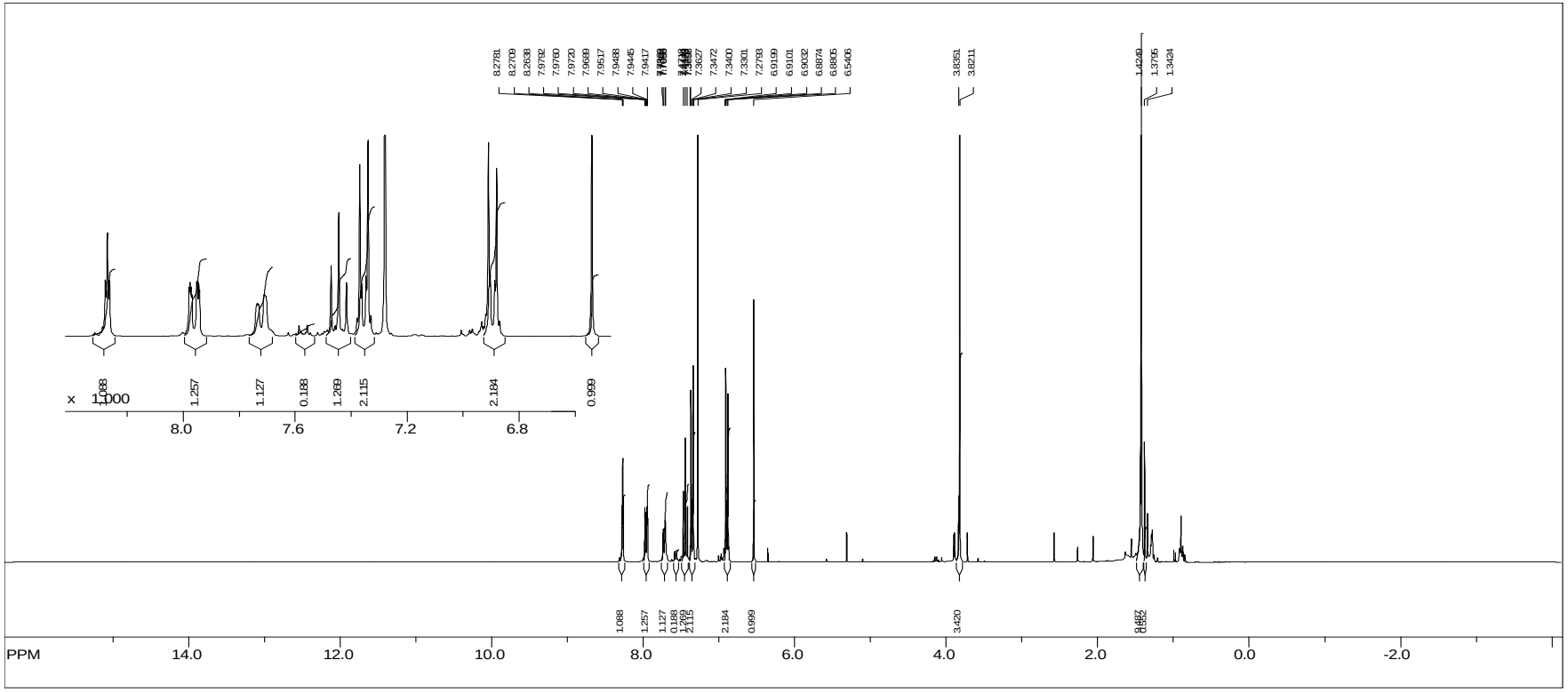
file: Z:\Laina\lmgxi\lmgxi_66d\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1932

freq. of 0 ppm: 75.467787 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

tert-Butyl 2-(4-methoxylphenyl)-6-nitro-1*H*-indole-1-carboxylate (378) and *tert*-Butyl 2-(4-methoxylphenyl)-4-nitro-1*H*-indole-1-carboxylate (378')



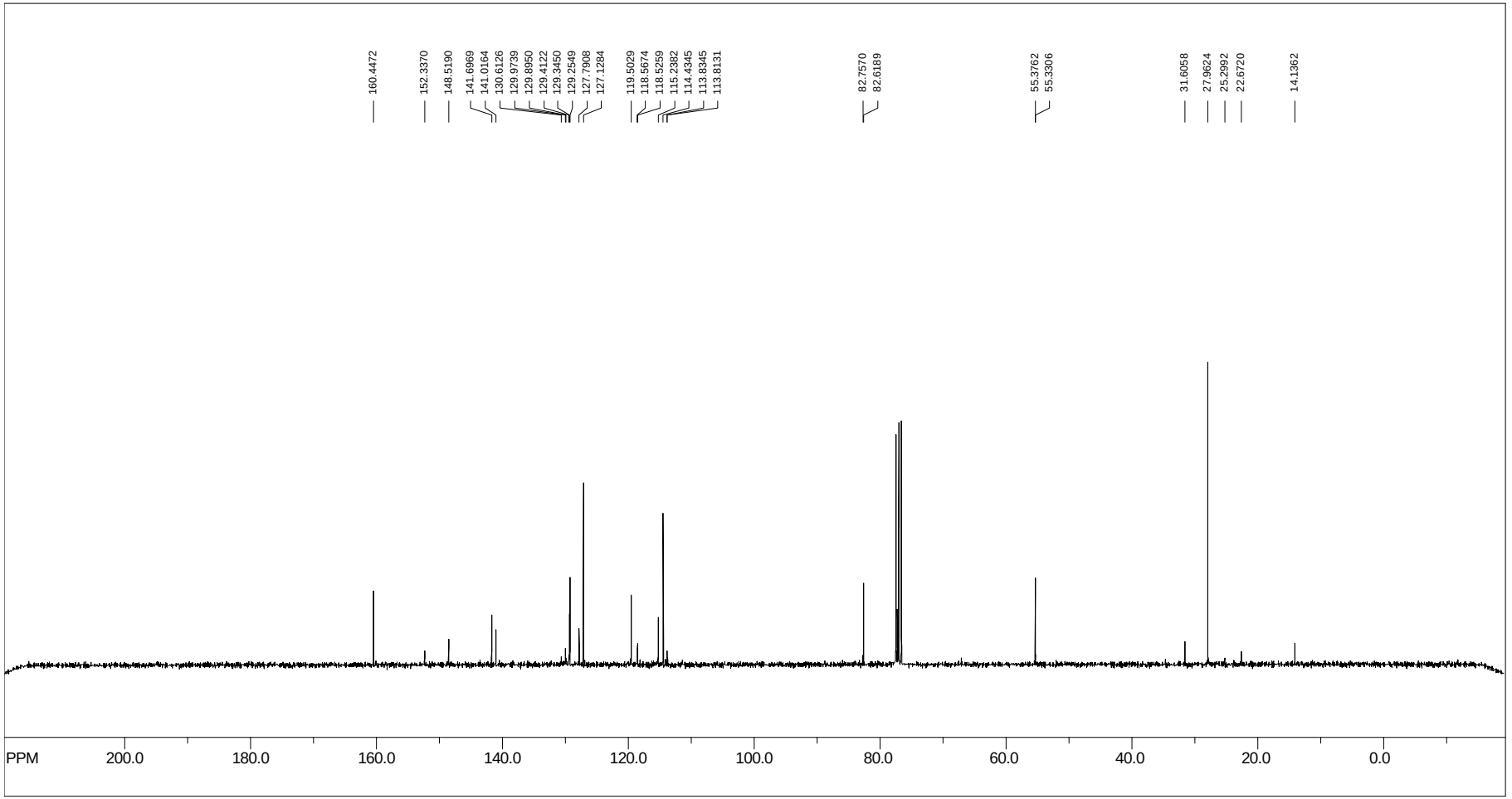
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



file: Z:\Laina\lmgx\lmgxi_67a\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

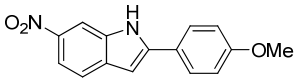
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 4



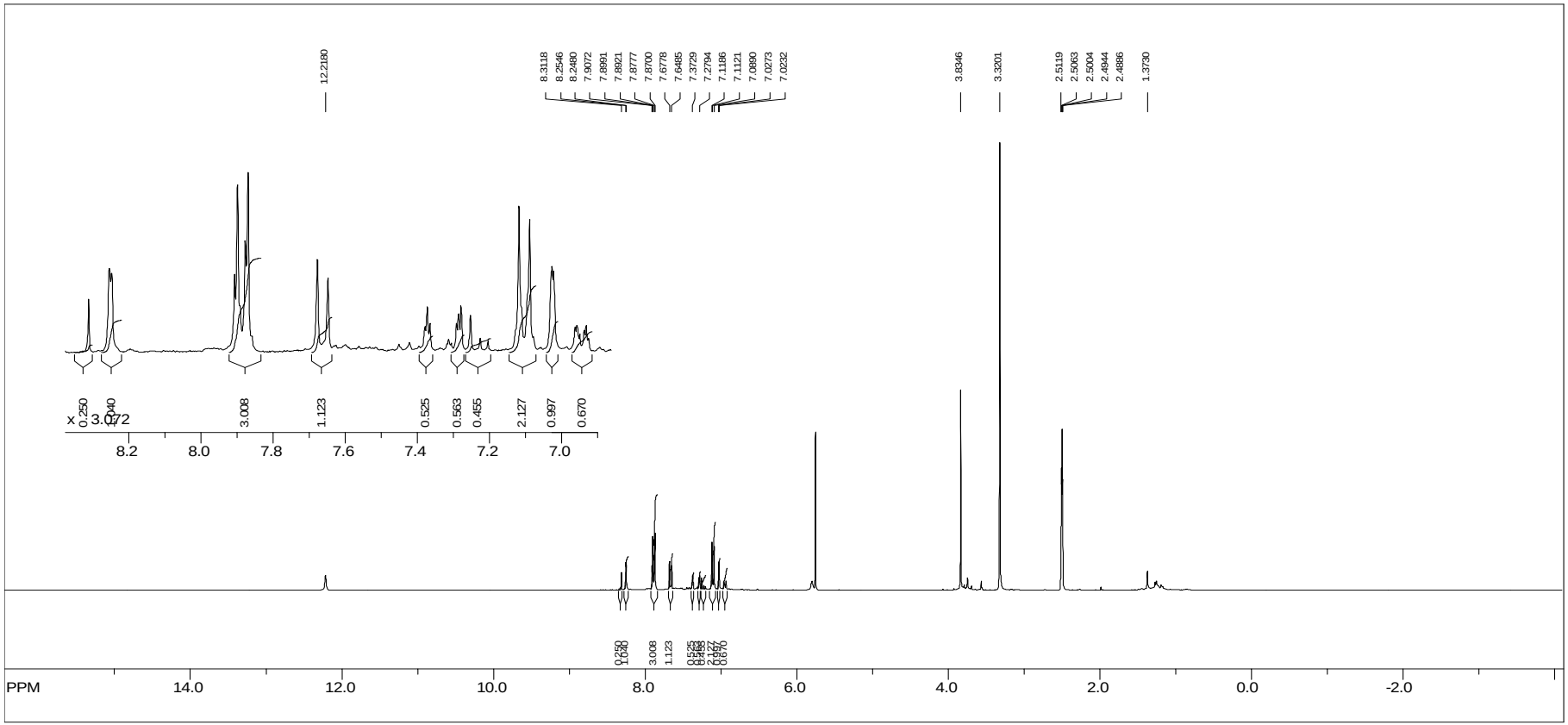
file: Z:\Laina\lmgxi\lmgxi_67a\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 763

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-(4-Methoxyphenyl)-6-nitro-1*H*-indole (379)



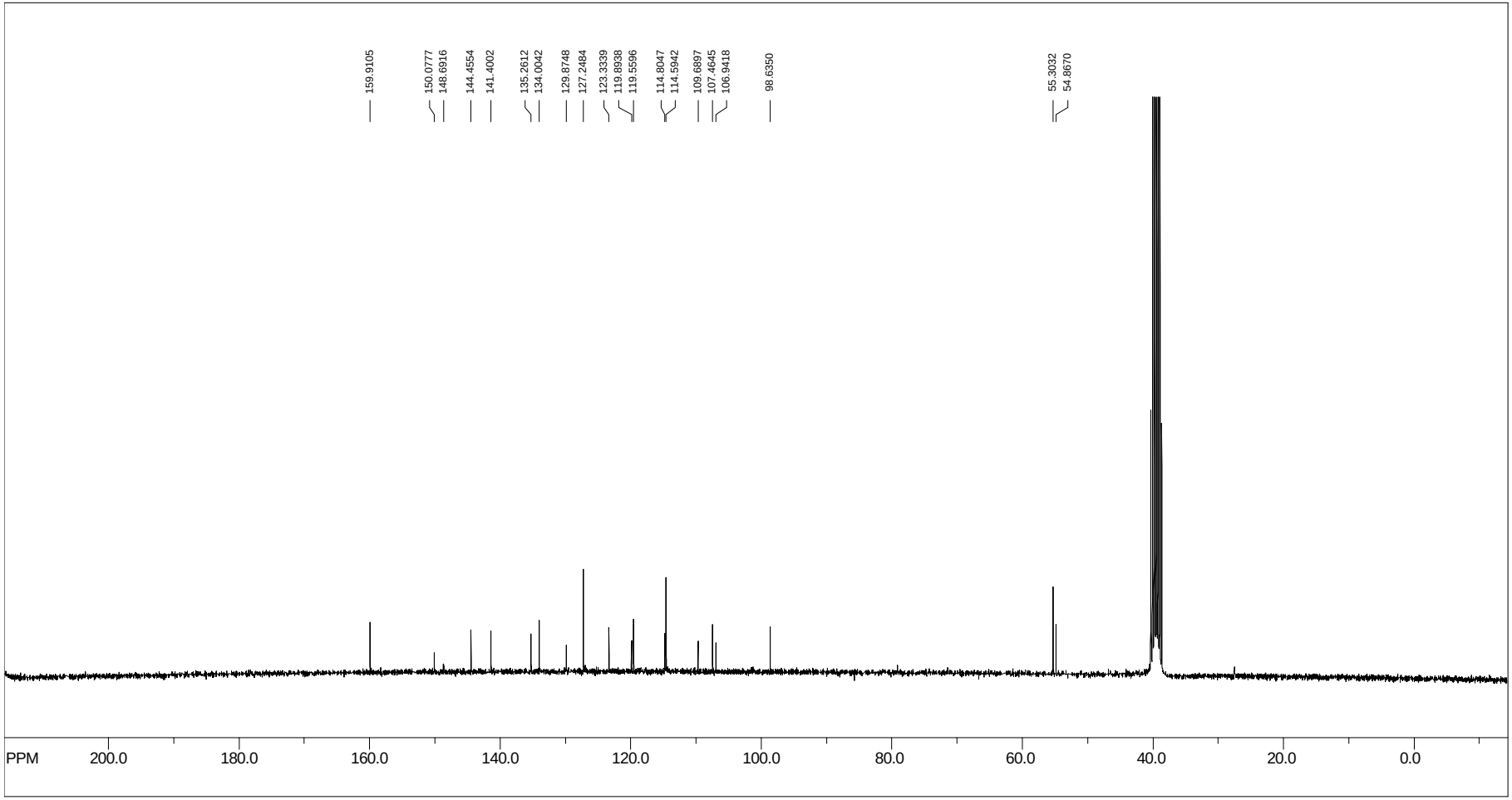
SpinWorks 2.5: PROTON DMSO {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgpi\lmgpi_67e\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

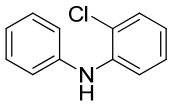
SpinWorks 2.5: C13CPD DMSO {C:\Bruker\TOPSPIN1.3} hultin 2



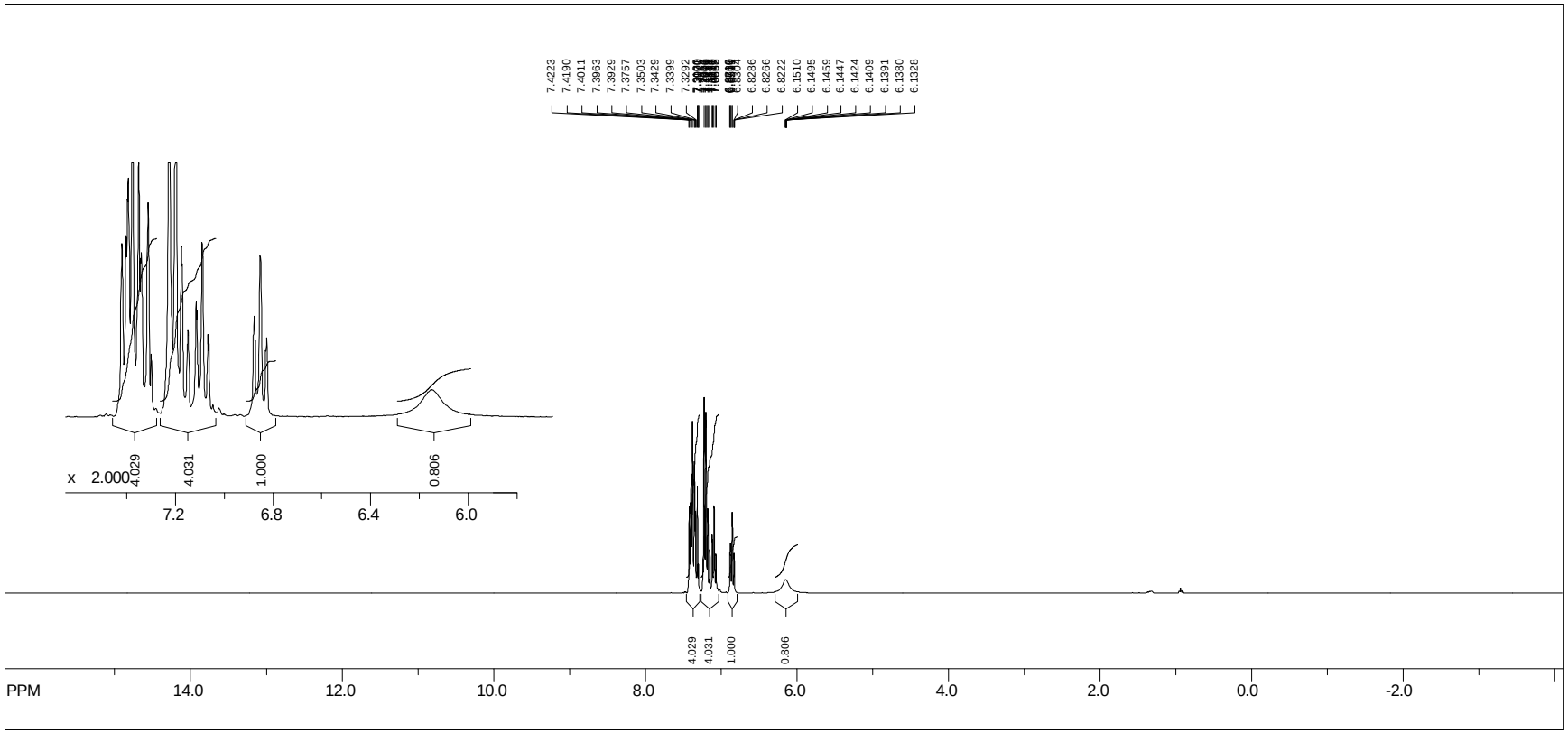
file: Z:\Laina\lmgxi\lmgxi_67e\3\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 11000

freq. of 0 ppm: 75.467787 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-Chloro-*N*-phenylbenzamine (380**)**



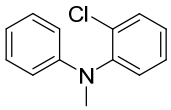
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



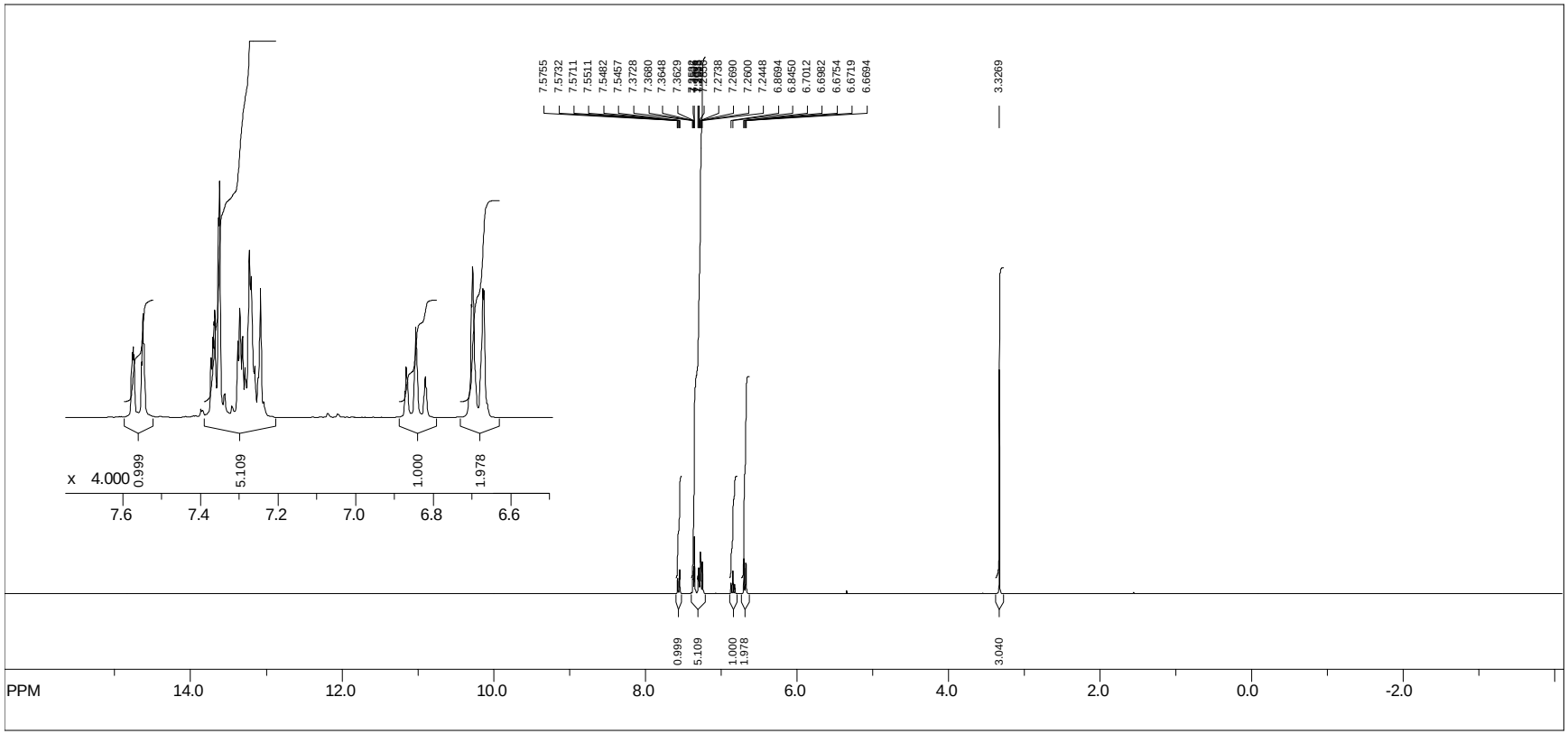
file: Z:\Laina\lmgxiii\lmgxiii_49a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 3

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

2-Chloro-*N*-methyl-*N*-phenylbenzamine (382)



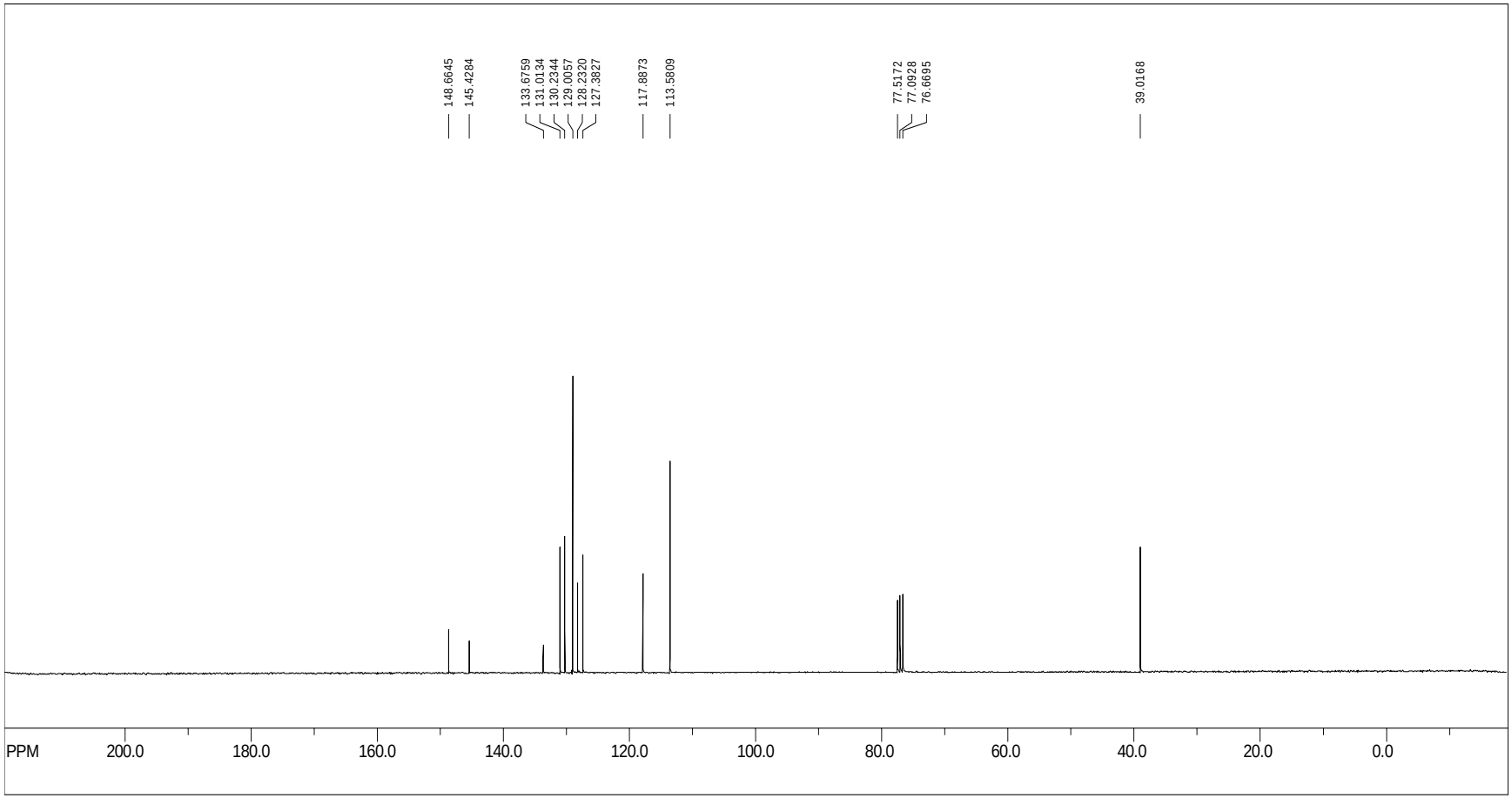
SpinWorks 2.5: N-Methyldiarylamine



file: Z:\Laina\lmgxiv\lmgxiv_50a\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 8

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

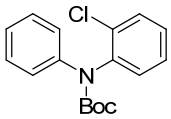
SpinWorks 2.5: N-Methyldiarylamine



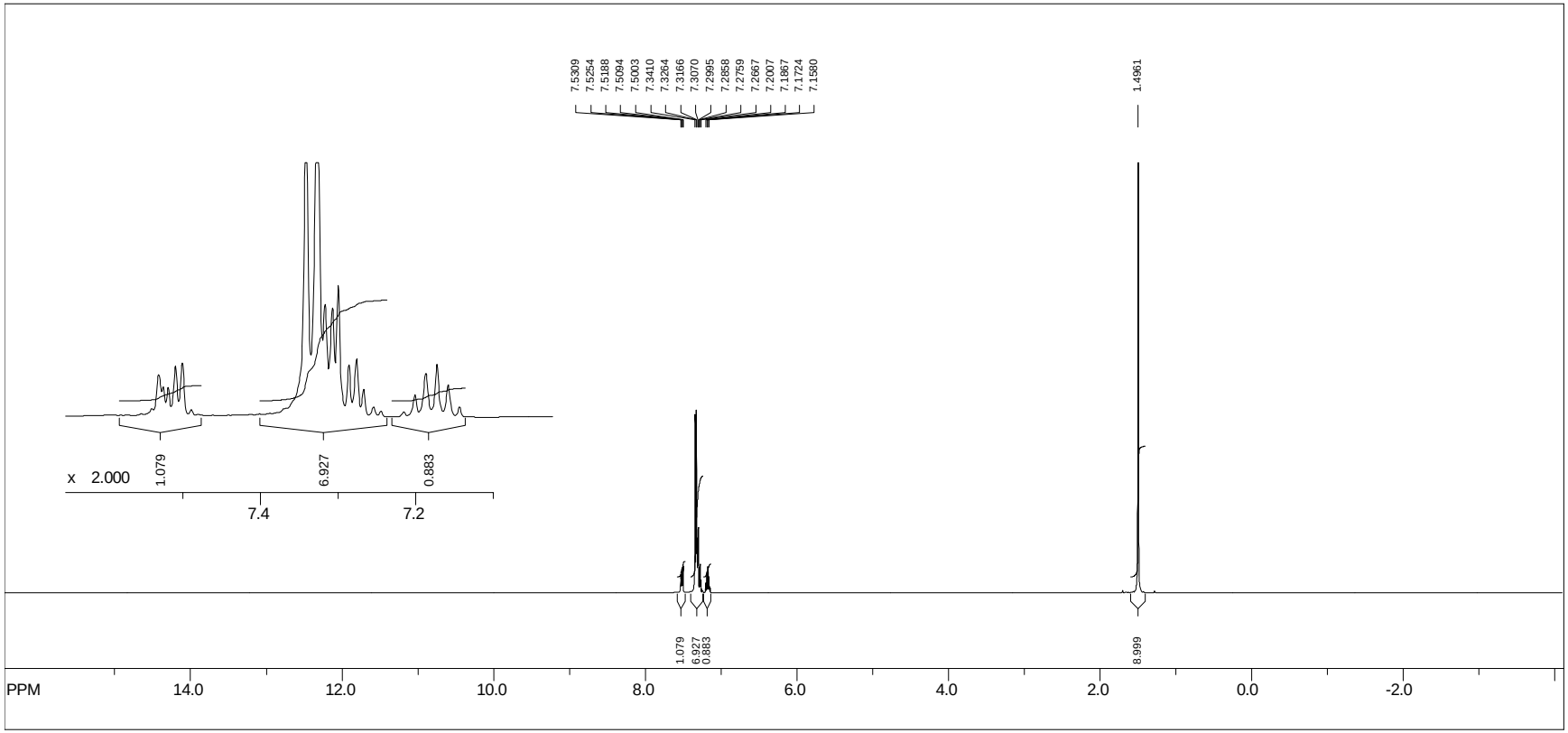
file: Z:\Laina\lmgxiv\lmgxiv_50a\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

tert-Butyl 2-chlorophenyl(phenyl)carbamate (384)



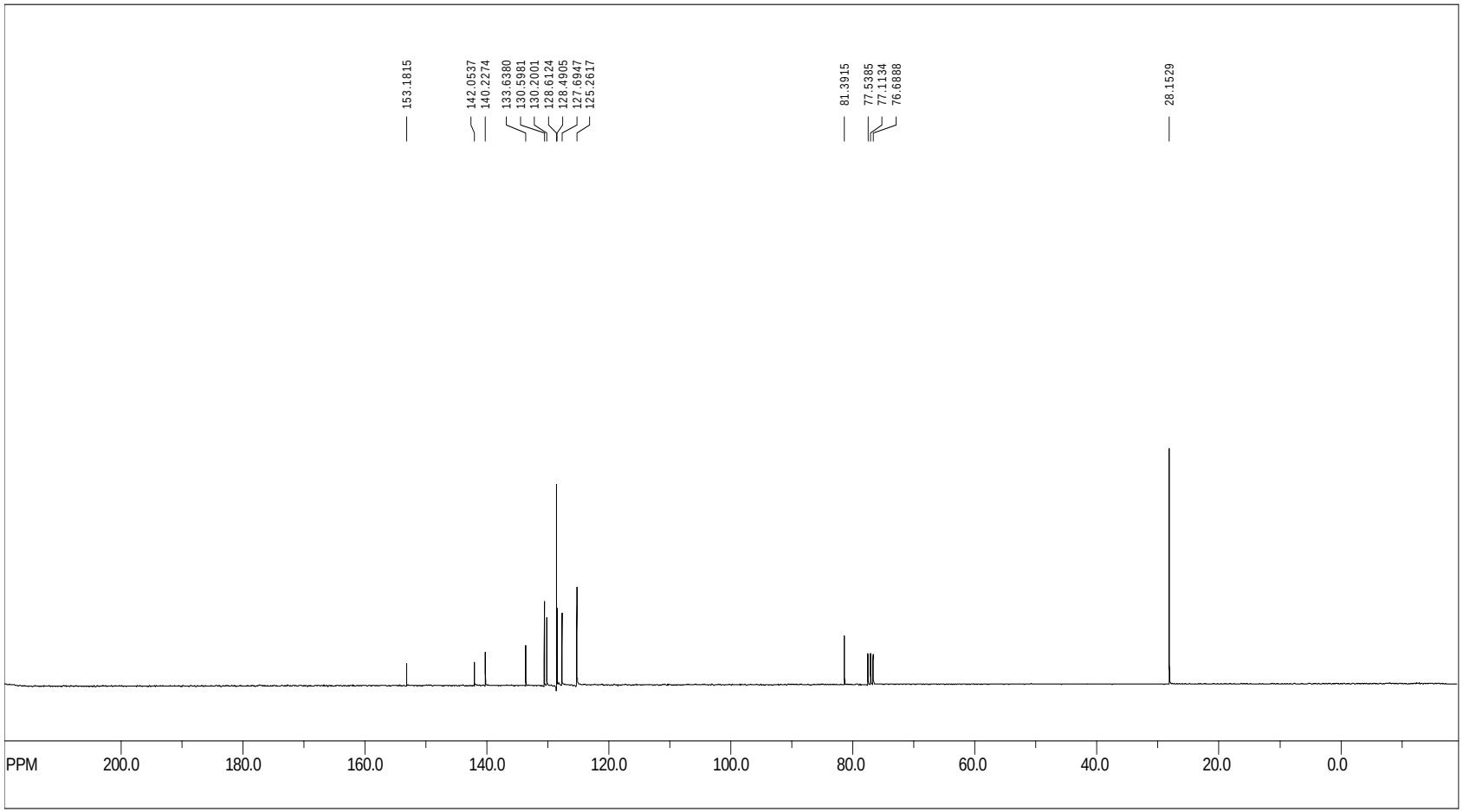
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



file: Z:\Laina\lmgxv\lmgxv_30b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 2

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

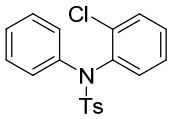
SpinWorks 2.5: C13CPD CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 2



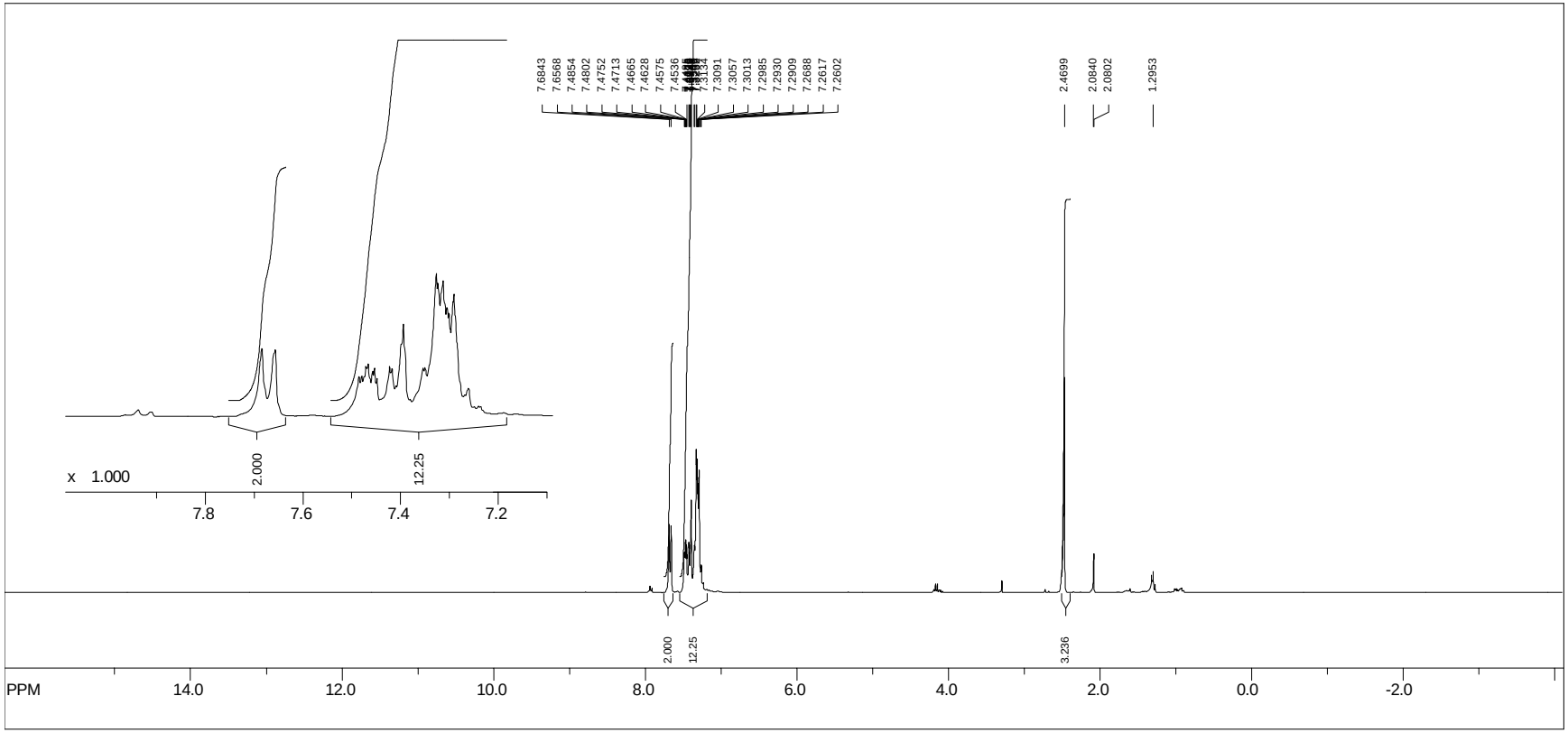
file: Z:\Laina\lmgxv\lmgxv_30b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 512

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

N-(2-chlorophenyl)-4-methyl-*N*-phenylbenzenesulfonamide (386)



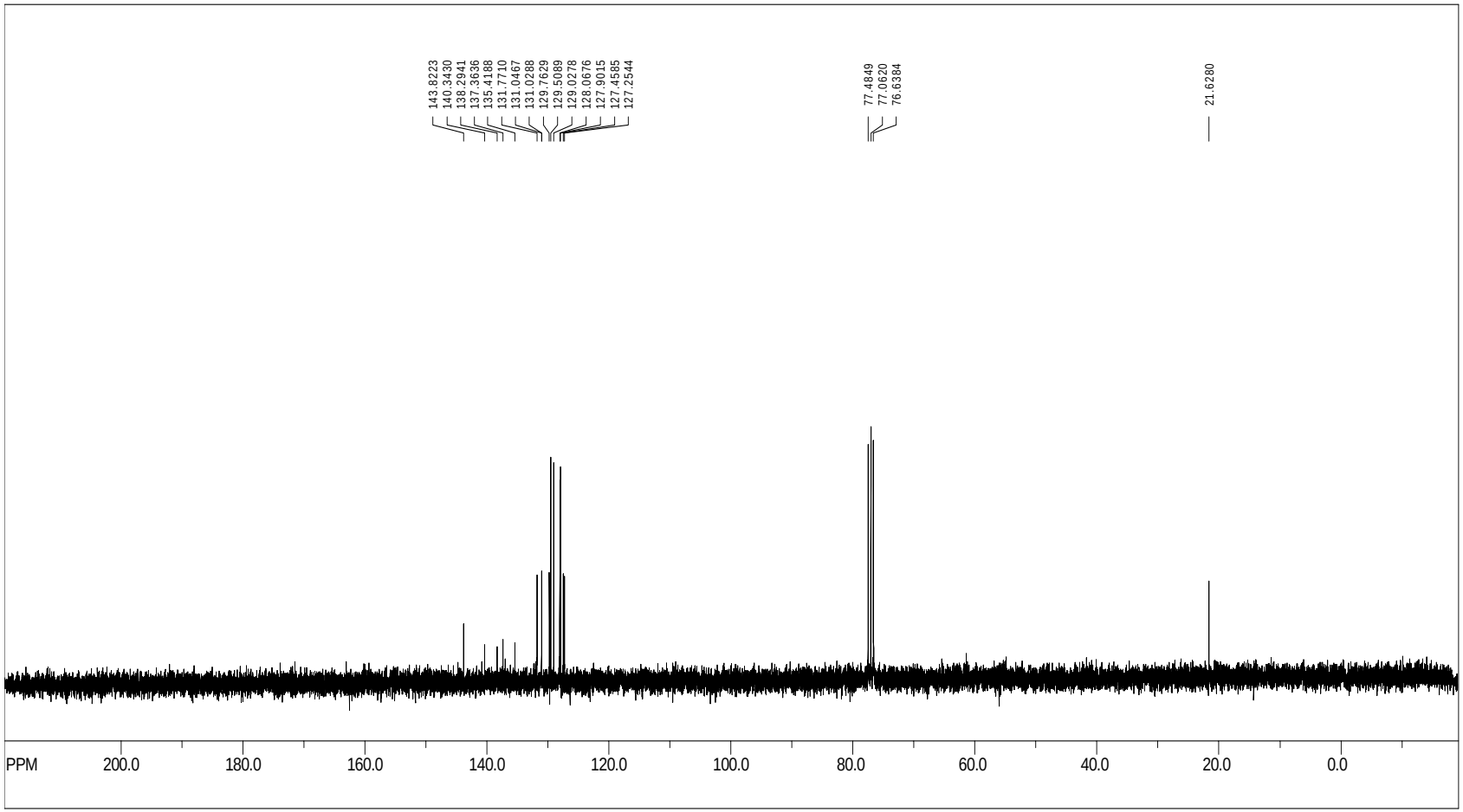
SpinWorks 2.5: PROTON CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgx\lmgxv_27b\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 65536 points
width: 6172.84 Hz = 20.567092 ppm = 0.094190 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000

SpinWorks 2.5: C13CPD256 CDCl3 {C:\Bruker\TOPSPIN1.3} hultin 1



file: Z:\Laina\lmgxv\lmgxv_27b\2\fid expt: <zgpg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 36

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000