SYNTHESIS OF *p*-HYDROXYDIARYLKETONES AND THEIR REACTIONS WITH OXIDIZING CONDITIONS

by

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ABSTRACT:

A detailed study of the synthesis of hydroxydiarylketones by the Fries rearrangement of esters containing methoxy and nitro group has been carried out. Under specific conditions methoxy esters rearranged to give methoxy hydroxydiarylketones and dihydroxydiarylketones as the major and minor products respectively. These reaction conditions are also responsible for the cleavage of the methyl group on the methoxy group. Suitable conditions were established for esters containing -OMe group(s) to minimize cleavage. These conditions were studied and adjustments were made to optimize the yields of the required methoxy hydroxydiarylketones. The yields of the methoxy hydroxydiarylketones were higher when chlorobenzene (b.p. 133 °C) was used as the solvent.

Oxidation of methoxy hydroxydiarylketones and nitro hydroxydiarylketones with lead tetraacetate in a variety of solvents and solvent mixtures has been studied. Acetoxylation occurred exclusively at C2 to give 2-acetoxylated derivatives. The nature of the group substituted on the second phenyl ring (MeO-, O_2N-, H) did not affect the acetoxylation position. The solvent/solvent mixture used for the reactions seemed to have a great effect on the yields and cleanness of the reaction. It was found that the yields were higher when acetic acid was used as the solvent.

When ceric ammonium nitrate was used as oxidant, all hydroxydiarylketones were oxidized to give the cleaved acids. The yield of acid depended on the reaction solvent used. The highest yield was obtained when acetic acid methanol mixture was used as the solvent. The phenyl ring containing the hydroxy group was not recovered, nothing was detected which corresponded to the phenol used.

Bromine was also used to oxidize the hydroxydiarylketones. As one of the

characteristic properties of phenols is the rapidity with which they undergo nuclear substitution in available *ortho* and *para* - positions by electrophilic reagents such as bromine, bromo substituted hydroxydiarylketones were obtained.

In general, no compound (product) was detected consistent with a retro-Fries rearrangement. At the same time, the possibility of a retro-Fries rearrangement cannot been excluded, especially when ceric ammonium nitrate was used as an oxidant.

TABLE OF CONTENTS:

Chapter 1

INTRODUCTION

The main objective of this research was to develop efficient syntheses of hydroxydiarylketones and to study their reaction under selected oxidizing conditions. The hydroxydiarylketones have many industrial applications and also may be potent bactericides. They find very important applications as stabilizers in the manufacturing of paints and vanishes, plastics, films, natural or synthetic rubbers. Many hydroxydiarylketones and some of their derivertives are used in the metallurgical industry, either for the extraction and separation of metals or for their selective estimation in ores and alloys. Some hydroxydiarylketones have properties which are useful in the pharmaceutical industry and in perfumery. Moreover, hydroxydiarylketones are important, mainly as starting materials in organic synthesis. Some hydroxydiarylketones occur naturally.

Although several reactions allow the preparation of hydroxydiarylketones (Friedel-Crafts reaction, Fries rearrangement, Hoesch and Nencki reactions), the Fries rearrangement is the most suitable process. It is easy to perform, the isomer separation is straightforward and the yields are good. The Fries rearrangement has also been carried out photochemically. The last review on Fries rearrangement dates from 1992.[1] In this section the Fries reaction is discussed.

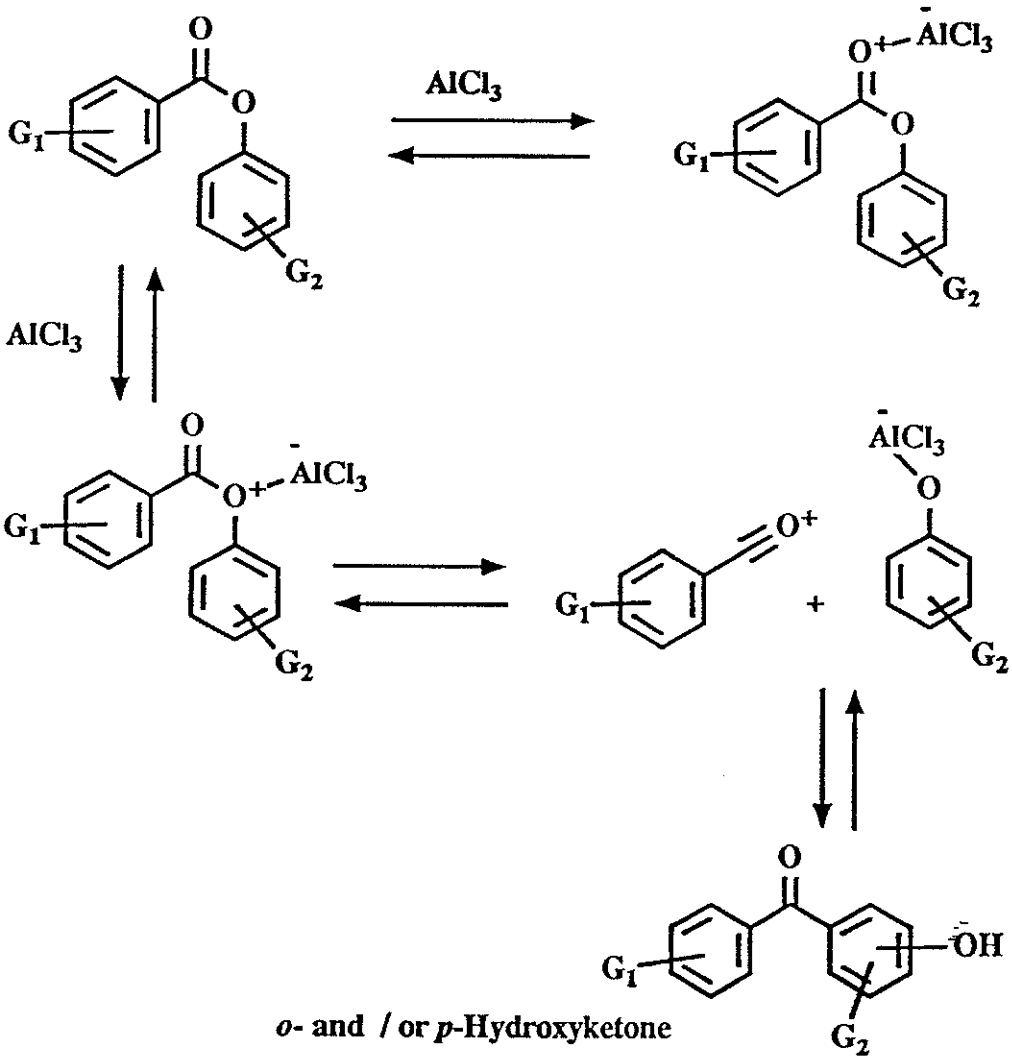
Hydroxydiarylketones prepared by Fries rearrangement can be oxidized with a variety of oxidants. Bromine (Br_2), lead tetraacetate (LTA), and ceric ammonium nitrate (CAN), are some of the oxidants which are expected to oxidize these compounds. A literature survey was made and the specific oxidative behaviors of these oxidants towards hydroxydiarylketones were identified. A review on oxidation of compounds related to hydroxydiarylketones using the mentioned oxidants is given in this section. Simple phenols and phenols with substituents at *ortho* and *para* position are good examples.

1.1: Preparation of hydroxydiarylketones:

A literature survey was made on methods for the preparation of the hydroxydiarylketones. We chose the Fries rearrangement method as the best method for hydroxydiarylketone preparation. The method is well documented[1-13] and various types of esters have been reported to rearrange to the hydroxydiarylketones under Fries conditions. $AlCl_3$ is the most commonly used catalyst to carry out the Fries rearrangement. The solid reagent is easier to handle compared to other Lewis acids. Some specific catalysts have been used for rearrangement of esters (zeolites and sulfonated cation exchange resins) but the yields obtained are not of preparative interest. In general, phenyl esters provide *ortho*-hydroxydiarylketones and *para*-hydroxydiarylketones. The yields of *ortho* &/or *para* products depends on the experimental conditions. Temperature and time are the two main factors which determine the product(s). On the other hand, in carrying out the reaction in refluxing solvents (temperature control), the formation of the desired products is preponderant. The solvents are chosen so that the intended temperature can be attained and easly maintained for the required length of time (until the reaction is completed).

Only in one example, published in 1961[8], was it suggested that the reaction was intermolecular. Munavalli[9] in 1972 suggested that in the Fries rearrangement intermolecular and intramolecular acylation are competitive, and that one or other can be almost totally suppressed by lowering or rising the temperature. In 1974 Martin [10] reviewed the Fries rearrangement and concluded that the mechanism was intermolecular. A literature survey showed that a predominantly intramolecular[10-13] rearrangement mechanism was favored by most authors. A

recent review by Martin[1] summarized enough evidence to support an intramolecular mechanism. The proposed mechanism is given below;



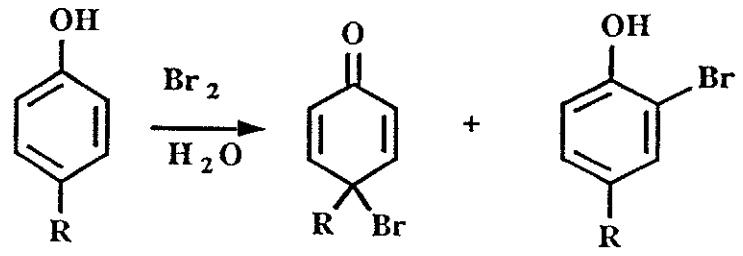
Scheme 1 Fries Rearrangement

Nothing has been mentioned in the literature on how to best prevent or reduce the cleavage of cleavable groups under the reaction conditions, e.g. Me on methoxy group. This research has developed suitable conditions for Fries reaction of diaryl esters containing methoxy group. These conditions are given in the Results and Discussion section.

1.2: Bromination of Phenols:

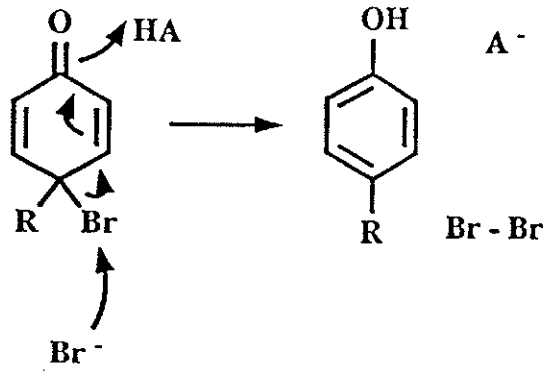
Electrophilic bromination of simple phenols to produce brominated phenols is well known and documented. Bromination is confirmed to proceed *via* 2,5-cyclohexadienone intermediates. The intermediate derived from 2,6-dimethylphenol behaves similarly to the intermediate derived from unsubstituted phenol. The only difference is that the former rearranges more slowly. This means that the intermediate is less labile (has a longer lifetime) than a derivative derived from a simple phenol. In general, phenols bearing bulky groups at position 2 and 6 react with bromine to give cyclohexadienone of sufficient lifetime to be observable.[14] These "*ipso*-dienones" (cyclohexadienones) are also formed during bromination of phenols and phenols bearing alkyl groups at position 2, 3, 5 and/or 6. These *ipso*-dienones account for about 10% of the initial consumption of bromine.[15]

Scheme 2 below shows the two possible products when phenols with an alkyl group at the *para* position are subjected to bromination conditions. Only *ortho* bromo-products are isolated.



Scheme 2 Bromination of Phenol

Under the reaction conditions *ipso*-dienones are labile and decompose by debromination which is induced by Br^- and catalyzed by proton and general acids. As a consequence they are converted to *ortho*-bromo products. A debromination mechanism suggested by Tee's group[16] is shown below in Scheme 3.



Scheme 3 Debromination Mechanism

Based on these facts we decided to study the bromination of the hydroxydiarylketones prepared by Fries rearrangement. Hydroxydiarylketones are

expected to behave like simple phenols, i.e. *ipso*-dienones are expected to form during bromination. These *ipso*-dienones are possible intermediates for the retro-Fries reaction.

Beside electrophilic bromination of phenols, bromine dehydrogenates alcohols to carbonyl compounds[17] (secondary alcohols in preference to primary alcohols[17a]) and hydrazo compounds to azo compounds[18]and oxidizes sulfides to sulfoxides[19] and disulfides to sulfonic acids.[20] Benzyl alkyl ethers are degraded to benzaldehyde.[14] Phenols are oxidized to quinones.[21]

1.3: Oxidation with Lead Tetraacetate (LTA):

Systematic studies, especially by Wessely[22] and his group, have brought order to the data on phenol oxidation. In reaction the of lead tetraacetate, acetoxy radicals are the reactive species.

A number of mechanism speculations has been reported.[23-27] Using electron spin resonance (esr) spectroscopy, some authors[24] found that radicals were present during the oxidation of phenols by LTA. However, the work of other authors[25] made it probable that the observed radicals were formed by air oxidation and were not involved in the main reaction. These authors[25] regarded the latter as ionic because of the solvent dependence, catalysis by boron trifluoride, and very high rate of reaction . Most authors[23,24] assume that the aryl intermediates dissociate into radicals $(AcO)_3Pb^{\cdot}$ and $ArO^{\cdot}$. The aryl radical exists in two resonance structures which react with acetoxy radicals to form *ortho* and *para* quinone. Scheme 4 below is the general mechanism proposed by Criegee.[23a]

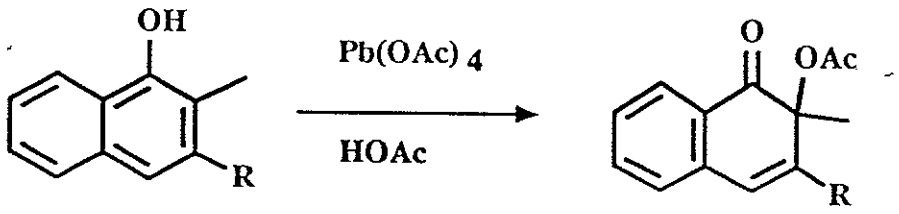
LTA causes one electron oxidations resulting in the formation of quinones from phenols and from aromatic amino compounds with *p*-amino groups.

As mentioned above, the nature of the groups, R_1, R_2 and R_3 controls the acetoxylation preference. It has been reported that the introduction of a Me - group into the *ortho* or *para* position of a simple phenol generally results in a higher proportion of acetoxylation at that position.[28,29]

This phenol oxidation, which has become known as Wessely[22] acetoxylation, has been the subject of a number of studies[30] due to interest in the mechanism of the reaction and its synthetic potential. Despite this, only a few such oxidations have been reported.

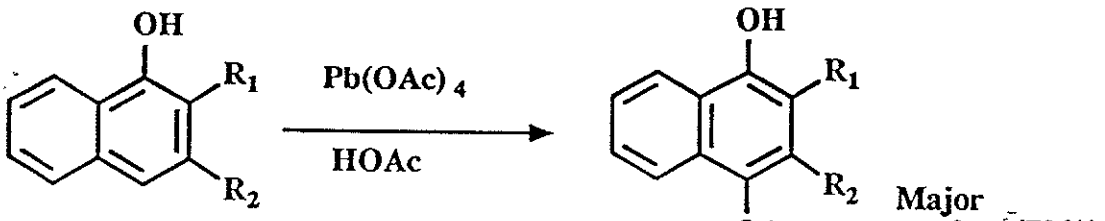
Lead tetraacetate oxidizes a variety of compounds, some of which are listed below. The addition of acetoxy radicals across double bonds produces vicinal diacetates, and their attack at benzylic positions and at α positions with respect to carbonyl groups produces benzylic acetates and α-acetoxy ketones respectively. Primary alcohols are converted (dehydrogenated) to aldehydes, and primary amines are converted into nitriles. Ketone hydrazones are transformed into diazo compounds. Also, vicinal diols undergo oxidative cleavage of the carbon chains in nonaqueous media.

Among the few authors who have reported on the oxidation of the phenolic compounds with lead tetraacetate were Pinhey and his group,[28] who performed a detailed study on the acetoxylation of 1-naphthols. In the case of 1-naphthol the main product was 4-acetoxy-1-naphthol (attack at C_4) and the minor product was 2,2-diacetoxynaphthalen-1(2H)-one (attack at C_2). 4-Acetoxy-1-naphthol was oxidized further to 1,4-naphthoquinone (attack at C_4).



Scheme 5 Acetoxylation of phenols with a methyl group substituent

They also found that when the *ortho* position to the hydroxyl group was substituted by an alkyl group other than Me group and the *para* position is unsubstituted, the acetoxylation preference changes. Scheme 6 below shows that acetoxylation occurred at *para* position only.



(R_1, R_2 = Me)

Scheme 6 Acetoxylation of phenols with alkyl groups other than methyl group

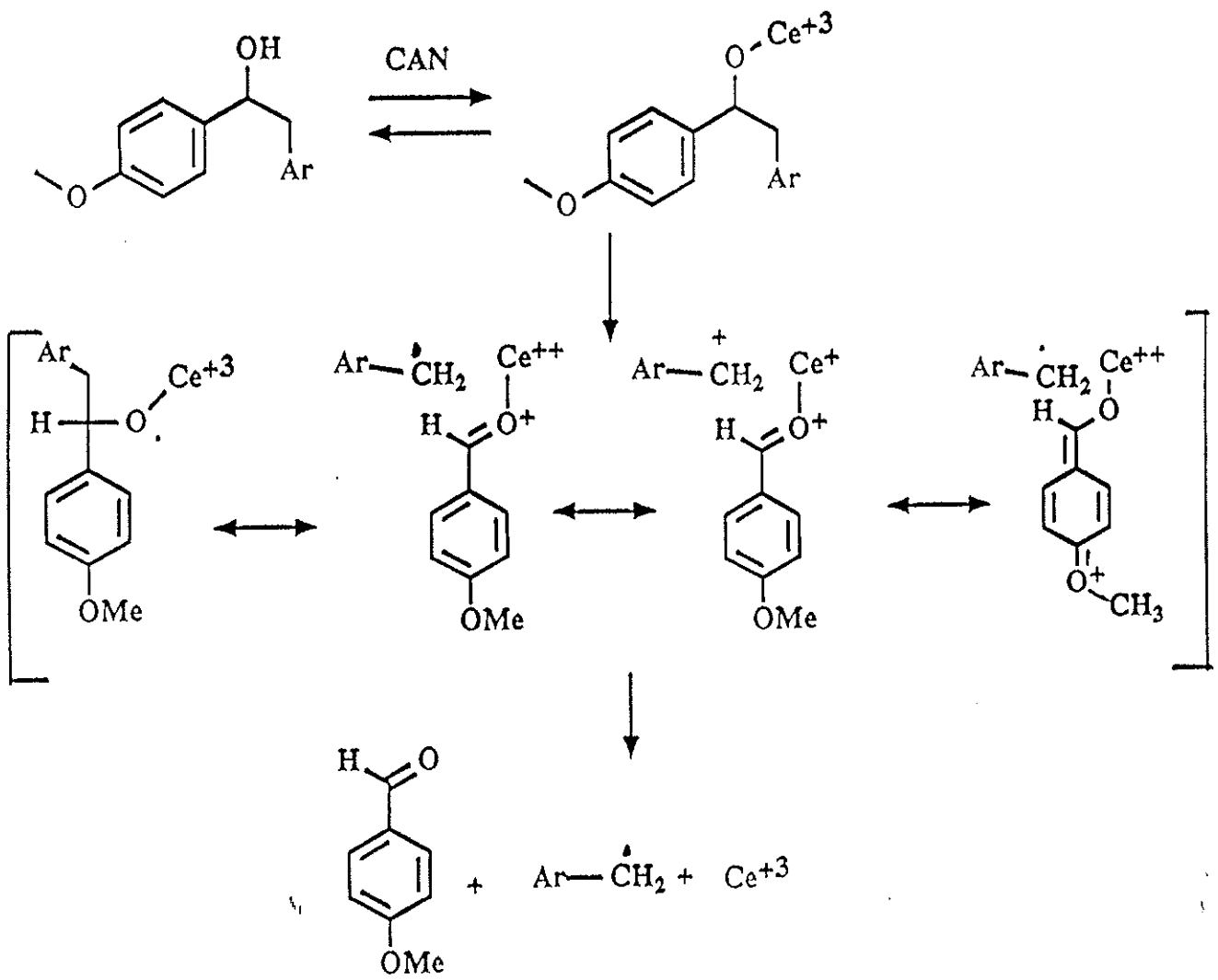
The oxidation of phenolic compounds with lead tetraacetate is well documented. We investigated the oxidation of hydroxydiarylketones with and without methyl groups at *ortho* position to the hydroxyl group.

1.4: Oxidation with Ceric Ammonium Nitrate (CAN):

The cerium (IV) ion is a typical one equivalent oxidant which has proved to be useful for the synthesis of certain aryl aldehydes from the corresponding substituted toluenes wherein selective oxidation of the methyl group is achieved.[31] In some cases, when the reaction was left for a long time, both aldehydes and carboxylic acids were produced.[17] However, in aqueous acetic acid, the reaction was reported as unsuccessful with strong electron donating groups. In contrast, other workers have reported successful oxidations of both of these types of compounds with CAN, and the reagent has been applied in steroid chemistry.[18] CAN is useful for acetoxylation of aromatic side chains in benzylic positions,[31c,32] oxidizes alcohols to aldehydes[33] and phenols to quinones.[34] The reagent also oxidizes methylene or methyl groups that are adjacent to aromatic rings to carbonyl groups,[31] cleaves vicinal diols to aldehydes or ketones, and α-hydroxy ketones to acids.[35] Diaryl sulfides can be converted to sulfoxides,[36] carbonyl compounds can be recovered from their oximes and semicarbazones[34a,37] and carboxylic acids from their hydrazides[38] under mild conditions. More frequently, the benzylic hydrogen is replaced by an acetoxy group on refluxing with ceric ammonium nitrate in 100% acetic acid or with lead tetraacetate.

Ceric ammonium nitrate is a common oxidant used to generate radical cations from a variety of aromatic hydrocarbons. It has been used as a method of nitration, to catalyze opening of unsaturated epoxides, to remove a protecting group (N-protecting group e.g. di-(4-methoxyphenyl)methyl or ('dimethoxybenzhydryl', DMB)[39] and to effect oxidative-cleavage of 1,2-diarylethanols to corresponding aldehydes. The appearance of a red color has

been cited as a marker for the complex formation between Ce(IV) and hydroxylic substrates.[40,41] The oxidation mechanism has been studied by various researchers. At first, the mechanism of this type of reaction was assumed to be a two-electron process.[42] Later, in 1988, Fisher's group[40] gave evidence to support a one-electron process instead of a two-electron process. They proposed that the mechanism of oxidative cleavage of 1,2-diarylethanols by ceric ammonium nitrate was a one-electron process - shown as Scheme 7 below. Up to this time, there are no clearly documented two-electron oxidative cleavage of alcohols. There have been no reports so far about the oxidation of phenols with ceric ammonium nitrate.



Scheme 7 Mechanism of oxidative cleavage of benzylic alcohol

Due to its chemical behavior described above, CAN was chosen as one of the oxidants in this study.

1.5: Retro-Fries Reaction:

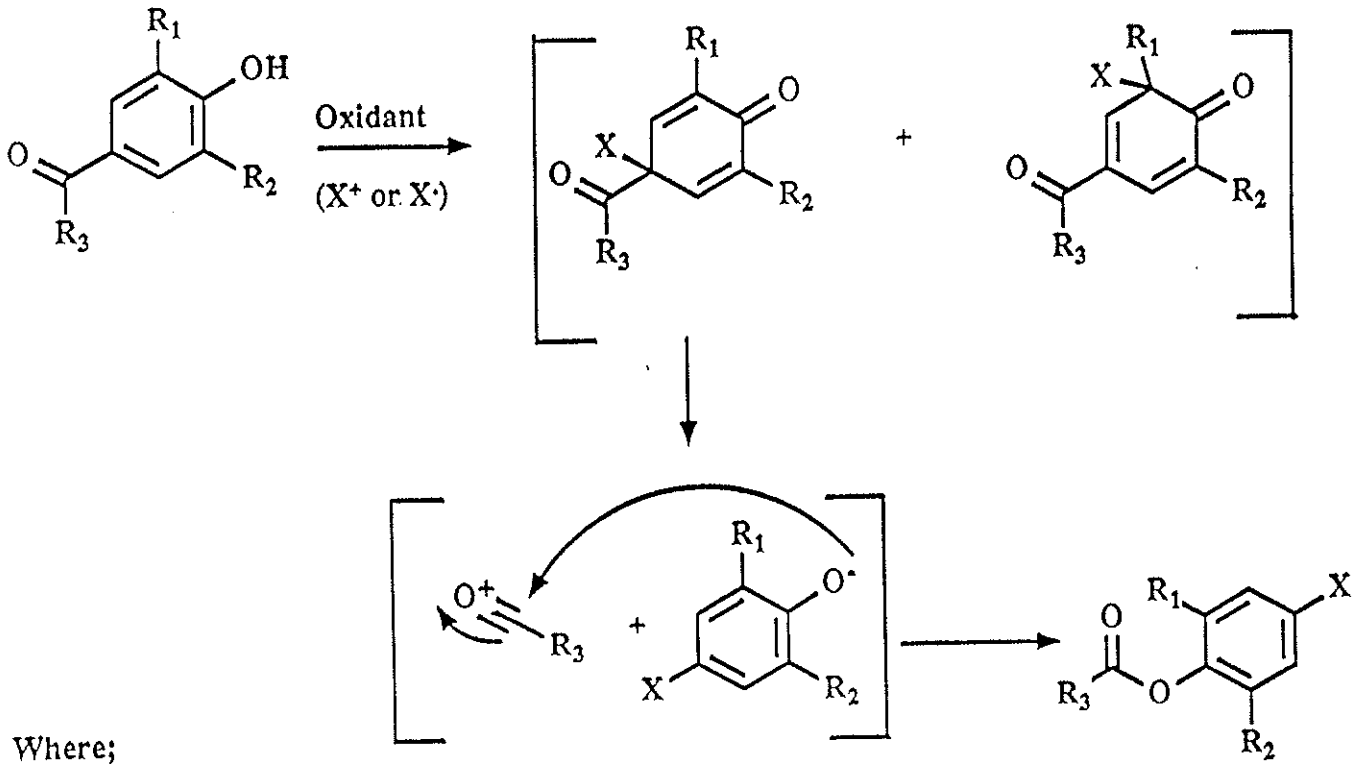
The main goal of this work is to prepare the hydroxydiarylketones and use them (as starting materials) to study the retro-Fries reaction. In the time since the Fries reaction was discovered, there has only been a few attempts made to perform (effect) the reverse reaction i.e. retro-Fries reaction. The attempts performed by heating the hydroxydiarylketones in presence of a Lewis acid at a high temperature, were unsuccessful. We have chosen to use the oxidation method to reverse this reaction. The oxidants are carefully chosen to suit this goal.

Hydroxydiarylketones are commonly prepared in high yields by Fries rearrangement of the corresponding esters. As each step in the reaction is known to be reversible, as shown in the reaction mechanism (Scheme 1), it should be possible, with the right reagent and under suitable conditions to reverse the Fries reaction. That is, it should be possible, starting with the hydroxydiarylketones to form the corresponding esters. Bromine, Lead Tetraacetate and Ceric Ammonium Nitrate are known to be good oxidants (as indicated above) due to their individual oxidative behaviors, i.e. bromination, acetoxylation, nitration and oxidative cleavage, respectively. These oxidants are expected to be able to introduce a substituent on the phenyl ring or possibly to cleave the bond and make it possible to reverse the Fries reaction.

Before the experimental work began, a mechanism was proposed for each oxidant, to show the putative course of the reaction. These mechanisms were derived from the documented facts from the literature, and the experimental conditions were designed accordingly. Expected mechanisms for retro-Fries rearrangement (for each individual oxidant) are shown in the results and discussion

section. For each oxidant, one or two expected mechanisms are given to explain how the oxidant could cause the reverse reaction.

In general, the mechanism is expected to proceed to give a retro-Fries reaction (Scheme 8). As documented in the literature, the reactive species X (for the chosen oxidants) are either radicals or positively charged (electrophiles).



Where;

$R_1 = R_2 =$ H or Me

R_3 = Me, *p*-Methoxy phenyl, *p*-Nitro phenyl

Scheme 8 The expected mechanism for a retro-Fries reaction

As systems (of chemical reactants) tend to move towards their most stable state, we might expect that the more stable the products are compared with the starting materials, that the further over to the former's favor any equilibrium between them might be expected to lie. In seeking their most stable condition, systems tend towards minimum energy and maximum entropy.

Under Fries conditions the hydroxydiarylketone products, would be more stable than the intermediate(s), thus favoring the reaction. A big challenge for a retro-Fries process (the goal of this project) is the decomposition of an intermediate into products (esters). Since free energy of activation $\Delta G_2^{\#}$ is larger than $\Delta G_1^{\#}$ (see diagram 1 below), suitable conditions have to be established / chosen to make it possible for the intermediate(s) to be converted into product(s) (esters).

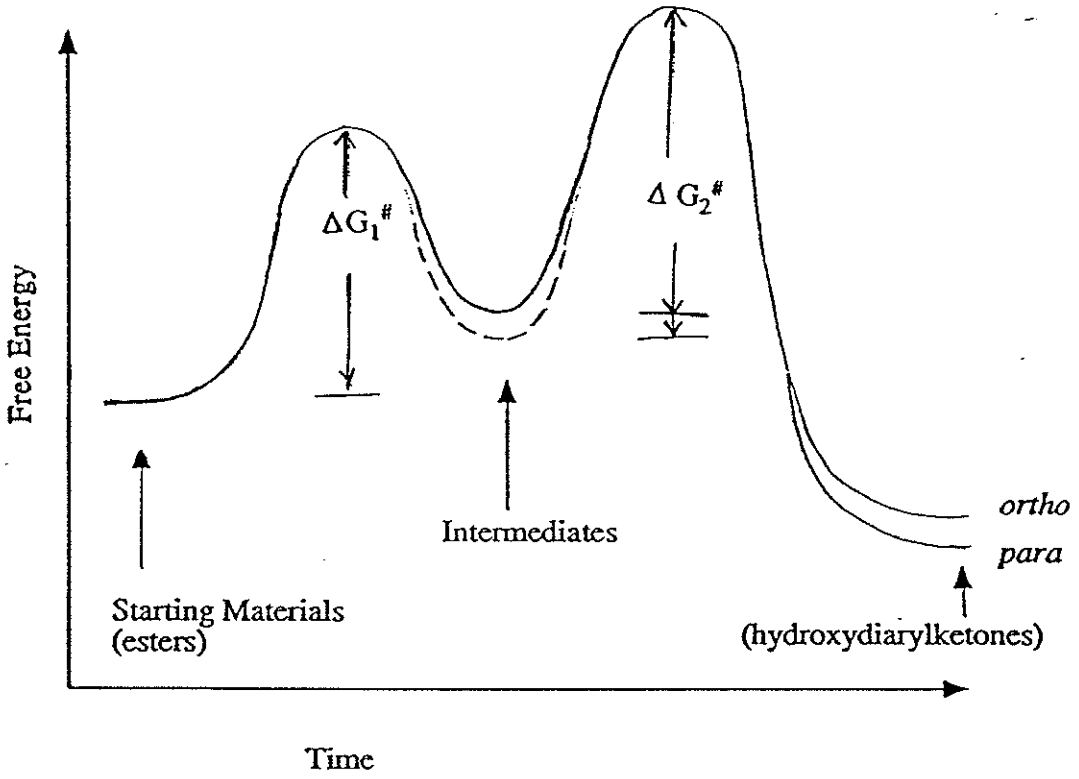


Diagram 1

Three oxidants are used in the process of oxidizing the compounds prepared by the Fries-rearrangement method. A survey of literature on these three oxidizing agents (as indicated above) allowed us to come up with three possible reactions all of which have the potential for reversing the Fries rearrangement. So far only a few attempts[13,43-47] have been reported on retro-Fries reaction. The reaction was performed with a strong protic acid (trifluoromethanesulfonic acid (TFMS)), as catalyst. Apart from isomeric ketones and esters, phenols and ketoesters were also isolated. The authors[13] suggested a dissociative mechanism

and an intermolecular process. This shows that it is possible to reverse the Fries reaction provided the reaction conditions are carefully designed/selected. We propose three equations to show how retro-Fries reaction is expected to take place which are given in the Discussion part of this thesis.

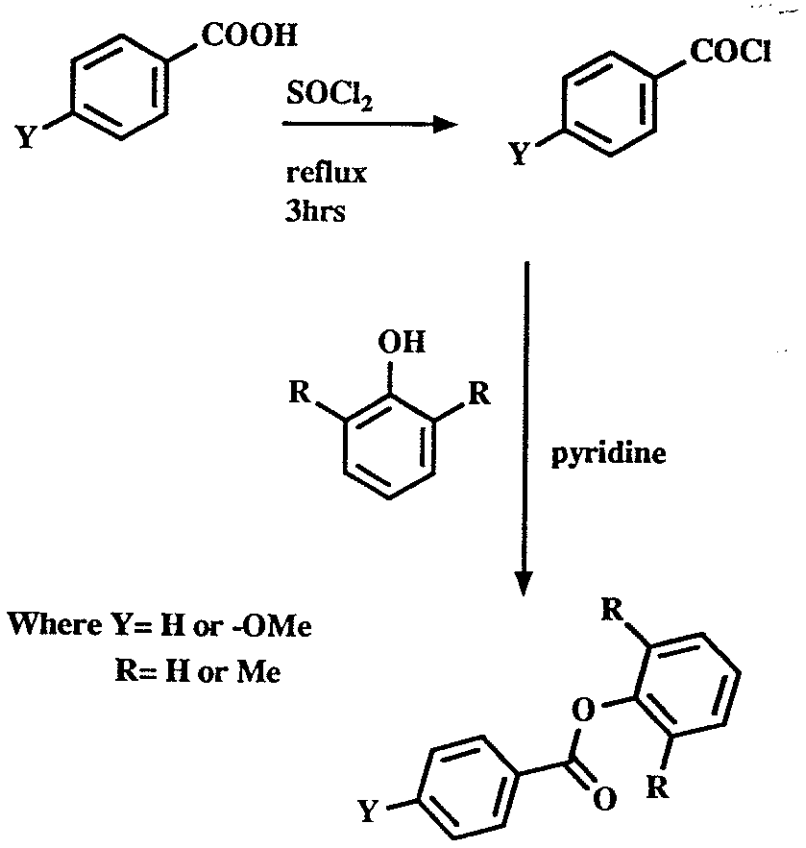
Chapter 2

RESULTS AND DISCUSSION

2.1: Fries Rearrangement:

As mentioned in the Introduction, hydroxydiarylketones were prepared by Fries reaction because it is the most suitable method. In 1908, Fries discovered the rearrangement of the ester to ketone when subjected to a Lewis acid.[48] There is no doubt that the mechanism involved is intramolecular, as indicated in the Introduction.

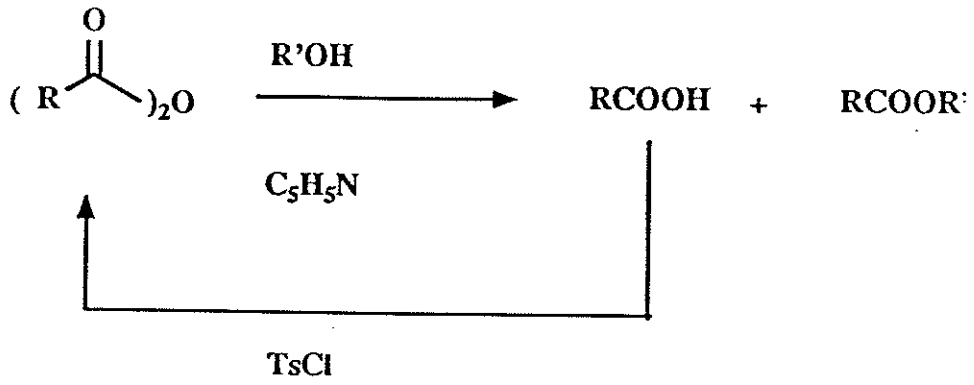
Carboxylic acids used to prepare the esters had one of the following *para*-substituents; H, $-NO_2$, and -OMe. Esters without a nitro group were prepared by using the Schotten - Baumann technique; i.e. the acid chloride was added in portions followed by vigorous shaking to a mixture of equivalent moles of phenol in pyridine. The mixture was left to cool to room temperature, and the ester subsequently precipated on addition of cold water. See a general Scheme below;



Scheme 9 Preparation of esters with no nitro group substituent

This method of preparation was not satisfactory for esters with a nitro group at position 4. As yields were very low we decided to prepare them by using another method; *para*-nitrobenzoic acid was dissolved in pyridine and two molecular equivalents of TsCl was added. The solution was then chilled in ice and one molecular equivalent of the phenol was added. The solution was kept cold or warm (depending on the ester prepared) for one hour and then poured into three

volumes of an ice and water mixture. Solid esters were collected by filtration. This method is convenient for the *in situ* preparation of acid anhydrides in pyridine for use in formation of esters. Refer to Scheme 10.

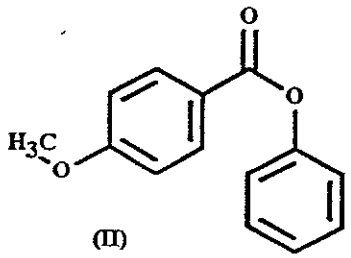


Scheme 10 Preparation of esters with a nitro group substituent

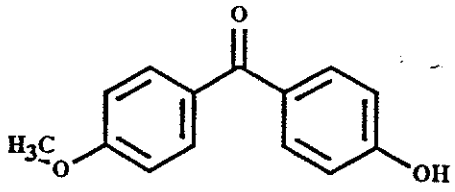
We studied the rearrangement of these esters subjected to two Lewis acids - $AlCl_3$ and BF_3. The reaction was performed at different temperatures and was repeated several times to make sure the results can be reproduced. The first attempts (with $AlCl_3$) were performed using the following method. The reaction was started in refluxing CS_2, the solvent was distilled off after 3 hours and then the solid residue was heated at 150 °C for three hours. As the methyl group on methoxy group showed a tendency of being cleaved (100% cleavage) at this temperature, the reaction was repeated at different temperatures lower than 150 °C. The results are shown in Table 1 and 2 below;

TABLE I:

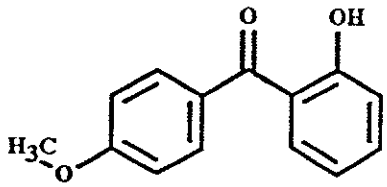
Starting Material (s.m.) Compound II		Products (%)				Recovered s.m.%
Temperature °C	Time (hr)	III	IV	V	VI	
23 (Room temp.) and 90	3	-	-	-	-	95
120	3	-	19	-	-	74
120	12	10	32	-	-	50
125	3	trace	46	-	-	48
125	12	14	49	-	-	26
130	3	29	20	trace	trace	40
135	3	50	-	trace	-	40
135	5	63	-	15	-	0
140	3	-	-	78	-	0
145	6	-	-	83	-	0



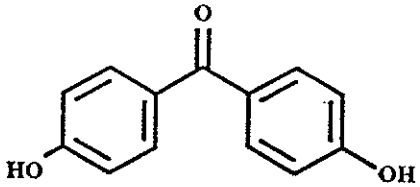
(II)



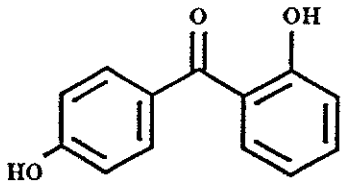
(III)



(IV)



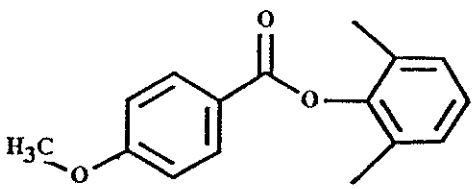
(V)



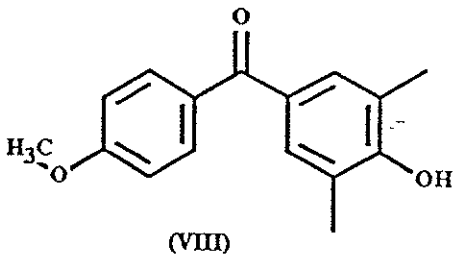
(VI)

TABLE 2:

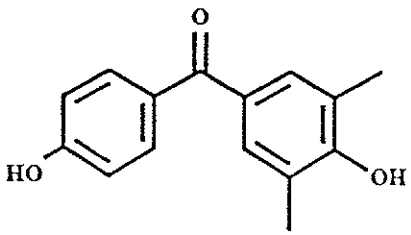
Starting Material (s.m.) VII		Products (%)		Recovered s.m. (%)
Temperature (°C)	Time (hr)	VIII	IX	
23 (Room temp.) and 90	3	-	-	90
90 - 95	3	20	-	70
125	3	42	-	50
125	6	56	-	35
135	3	58	trace	20
135	6	62	12	11
140	3	18	48	14
> 140	3	-	82	0



(VII)

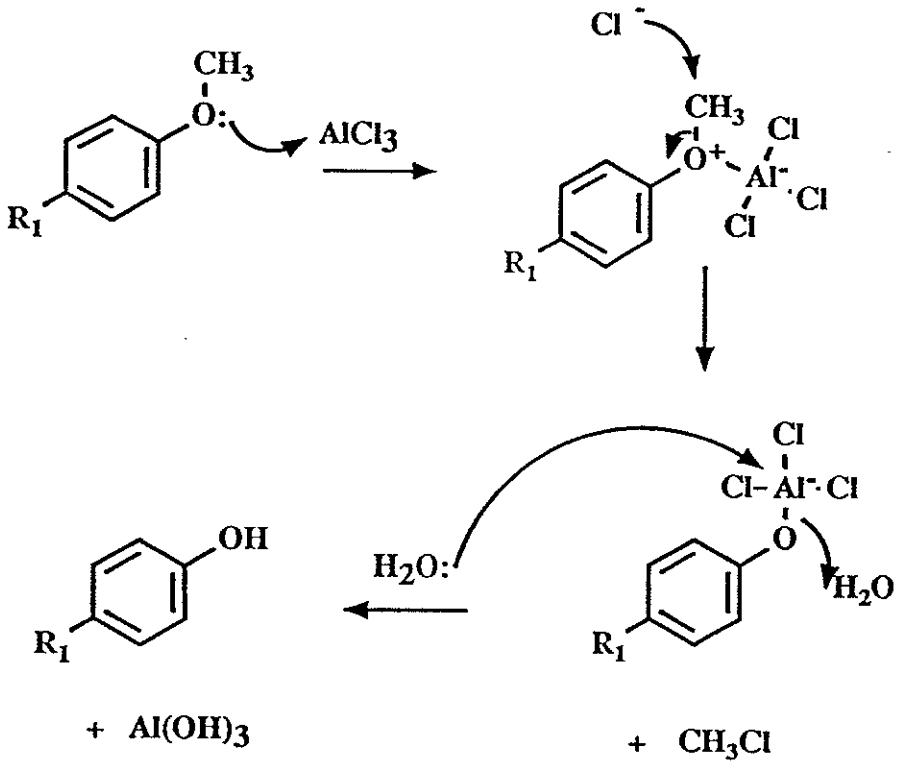


(VIII)



(IX)

The methyl ether cleavage mechanism is shown below:



Scheme 11 Methyl ether cleavage mechanism

Another attempt was made to maximize the yields of the products containing methoxy group(s), by finding a suitable solvent which could be used for this reaction. Chlorobenzene, which boils at 133 °C, was found to be a highly suitable one. As the the boiling temperature is sufficiently close to 135 °C the temperature at which the highest yield of the methoxy hydroxyketone was obtained

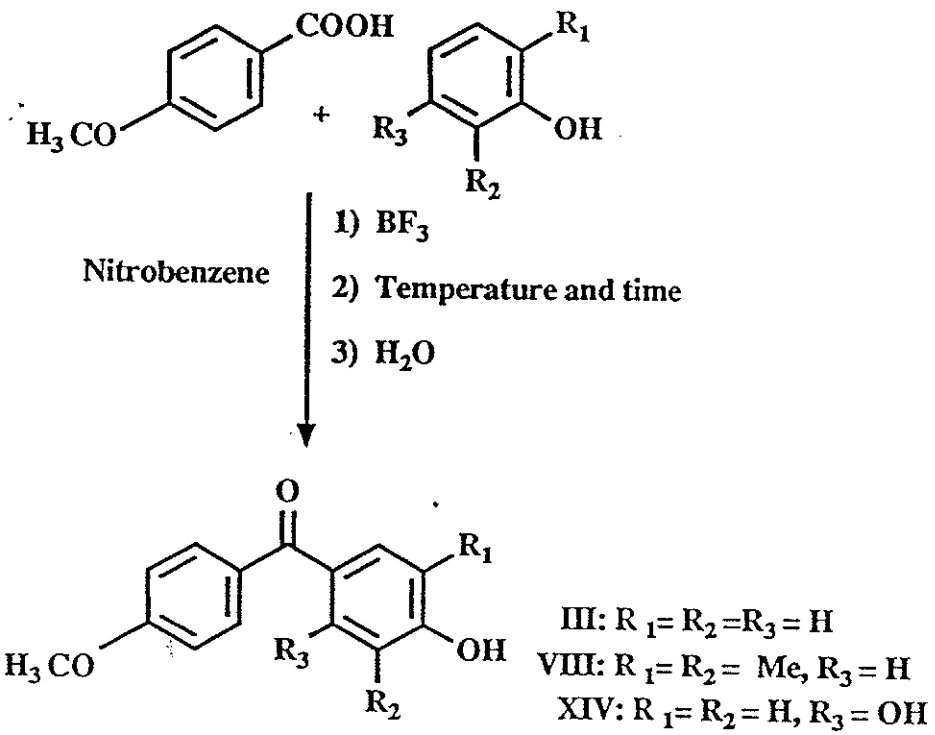
when the residue was heated without a solvent (the first attempt).

As esters without methoxy group can be rearranged readily to hydroxydiarylketones at higher temperatures, there is no cleavage to worry about. Conversely, as electron withdrawing groups (like $-NO_2$) slow the reaction, more time for the reaction is needed in order to obtain reasonable yield. Nitro esters, when heated for too long (with or without solvent) under Fries conditions, form tarry materials, from which it is difficult to isolate products. When both *para* and *ortho* hydroxy products are possible, the time of reaction becomes a factor on the *para*/*ortho* ratio. When nitro esters were subjected to Fries conditions at 133 °C (refluxing chlorobenzene), six hours and thirty minutes were found to be the appropriate time for the maximum yield of the *para* hydroxy product. Beyond that, the yield of *para* hydroxy product starts to decrease and the *ortho* hydroxy product starts to increase.

Another attempt was made to synthesize the hydroxydiarylketones at a lower temperature (than when $AlCl_3$ was used as a Lewis acid). The esters were dissolved in nitrobenzene (b.p. 210.9 °C) and BF_3 gas was bubbled through until the solution was saturated. The reaction was completed after heating the saturated solution for 45 minutes at 80 °C in a sealed container. The reaction was very clean and no cleavage of methoxy groups was observed. See Table 3 and 4. This procedure is not useful for the compounds with an electron withdrawing group, e.g. NO_2. The temperature is not high enough to drive the reaction forward, and higher temperatures and longer reaction times are needed to obtain the same yields.

TABLE 3:

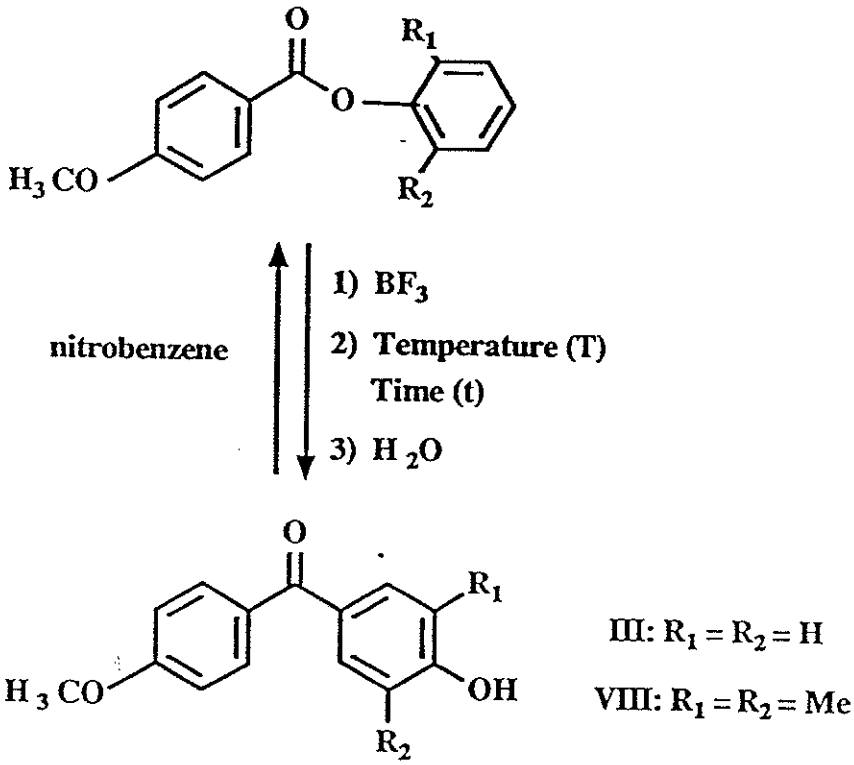
R^1	R^2	R^3	Temperature (°C)	Time (t)	Product	Yield %
H	H	H	80	14 hr	III	92
H	H	-OH	80	45 min.	XIV	94
$-CH_3$	$-CH_3$	H	80	14 hr	--	0
$-CH_3$	$-CH_3$	H	125-130	5 hr	VIII	61
$-CH_3$	$-CH_3$	H	125-130	10 hr	VIII	76



III: $R_1 = R_2 = R_3 = H$
VIII: $R_1 = R_2 =$ Me, $R_3 = H$
XIV: $R_1 = R_2 = H$, $R_3 = OH$

TABLE 4:

R^1	R^2	Temperature (°C)	Time (t)	Product	Yield %
H	H	80	6 hr	III	92
H	H	110	4 hr	III	92
$-CH_3$	$-CH_3$	80	5 hr	VIII	94
$-CH_3$	$-CH_3$	110	3 hr	VIII	92



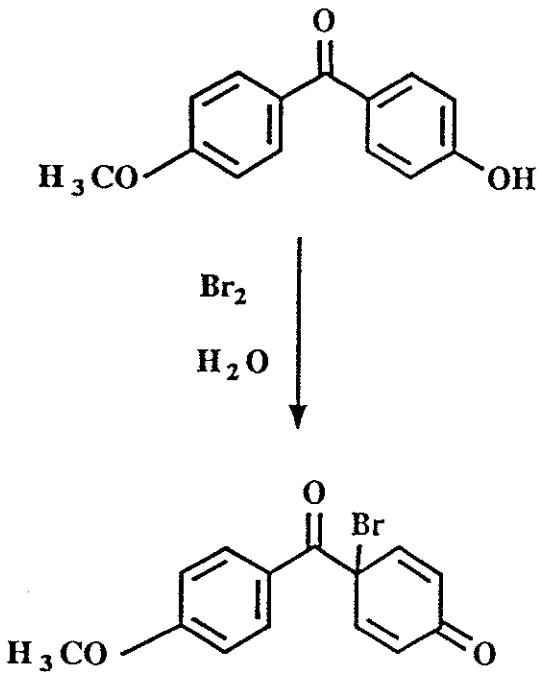
III: $R_1 = R_2 = H$

VIII: $R_1 = R_2 = Me$

2.2: Bromination of *p*-hydroxydiarylketones:

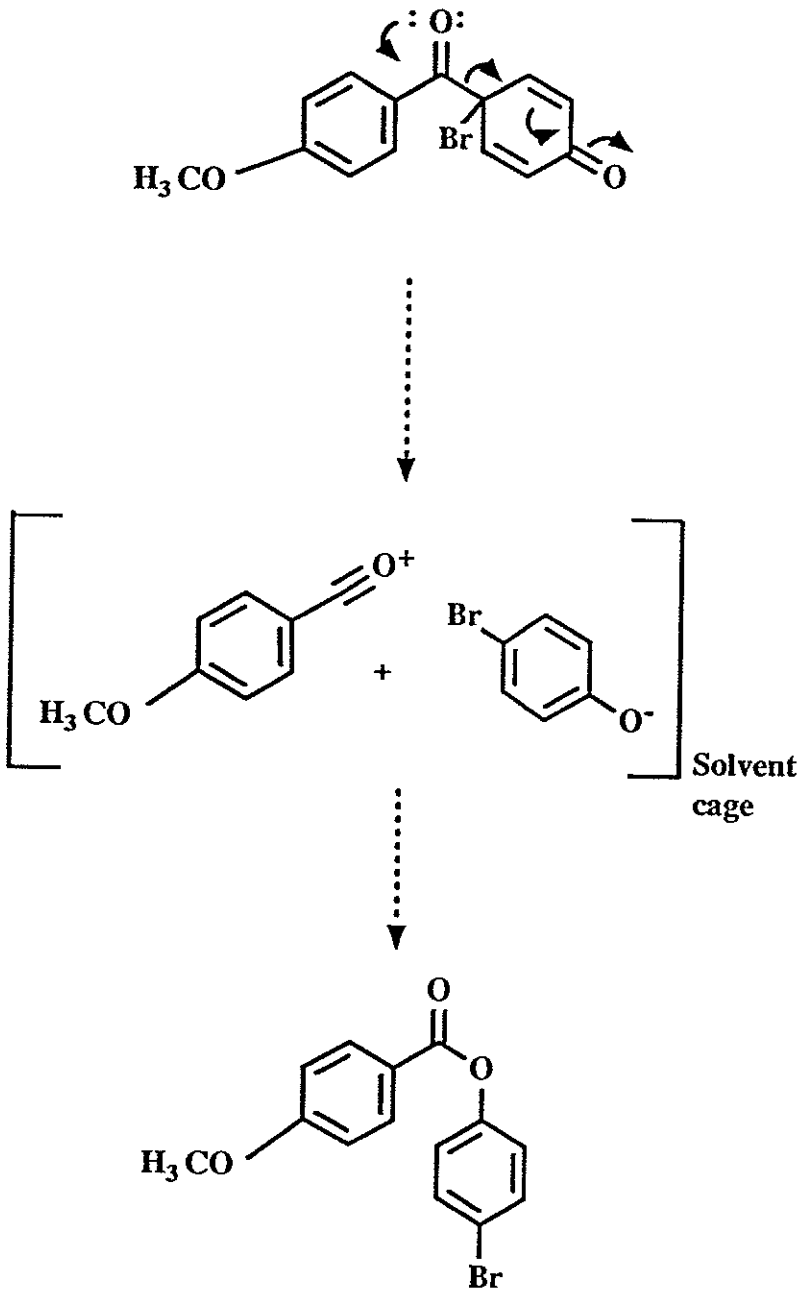
Bromination of simple phenols, as mentioned earlier, proceeds *via* *ipso*-dienone intermediates. This fact led us to invesatigate whether *ipso*-dienones would be formed during bromination of phenols bearing a ketone group at position 4 (hydroxydiarylketones).

The above statement means that the following occurs when the hydroxydiarylketone is undergoing bromination;



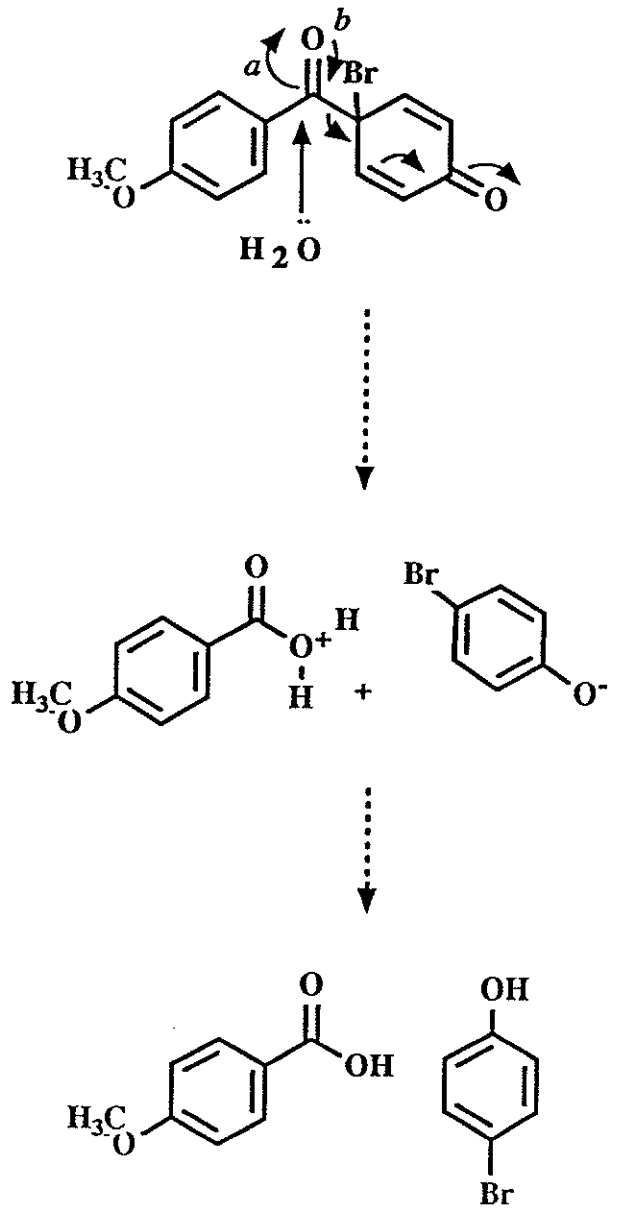
Scheme 12 Formation of the *ipso*-dienone

The *ipso*-dienones have only been observed when the bromination is performed in aqueous solution. It is also known that these *ipso*-dienones are labile and undergo debromination to regenerate the aromatic ring. We decided to utilize their existence, and use harsher conditions (than those described in the literature) to try to convert the dienones into esters (retro-Fries rearrangement) or the acid and phenol. In order for this to happen, the acyl-aryl bond must be broken. Electron donating groups were considered appropriate substituents in the hydroxydiarylketone to assist in breaking the bond (methoxy group was used in our case). A second factor considered to be of help is the reaction temperature. Thus the reaction was performed at different high temperatures. The reaction time was the third factor considered, and the reaction was performed for different time length (from a few minutes to several weeks). In general, the experimental conditions were designed with a hope that the following might occur:



Scheme 13 Retro-Fries reaction by bromination

Since the bromination is made in the presence of water, direct nucleophilic attack on the carbonyl is possible. If the attack occurs the following mechanism is expected;

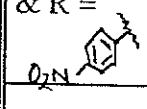


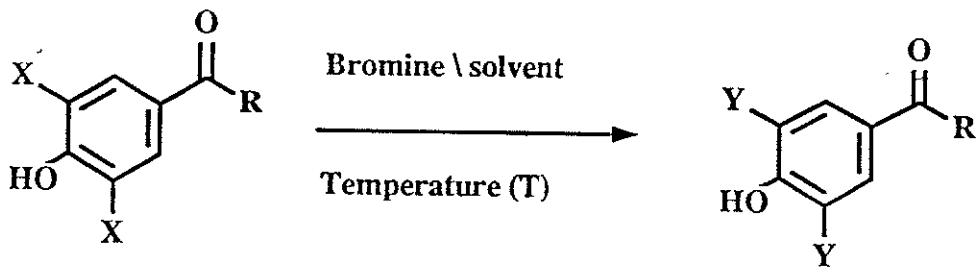
Scheme 14 Bromination in the presence of water

Both predictions are possible and this study was performed with a view to determine the products.

Bromine substituted hydroxydiarylketones were obtained (in a high yield) in case of the compounds with available *ortho* positions. Compounds with unavailable *ortho* positions did not give any new products and the starting materials were recovered (see Table 5).

TABLE 5:

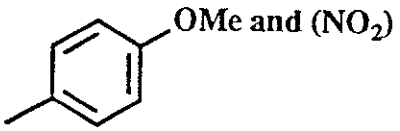
Starting Material (s.m.)	Solvent	Temperature (°C)	Bromine (mole equivalents)	Product	% Yield of product
X =H & R = CH_3	1)EtOH 2)$EtOH_{aq}$	Room temperature (r.t.) 23	2 equivalents	Y = Br	98
	"	55	2 equivalents	Y = Br	98
	"	55	3 equivalents	Y = Br	97
X = CH_3 & R = 	"	r.t.	2 equivalents	Y = Br	99
	"	55	2 equivalents	Y = Br	99
	"	55	3 equivalents	Y = Br	97
X = CH_3 & R = 	"	r.t.	2 equivalents	Y = Br	79
	"	55	2 equivalents	Y = Br	85
	"	55	3 equivalents	Y = Br	90



Where; X = H, and Me

Y = Br, and Me

R = Me, or



Scheme 15 Bromination of *p*-hydroxydiarylketones and *p*-hydroxyacetophenone

It was found that experimental results were not in our favor. I.e. the expected / predicted (retro-Fries rearrangement) reaction did not occur. Since it is known that *ipso*-dienones are formed during aqueous bromination of the phenols having alkyl groups at position 4, it is possible that hydroxydiarylketones also do form the *ipso*-dienones during bromination. As with the reported[14-16] *ipso*-dienones, the *ipso*-dienones formed by the hydroxydiarylketones are also expected to be labile.

The life time of known *ipso*-dienones has not yet been reported but it is known that these *ipso*-dienones do account for about 10% of the initial consumption of bromine. Our results suggest several reasons why the anticipated products were not obtained, and those reasons are:

First; the lifetime of the *ipso*-dienones is too short for any other reaction to

take place. I.e. bromination is very fast.

Second; it may be that the experimental conditions are not suitable for the reaction and a temperature lower than the room temperature may be needed for the reaction to take place. Since the *ipso*-dienones are labile, they may be less labile at lower temperature - and this will increase their lifetime.

Third; the bond to be broken (acyl-aryl bond), in order for the retro-Fries rearrangement to occur, may be too strong i.e. it will never be broken even if the lifetime of the *ipso*-dienones is reasonably long.

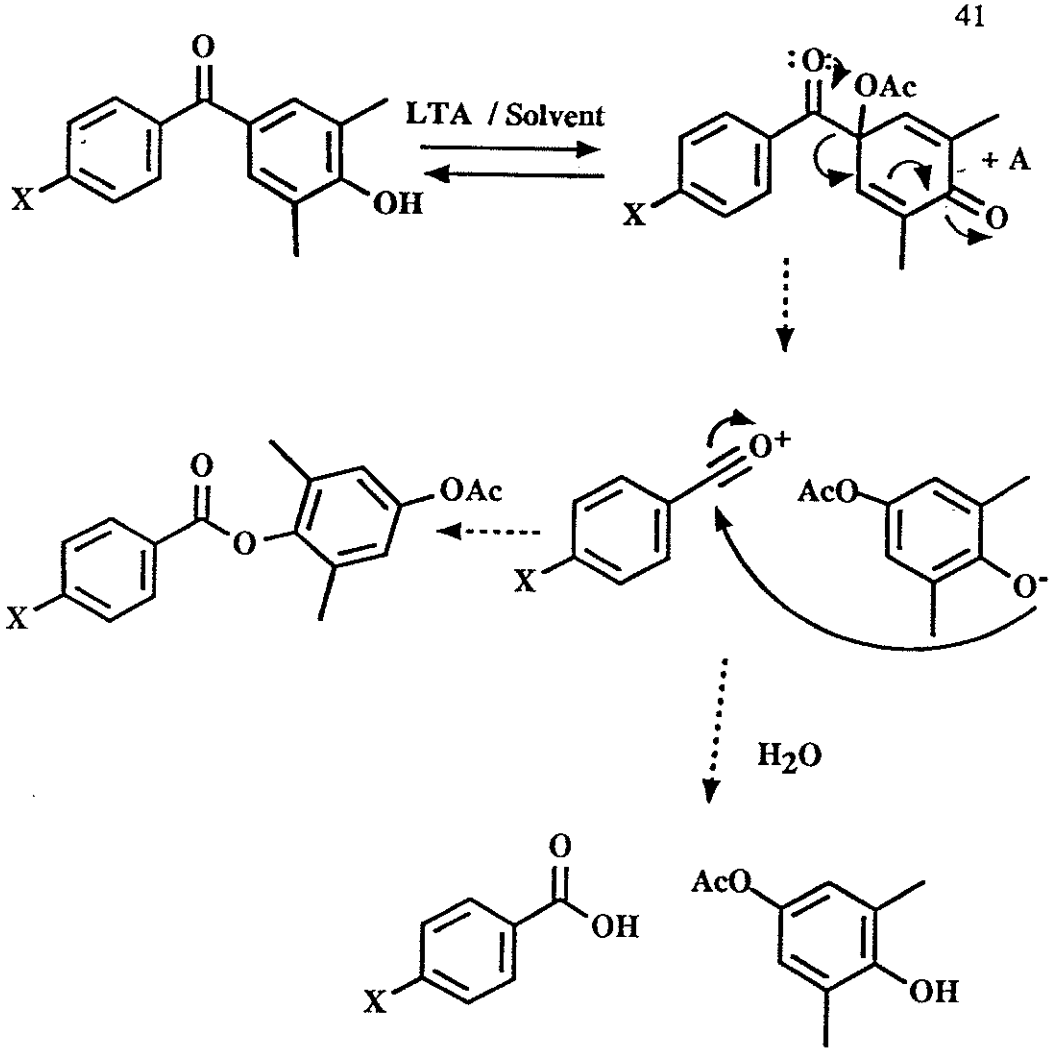
Although its reported that the rate of decomposition of the *ipso*-dienones and of the attack on position 4 are not sensitive to the nature of the alkyl substituents, the hydroxydiarylketones (phenols with a ketone at position 4) may behave differently.

Fourth; possibly hydroxydiarylketones do not form the *ipso*-dienones during bromination. The existence of *ipso*-dienones during the bromination of the phenols having a ketone at position 4, has not been confirmed yet. This point would be worth further investigation with smaller models.

2.3: Acetoxylation with Lead Tetraacetate:

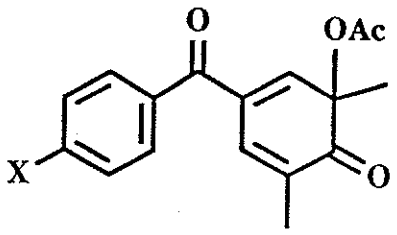
Lead tetraacetate is known to perform acetoxylation of phenols at *ortho* & / *para* positions. It is also confirmed that the introduction of a Me group into the *ortho* or *para* position of a simple phenol generally results in a higher proportion of acetoxylation at that position. In fact, a position with a methyl group is more preferred than any other alkyl group.[29,30] Studies have not been made on the phenols with a ketone group at any position. Based on known work we thus investigated whether, when lead tetraacetate is used to oxidize hydroxydiarylketones (phenols with a ketone substituent in para position), acetoxylation would be produced at *para* position.

If the above statement is true, it is reasonable to propose Scheme 16. *p*-Dienone acetates are expected to undergo cleavage of the bond (as indicated in Scheme 16) to allow the retro-Fries reaction to take place as shown below;



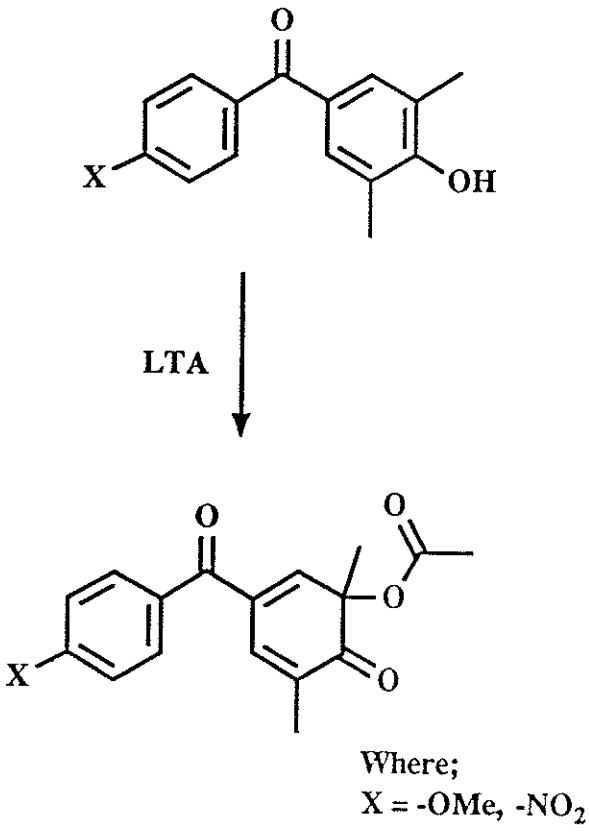
Where; X = -OMe, - NO_2

A =



Scheme 16 Retro-Fries reaction by acetoxylation

Phenols used in this work had a ketone group at *para* position (hydroxydiarylketones), with or without methyl groups at *ortho* positions. The ketone group did not change the acetoxylation preference, e.g. for the hydroxydiarylketones with methyl groups at the *ortho* positions, the acetoxylation was exclusively at the *ortho* position. See Table 6 and Scheme 17 below. The same was observed for hydroxydiarylketones without methyl groups, where the preference of acetoxylation was exclusively at the unsubstituted ortho position. The introduction of a ketone group at the *para* position of a phenol did not influence acetoxylation at that position.



Where;
X = -OMe, $-NO_2$

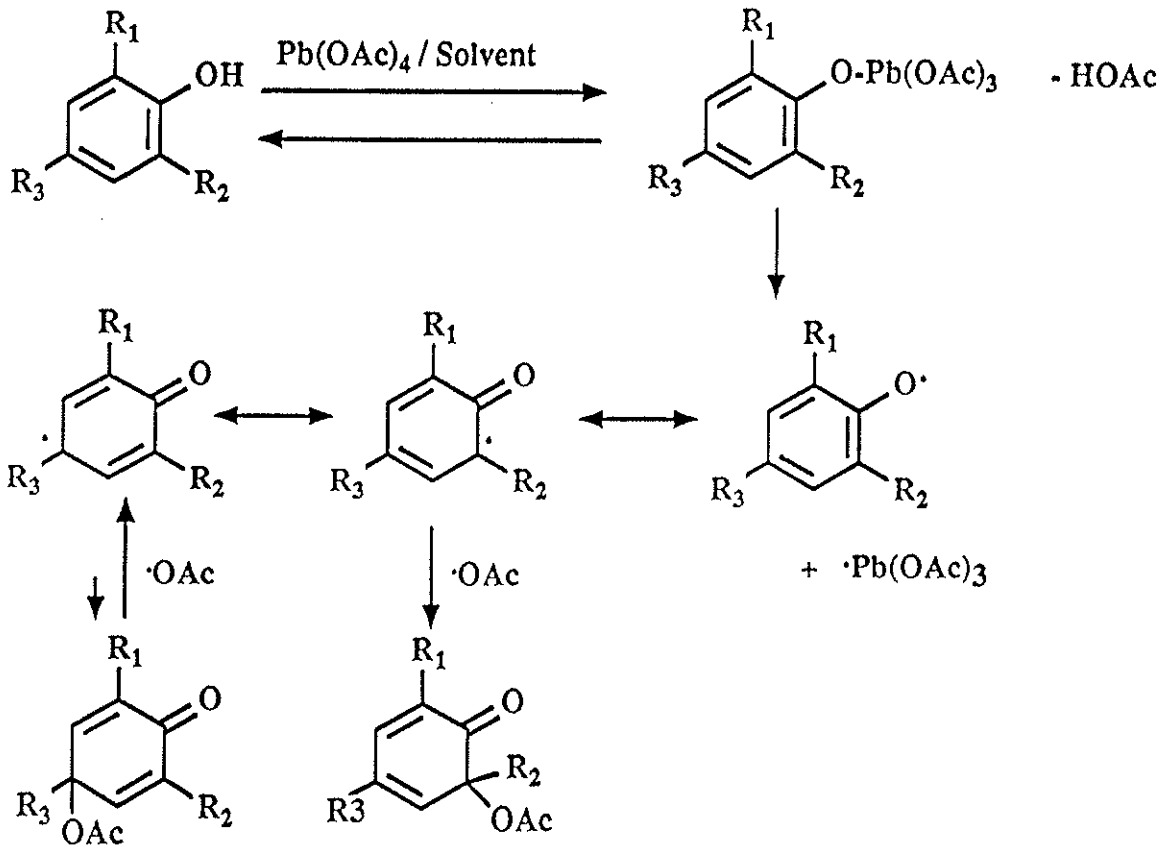
Scheme 17 Wessely oxidation.

TABLE 6:

Starting material (s.m)	Experimental Condition	Time (hrs)	% Yield	Recovered s.m %
X= -O-CH_3	Benzene / Reflux	15	55	21
	Benzene / MeOH / 65°C	6	78	5
	Benzene / MeOH / Reflux	6	78	0
	Benzene / AcOH / Reflux	6	60	0
	Benzene / AcOH / MeOH / Reflux	6	77	0
	AcOH / Reflux	6	70	0
	AcOH / MeOH / Reflux	6	89	0
	MeOH / Reflux	6	81	0
X= -NO_2	Benzene / Reflux	15	51	15
	Benzene / MeOH / 65°C	6	70	8
	Benzene / MeOH / Reflux	6	71	5
	Benzene / AcOH / Reflux	6	56	5
	Benzene / AcOH / MeOH / Reflux	6	72	6
	AcOH / Reflux	6	70	5
	AcOH / MeOH / Reflux	6	76	0
	MeOH / Reflux	6	72	0

The experimental results can be explained by considering the steric effect and the stability of the intermediates of the reaction. The ketone substituent on the phenol may be a very large group, and thus may block the acetate group from attacking the para position. Alternatively if the attack at *para* position did occur, the intermediates are perhaps too labile to produce the acetoxylated products.

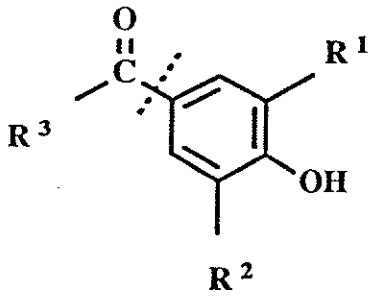
Phenols with alkyl groups other than methyl group and unsubstituted para position react with LTA to give *para*-dienone monoacetate. *Para*-dienone diacetates have never been found, possibly because they are too unstable. The phenyl ketone group on the *para* position of the phenol is much bigger than one acetate group. If *para*-dienone diacetate is too unstable to exist, it may be assumed that the expected intermediate (compound) is also too unstable to form. Scheme 18 explains the most reasonable mechanism for the reaction. The aryl intermediate dissociates into the radicals $(AcO)_3Pb\cdot$ and $ArO\cdot$. The aryl radical is a hybrid of three resonance structures of which two can form two possible products. *Para*-dienone acetate, as mentioned above is very unstable, therefore it decomposes back to the *para*-aryl radical.



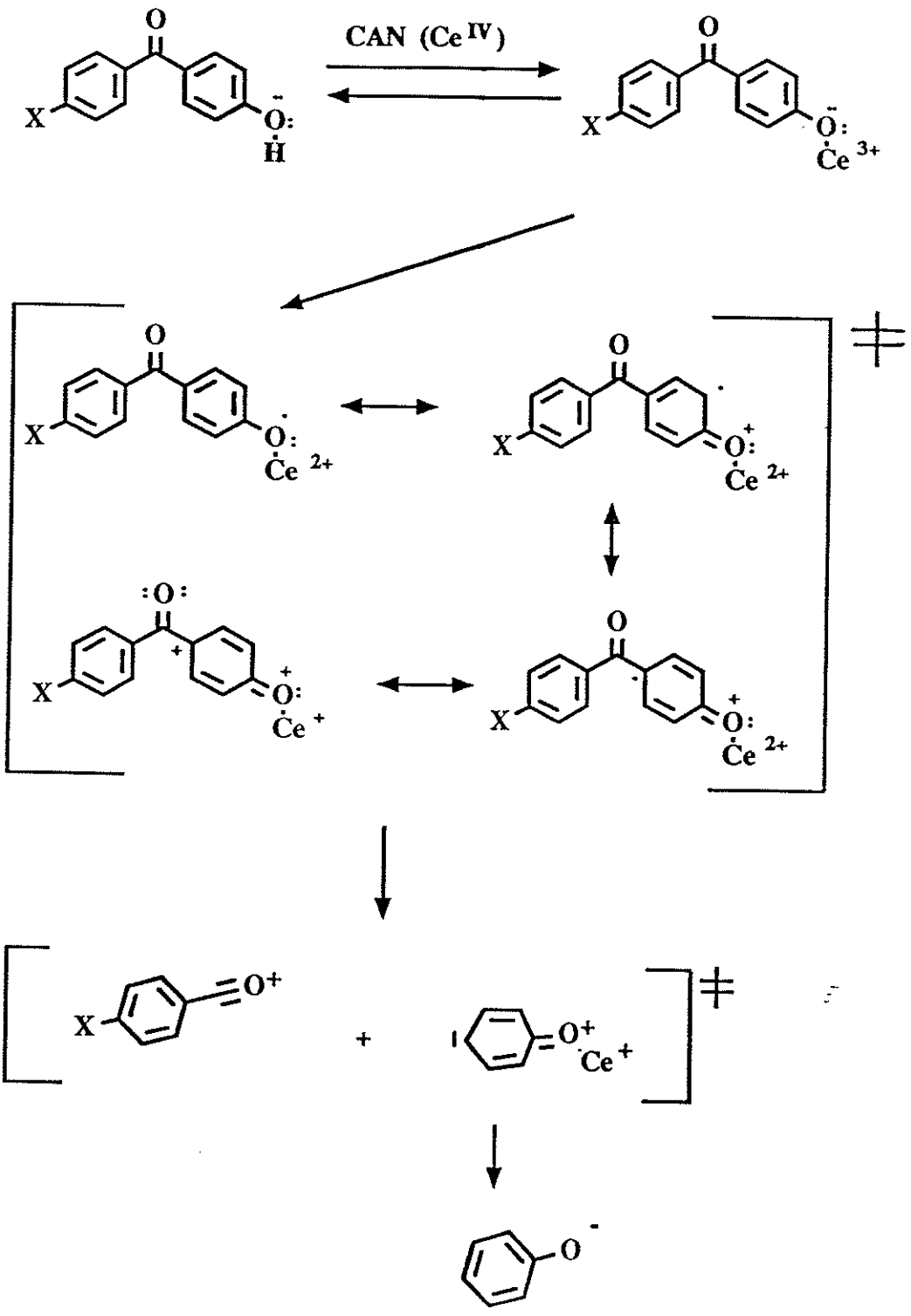
Scheme 18 Acetoxylation of *p*-hydroxyketones

2.4: Oxidation with Ceric Ammonium Nitrate:

Ceric ammonium nitrate is a common oxidant used to generate radical cations from a variety of aromatic hydrocarbons. It has been reported[49] that the oxidant does cleave some conjugated ketones to give two carboxylic acids. The same author[49] reported the nitration of the phenolic group of the 2'-hydroxychalcone at the position *para* to the hydroxyl group. From these and other facts mentioned in the Introduction, it would be expected that Ceric ammonium nitrate will nitrate the hydroxydiarylketone, and / or cleave the acyl-aryl bond to make retro-Fries rearrangement possible.

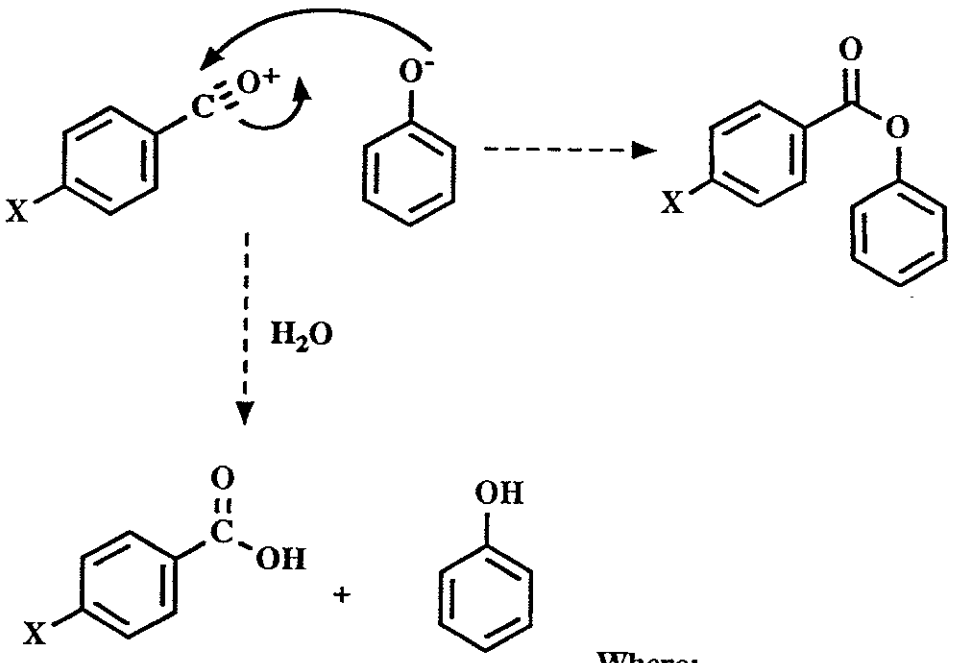


Dhar[49] suggested a mechanism for each of their observations. Some of the processes in their mechanisms can take place during the reaction of the hydroxydiarylketone with ceric ammonium nitrate. At the same time the cleavage of the benzylic alcohols with this oxidant may be of help in predicting what will happen to hydroxydiarylketones when subjected to the same conditions. Scheme 19 is what we anticipated would happen;



Scheme 19 Cleavage of the acyl-aryl bond

and hopefully, the following would ensue



Where;

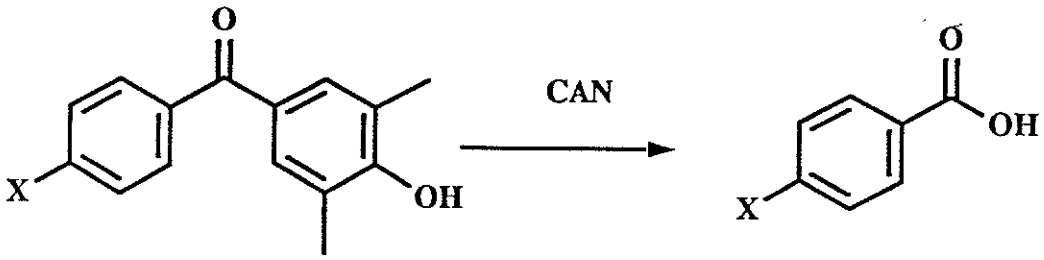
X = -OMe, $-NO_2$

Scheme 20 Retro-Fries reaction and / or formation of the acid and phenol.

When selected hydroxydiarylketones were treated with CAN, neither nitration products nor the correponding esters were detected. In general, it was found that the physical data and spectral information of the products obtained matched with that of the corresponding acids used to prepare the compounds. The phenolic part of the molecule (hydroxydiarylketone) was not detected. See Table 7.

TABLE 7:

Starting Material (s.m)	Experimental Condition	Time (hr)	% Yield of the acid	Recovered s.m %
X= -O-CH_3	AcOH / MeOH / Reflux	8	90	0
	AcOH / Reflux	8	77	12
	AcOH / H_2O / Reflux	8	80	0
	MeOH / H_2O / Reflux	8	69	0
	MeOH / Reflux	8	67	0
	THF / Reflux	8	72	0
	THF_{aq} / Reflux	8	67	0
	MeCN / Reflux	8	62	15
	$MeCN_{aq}$ / Reflux	8	67	5
X= -NO_2	AcOH / MeOH / Reflux	8	82	0
	AcOH / Reflux	8	72	0
	AcOH / H_2O / Reflux	8	72	0
	MeOH / H_2O / Reflux	8	67	0
	MeOH / Reflux	8	62	0
	THF / Reflux	8	72	0
	THF_{aq} / Reflux	8	64	0
	MeCN / Reflux	8	56	10
	$MeCN_{aq}$ / Reflux	8	56	0

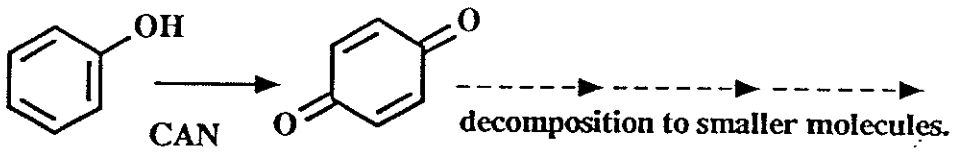


Where;
X = -OMe, -NO_2

Scheme 21 Oxidative cleavage of *p*-hydroxydiarylketones to acids

The acyl cation was determined to be the intermediate in the case of oxidative cleavage. This was established by carrying out the reaction in the presence of pure (redistilled and dried) alcohol (methanol and tertiary butyl alcohol) instead of other solvents indicated in Table 7. The products were identified as esters of the corresponding acids (the methyl ester (XX) and the tertiary butyl ester (XXI)). These observations suggest that the mode of cleavage takes place *via* the acyl cation as shown in Scheme 21.

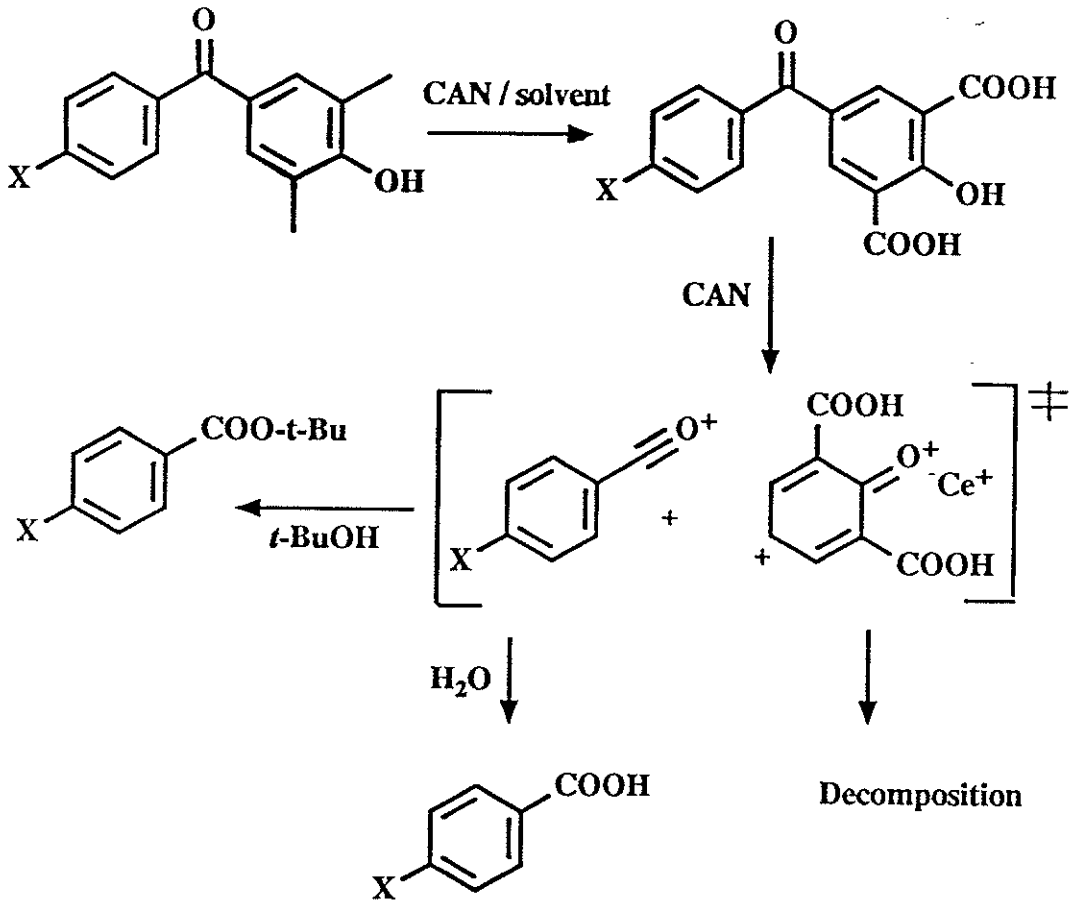
One question is still unanswered, that of the fate of the other part of the molecule, as nothing was detected corresponded to the part which had a hydroxyl group. To possibly answer this an experiment was made under the same conditions using a simple phenol instead of the hydroxydiarylketone. Phenol was oxidized to the quinone and then the dienone was further oxidized to smaller molecules. An attempt was made to separate the components without any success as the mixture was very complex. Scheme 22 below is a speculation of what might have happened to the quinone.



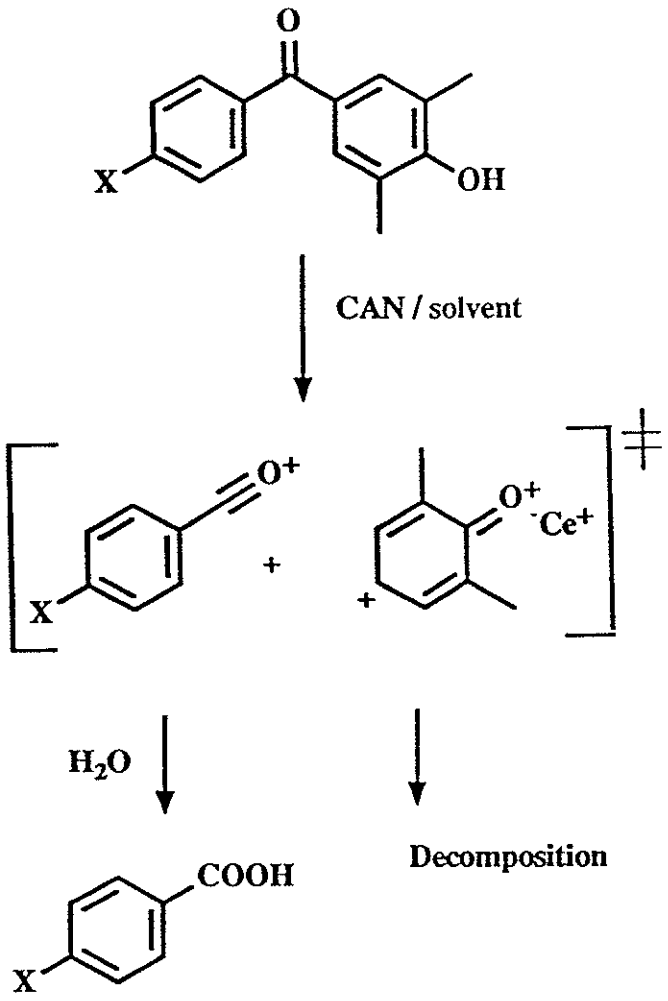
Scheme 22 Decomposition of phenol to smaller molecules.

It is also known that, ceric ammonium nitrate oxidizes methyl groups that are adjacent to aromatic rings to aldehydes or carboxylic acids. It is therefore possible that the methyl groups on the hydroxydiarylketones were oxidized to carbonyl groups (aldehydes and maybe further to carboxylic acids). If this happened, the sequence of the oxidation is not known. The question is whether the

oxidant oxidizes the methyl groups first before cleaving the bond (Scheme 23), or cleaves the bond first to produce the acyl cation and then oxidizes the methyl groups substituted on the phenolic ring (Scheme 24). Another possibility is that all oxidation processes occur simultaneously to produce the isolated product.



Scheme 23 Oxidation of the methyl group before the decomposition of the phenolic ring.



Scheme 24 Cleavage of acyl-aryl bond before the decomposition of the phenolic ring

As we have seen above, it does not matter which process takes place first, since all routes end with the same product, i.e. the corresponding carboxylic acid. The other part of the molecule, the part containing the hydroxyl group, is completely destroyed. No aromatic or quinone compounds were detected.

There is another possible explanation on how the oxidation could have taken place, and that is after retro-Fries rearrangement. If the oxidative cleavage to produce the acyl cation is faster than the oxidation of the phenolic ring (destruction of the other part of the molecule, i.e. the phenolic part), it is possible that the corresponding esters were formed. These esters were not detected / isolated because they were subjected to further oxidation. It has been reported that ceric ammonium nitrate cleaves esters[50] to give the corresponding carboxylic acids. Nothing was reported in this paper[50] about the other part of the molecule. They only reported the isolation of the corresponding acids.

Since the esters formed are reactive to the oxidant, they may undergo further oxidation (oxidative cleavage) to produce the corresponding carboxylic acids. This possibility of ester formation (retro-Fries rearrangement) is only possible, as said before, if the process is faster than the decomposition process. Oxidative cleavage of esters with ceric ammonium nitrate also gives the corresponding carboxylic acids.

The nature of X (electron withdrawing or electron donating group) did in fact influence the yields of the products but not the results. The corresponding carboxylic acid was isolated in each case. From our results, we cannot conclusively say that the retro-Fries rearrangement did not take place.

Chapter 3

CONCLUSION

CONCLUSION:

In fact, we verified that the experimental conditions stated can be optimized to transform the esters containing a methoxy group(s) into hydroxydiarylketones without demethylation. This is effected by controlling the temperature. Chlorobenzene as solvent was very effective for the rearrangement of the methoxy esters. Chlorobenzene boils at 133 °C, which is an ideal temperature for effecting the Fries rearrangement without demethylation. Temperatures higher than 133 °C were found not suitable, as then demethylated products were isolated in a higher yield. Time was another factor that needed to be monitored, as too brief reaction times led to higher yields of *ortho*-hydroxydiarylketones and too long periods of reaction led to demethylation. In refluxing chlorobenzene, methoxy esters needed 2.5 hours to give the highest yield of the hydroxydiarylketones without demethylation. On the other hand, solvents like nitrobenzene are suitable when the esters do not contain a methoxy group. For the esters prepared from phenols with substituted *ortho* position, and also which lack methoxy groups, there is no concern about the time and temperature. This is because there is only one possible product, *para* hydroxydiarylketone.

Bromination reaction gave the bromine substituted products. Thus the results are not in our favor. Only ring bromination reaction took place, and no cleavage of the bond was detected. The nature of the substituent (electron donating or electron withdrawing group) on the ring did not affect the products and the yields of products.

The methoxy substituent on *p*-hydroxydiarylketones does not influence the course of the rearrangement. No product was obtained with a substituent at *para*

position. CAN did not nitrate, LTA did not acetoxylate at *para* position, bromine did not brominate the hydroxydiarylketone at the *para* position.

It appears that, in general, these oxidants do not induce the retro-Fries rearrangement of p-hydroxydiarylketones.

Chapter 4

EXPERIMENTAL PROCEDURE

GENERAL:

Where more than one product were obtained flash chromatography was used to separate the products. The column (diameter = 1 cm) packed with silica gel 60 (25 cm long) was used and the eluent was ethyl acetate : hexane (3:2). All solid products were recrystallized from ethanol, and distillation was used to purify liquid products.

Melting points (m.p.) were determined on a Gallenkamp melting point apparatus. Infrared (ir) spectra were recorded on a Parkin-Elmer model 881. Ir samples were run as thin films (KBr plates). Proton nuclear magnetic resonance (^{1}H nmr) were recorded on Brucker Aspect 3000 spectrometer at 300 MHz and carbon thirteen nuclear magnetic resonance (^{13}C nmr) at 75.47 MHz. Except where otherwise stated the spectra were obtained on solutions in deuterated chloroform with tetramethylsilane as internal reference. The following abbreviations are used: s = singlet, d = doublet and m = multiplet. Mass spectra were obtained on a V.G analytical 7070E mass spectrometer using electron impact.

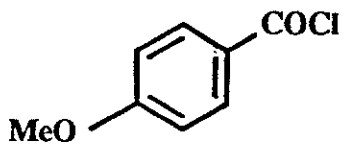
FRIES REARRANGEMENT USING $AlCl_3$ AS A LEWIS ACID:

A) 4-Methoxybenzoyl chloride (I)

(i) 4-Methoxybenzoic acid (6.09 g, 0.04 mol) was dissolved in thionyl chloride (9.52 g, 0.08 mol) then suspended in petroleum ether (50 mL), and dry $AlCl_3$ (0.8 g, 0.003 mol) was added. After three hours of heating at reflux temperature, the petroleum ether and excess thionyl chloride were removed by distillation. A pale yellow oil, which solidified at room temperature (25 °C), was obtained. Infrared and nmr spectra characteristics were identical to those reported in the literature.

(ii) Compound I can also be obtained by dissolving the acid in excess thionyl chloride and then heating under reflux for five hours. The excess solvent was removed by distillation.

The acid chloride was purified by distillation under high vacuum. The observed boiling point at 1.0 mm pressure was 90 °C (262 °C at 760 mm pressure).



(I)

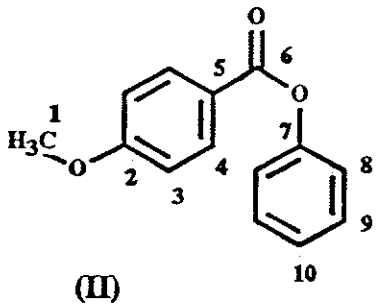
B) 4-Methoxyphenyl benzoate (II)

The reaction of 4-methoxybenzoyl chloride with phenol was carried out using the Schotten-Baumann technique. The acid chloride (2.5 g, 0.015 mol) was added in portions followed by vigorous shaking to a mixture of phenol (1.41 g, 0.015 mol) and pyridine (25 mL). The mixture was left to cool to room temperature, the ester subsequently precipitated out on addition of cold water 100 mL. The product was filtered, washed with cold water and recrystallized from ethanol. Compound II (3.05 g, 0.0134 mol,89%) was obtained which melted at 70-71 °C. Compound II had;

^{1}H-nmr (CCl_4) (δ,ppm): 3.87 (s, 3H), 6.90 (m, 2H), 7.16 (m, 3H), 7.34 (m, 2H);

^{13}C-nmr (CCl_4) (δ, ppm): C_1 (55.10), C_2 & C_6 (162.39, 162.22), C_3 (114.18), C_4 & C_8 (128.11, 131.25), C_5 (121.81), C_7 (149.97), C_9 (121.4), C_{10} (126.55);

MS(EI): 228 (2), 135 (100), 107 (6.1), 77 (12.5). Exact mass calculated for compound (II): 228.0783; found 228.0778.



(II)

C) 4-Hydroxy-4'-methoxybenzophenone (III)

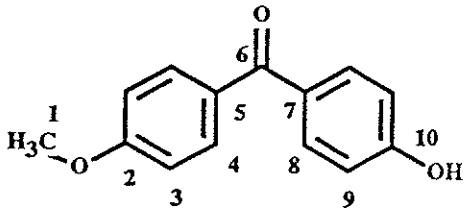
To a stirred mixture of $AlCl_3$ (2.66 g, 0.02 mol) in CS_2 (40 mL) placed in a 100 mL round bottomed flask was added slowly compound II (2.28 g, 0.02 mol) in of CS_2 (15 mL). When all the ester (in 15 mL CS_2) was introduced, the reaction mixture was refluxed gently on the water bath for three hours (until the evolution of HCl ceased). The solvent was distilled off and the flask was placed in a graphite bath maintained at 149-152 °C for 3 hours, cooled and treated with cold 5% HCl (50 mL) to decompose the $AlCl_3$. The mixture was allowed to stand overnight so that the product could solidify. The product was filtered, dissolved in 10% NaOH (15 mL) and the non phenolic products were extracted with three portions of ether (15 mL each). Acidification with 50% HCl (10 mL) of the alkaline solution afforded 4,4'-dihydroxybenzophenone (V) (m.p. 204-6 °C) instead of the expected compound (III). ^{1}H-nmr did not show the three-methyl protons (-O-CH_3) but only the aromatic protons; 6.9 (m, 4H), 7.7 (m, 4H).

The experiment was repeated at different temperatures and four products were detected as shown in Table 1 (page 25).

Compound III melts at 153 °C and had **ir (KBr):** 3260-3380 cm^{-1} (O-H), 2840 cm^{-1} (O-CH_3), 1620-1645 cm^{-1} (C=O).

^{1}H-nmr ($CDCl_3$ + DMSO-D_6) (δ,ppm): 3.87 (s, 3H), 6.85 (m, 2H), 6.98 (,2H), 7.61 (, 2H), 7.70 (, 2H);

^{13}C-nmr (DMSO-D_6)(δ, ppm): C_1 (55.36), C_2 & C_{10} (161.31, 162.17), C_5 & C_7 (128.39, 130.18), C_6 192.92), C_3 & C_9 (113.54, 114.96), C_4 & C_8 (131.52, 131.99); MS(EI): 228 (66.20), 197 (10.0), 135 (100), 93 (10.8), 77 (13.8). Exact mass calculated 228.0783; found 228.0799



(III)

D) 4-Methoxyphenyl-2',6'-dimethylbenzoate (VII)

In a manner similar to that described above for synthesis of the ester II, 4-methoxybenzoylchloride (2.50 g, 0.015 mol) and 2,6-dimethylphenol (1.83 g, 0.015 mol) were used. The product was recrystallized from ethanol and the yield was 3.02 g (0.012 mol, 79%) and m.p. 43 °C.

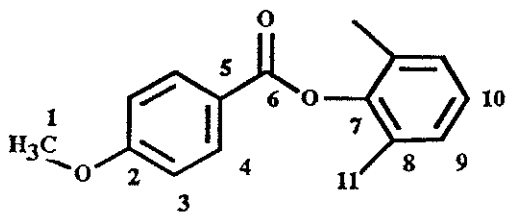
Compound (VII had **ir (KBr)**; 2838 cm^{-1} ($-OCH_3$), 2875 cm^{-1} ($-CH_3$), 1640 cm^{-1} (C=0).

^{1}H-nmr (CCl_4) (δ, ppm): 2.14 (s, 6H), 3.80 (s, 3H), 6.89 (m, 2H), 6.98 (m, 3H), 8.10 (m, 2H);

^{13}C-nmr (DMSO-D_6)(δ, ppm): C_1 (54.78), C_2 & C_6 (162.44,163.31), C_3 (113.44), C_4 & C_9 (128.07, 131.78), C_5 (121.67), C_7 (148.29), C_8 (129.92), C_{10} (125.15), C_{11} (16.25).

MS(EI): 256 (2), 180 (3.6), 152 (3.6), 135 (100), 107 (5.7), 92 (7.8), 77 (12.2).

Exact mass calculated 256.1095; found 256.1086.



(VII)

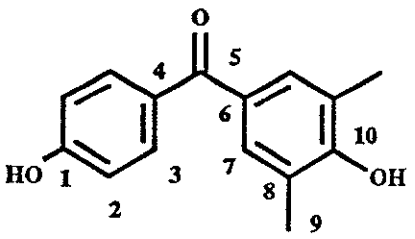
E) 4-Hydroxy-3,5-dimethyl-4'-methoxybenzophenone (VIII)

In a manner similar to that described above for synthesis of III, the Fries rearrangement was conducted to the point where the reaction mixture was treated with 5% HCl. The solid residue was extracted with three portions of ether (15 mL each), the ether solution was then extracted with two portions of 10% NaOH (15 mL each). Acidification of the alkaline extracts with dilute HCl afforded 4,4'-dihydroxy-3,5-dimethylbenzophenone (IX) (90%) m.p. 204 °C instead of the expected compound VIII.

Compound IX had **ir (KBr)**: 2810-3215 cm^{-1} (O-H), 1690 cm^{-1} (C=O), 2868 cm^{-1} ($-CH_3$);

^{1}H-nmr (DMSO-D_6) (δ, ppm): 2.22 (s,6H), 6.88 (δ, 2H), 7.33 (s, 2H), 7.59 (d, 2H), 9.05 (s,1H), 10.23 (s, 1H);

^{13}C-nmr (DMSO-D_6): (δ, ppm): C_1 & C_9 (157.07,160.99), C_2 (114.82), C_3 & C_7 (131.60, 130.26),C_4 & C_6 (128.84,128.70), C_5 (193.25), C_8 (123.18) and C_{10} (16.50). **MS(EI)**: 242 (11.2), 121 (100), 93 (21.1), 77 (40.0). Exact mass calculated 242.0939; found 242.1007.



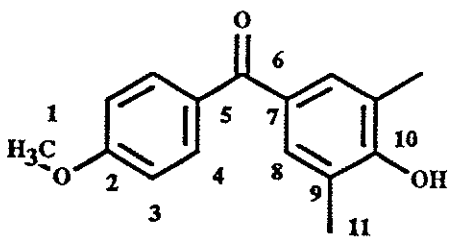
(IX)

Compound VIII was obtained at lower temperatures as indicated in Table 2. Compound VIII melted at 124-125 °C and had **ir (KBr)**: 3255- 3370 cm^{-1} (O-H), 2838 cm^{-1} ($O-CH_3$), 1625-1645 cm^{-1} (C=O)

^{1}H-nmr (DMSO-D_6) (δ, ppm): 2.18 (s, 6H), 3.89 (s, 3H), 6.98 (m, 2H), 7.35 (s, 1H), 8.18 (m, 2H);

^{13}C-nmr (DMSO-D_6) (δ, ppm): C_1 (55.36), C_2 & C_{10} (161.31,160.99), C_3 (113.54), C_4 & C_8 (131.52, 130.25), C_5 & C_7 (128.39, 130.30), C_6 (193.25), C_9 (123.62), C_{11} (16.50);

MS(EI): 256 (8), 242 (3), 135 (100), 121 (96), 107 (60), 93 (19), 77 (39.5). Exact mass calculated 256.1095; found 256.1110.



(VIII)

As the two tables (1 and 2 page 23 and 25 respectively) show, the required compounds are obtained at a higher yield at a reaction temperature of135 °C. To utilize this, the experiment was repeated using chlorobenzene as a solvent which boils at 133 °C. All esters used dissolve in chlorobenzene.

F) General procedure:

To a stirring mixture of $AlCl_3$ (0.133 g, 0.001 mol) in chlorobenzene (35 mL) placed in a 100 mL round bottomed flask was added slowly the ester (0.0005 mol) chlorobenzene (15 mL). When all the ester was introduced, the reaction mixture was refluxed gently for 5 hours. The mixture was cooled and treated with 5% HCl (50 mL) and allowed to cool to room temperature. The mixture was then extracted by diethyl ether. The organic extract was washed by cold water and then extracted by 10% NaOH (methoxy group containing compounds) or by 15% NaOH (nitro group containing compounds). Acidification (with dilute HCl) of the alkaline extracts afforded the corresponding methoxy hydroxydiarylketone compounds III and VIII were obtained in yields of 70% and 78% respectively).

G) Phenyl-4-nitrobenzoate (X)

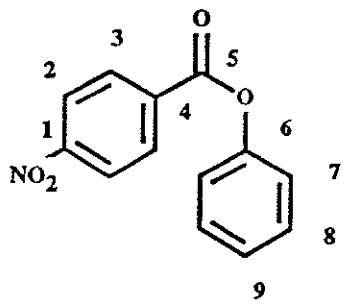
4-Nitrobenzoic acid (3,34 g, 0.02 mol) was dissolved in pyridine (50 mL) and two molecular equivalent of p-TsCl was added. The solution was chilled in an ice bath and one molar equivalent of phenol was added. The solution was kept cold (in ice water bath) for one hour and then poured into an ice water mixture (150 mL). The ester was collected by filtration, white solid m.p. 128-9 °C (75%). When the solution was heated and maintained at 64 °C for 1 hour, the yield was raised to 90%.

The compound had **ir (KBr)**; 1690,1240 cm^{-1} (C=O), 1510, 1390 cm^{-1} ($-NO_2$);

^{1}H-nmr ($CDCl_3$) (δ, ppm): 7.22 (m, 2H), 7.24 (m, 1H), 7.46 (m, 2H) and 8.37 (m,4H);

^{13}C-nmr (CCl_4) (δ, ppm): C_1 & C_6 (150.88, 150.49), C_9 (126.38), C_3 & C_8 (129.64, 131.25), C_2 & C_7 (123.68, 121.38), C_4 (134.96), C_5 (163.26);

MS(EI): 243 (12.5), 151 (8.0), 150 (100), 104 (29.1), 92 (11.4), 76 (20.8). Exact mass calculated; 243.0529; found 243.0544.



(X)

H) 4-Hydroxy-4'-nitrobenzophenone (XI)

Phenyl 4-nitrobenzoate (2.43 g, 0.01 mol) was heated with anhydrous $AlCl_3$ (1.71 g, 0.013 mol) at 125 °C for two hours and then cooled to room temperature. The solid mixture was treated with 5% HCl followed by three extractions with ethyl acetate (25 mL each). The organic layer was then extracted with 5% $NaHCO_3$ (25 mL) to remove the acid (if any), then two extractions of 5% Na_2CO_3 (25 mL each) to remove 4-hydroxy-4' -nitrobenzophenone. The last two extractions were made with of 5% NaOH (25 mL each) to remove 2-hydroxy-4'-nitrobenzophenone. The basic extracts were acidified by HCl to

recover the two products, 4-hydroxy-4'-nitrobenzophenone (0.68 g, 28%, m.p. 193.5-194.5 °C) and 2-hydroxy-4'-nitrobenzophenone (0.18 g, 7.4%, m.p. 113 °C) were obtained. 50% of the ester was recovered.

I) 2,6-Dimethylphenyl-4'-nitrobenzoate (XII)

Using the same procedure described for compound X, the solution was heated and maintained at 65 °C for three hours a slightly yellow product (crystals) was obtained (96%, m.p. 92-93 °C).

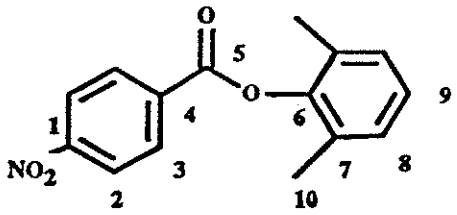
The compound had **ir (KBr)**: 1692, 1239 cm^{-1} (C=O), 1512, 1391 cm^{-1} ($-NO_2$), 2870 cm^{-1} ($-CH_3$);

^{1}H-nmr ($CDCl_3$) (δ, ppm): 2.19 (s, 6H), 7.12 (m, 3H), 8.37 (m, 4H);

^{13}C-nmr ($CDCl_3$) (δ, ppm): C_1 (126.48), C_2 & C_8 (128.77,131.22), C_3 (129.99), C_4 & C_6 (147.96, 150.92), C_5 (162.91), C_7 (134.57), C_9 (123.77), C_{10}(15.87)

MS(EI): 271 (10), 151 (8), 150 (100), 149 (17),122 (20),121 (11), 120 (15), 107 (18), 104 (24), 92 (9),

91 (10), 79 (26), 77(13), 76 (76). Exact mass calculated; 271.0841; found 271.0857.



(X)

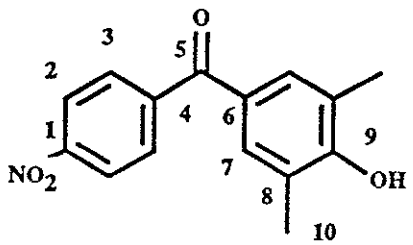
J) 4-Hydroxy-3,5-dimethylphenyl-4'-nitrobenzophenone (XIII)

2,6-Dimethylphenyl 4-nitrobenzoate (2.71 g, 0.01 mol) was heated with anhydrous $AlCl_3$ (1.71 g, 0.013 mol) at 125 °C for two hours and then cooled to room temperature. The solid mixture was treated with 5% HCl followed by three extractions with ethyl acetate (25 mL each). The organic layer was then extracted with 5% $NaHCO_3$ (25 mL) to remove the acid (if any), then two extractions of warm 10 % NaOH (25 mL each) to remove 4-hydroxy-3,5 - dimethylphenyl-4'-nitrobenzophenone. The basic extract was then acidified by HCl to recover the product, 4-hydroxy-3,5-dimethylphenyl-4' -nitrobenzophenone (1.45 g, 59%, m.p. 155-156.5 °C) was obtained. 31% of the ester was recovered.

Compound XIII had **ir (KBr)**: 1691, 1241 (C=O), 1510, 1391 cm $^{-1}$ ($-NO_2$), 2812-3390 cm $^{-1}$ (O-H);

^{1}H-nmr ($CDCl_3$) (δ, ppm): 2.29 (s, 6H), 5.21 (s, 1H), 7.49 (s, 2H), 7.85 (m, 2H), 8.32 (m, 2H).

^{13}C-nmr ($CDCl_3$) (δ, ppm): C_1 (123.22), C_2 (123.39), C_3 & C_7 (130.24), C_4 & C_6 (129.10, 130.50), C_5 (193.80), C_8 (122.80), C_9 (157.19) and C_{10} (15.85).



(XIII)

4.2: FRIES REARRANGEMENT USING BF_3 AS A LEWIS ACID:

K) 4-Hydroxy-4'-methoxybenzophenone (III)

(i) Phenol (1.00 g, 0.01 mol) and *p*-methoxybenzoic acid (3.00 g, 0.02 mol) were suspended in nitrobenzene (30 mL), and then BF_3 gas was bubbled through until all the starting materials were dissolved (saturation). The mixture was heated at 80 °C (in the water bath) for 14 hours. The reaction was monitored by TLC to ensure the completion. The reaction mixture was cooled to room temperature before the addition of water. The solid product was filtered from the solution mixture and washed with a very dilute Na_2CO_3 solution and then dried (m.p. 153 °C). The spectra obtained were identical those obtained previous for compound III.

(ii) The reaction was completed faster (5 hours) when the ester was used as the starting material. See Table 3 and 4 (page 30 and 31 respectively).

L) 4-Hydroxy-3,5-dimethyl-4'-methoxybenzophenone (VIII)

In a manner to that described above for compound III, the Fries rearrangement was conducted to afford compound VIII. Again see Table 3 and 4.

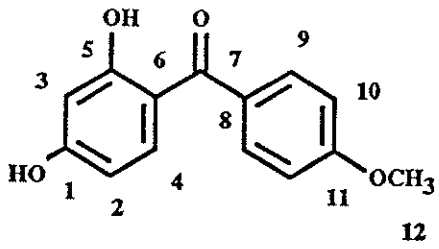
M) 2,4-Dihydroxy-4'-methoxyphenylbenzophenone (XIV)

In a manner to that described above for compound III, resorcinol was used instead of phenol to obtain compound XIV by heating the reaction mixture for only 45 minutes. The pure compound melts at 165 °C (94% yield). Compound XIV had **ir (KBr)**: 2810 - 3400 cm^{-1} (O-H), 1645 cm^{-1} (C=O), 2840 cm^{-1} ($-OCH_3$);

^{1}H-nmr (DMSO-D_6) (δ,ppm): 3.85 (s, 3H), 6.39 (m, 2H), 7.08 (m, 2H), 7.41 (d, 1H), 7.63 (m, 2H), 10.58 (s, 1H), 12.10 (, 1H);

^{13}C-nmr (DMSO-D_6) (δ, ppm): C_1, C_5 & C_{11} (152.02, 163.78, 164.09), C_2 & C_3 (107.76, 102.63) C_4 (134.70), C_6 (112.77), C_7 (197.08), C_8 (130.21), C_9 (131.09), C_{10} (113.57), C_{12} (55.37).

MS(EI): 244 (64.3), 243 (46.7), 137 (56.6), 136 (36.2), 135 (54.6), 108 (100), 92 (10.9), 77 (14.9). Exact mass calculated 244.0781; found 244.0783.



(XIV)

4.3: OXIDATION OF THE *p*-HYDROXYDIARYLKETONES:

The oxidation was made by using the following oxidants;

(a) Bromine - Br_2,

(b) Lead Tetraacetate - LTA and

(c) Ceric Ammonium Nitrate - CAN

The oxidation was made under different experimental conditions. The experimental procedures given below are general and were followed when all individual experiment were made. Refer to Tables 5, 6 and 7 (page 37, 43 and 48 respectively).

4.3 (a): OXIDATION WITH BROMINE - Br_2:

General procedure;

The hydroxydiarylketone (1.95×10^{-4} mol) was dissolved in an aqueous solvent and 2 (or 4) equivalents of Br_2 were added, depending on how many bromine substitutions are anticipated to take place. The orange solution was left to stand until the color disappeared and then a saturated solution of $NaHSO_3$ was added to remove any traces of elemental bromine present. Solid products were obtained and analyzed as indicated below. The same procedure was followed when excess bromine was used and solid products were obtained and analyzed. See Table 5 (page 37).

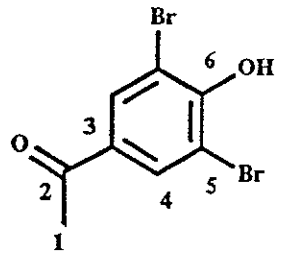
i) 3,5-Dibromo *p*-hydroxyacetophenone (XV)

The compound has a m.p. of 174-175 °C and had the following characteristics;

^{1}H-nmr (DMSO-D_6) (δ,ppm): 2.6 (s, 3H), 6.4 (s, 1H), 8.2 (s, 2H);

^{13}C-nmr (DMSO-D_6) (δ, ppm): C_1 (26.23), C_2 (194.14), C_3 (131.92), C_4 (132.57), C_5 (110.07), C_6 (153.26)

MS(EI): 294 (36.3), 281 (50.9), 279 (100.0), 277 (51.5), 62 (21). Exact mass calculated 293.8714; found 293.8699



(XV)

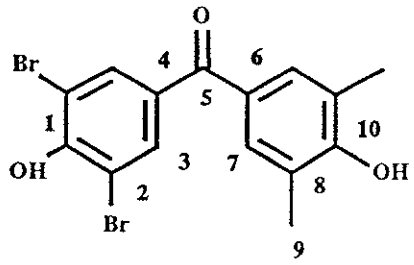
ii) 3,5-Dibromo-4,4'-dihydroxy-3',5'-dimethylphenylbenzophenone (XVI)

Compound XVI melts at 216-218 °C and had the following spectral characteristics;

^{1}H-nmr ($CDCl_3$) (δ, ppm): 2.30 (s, 6H), 5.15 (s, 1H), 6.25 (s, 1H), 7.44 (s , 2H),

7.90 (s, 2H);

^{13}C-nmr ($CDCl_3$) (δ, ppm): C_1 & C_{10}(156.23, 160.89), C_2 (110.11), C_3 & C_7(133.01, 129.81), C_4 & C_6 (133.86, 129.81), C_5 (192.99), C_8 (123. 36), C_9 (16.89); **MS(EI):** 400 (11.4), 150 (10.6), 149 (100.0), 91 (11.7), 77 (13.9). Exact mass calculated 399.9133; found 399.9146.



(XVI)

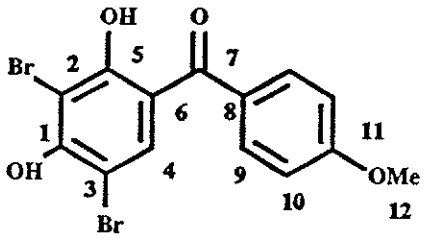
iii) 3,5-Dibromo-2,4-dihydroxy-4'-methoxyphenylbenzophenone (XVII)

Compound XVII melts at 157-158.5 °C and had the following spectral characteristics;

^{1}H-nmr ($CDCl_3$) (δ, ppm): 3.9 (s, 3H), 6.0 (s, 1H), 6.4 (s, 1H), 6.98 (s, 2H), 7.78 (m , 2H), 7.91 (s, 1H);

^{13}C-nmr ($CDCl_3$) (δ, ppm): C_1, C_5 & C_{11} (157.79, 158.12, 160.04), C_2 & C_3 (95.81, 101.63), C_4 & C_9 (132.94, 130.01), C_6 & C_8 (120.55, 129.07), C_7 (196.78), C_{10} (110.87), 160.89), &), C_{12} (55.44);

MS(EI): 402 (8.2), 294 (10.8), 135 (31.4), 108 (100), 92 (10.6), 77 (17.7). Exact mass calculated 401.8925; found 401.8954.



(XVII)

4.3 (b): OXIDATION WITH LEAD TETRAACETATE - LTA:

General procedure;

The hydroxydiarylketone (3.9 X 10^{-4} mol) was dissolved in the desired solvent (15 mL) and LTA (2 equivalents) were added to a stirring solution. A brownish solution was obtained which was heated under reflux for a period shown in Table 6 (page 40). The hot solution was left to cool to room temperature and then diluted with cold water (50 mL). The product was obtained by filtration.

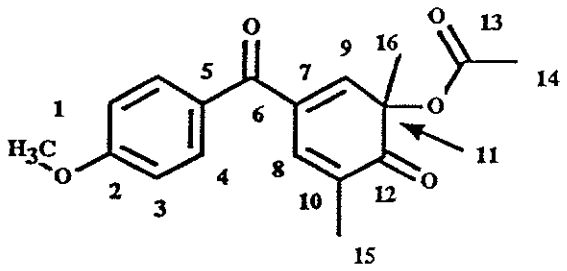
When compound VII was used as the starting material the product obtained (XVIII) melted at 152-153 °C and the following spectral values were obtained;

ir (KBr): 2838 cm^{-1} (-OCH_3), 1400-1450, 2870 cm^{-1} (-CH_3), 1680 cm^{-1} (-C=C-), 1660-1750 cm^{-1} (-C=O);

^{1}H-nmr ($CDCl_3$) (δ, ppm): 1.45 (s, 3H), 2.02 (s, 3H), 2.14 (s, 3H), 3.88 (s, 3H), 6.57 (m, 1H), 6.95 (m,2H), 7.26 (m, 1H), 7.78 (m, 2H).

^{13}C-nmr ($CDCl_3$) (δ, ppm): C_1(55.51), C_2 (163.58), C_3(113.82), C_4 (132.09), C_5, C_7 & C_{10}(128.89, 132.35), C_6 & C_{12} (192.66, 197.83), C_{13} (169.91), C_8 & C_9 (135.68, 145.63),C_{11}(78.66), C_{14} & C_{16} (20.74, 23.28), C_{15} (15.44)

MS(EI): 314 (2), 272 (9), 257 (9.9), 256 (58.8), 241 (19.9), 230 (13.7), 149 (76.2), 135 (100.0), 92 (13. 1) 77 (24.1). Exact mass calculated 314.3412; found 314.1125.



(XVIII)

For various compounds and conditions, see Table 6 page 43.

4.3 (c): OXIDATION WITH CERIC AMMONIUM NITRATE - CAN:

General procedure;

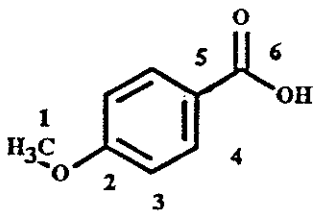
The hydroxydiarylketone (3.9 X 10^{-4} mol) was dissolved in the desired solvent (15 mL) and CAN (2 equivalents) were added to a stirring solution. A yellow solution was obtained which was heated under reflux for 8 hours. The hot solution was left to cool to room temperature and then diluted with cold water (50 mL). The product was obtained by filtration or extraction by ethyl acetate (20 mL) depending on the solvent (or mixture of the solvents) used. This was made because with some solvents the product did not precipitate. When the product was obtained by filtration, the aqueous layer was extracted with ethyl acetate and the analysis was done on the residue. With a few experimental conditions the starting material was recovered in a low percentage and with other conditions the spectra were too complex to identify the components. The solid products obtained were found to be acidic and melting points were also found.

When compound VII was used as the starting material the product obtained (XIX) melted at 182 °C and the following spectra values were obtained;

Ir (KBr): 2830 cm^{-1} ($-OCH_3$), 1600 cm^{-1} (-C=O);

^{1}H-nmr ($CDCl_3$) (δ, ppm): 3.88 (s, 3H), 6.94 (m, 2H), 8.07 (m, 2H);

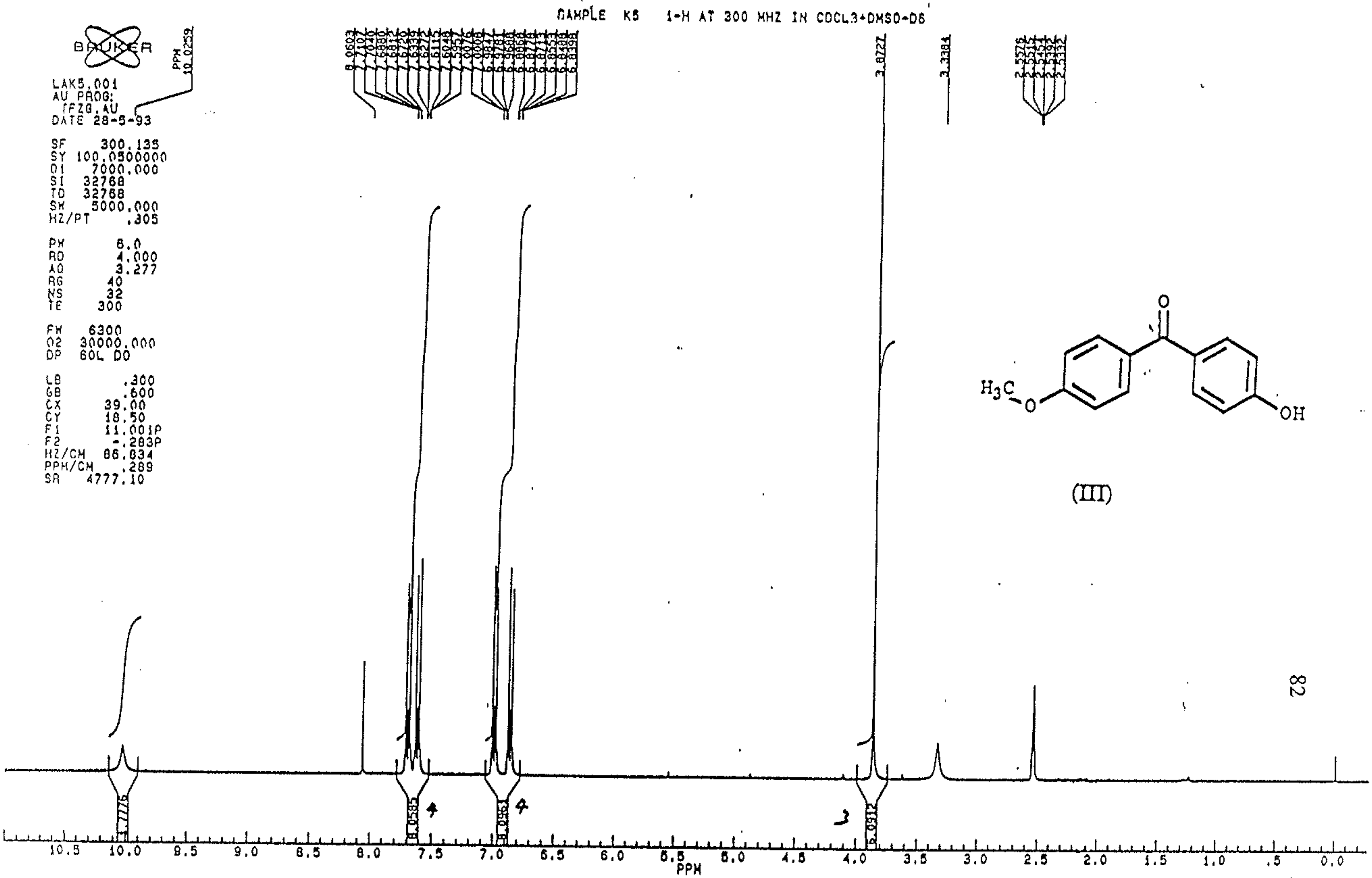
^{13}C-nmr ($CDCl_3$) (δ, ppm): C_1 (55.47), C_2 (164.00), C_3(113.73), C_4 (132.32), C_5 (121.60), C_6 (171.35). Exact mass found was 152.1801. The above information matches with that of 4-methoxybenzoic acid.



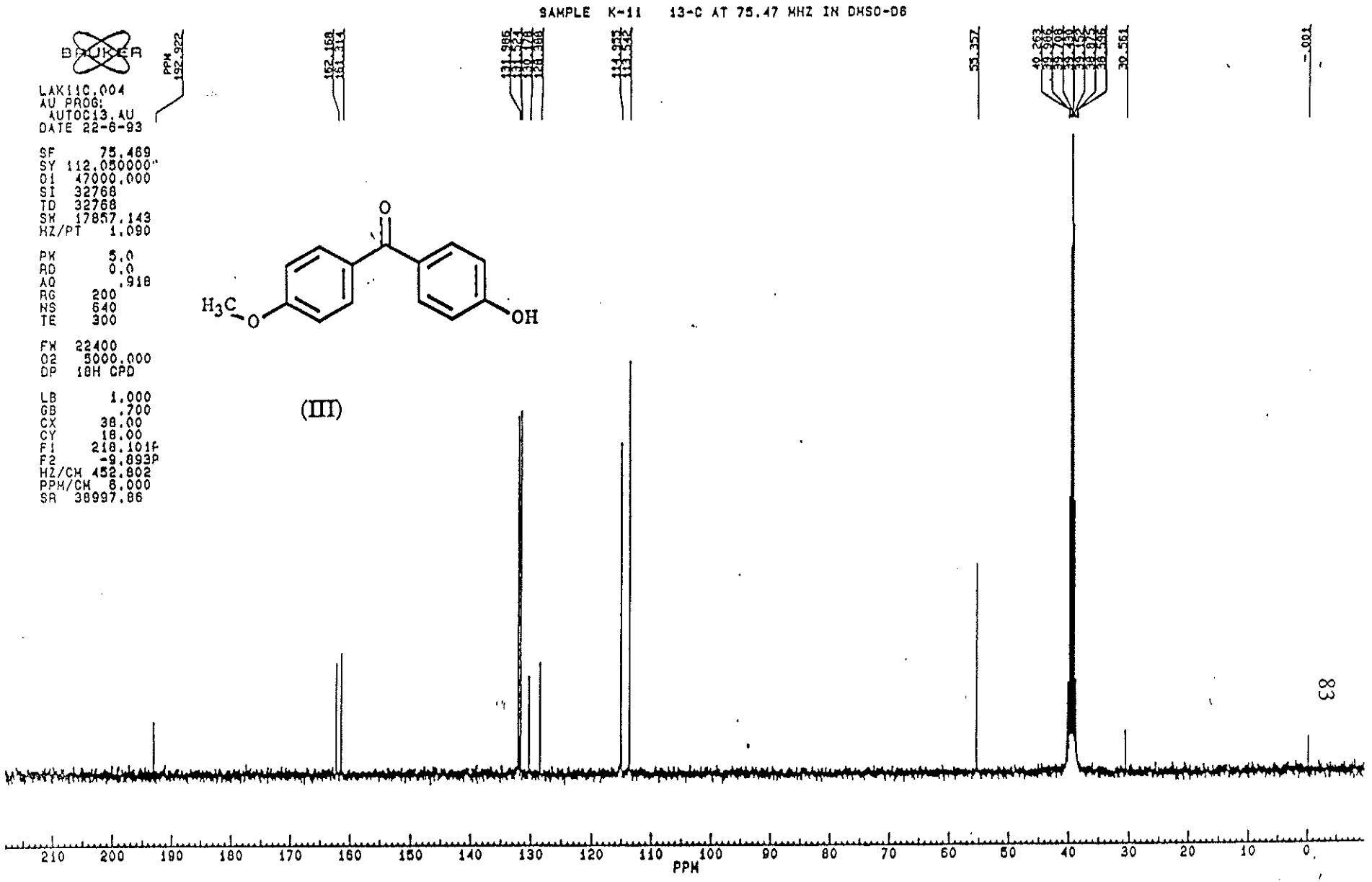
(XIX)

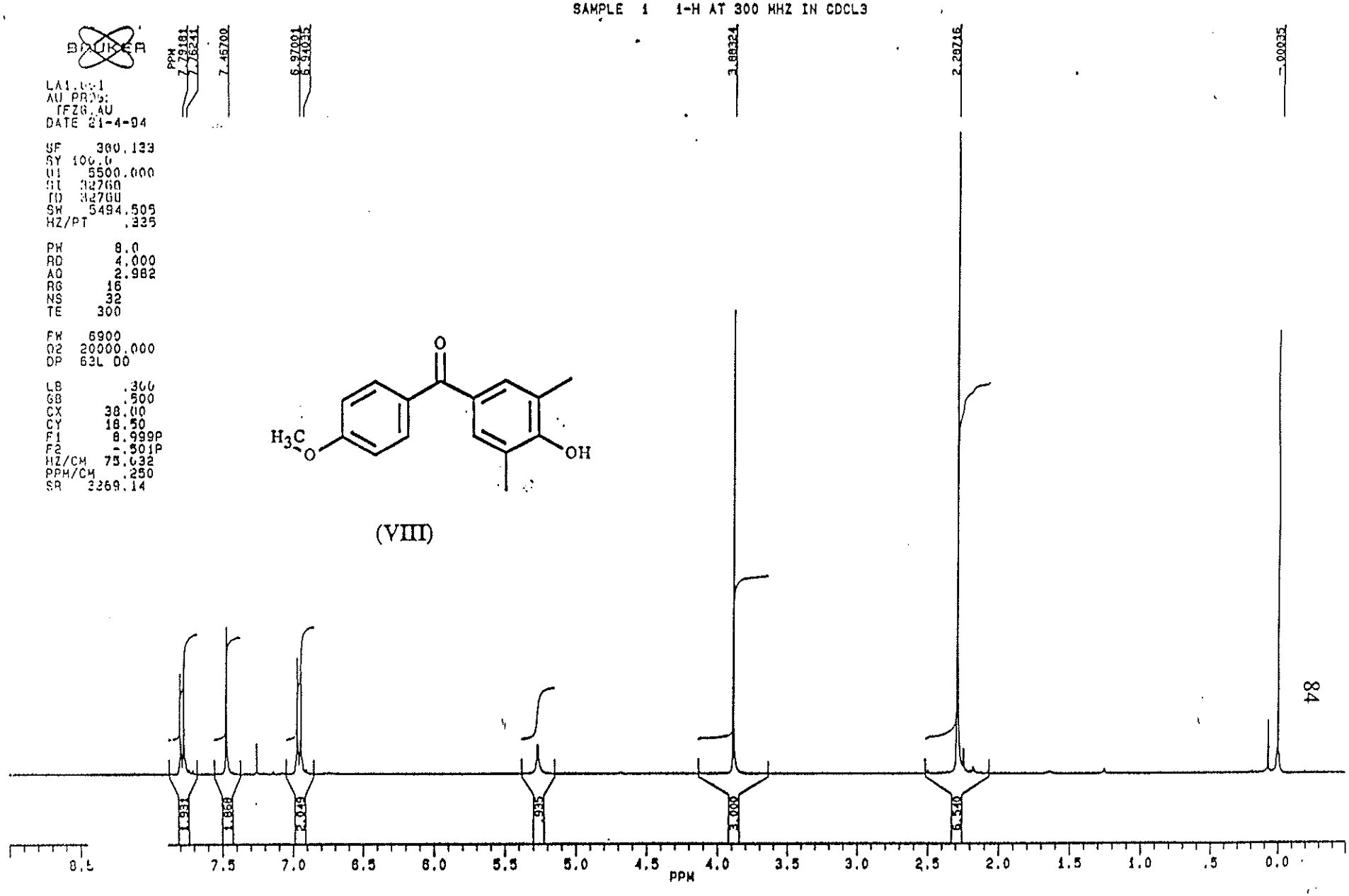
Other acids formed during the oxidation of the hydroxydiarylketones corresponded to the acids used to prepare their esters.

NMR SPECTRA

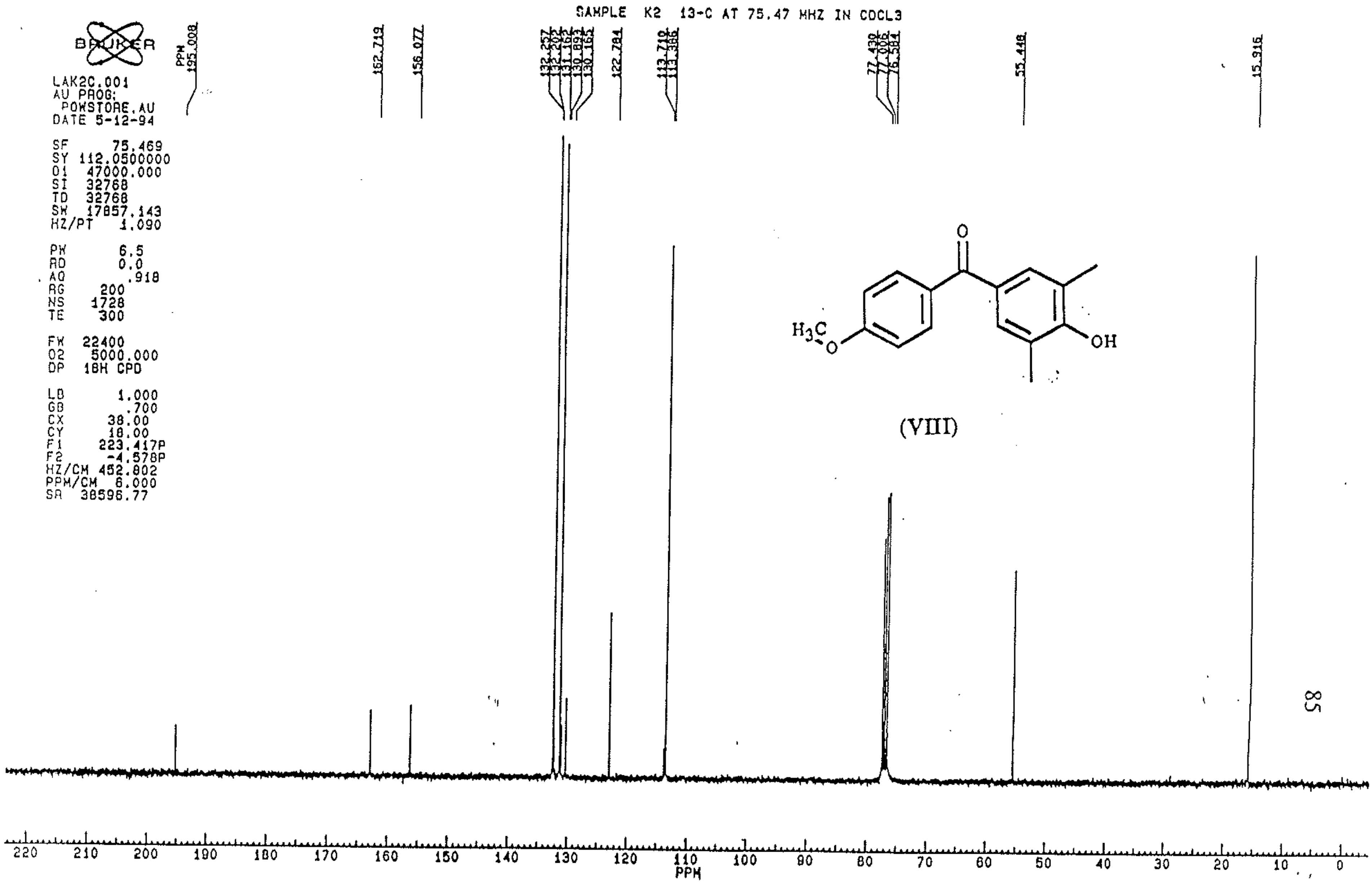

SAMPLE K5 1-H AT 300 MHZ IN CDCL3+DMSO-D6
BRUKER
LAK5.001
AU PROG:
FFZG.AU
DATE 28-5-93
SF 300.135
SY 100.0500000
O1 7000.000
SI 32768
TD 32768
SW 5000.000
HZ/PT .305
PW 6.0
RD 4.000
AQ 3.277
RG 40
NS 32
TE 300
FW 6300
O2 30000.000
DP 60L DO
LB .300
GB .600
CX 39.00
CY 18.50
F1 11.001P
F2 -.283P
HZ/CM 86.834
PPM/CM .289
SR 4777.10
PPM
10.0259
3.8727
3.3384
4
4
3
H3C
O
OH
PPM

(III)


SAMPLE K-11 13-C AT 75.47 MHZ IN DMSO-D6
BRUKER
PPM
192.922
152.168
151.314
131.986
131.524
130.178
128.368
114.923
113.542
55.357
40.263
39.908
39.708
39.453
39.152
38.872
38.596
30.561
-.001
LAK11C.004
AU PROG:
AUTOC13.AU
DATE 22-6-93
SF 75.469
SY 112.050000
O1 47000.000
SI 32768
TD 32768
SW 17857.143
HZ/PT 1.090
PW 5.0
RD 0.0
AQ .918
RG 200
NS 640
TE 300
FW 22400
O2 5000.000
DP 18W CPD
LB 1.000
GB .700
CX 38.00
CY 18.00
F1 218.101P
F2 -9.893P
HZ/CM 452.802
PPM/CM 6.000
SR 38997.86
O
H3C
O
OH
(III)
83
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
PPM


SAMPLE 1 1-H AT 300 MHZ IN CDCL3
BRUKER
PPM
7.79181
7.78241
7.46700
6.97001
6.94035
3.88324
2.29746
-.00935
LA1.001
AU PROG:
TFZG.AU
DATE 21-4-94
SF 300.133
SY 100.0
O1 5500.000
SI 32768
TD 32768
SW 5494.505
HZ/PT .335
PW 8.0
RD 4.000
AQ 2.982
RG 16
NS 32
TE 300
FW 6900
O2 20000.000
DP 63L 00
LB .300
GB .500
CX 38.00
CY 18.50
F1 8.999P
F2 -.501P
HZ/CM 75.032
PPM/CM .250
SR 3269.14
O
H3C
O
OH
1.931
1.868
2.049
.935
3.000
6.340
8.5
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
PPM

(VIII)


SAMPLE K2 13-C AT 75.47 MHZ IN CDCL3
BRUKER
LAK2C.001
AU PROG:
POWSTORE.AU
DATE 5-12-94
SF 75.469
SY 112.0500000
O1 47000.000
SI 32768
TD 32768
SW 17857.143
HZ/PT 1.090
PW 6.5
RD 0.0
AQ .918
RG 200
NS 1728
TE 300
FW 22400
O2 5000.000
DP 18H CPD
LB 1.000
GB .700
CX 38.00
CY 18.00
F1 223.417P
F2 -4.578P
HZ/CM 452.802
PPM/CM 6.000
SR 38596.77
PPM
195.008
162.719
156.077
132.257
131.163
130.893
130.163
122.784
113.719
113.366
77.430
77.006
76.584
55.448
15.916
O
H_3C
O
OH
(VIII)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
PPM

SAMPLE K-21 1-H AT 300 MHZ IN DMSO-D6

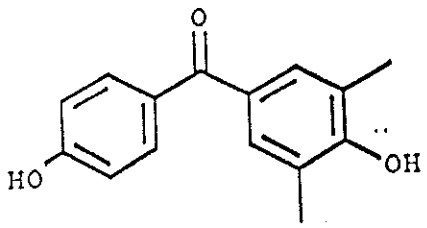
LAK21.001
AU PROG:
ZFZG.ad
DATE 17-6-93

SF 300.135
SY 100.0500000
O1 7000.000
SI 32768
TD 32768
SW 5000.000
HZ/PT .305

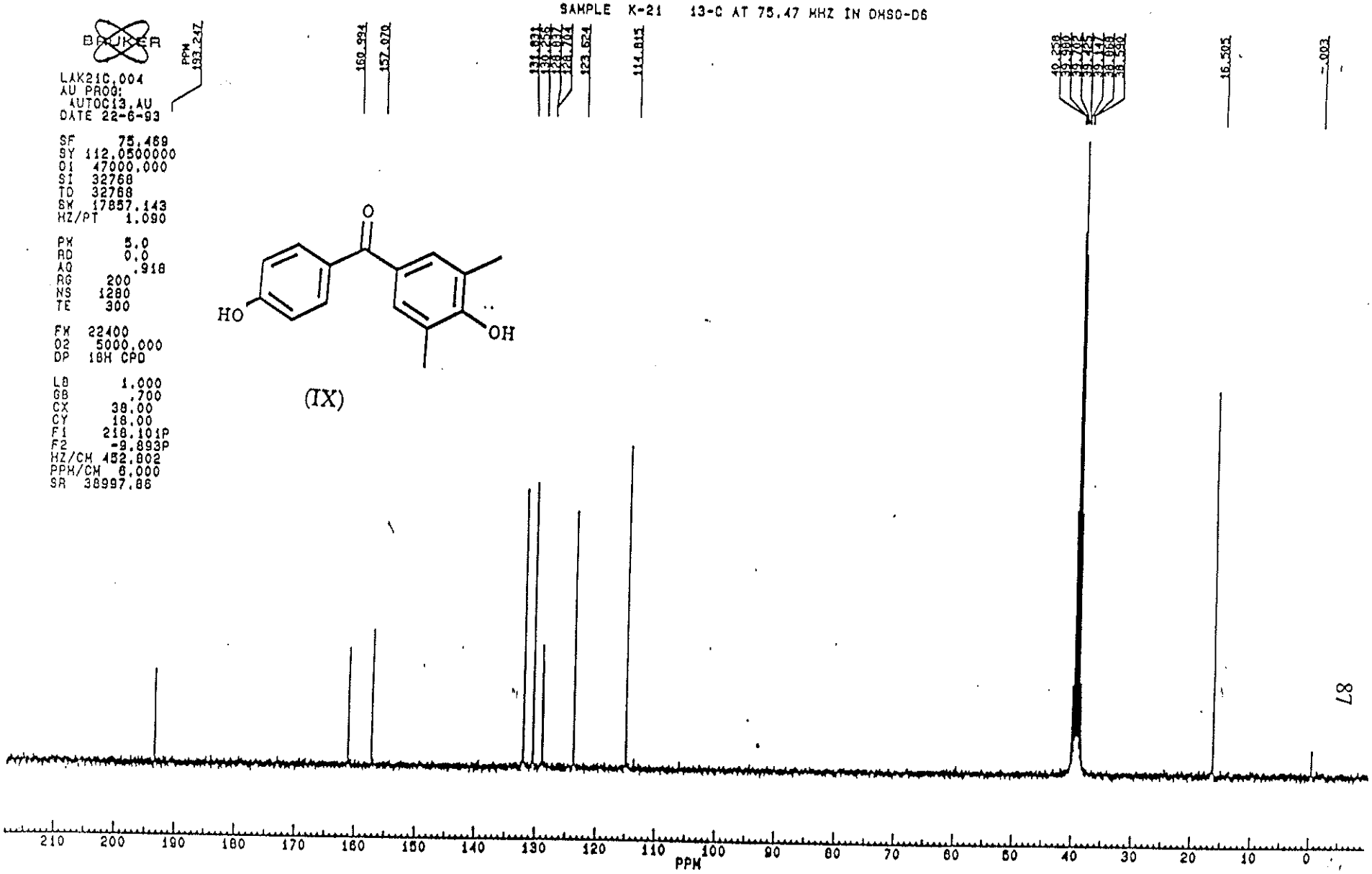
PW 6.0
RD 4.000
AQ 3.277
RG 16
NS 32
TE 300

FW 6300
O2 30000.000
DP 60L DO

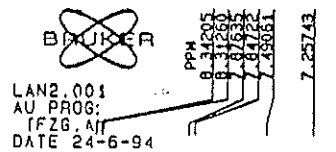
LB .300
GB .600
CX 39.00
CY 22.00
F1 11.001P
F2 -.699P
HZ/CM 90.035
PPM/CM .300
SR 4787.78



(IX)


SAMPLE K-21 13-C AT 75.47 MHZ IN DMSO-D6
BRUKER
PPM 193.247
160.994
157.070
131.831
130.256
128.017
126.704
123.624
114.815
16.505
-.003
LAK21C.004
AU PROG:
AUTOC13.AU
DATE 22-6-93
SF 75.469
SW 112.0500000
OI 47000.000
SI 32768
TD 32768
SW 17857.143
HZ/PT 1.090
PW 5.0
RD 0.0
AQ .918
RG 200
NS 1280
TE 300
FW 22400
O2 5000.000
DP 18H CPD
LB 1.000
GB .700
CX 38.00
CY 18.00
F1 218.101P
F2 -9.893P
HZ/CM 452.802
PPM/CM 6.000
SR 38997.86
HO
OH
O
(IX)
87
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
PPM

SAMPLE N2 1-H AT 300 MHZ IN COCL3



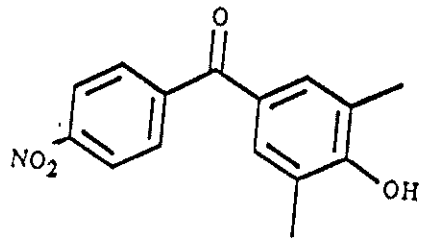
LAN2.001
AU PROG:
[FZG.AU]
DATE 24-6-94

SF 300.133
SY 100.0
O1 5500.000
SI 32768
TD 32768
SW 5494.505
HZ/PT .335

PW 8.0
RD 4.000
AQ 2.982
RG 100
NS 32
TE 300

FW 6900
O2 20000.000
DP 63L DO

LB .300
GB .500
CX 38.00
CY 18.50
F1 9.003P
F2 -.497P
HZ/CM 75.032
PPM/CM .250
SR 3368.13



(XIII)

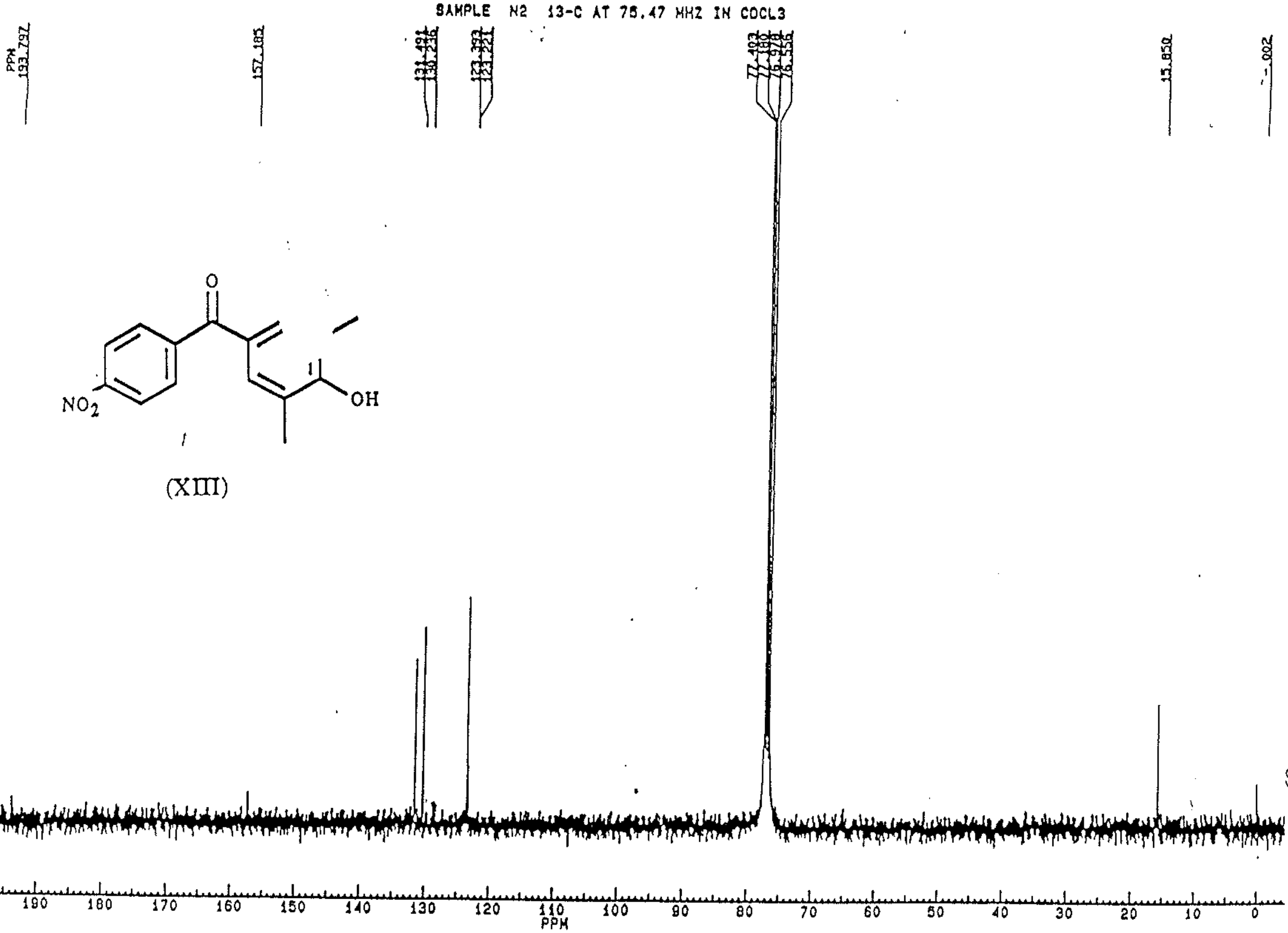
LAN2CC.004
AU PROG:
AUTOC13.AU
DATE 25-6-94

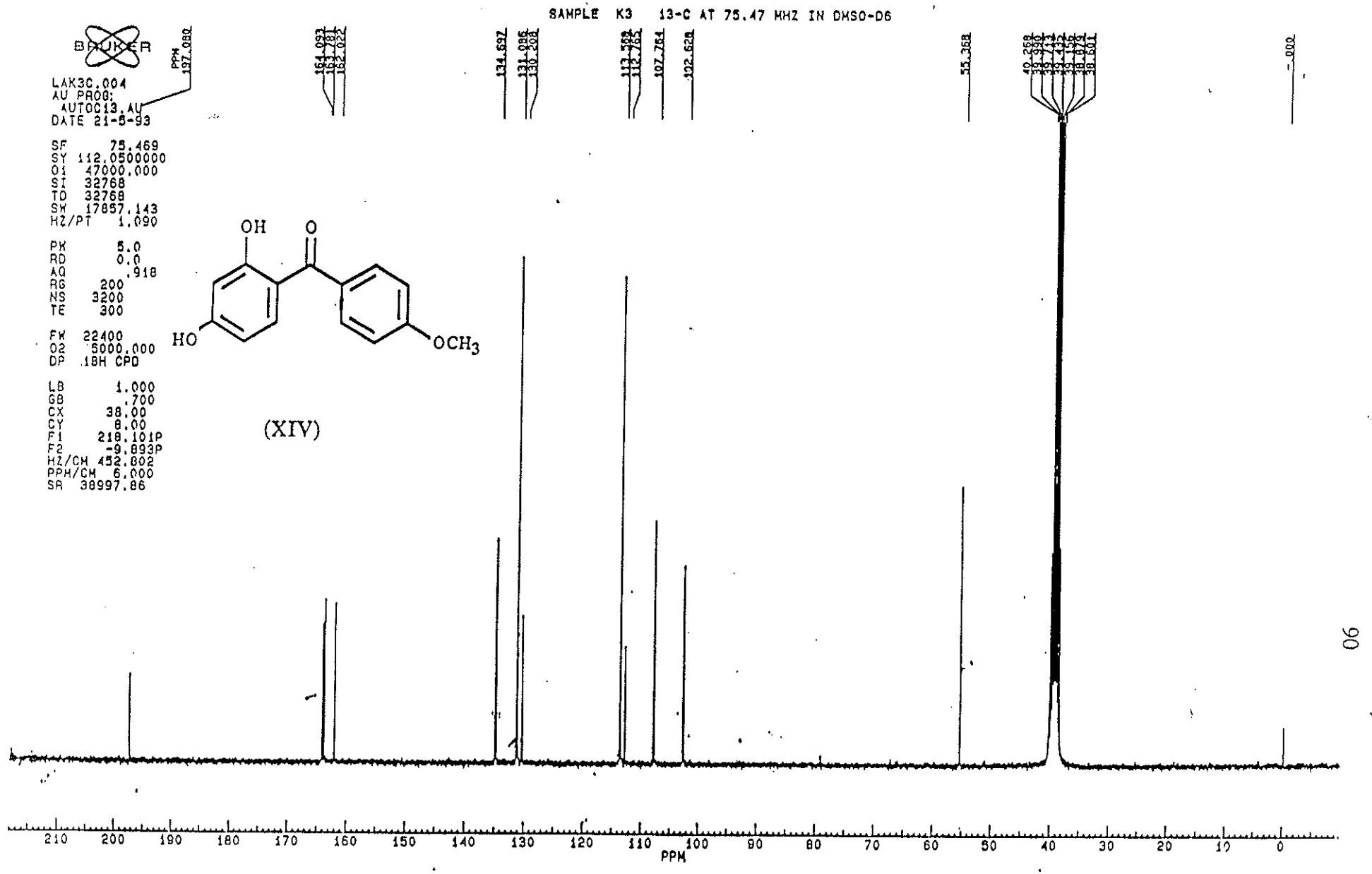
SF 75.469
SY 112.0500000
O1 47000.000
SI 32768
TD 32768
SW 17857.143
HZ/PT 1.090

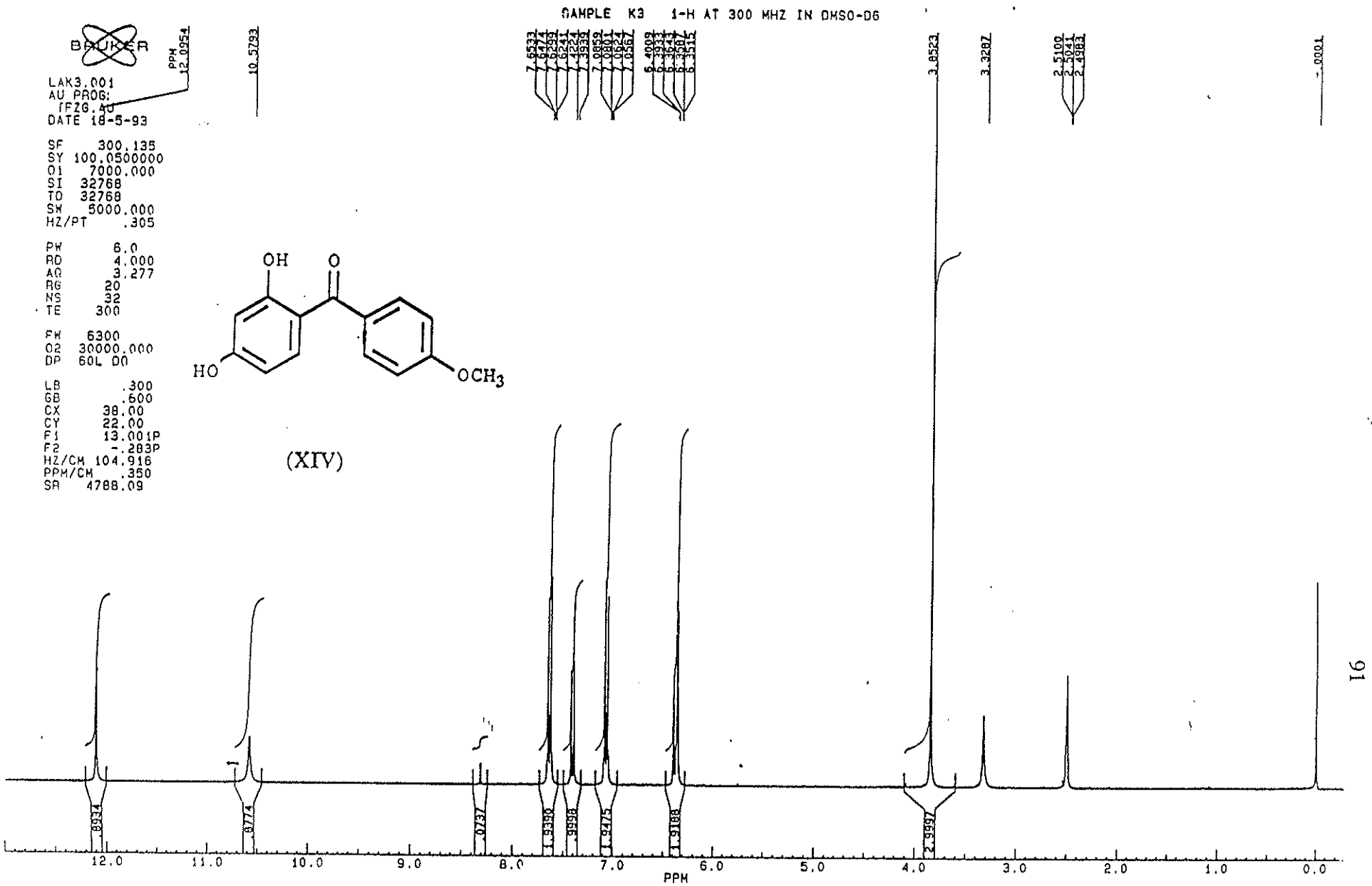
PW 5.0
RD 0.0
AQ .918
RG 200
NS 4800
TE 300

FW 22400
O2 5000.000
DP 18H CPD

LB 1.000
GB .700
CX 38.00
CY 6.00
F1 223.417P
F2 -4.578P
HZ/CM 452.002
PPM/CM 6.000
SR 38596.77

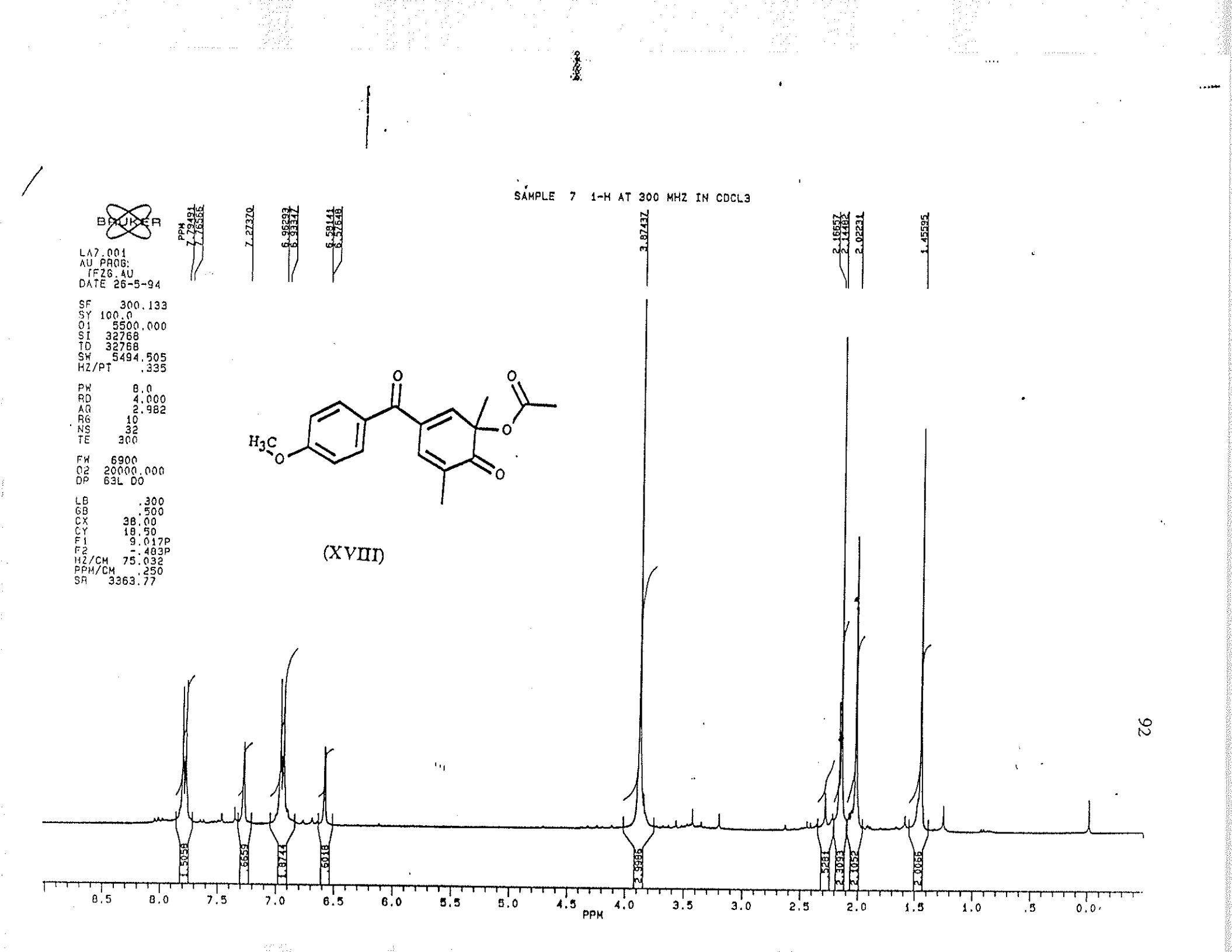



SAMPLE K3 13-C AT 75.47 MHZ IN DMSO-D6
BRUKER
LAK3C.004
AU PROG:
AUTOC13.AU
DATE 21-6-93
SF 75.469
SY 112.0500000
OI 47000.000
SI 32768
TD 32768
SW 17857.143
HZ/PT 1.090
PK 5.0
RD 0.0
AQ .918
RG 200
NS 3200
TE 300
FW 22400
O2 5000.000
DP .1BH CPD
LB 1.000
GB .700
CX 38.00
CY 8.00
F1 218.101P
F2 -9.893P
HZ/CM 452.802
PPH/CM 6.000
SR 38997.86
PPM
197.080
164.033
163.781
162.022
134.692
131.086
130.208
113.558
112.762
107.764
102.628
55.368
40.258
39.840
39.423
39.006
38.589
38.171
38.001
-.000
OH
O
HO
OCH3
(XIV)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
PPM

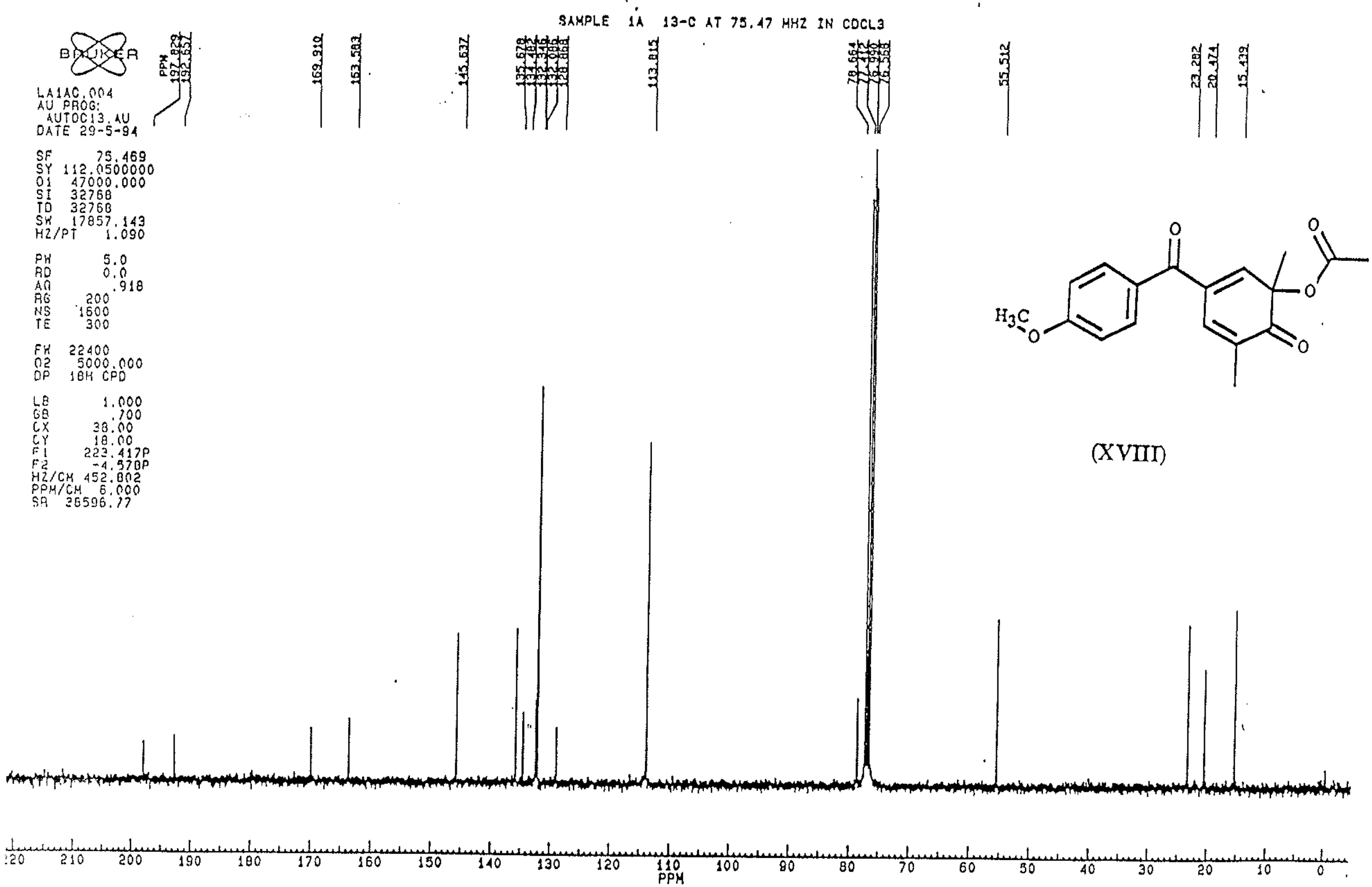

SAMPLE K3 1-H AT 300 MHZ IN DMSO-D6
BRUKER
LAK3.001
AU PROG:
[FZG.AU
DATE 18-5-93
SF 300.135
SY 100.0500000
O1 7000.000
SI 32768
TD 32768
SW 5000.000
HZ/PT .305
PW 6.0
RD 4.000
AQ 3.277
RG 20
NS 32
TE 300
FW 6300
O2 30000.000
DP 60L D0
LB .300
GB .600
CX 38.00
CY 22.00
F1 13.001P
F2 -.283P
HZ/CM 104.916
PPM/CM .350
SR 4788.09
PPM
12.0954
10.5793
7.6533
7.6474
7.6299
7.6241
7.4224
7.3939
7.0859
7.0801
7.0624
7.0567
6.4009
6.3933
6.3641
6.3587
6.3515
3.8523
3.3287
2.5100
2.5041
2.4981
-.0001
0.9934
0.9774
0.9737
1.9380
0.9998
1.9475
1.9188
2.9997
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

OH
O
HO
OCH3

(XIV)


SAMPLE 7 1-H AT 300 MHZ IN CDCL3
BRUKER
LA7.001
AU PROG:
FFZ6.AU
DATE 26-5-94
SF 300.133
SY 100.0
O1 5500.000
SI 32768
TD 32768
SW 5494.505
HZ/PT .335
PW 8.0
RD 4.000
AQ 2.982
RG 10
NS 32
TE 300
FW 6900
O2 20000.000
DP 63L DO
LB .300
GB .500
CX 38.00
CY 18.50
F1 9.017P
F2 -.483P
HZ/CM 75.032
PPM/CM .250
SR 3363.77
PPM
7.78491
7.76566
7.27370
6.96233
6.93347
6.58141
6.57648
3.87437
2.16557
2.14482
2.02231
1.45595
1.5058
.5659
1.8744
.5018
2.9996
.5281
2.3093
2.1052
2.9066
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
H3C
O

(XVIII)


SAMPLE 1A 13-C AT 75.47 MHZ IN CDCL3
BRUKER
LA1AC.004
AU PROG:
AUTOC13.AU
DATE 29-5-94
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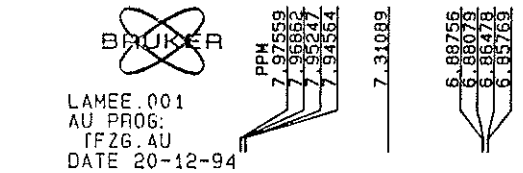
SY 112.0500000
O1 47000.000
SI 32768
TD 32768
SW 17857.143
HZ/PT 1.090
PW 5.0
RD 0.0
AQ .918
RG 200
NS 1600
TE 300
FW 22400
O2 5000.000
DP 18H CPD
LB 1.000
GB .700
CX 38.00
CY 18.00
F1 223.417P
F2 -4.578P
HZ/CM 452.802
PPM/CM 6.000
SR 26596.77
PPM
197.829
192.557
169.910
163.583
145.537
135.678
113.815
78.664
55.512
23.282
20.474
15.439
PPM
O
O
O
H3C
O
O

(XVIII)

SAMPLE MEE 1-H AT 300 MHZ IN CDCL3



PPM
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7.96852
7.95247
7.94564
7.31089
6.88756
6.88079
6.86478
6.85769
3.84900
3.79123

LAMEE.001
AU PROG:
TFZG.AU
DATE 20-12-94

SF 300.133
SY 100.0
O1 5500.000
SI 32768
TD 32768
SW 5494.505
HZ/PT .335

PW 6.0
RD 4.000
AQ 2.982
RG 1
NS 32
TE 300

FW 6900
O2 20000.000
DP 63L D0

LB .300
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CX 38.00
CY 18.50
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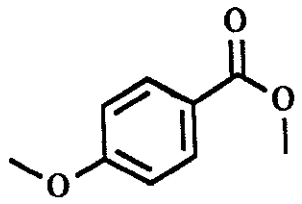
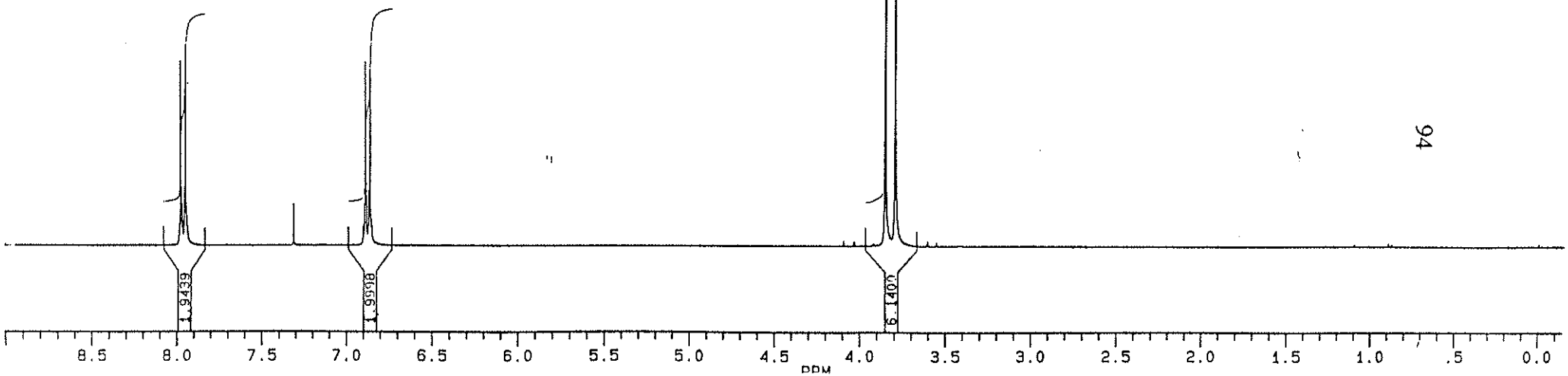
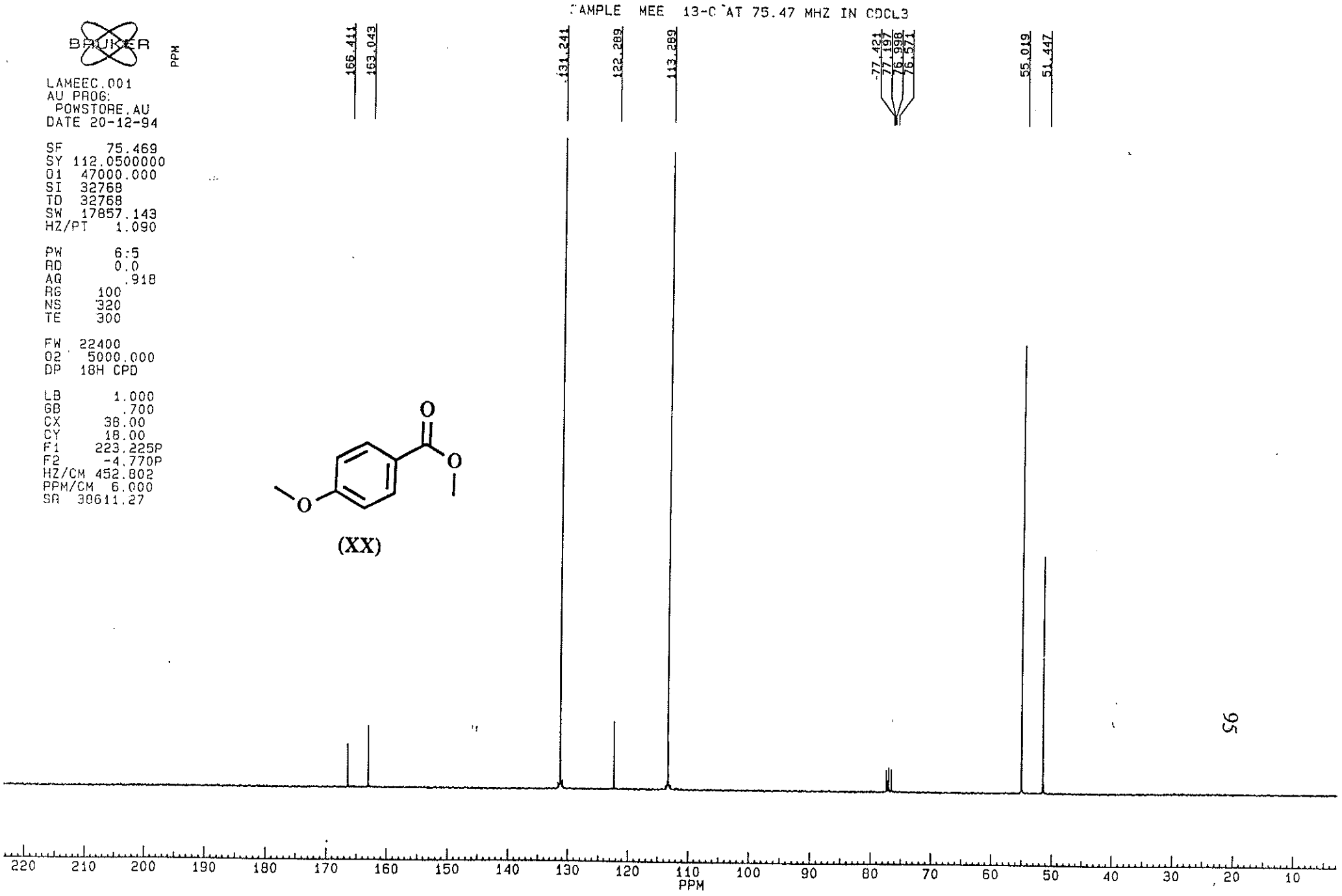
HZ/CM 75.032
PPM/CM .250
SR 3351.36



(XX)




SAMPLE MEE 13-C AT 75.47 MHZ IN CDCL3
BRUKER
PPM
LAMEEC.001
AU PROG:
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SY 112.0500000
O1 47000.000
SI 32768
TD 32768
SW 17857.143
HZ/PT 1.090
PW 6.5
RD 0.0
AQ .918
RG 100
NS 320
TE 300
FW 22400
O2 5000.000
DP 18H CPD
LB 1.000
GB .700
CX 38.00
CY 18.00
F1 223.225P
F2 -4.770P
HZ/CM 452.802
PPM/CM 6.000
SR 38611.27
166.411
163.043
131.241
122.289
113.289
77.421
77.197
76.998
76.571
55.019
51.447
O
O
O
(XX)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
PPM

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