THE UNIVERSITY OF MANITOBA

STUDIES ON

BENZO[C]THIOPHENES AND RELATED SYSTEMS

by

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ABSTRACT

To gain some insight on the special properties of the thiathiophthenes, the syntheses of two model systems have been attempted. While the synthesis of the first model system, the 4-thioacylbenzo[c]-thiophenes, has not been successful, the synthesis and properties of a variety of benzo[c]thiophene derivatives have been explored.

On the other hand, the second model system, 7-acetyl-3-methyl-anthranil, has been synthesized by reduction of 2,6-diacetylnitro-benzene. While the chemical properties of the compound indicate that it undergoes valency-tautomerism, spectroscopic studies indicate that this process is too slow to be detected on the NMR time-scale. Comparisons with other heterocyclic systems plus present evidence appear to favour the hypothesis that invokes the use of sulfur d-orbitals in the bonding of the central sulfur atom of thiathiophthenes to explain their symmetry in solution.

A variety of thiophene analogues of triptycene which contain the benzo[c]thiophene element of structure have been prepared. Anthracenes react with diacetyl- and dibenzoylethylenes and dibenzoylacetylene to give substituted bicyclooctadienes and -trienes as Diels-Alder type adducts. Sulfurization of the former give thiophene analogues of triptycene in which one ortho linked benzene ring is replaced by a five-member heterocyclic system; but the latter give mixtures of the thiophenes and the corresponding furans. Attempted preparation of triptycene analogues in which two ortho linked benzene rings are replaced by heterocyclic systems was unsuccessful. Attempted retro Diels-Alder reactions of the thiophene analogues to produce dehydrothiophenes were also unsuccessful.

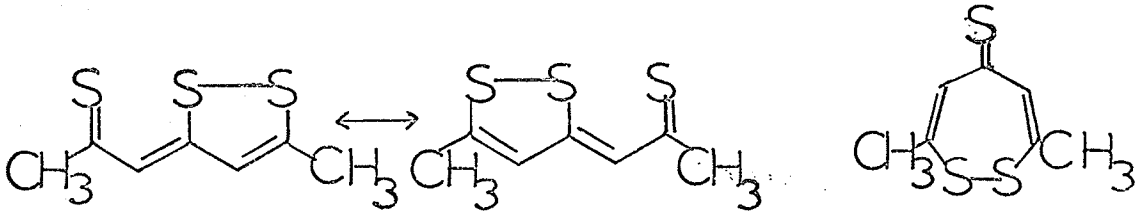
TABLE OF CONTENTS

EXPERIMENTAL PROCEDURES AND RESULTS

INTRODUCTION

PART A THIATHIOPHTHENES

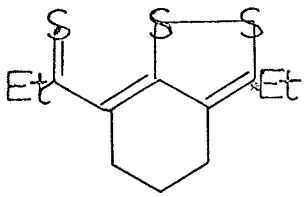
Ever since Bezzi et al. (1) proposed the structure 1 for a compound (2) obtained by the treatment of diacetylacetone with phosphorus pentasulfide in benzene to which he gave the name dimethyl thiathiophthene, many workers have attempted to explain the special properties of this compound. It may be named 5-methyl-3-thioacetylmethylene-1,2-dithiole, but in accordance with its symmetry, is perhaps better named as a 1,6,6aS(1V)-trithiapentalene derivative.



1a 1b 2

In this thesis, for convenience, the name thiathiophthene will be employed. Arndt (2) had erroneously proposed the 1,2-dithiepin structure 2 to the reaction product. However, Bezzi's X-ray structure determination studies have shown that the sulfur atoms are all collinear and equally spaced at a distance of 2.36×10^{-8}cm, which is greater than the normal S-S bond length of 2.04×10^{-8}cm. These results led the above workers to suggest that Arndt's compound is characterized by single bond-no bond resonance, 1a <—> 1b, and that 1a and 1b are contributing structures to a symmetrical resonance hybrid.

Many other thiathiophthenes have since been prepared. By applying Arndt's method, Behringer et al. (3) synthesized the interesting bridged thiathiophthene 3 in 59% yield from 2,6-dipropionylcyclohexanone.



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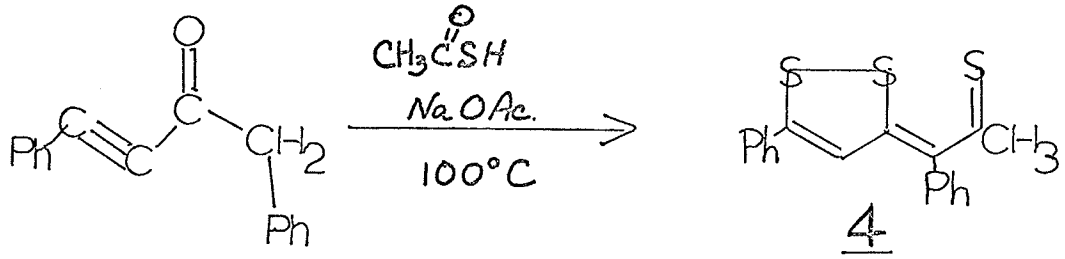
Another thiathiophthene 4 was obtained by the simultaneous introduction of all three sulfur atoms in a reaction outlined below, first introduced by Behringer and his co-workers (4).



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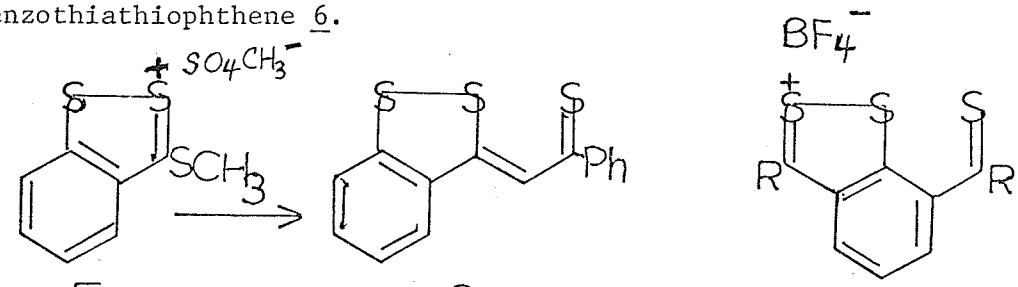
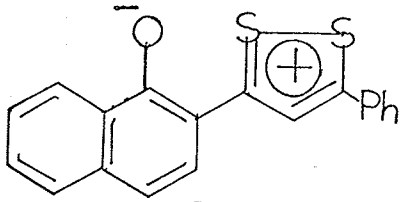
Behringer et al. (3) also discovered that aroylacetonitriles condense with "trithionium salts" such as 5 to give, ultimately, the benzothiathiophthene 6.

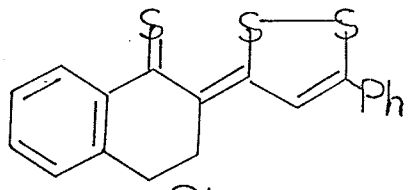


5 6 7

Except for the interesting cationic species 7 recently described by Brown, Leaver, and Rawlings (5), no other thiathiophthenes fused to an aromatic ring seem to have been reported, although closely related systems such as 8a and 8b are known (6,7).



8a



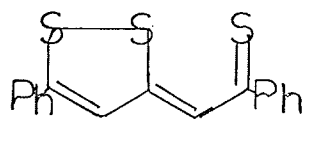
8b

Further evidence of symmetry was provided by Hertz et al. (8) in their nuclear magnetic resonance studies of thiathiophthenes. They found that both methyl protons of 1 were equivalent. Similarly both methine protons were equivalent.

Dingwall et al. (9) have found evidence for ring current, ie. aromaticity, in the strong deshielding of the ring protons. Hence, the thiathiophthene system would appear to possess some aromatic character.

Leaver et al. (10) originally argued that the symmetrical structure for compound 1, as proven by X-ray crystallography and N.M.R. studies, may be caused by rapid tautomerism instead of single bond-no bond resonance. They found that although compounds 10 and 11 cannot exhibit resonance of the type described for 9, their ultraviolet and visible spectra resembled that of 9. Furthermore, wavelengths of visible maxima of compounds 9, 10, and 11 differed from those of the corresponding ketones (12, 13, and 14 respectively) by roughly the same increments (67 mμ, 69 mμ, and 60 mμ respectively).

Nevertheless, their data was later (see below) interpreted in terms of tetravalent sulfur structures.



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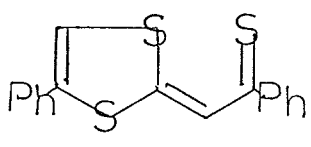

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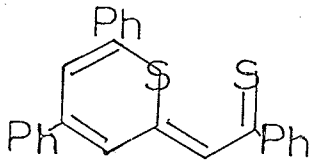

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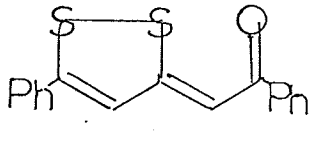

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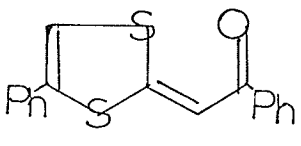

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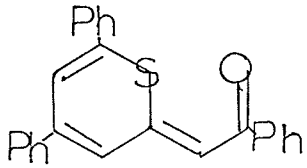
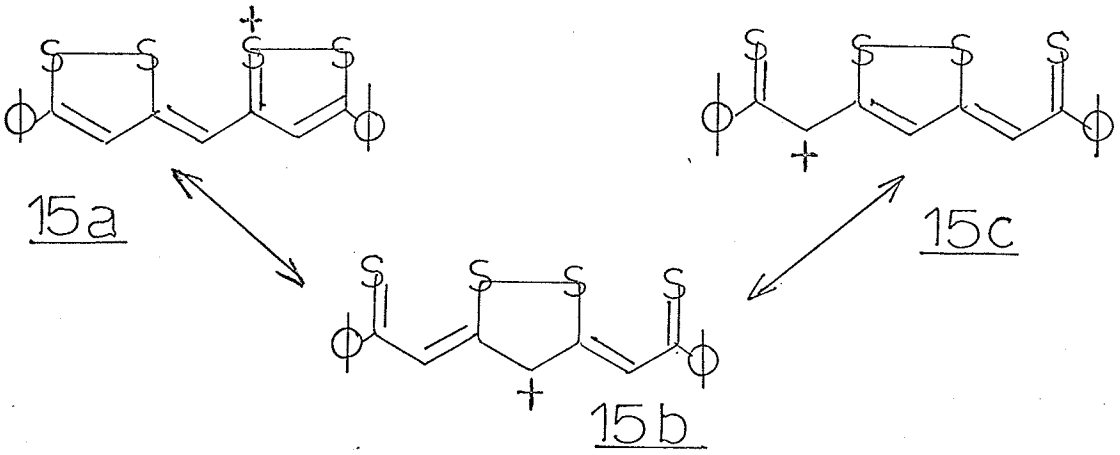


14

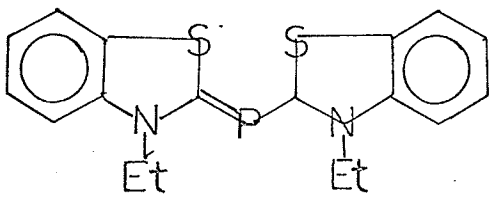
Maeda (11) and more recently, Gleiter and Hoffman (12) using calculations involving simple L.C.A.O. approximations, have invoked the use of sulfur d-orbitals in the bonding of the central sulfur atom giving tetravalent sulfur structures to explain the symmetry of the thiathiophthenes.

In 1966 Klingsberg (13) postulated that the unusually short distance of $3.0\text{-}3.1\times10^{-8}$cm between the two internal sulfur atoms of dithiolocyanine perchlorates 15 indicated that partial bonding between the sulfur atoms is possible. This led him to formulate the compound as a resonance hybrid to which canonical structures of the types 15b and 15c make minor contributions; ie, single bond-no bond resonance as an explanation for this phenomenon.



15a 15c 15b

Klingsberg's hypothesis was disputed by Leaver et al. (14) for two reasons: (a) no evidence had yet been presented to indicate that the disulfide bonds in the dithiole nuclei are unusually long, and (b) the central S-S distance is no shorter than the value of 2.95×10^{-8} cm. found for the phosphacyanine 16 in which no-bond resonance is highly improbable. They suggested that the partial interannular bonding in these cyanines is due to the overlap of sulfur 3d orbitals, ie, the expansion of the valence shell of the two internal sulfur atoms. Hence, in terms of resonance symbolism they described the structure of 15 as 17, which contains a tetravalent sulfur.



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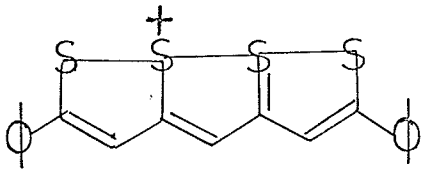
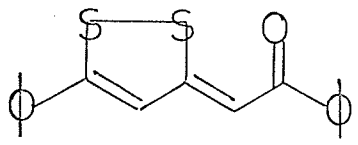
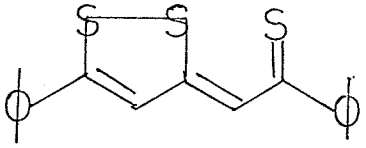


17

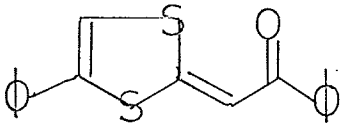
More recently Brown, Leaver, and McKinnon (15) on the basis of their ultraviolet and visible spectra studies of dithiolylidene ketones, 1,6,6aS(1V)trithiapentalenes, and analogous compounds (compounds 9 to 24), rejected the single bond-no bond resonance hypothesis. Since the compounds 9 to 11 and also 18 to 19 are seen to be members of an iso-π-electronic series, their electronic spectra should be similar. In fact these investigators found each of these spectra contains a strong, symmetrically-shaped band with the maximum falling in the 415-475nm range for the ketones and in the 485-545nm for the thiones. The difference in bathochromic shift ($\Delta\nu$) between the ketones and the corresponding thiones were found to be higher (425 and 435mm^{-1}) for 4H-pyrans 18 and 4H-thiopyrans 19 than for 9,10, and 11 (236,245, and 339mm^{-1} respectively). Since the pairs of compounds that show low values of $\Delta\nu$ are those in which a bonding interaction is possible between the exocyclic and endocylic heteroatoms, these investigators suggested that the thiones of 9,10 and 11 are better represented by bicyclic formulae such as 20,21, and 22 than the classical formula ascribed to thiathiopthenes 1.

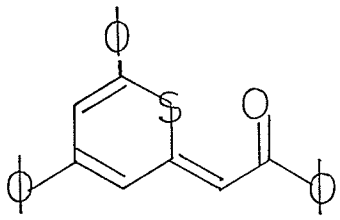


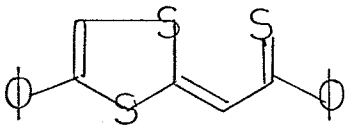


9

ϕ= PHENYL







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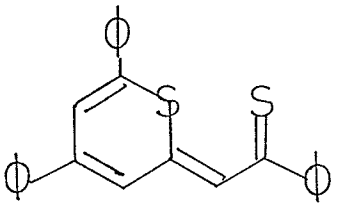

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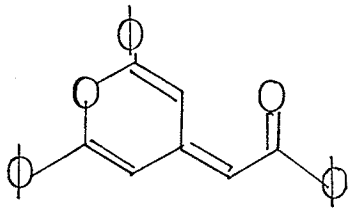

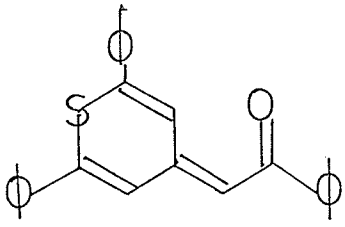

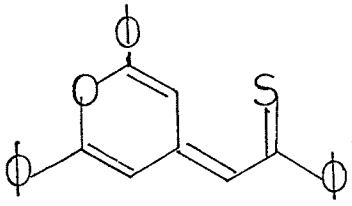

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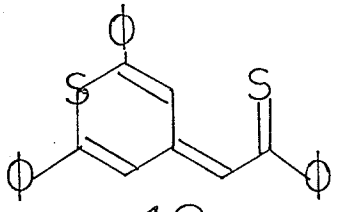

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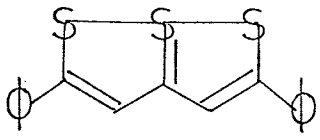

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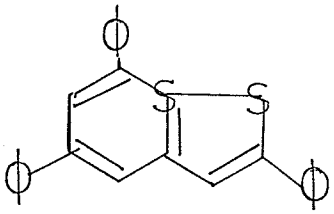

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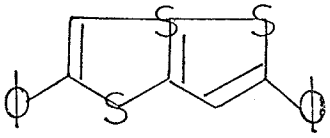
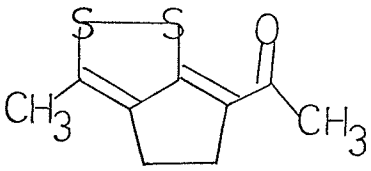
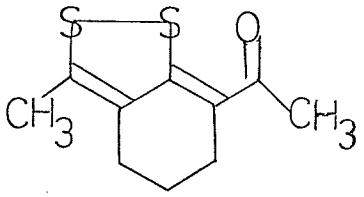
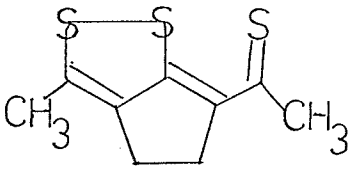


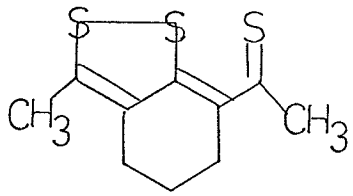
21

Brown, Leaver, and McKinnon reinforced their arguments when they found the $\Delta\nu$ value of 23 higher than 24 as expected. If the low values of $\Delta\nu$ are indeed caused by bonding between sulfur atoms, which, in the classical structures of the thiones, are formally non-bonded, then 23 should show a relatively higher $\Delta\nu$ value due to the larger bond angle between the thione sulfur and the neighbouring ring sulfur of 23. This distortion is caused by the thioacylmethylene-1,2-dithole system peri-fusion with a five-membered ring. On the other hand, the larger ring homologue 24 does not suffer from this type of distortion, and thus would be expected to have a lower $\Delta\nu$ value.







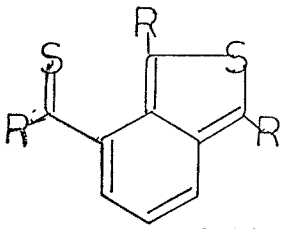


23 24

Thus, the unique characteristics of 3-thioacylmethylene-1,2-dithioles have been attributed: (a) to rapid tautomerism, (b) to utilization of sulfur d-orbitals giving a tetravalent sulfur structure, and (c) to single bond-no bond resonance. Even though no single one of the above hypotheses

gives a thorough account of the special properties of 1, the theories involving d-orbitals appear to provide the most satisfactory explanation of the facts.

However, despite conclusions reached above, it is of interest to determine to what extent the symmetrical properties of the thiathiophthenes could be approached or parallelled by related systems in which the central atom might not be capable of valence shell expansion. Such systems might exhibit single bond-no bond resonance or valence-tautomerism. In searching for related compounds in which the central atom is incapable of valency shell expansion, the synthesis and properties of two model systems: 4-thioacylbenzo[c]thiophenes 25 and 7-acylanthranils 26, have been investigated to determine to what extent their properties approach those of the thiathiophthenes. Replacing the central sulfur atom S-S-S in the thiathiophthene system by a carbon to form S-C-S in the benzo[c]thiophene system, and by O-N-O or S-N-S in the anthranil or thioanthranil system would give molecules which are potentially symmetrical, according to hypotheses (a) or (c) above. Hence, if either or both systems (25, 26, and 27) were found to be symmetrical - i.e., with NMR showing the equivalence of alkyl or aryl substituents "R" and the protons on the aromatic ring with an AB_2 type of pattern, it would indicate that hypotheses of types (a) or (c) are not unimportant in describing the properties of thiathiophthenes.



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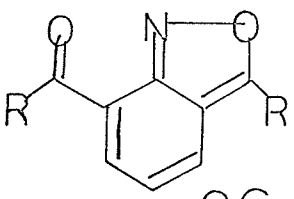

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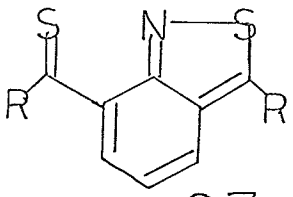
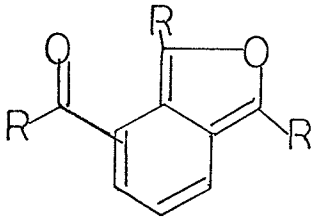


27

It is therefore pertinent to review the chemistry of the benzo[c]thiophene and anthranil systems. Some benzo[c]furan derivatives 28 might also exhibit the properties in question; however, studies on benzo[c]furans (16) have indicated that these are even less stable than benzo[c]thiophenes, and would be less suitable for investigation. The thioanthranil system 27 would also be desirable. However, it was expected from the outset that 27 might be prepared by suitable conversions from 26. As will be evident later, this was partially realized.



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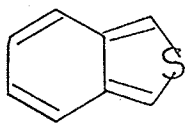

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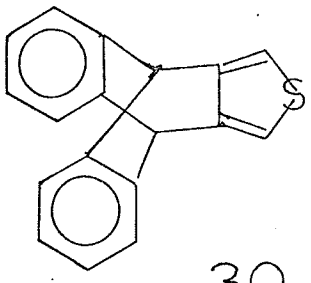


30

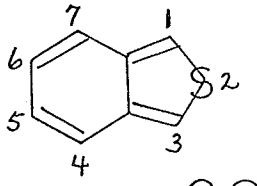
Another system which contains the benzo[c]thiophene 29 element of structure is that of a thiophene analogue of triptycene 30. Such compounds are of interest because it seems appropriate to investigate to what extent does replacing one ortho linked benzene ring of triptycene with a heterocyclic system have on the physical and spectroscopic properties of the molecule. Furthermore, some of our synthetic methods and reagents seemed amenable to the preparation of these, and it was decided to investigate certain syntheses and reactions of this and related systems.

Recent reviews by Klingsberg (13b) and Salmond (12b) have given an extensive background and insight to the thiathiophthenes and possible valence-shell expansion of sulfur heterocycles although these reviews deal with the topics from somewhat different viewpoints. It has also been found that in certain unsymmetrical thiathiophthene derivatives the S-S spacing is not equal; nevertheless, these unsymmetrical thiathiophthenes can be represented by bicyclic formulae which include tetravalent sulfur structures, according to Maeda (11) and Gleiter et al. (12a).

PART B BENZO[c]THIOPHENES

Introduction

Unlike benzo[b]thiophenes 31, very few derivatives of benzo[c]-thiophene 29 have been reported in the published literature.



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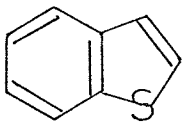
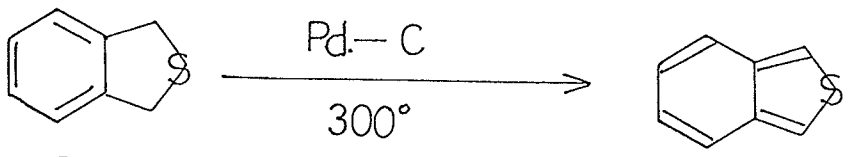


31

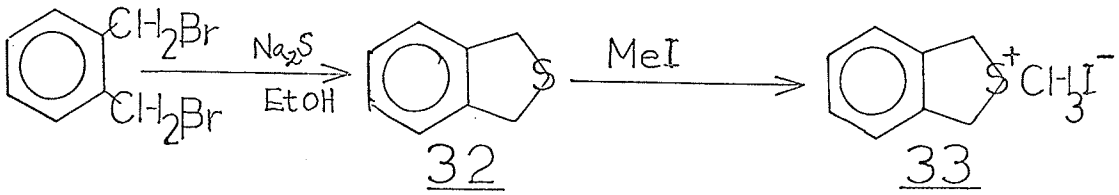
Benzo[c]thiophene (also known as isobenzothiophene or isothianaphthene) is an unstable compound which crystallizes in colourless platelets under nitrogen at -30°C. It was first prepared by Mayer et al. (17) in 65% yield from the catalytic vapour phase dehydrogenation of 1,3-dihydrobenzo[c]thiophene (32) over palladium-charcoal at 330°C in the absence of oxygen.



32 29

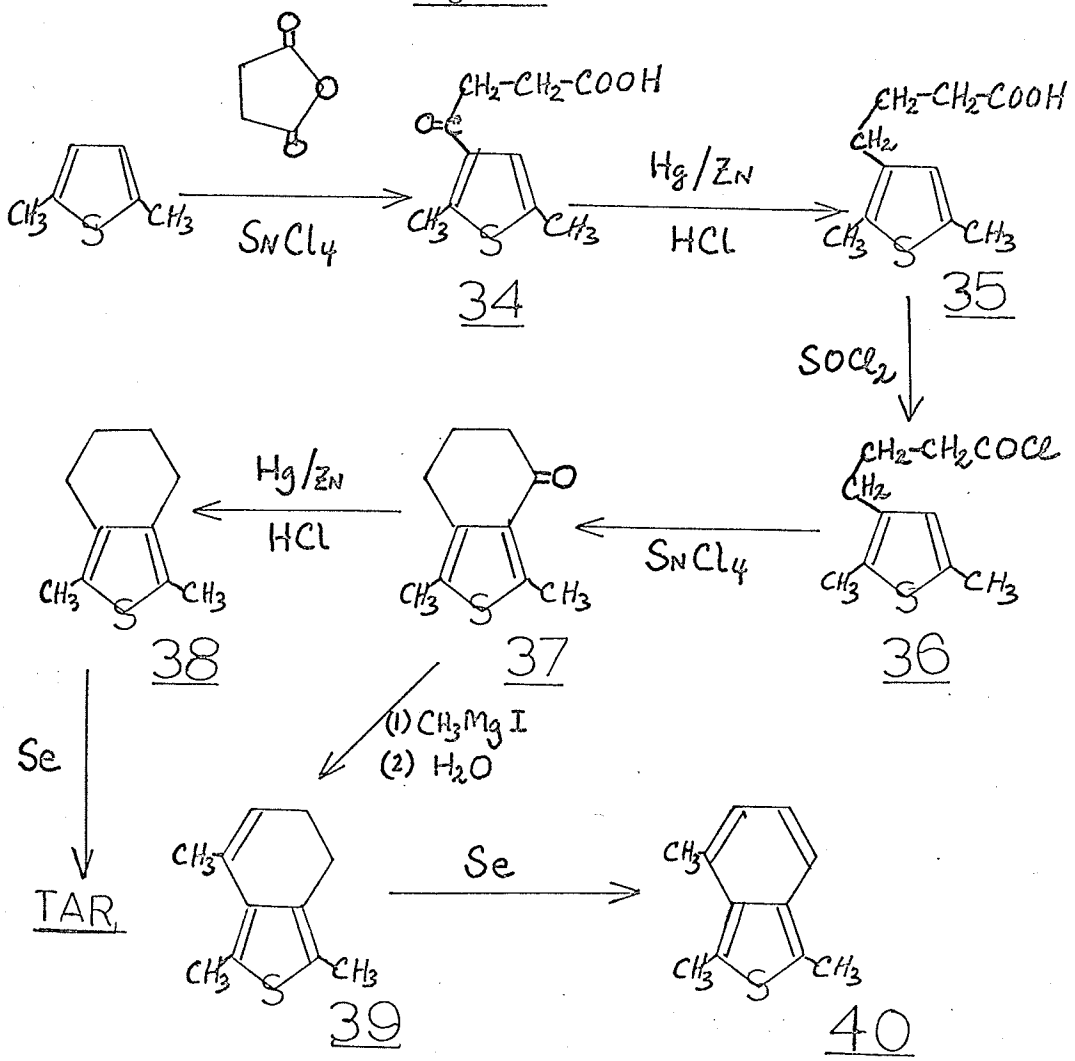
General Preparations

Whereas benzo[c]thiophene itself is unstable, more stable derivatives have been reported much earlier. 1,3-Dihydrobenzo[c]thiophene 32 has been prepared in fair yields from o-xylylene dibromide and potassium or sodium sulfide (18). The compound forms a crystalline methiodide salt 33 on reaction with methyl iodide.



Apart from the 1,3-dihydro derivatives, the fully aromatic ring system of benzo[c]thiophene is stable only if positions 1 and 3 are substituted with electron-donating groups, preferably phenyls. Figure I illustrates the procedures involved in the classical preparation of a homologue of benzo[c]thiophene, the 1,3,4-trimethyl derivative 40.

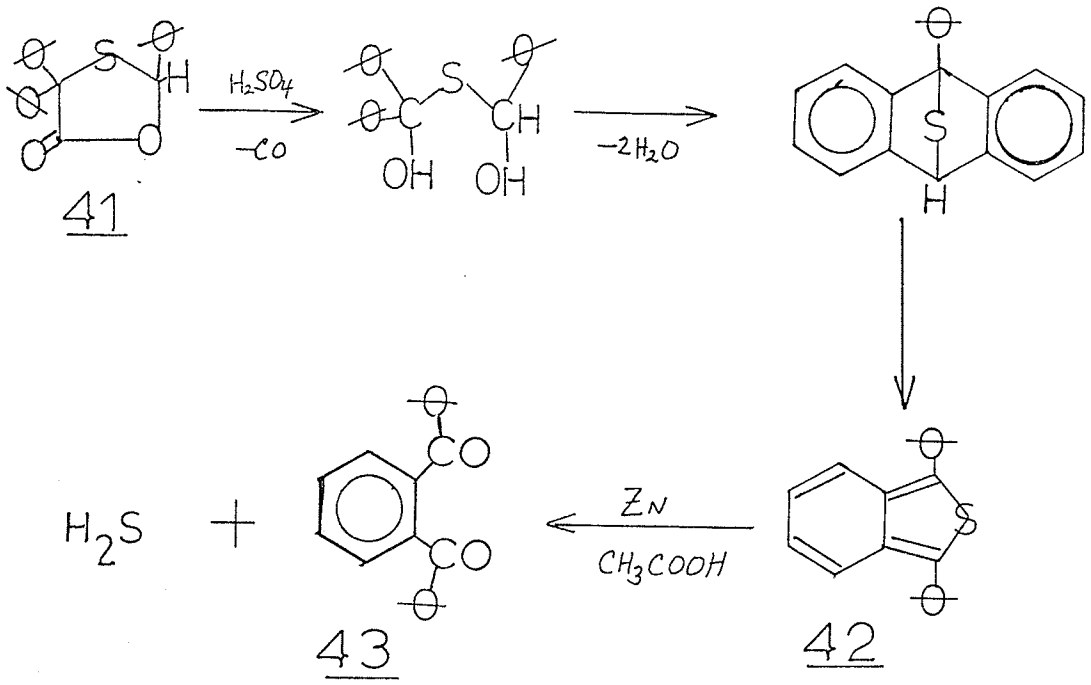
Figure I



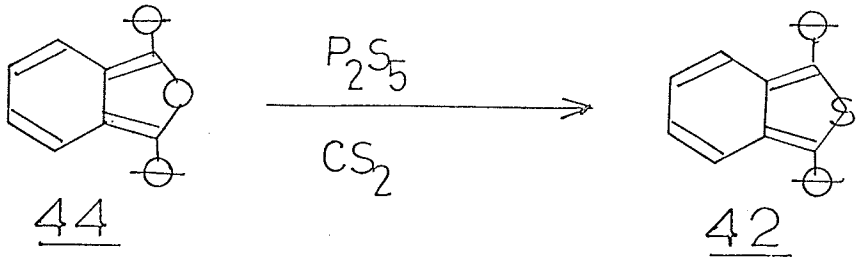
The first step was the Friedel-Crafts reaction involving 2,5-dimethylthiophene and succinic anhydride to give 2,5-dimethylthenoyl-3-(β-propionic acid) (34). This was followed by a Clemmensen reduction of the ketone to give 3-(2,5-dimethylthienyl)-γ-butyric acid (35). After conversion to the acid chloride 36 with thionyl chloride, ring closure was effected by the Fieser and Kennelly ring-closure method (19) yielding 1,3-dimethyl-4-keto-5,6,7-trihydrobenzo[c]thiophene (37) (20). Treatment of 37 with methyl magnesium iodide followed by hydrolysis produced 1,3,4-trimethyl-6,7-dihydrobenzo[c]thiophene (39). The Clemmensen reduction of 37 yielded 1,3-dimethyl-4,5,6,7-tetrahydrobenzo[c]thiophene (38). Both 38 and 39 were dehydrogenated on treatment with selenium at high temperatures. However, Buu-Hôi et al. (21) reported the isolation of only 1,3,4-trimethylbenzo[c]thiophene (40) in small yields. 1,3-Dimethylbenzo[c]thiophene was not detected; probably it is as unstable as the parent compound.

On the other hand, 1,3-diphenylbenzo[c]thiophene (42) is a very stable, bright yellow solid which exhibits green fluorescence in ultraviolet light. Bistrzycki et al. (22) in 1922 first reported the synthesis of 42 by a multiple-step reaction from the lactone of α-hydroxybenzylthiobenzilic acid (41) as outlined in Figure II. The structure of 42 was established by reductive rupture of the thiophene ring with zinc and acetic acid giving o-dibenzoylbenzene (43) and hydrogen sulfide.

Figure II

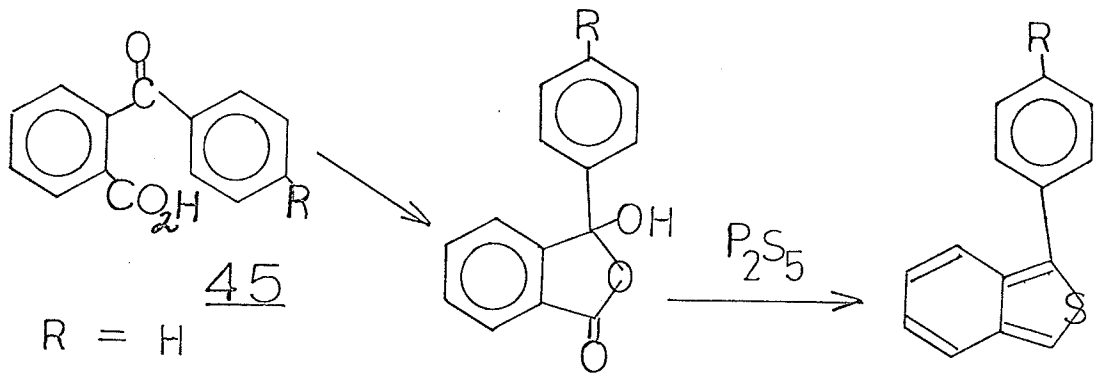


Later investigators (23) verified Bistrzycki's work and gave additional proof of structure by obtaining 42 from 1,3-diphenylbenzo-[c]furan (44) and phosphorus pentasulfide. Zinc amalgam was reported to reduce 42 to o-dibenzoylbenzene (24). Pyrolysis of 42 with zinc at 400° gave the known 9-phenylanthracene. Dufraisse and Daniel also revealed that both o-dibenzoylbenzene and 1,3-diphenylbenzo[c]furan over zinc dust at 400°C yielded 9-phenylanthracenes (23).



44 42

O'Brochta et al. (25) obtained 1-arylbenzo[c]thiophenes 46 by treating the hemiacetals of o-benzoylbenzoic acid 45 and its derivatives with phosphorus pentasulfide.



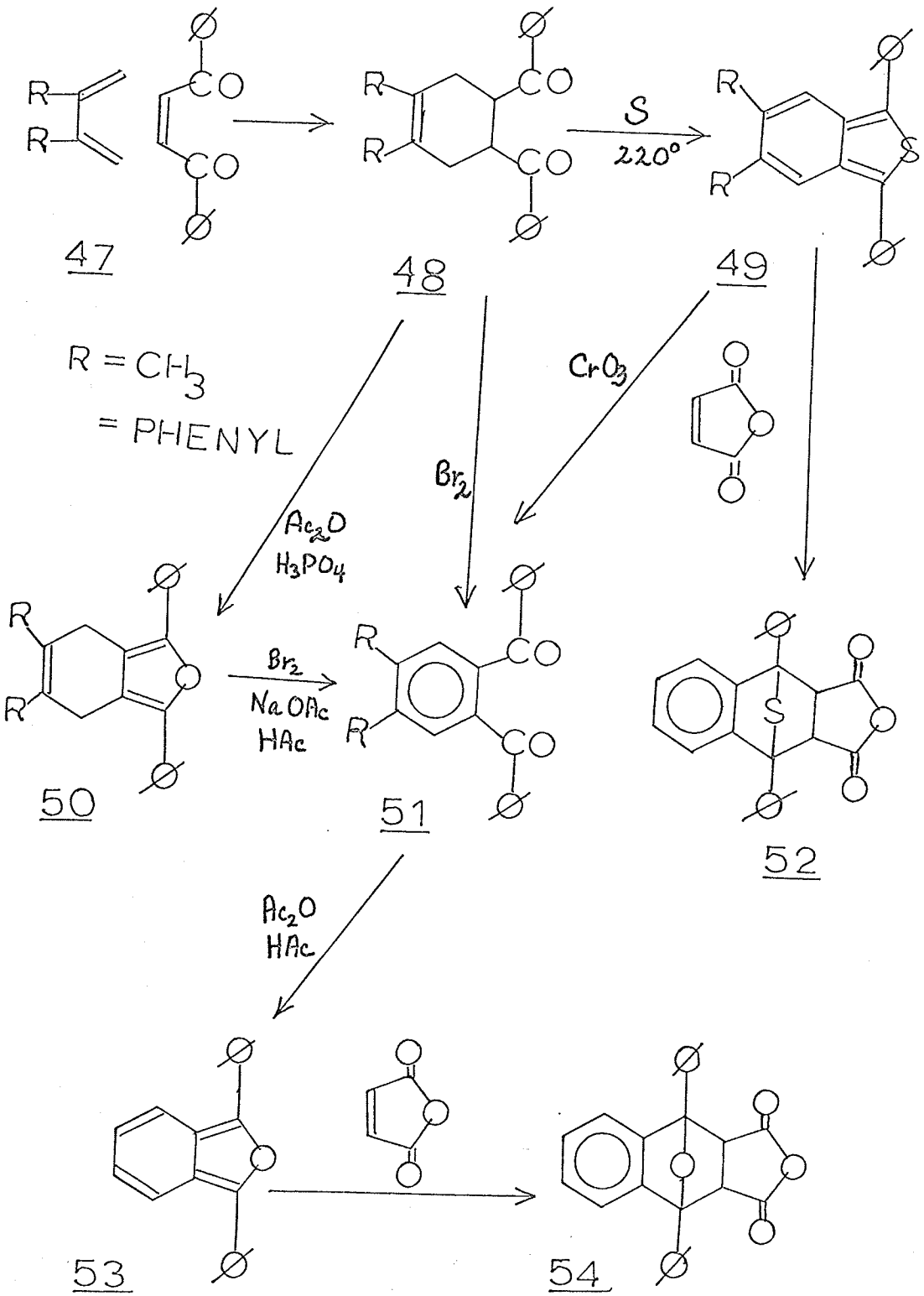
45

R = H
= CH_3
= Cl

46

By far the most efficient method in synthesizing 1,3-diphenylbenzo-[c]thiophenes is the Diels-Alder technique. Figure III illustrates the procedures involved in the preparation of benzo[c]thiophenes and benzo-[c]furans utilizing the Diels-Alder method.

Figure III


R
R
CO
CO
47
48
S
220°
49
R = CH3
= PHENYL
CrO3
Br2
Ac2O
H3PO4
Br2
NaOAc
HAc
50
51
52
Ac2O
HAc
53
54

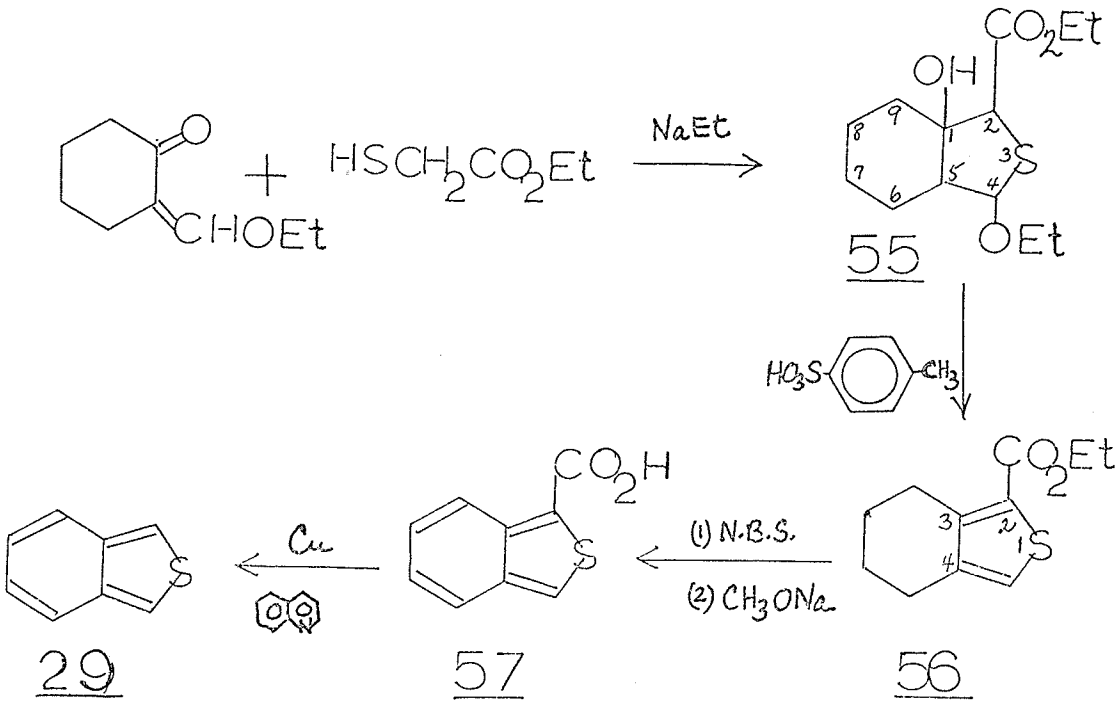
Adams and Gold (26) found that Diels-Alder reactions of 1,3-butadienes with diaroylethylenes 47 gave the corresponding diaroylcyclohexenes 48. The cyclohexenes were easily dehydrated to dihydrobenzo[c]furans 50 upon treatment with acetic anhydride and phosphoric acid. Treatment of 50 with bromine in an acetic acid solution containing sodium acetate yielded the dibenzoylbenzenes 51. The latter were converted into the highly fluorescent benzo[c]furans 53. These workers also noted that the benzo[c]furans were good dienes for Diels-Alder reactions, and that their adducts with maleic anhydride 54 could be aromatised to naphthalene derivatives on heating with HBr.

Further chemical and spectroscopic studies of aryl-substituted benzo[c]thiophenes were reported by Allen and Gates (27), who continued the work started by Adams and Gold. The former reported several new derivatives of 2,3-disubstituted 1,3-butadienes which reacted with dibenzoylethylenes to yield substituted diaroylcyclohexenes 48. These on treatment with sulfur at 220°C produced 5,6-disubstituted benzo[c]thiophenes 49. Addition of nitric or chromic acid in acetic acid to 49 afforded the same diketone 51 as that which was produced by reacting 50 with bromine in acetic acid solution also containing sodium acetate. Similarly to the benzo[c]furans, 1,3,5,6-tetraphenylbenzo[c]thiophene also formed Diels-Alder adducts 52 with maleic anhydride.

The analogy between the furan and thiophene series was further strengthened when Zweig et al. (28) investigated the electrochemiluminescence of aryl-substituted benzo[c]furans and benzo[c]thiophenes.

Both were found to exhibit green-yellow fluorescence on exposure to light. They found that, whereas all benzo[c]furan derivatives formed adducts with maleic anhydride, only 1,3,5,6-tetraphenylbenzo[c]thiophene underwent the same reaction.

Figure 1V



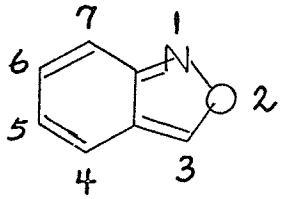
Recently, a novel synthesis of benzo[c]thiophene was reported by Tilak et al. (29) as illustrated in Figure 1V. Condensation of ethylmercaptoacetate with ethoxymethylcyclohexanone in the presence of sodium ethoxide yielded 2-carboethoxy-4-ethoxy-1-hydroxybicyclo-(4,3,0)-3-thianonane (55). Dehydration of 55 with p-toluenesulfonic acid afforded 2-carboethoxytetrahydrobenzo[c]thiophene (56) as a colorless liquid. Interaction of 56 with N-bromosuccinimide followed by treatment with sodium methoxide gave 1-carboxybenzo[c]thiophene (57).

Decarboxylation of the acid 57 by copper-quinoline treatment at 110°C gave benzo[c]thiophene (29) as a pale yellow liquid with naphthalene-like odour. The product decomposed after 15 minutes and rapidly on exposure to oxygen.

PART C ANTHRANILS

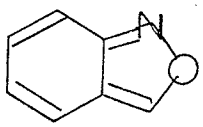
General Introduction

Anthranils are benzo derivatives of isoxazoles. Unlike benzo-[c]thiophene, anthranils are stable compounds at room temperature and have been known for over 50 years. Besides anthranil, other names such as anthroxan-2,1-3,4-; βγ-benzisoxazole; benzo[c]isoxazole; and benzpseudoxazole can be found in the literature in reference to the ring system 58. Anthranil and its 3-methyl derivative are colourless oily liquids with a characteristic odour.



58

In 1882 Friedlander (30) first regarded anthranil as the anhydride of anthranilic acid, and ascribed to it the lactam (59) or the lactim 60 formulae.



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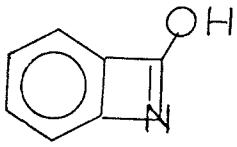

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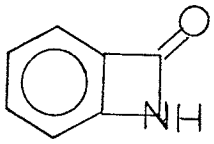

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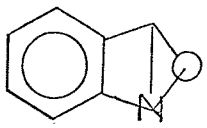

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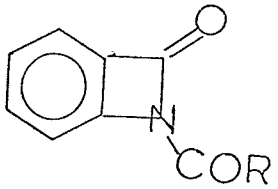
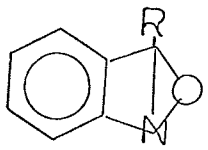


62

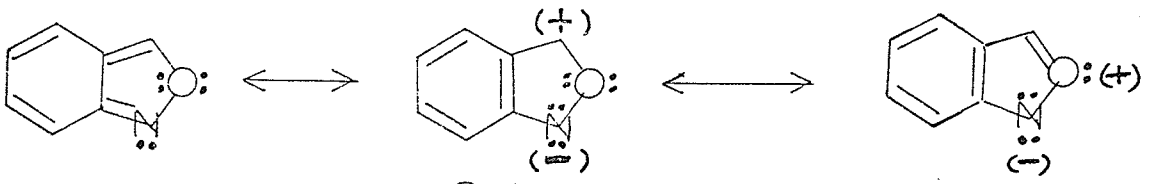


63

The following year Schillinger (31) proposed the tricyclic structure 61.

Heller (32) supported the lactam structure 59 proposed by Friedlander because the existence of acyl derivatives, which were at that time represented by 62, favoured the lactam structure. On the other hand, Bamberger et al. (33) insisted on the tricyclic structure 61 since the methyl and carboxy derivatives of anthranil were formed from starting materials in which the substituents were undoubtedly attached to carbon three 63. Physical methods including molar refraction (34,35), ultraviolet (36) and Raman spectroscopy (37) finally established 58 as the structural formula for anthranil.

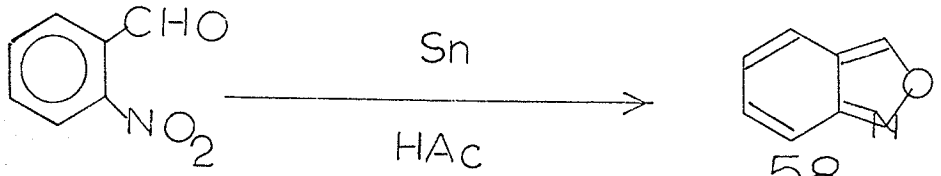
Anthranil may be regarded as a heteroaromatic 10π electron system. Its dipole moment, reported to be 3.06D (38), indicates a very polar molecule which may be attributed to contributions from canonical forms such as 64 and 65 to the ground state of the molecule.



64 65

General Preparations of Anthranils

Various anthranil derivatives can be prepared by reduction of o-nitroketones and o-nitroaldehydes with suitable reducing agents. Friedlander (30) first prepared anthranil in 1882 by reacting o-nitrobenzaldehyde with tin in acetic acid solution.



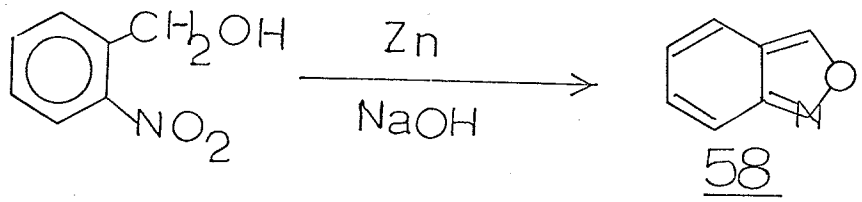
58

Later workers have prepared other derivatives of anthranil by reacting o-nitrocarbonyl compounds with other reducing agents such as:

1) Stannous chloride and hydrochloride acid (39)
2) Zinc and acetic acid (40)
3) Ammonium chloride or soda lime (41)
4) Ferrous sulfate and ammonia (42)
5) Sodium amalgam (41)
6) Sodium alkoxides (43)
7) Sodium dithionite (44)
8) Trialkylphosphites (45)
9) Hydrogen and platinum (46)

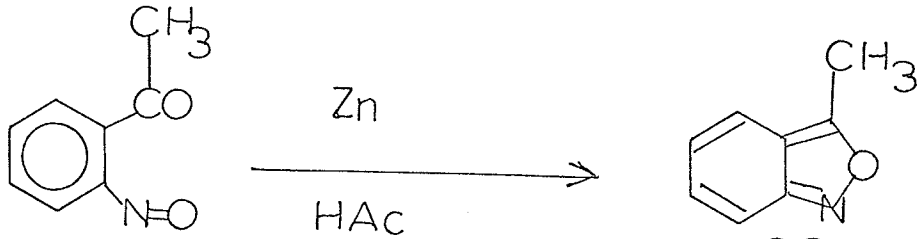
In this reaction the choice of reducing agent is often critical since further reduction leads to o-aminocarbonyl compounds (47).

Freundler (48) obtained anthranil, amongst other products, on reduction of o-nitrobenzyl alcohol with zinc and alkali.



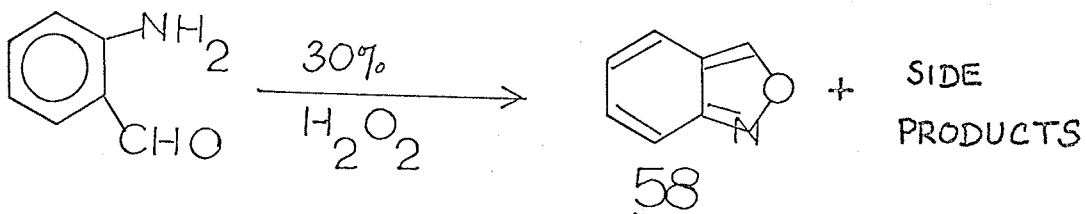
58

Heller (32) isolated 3-methylanthranil (66) on treatment of a o-nitrosoacetophenone with zinc and acetic acid.



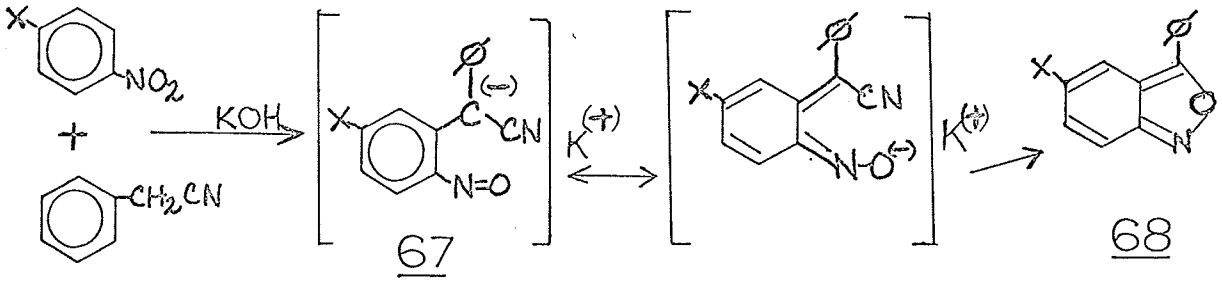
66

Although oxidative methods are less widely used in the preparation of anthranil and derivatives, Bamberger (49) reported the successful synthesis of anthranil in small yields by the oxidation of o-aminobenzaldehyde with 30% hydrogen peroxide. The production of side products was noted.



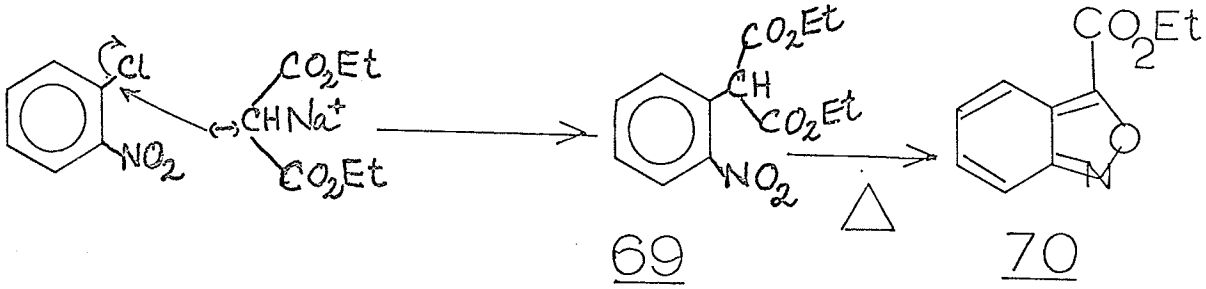
58

In 1960, Davis et al. (50) obtained 3-aryl-5-haloanthranils 68 on treatment of p-halonitrobenzenes with benzylcyanides in the presence of a large excess of methanolic potassium hydroxide.

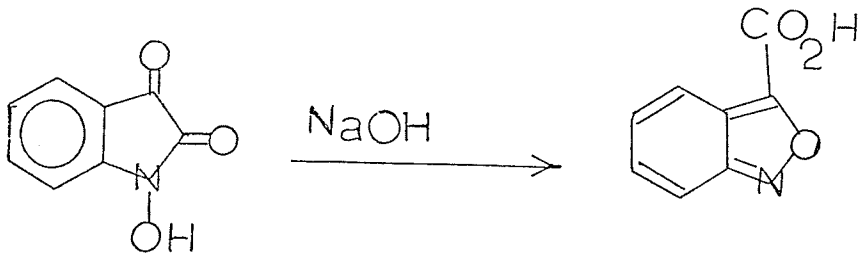


The intermediate 67 was isolated by Walker two years later (51).

Grob et al. (52) reacted o-chloronitrobenzene with diethyl sodiomalonate and obtained the product 69 which decomposed to ethyl anthroxanate (70) on distillation. The general mechanism involves the displacement of the halogen atom of o-chloronitrobenzene by diethyl sodiomalonate.

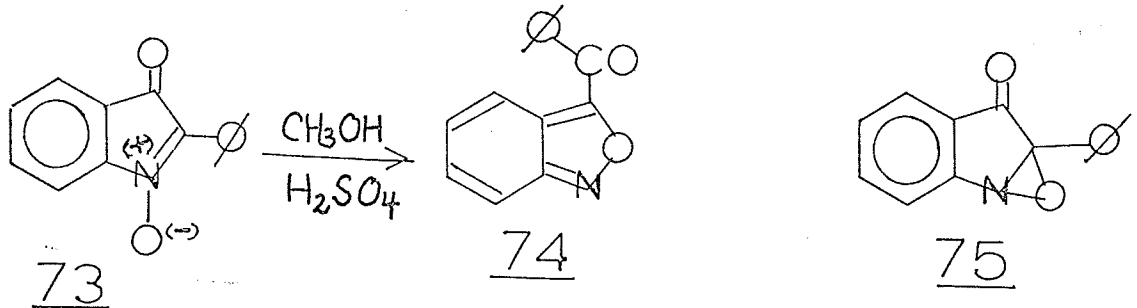


In general, anthranil and derivatives can also be prepared from other heterocycles. For example, N-hydroxyisatin (71) isomerizes to anthroxanic acid (72) in dilute sodium hydroxide solution.



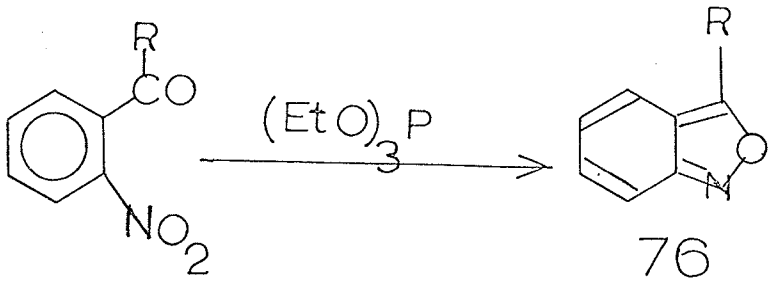
71 72

2-Phenylisatogen (73) rearranges in methanolic sulfuric acid to an isomeric compound, which was called 2-phenylisoisatogen and formulated as an oxazirane 75 by Ruggli et al, (55). Recent work has shown, however, that the product is 3-benzoylanthranil (74), formed by hydrolysis and recyclisation of the isatogen (56,57).



73 74 75

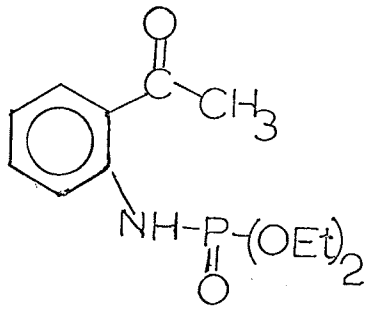
In 1970 Cadogan (58) reported the synthesis of 3-phenyl-anthranils 76 by treating o-nitrobenzophenone with triethylphosphite. On the other hand, when they treated o-nitroacetophenone with triethyl-phosphite under similar conditions, none of the expected 3-methyl-anthranil was isolated; instead, they obtained diethyl-N-(2-acetyl-phenyl)-phosphoramidate (77).



76

R = ∅

= ∅-CH=CH—



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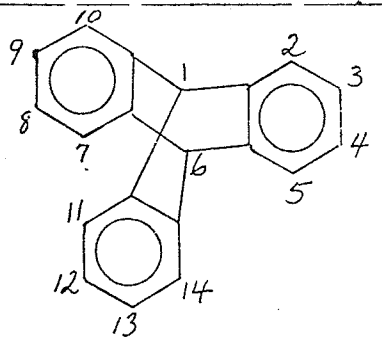
PART D HETEROCYCLIC ANALOGUES OF TRIPTYCENE

Introduction and Classical Preparations of Triptycene

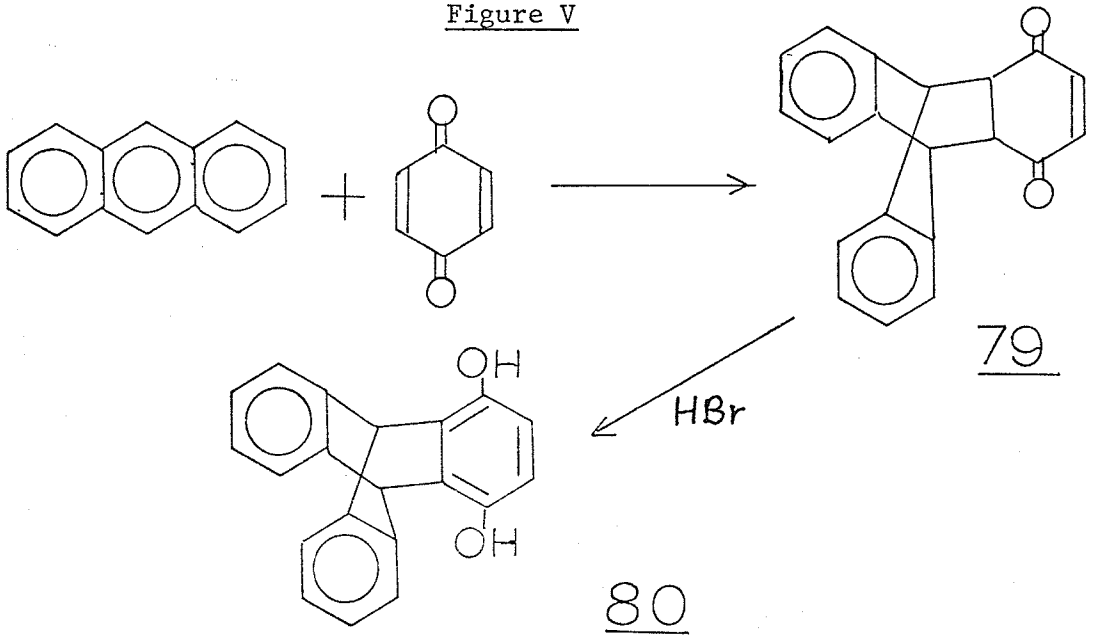


78

During the course of their studies on bicyclic ring systems (59,60), Bartlett et al. (61) reported the synthesis of triptycene (78), also known as 9,10-o-benzenoanthracene or tribenzobicyclo[2,2,2]-octatriene.

Actually triptycene is an analogue of the triphenylmethyl system in which the ortho positions of the three phenyl groups are united to a common CH. Bartlett called the compound triptycene because the shape of this ring system suggested to him the triptych of antiquity, which was a book with three leaves hinged on a common axis. Figure V illustrates Bartlett's classical synthesis of triptycene.

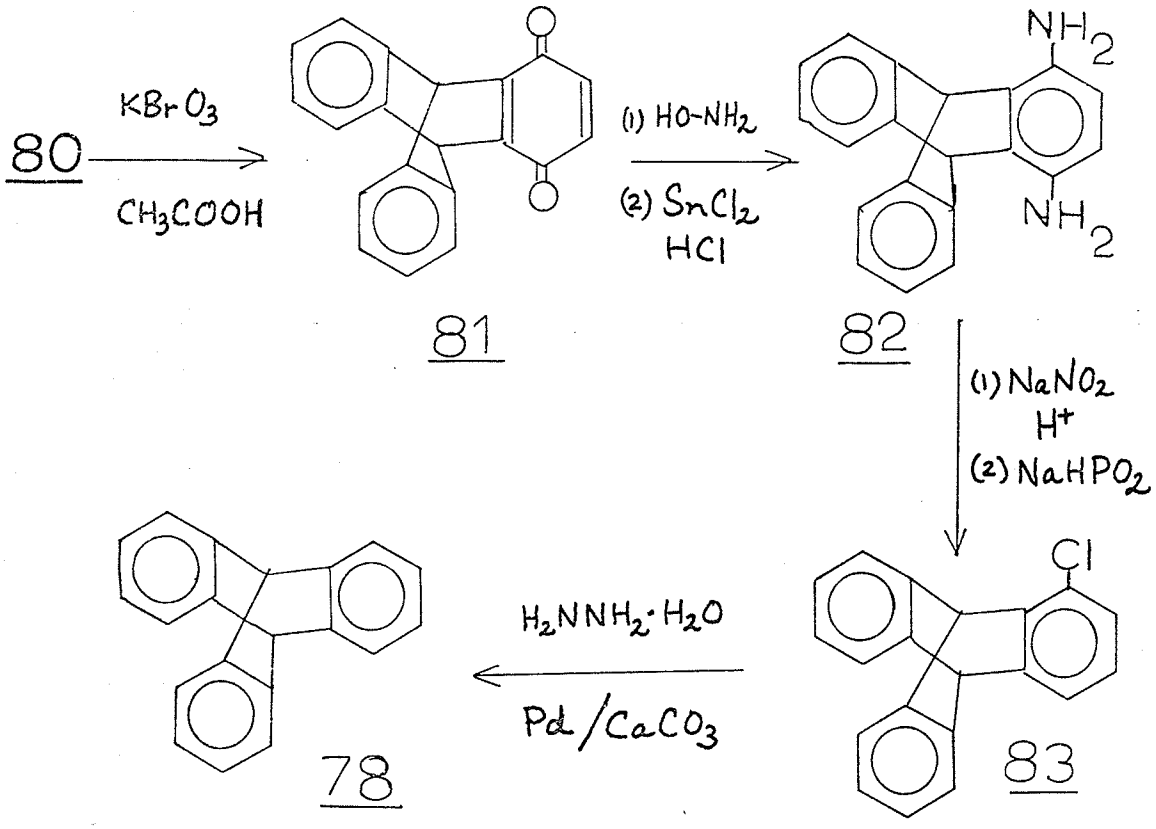
Figure V



79

80

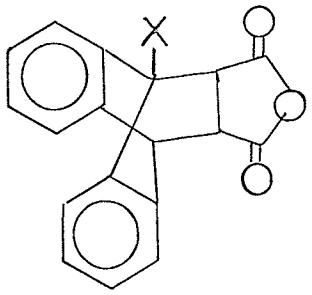
Figure V continued



By slightly modifying Clar's route (62) to the hydroquinone 80, the first step was the formation of the adduct 79 by heating anthracene and quinone in refluxing xylene for two hours. The adduct rearranged to the hydroquinone 80 on treatment with hydrobromic acid. Oxidation of the hydroquinone with potassium bromate in hot glacial acetic acid yielded the quinone 81. The latter was first reacted with hydroxylamine hydrochloride to produce the dioxime, and then reduced to the diamine 82 on treatment with stannous chloride in

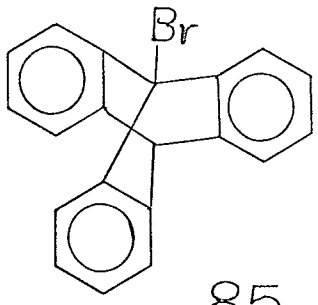
concentrated hydrochloric acid. Diazotization of the diamine in acetic acid-sulfuric acid mixture and sodium nitrite, followed by treatment with $NaHPO_2$ in HCl gave 2-chlorotriptycene (83). The final conversion step to triptycene was first reported by Busch and Stove (63). This consisted of treating the chloro compound 83 with palladium on calcium carbonate and hydrazine hydrate in ethanol-potassium hydroxide solution.

It has been shown by Barnett et al. (64) and by Bachmann (65) that maleic anhydride readily undergoes addition to 9-substituted products of anthracene, yielding dibenzobicyclooctadiene derivatives such as 84 with substituents at the bridge-head position. These are among the few compounds known up to that time which are structurally incapable of replacement reactions with Walden inversion.



84

X = Br
= NH_2
= OH
= NO_2



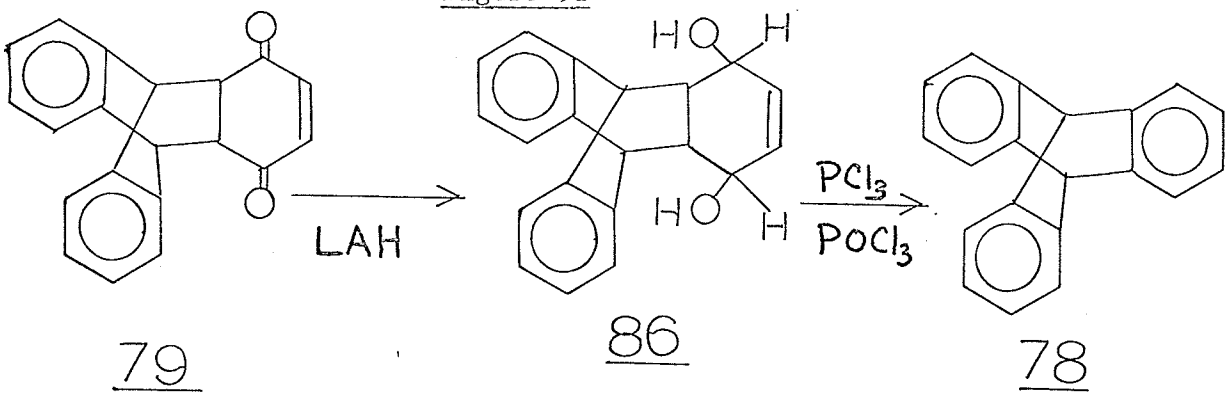
85

In a series of papers (59,60,61), Bartlett et al. have also reported that triptycene, similarly to compound 84, is structurally incapable of replacement reactions with Walden inversion. Although triptycene is an analogue of triphenylmethane, it is entirely lacking in the activity of its aliphatic hydrogen toward potassium exchange,

chlorination, and oxidation which characterizes triphenylmethanes. During the course of their studies on 1-bromotriptycene (85), Bartlett et al. (66) found that 1-bromotriptycene failed to undergo nucleophilic displacement even under the most drastic conditions. They suggested that triptycene is unfavourably constituted for conjugation involving the bridgehead carbon atoms because of the rigid bond angles in the interior of the bicyclo[2,2,2]octane ring system. This total absence of the resonance possibilities in the anion or the deactivating effect [called the Mills-Nixon effect (67)] involving the bridgehead carbon atoms, accounts for the special properties and behaviour of 1-bromotriptycene (85) as compared to triphenylmethanes. This also indicates that benzene rings fused on the bridges of the bicyclo[2,2,2]octane have a strongly deactivating influence upon the C-Br bond at position one. As will be evident in a later discussion, similar properties were discovered with respect to heterocyclic analogues of triptycene.

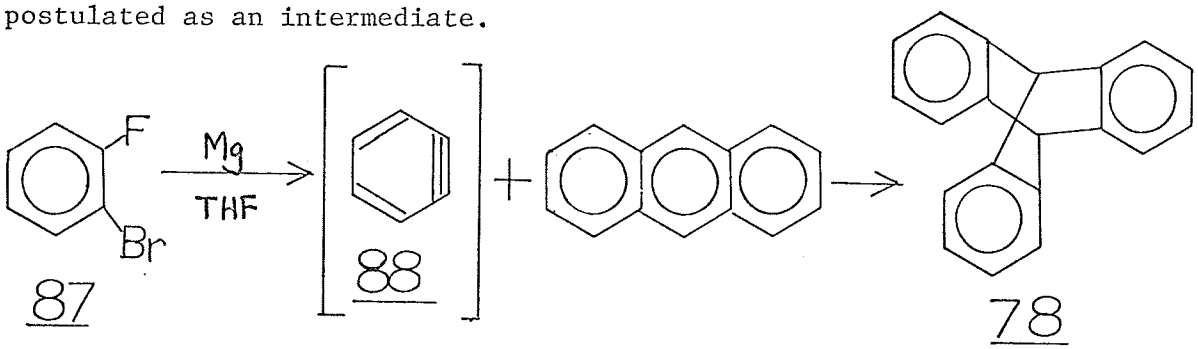
By modifying Bartlett's classical route, Craig and Wilcox (68) reported a shorter and more direct route to triptycene. When the adduct between anthracene and p-benzoquinone 79 was reduced with lithium aluminum hydride or sodium borohydride, a diol 86 was isolated. Treatment of 86 with PCl_3 and $POCl_3$ gave triptycene in fair yield (see Figure V1).

Figure VI



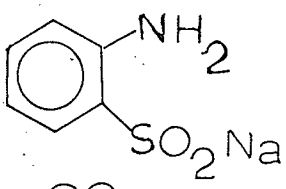
Preparation of Triptycene involving Benzyne

In 1956, Wittig and Ludwig (69) developed a novel route to triptycene from anthracene and dehydrobenzene or benzyne (88). Reaction of anthracene, o-fluorobromobenzene (87), and magnesium in tetrahydrofuran gave triptycene in 28% yield. The benzyne was postulated as an intermediate.

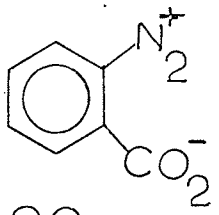


Later workers have prepared a series of triptycene derivatives by reacting benzyne with various anthracene derivatives. Wittig and Hoffmann (70) have prepared benzyne by the diazotization of compound 89 followed by heat induced decomposition of the diazonium salt. Stiles and Miller (71) prepared benzyne by decomposing benzene diazonium-2-carboxylate (90) on heating. In 1968 Stevens (72) used 2-azoxybenzoic acids 91 as benzyne precursors. Brewer et al. (73)

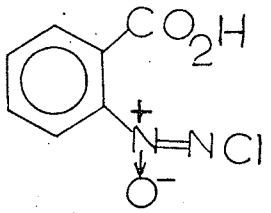
reported the addition reactions of tetrafluorobenzyne (92) with anthracene derivatives giving tetrafluorotriptycenes



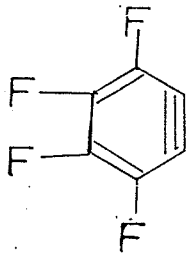
89



90



91



92

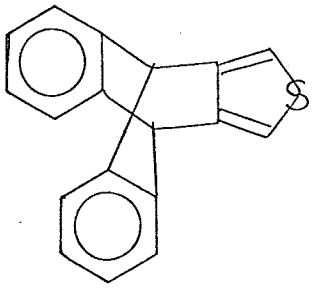
More recently, Schaefer et al. (74) analyzed the proton magnetic resonance spectrum of triptycene. The ring proton spectrum of triptycene was analyzed after the methine proton was decoupled. These workers discovered that the ring proton shifts in triptycene are greatly influenced by a combination of ring current, bond anisotropy and electron density (substituent effect) contributions. They also found that the proton coupling constants indicate a small amount of ring strain in the bonds near the methine carbons.

Heterocyclic analogues of triptycene

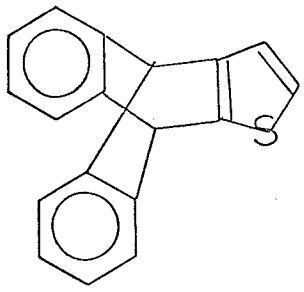
Although triptycene was synthesized by Bartlett et al. in 1942, only within the last fifteen years has research provided information

about other derivatives of triptycene. Likewise, little is known about the preparation and properties of heterocyclic analogues of triptycene. According to Longuet-Higgins' theory of isosterism (75), a -CH=CH- group of an aromatic system is electronically similar to the formally bivalent (-S-). Hence, when a heteroatom such as S,NH, or O replaces a -CH=CH-group in an aromatic ring, the new molecule formed should have similar properties to the original molecule. Thus, in theory at least, if one sulfur atom replaces a -CH=CH- group in one of the ortho linked benzene rings of triptycene, the new molecule is either 30a or 30b. This new molecule should have similar properties to triptycene. Two sulfur atoms replacing two -CH=CH- groups in two different aromatic rings of triptycene would produce either 93a,93b,93c', or 93c^2. Since compounds 93c' and 93c^2 are non-superposable and are mirror images of one another, they are enantiomers. Similarly, if all three benzene rings of triptycene contain a sulfur as a heteroatom, the new molecule formed is one of four possibilities: 94a,94b,94c, or 94d.

Group A

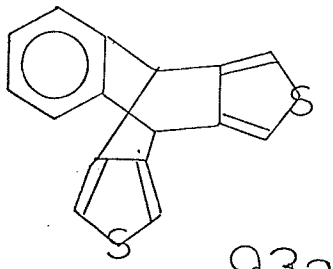


30a

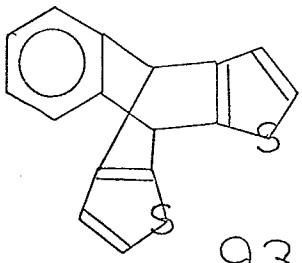


30b

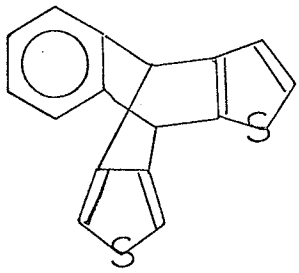
Group B



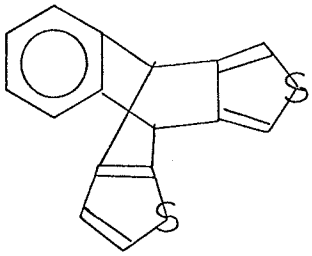
93a



93b

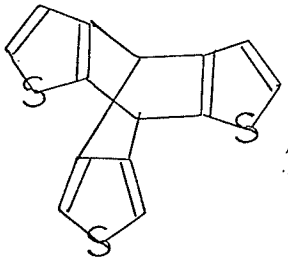


$93c^1$

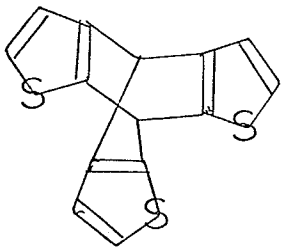


$93c^2$

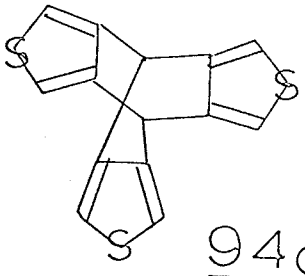
Group C



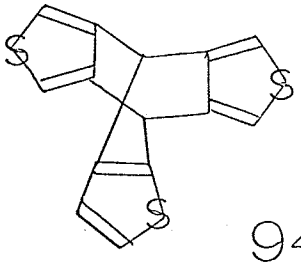
94a



94b



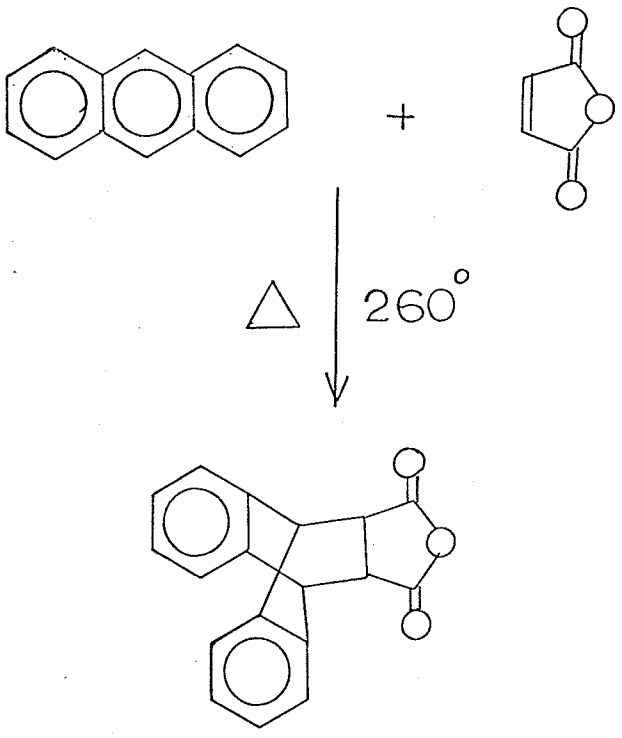
94c



94d

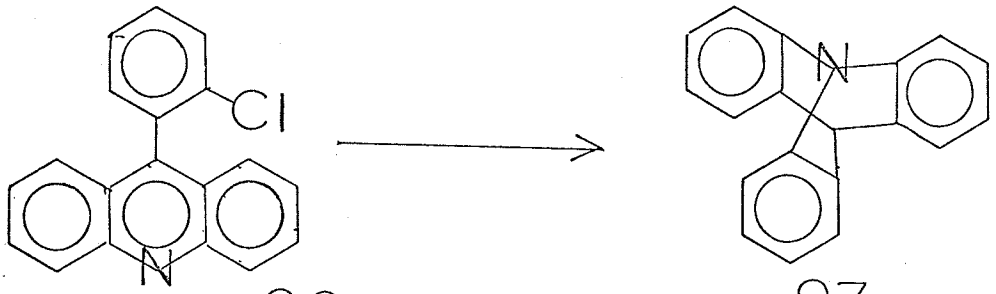
None of the foregoing heterocyclic analogues of triptycene has yet been reported in the published literature. The object of the present study was to investigate the synthesis and properties of some heterocyclic analogues of triptycene, with special emphasis on Group A and Group B derivatives, and sulfur as the heteroatom.

The first attempt to synthesize a heterocyclic analogue of triptycene was by Diels and Alder (76), who prepared anthracene-9,10-endo-2,β-succinic anhydride (95) by fusing a mixture of anthracene and maleic anhydride just below 260°C.



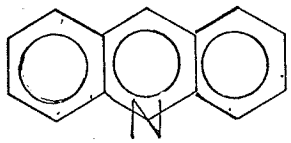
95

Bachmann and Kloetzel (77) reported the preparation of a series of adducts involving anthracene derivatives and maleic anhydride. They made a systematic study to determine the conditions for securing the maximum yields of the adducts, and found that methyl groups in the 9,10-positions of anthracene greatly increased the reactivity of these positions with respect to addition of maleic anhydride, while a 1,2-benzo group or 9,10-phenyl groups decreased the activity of the molecule.



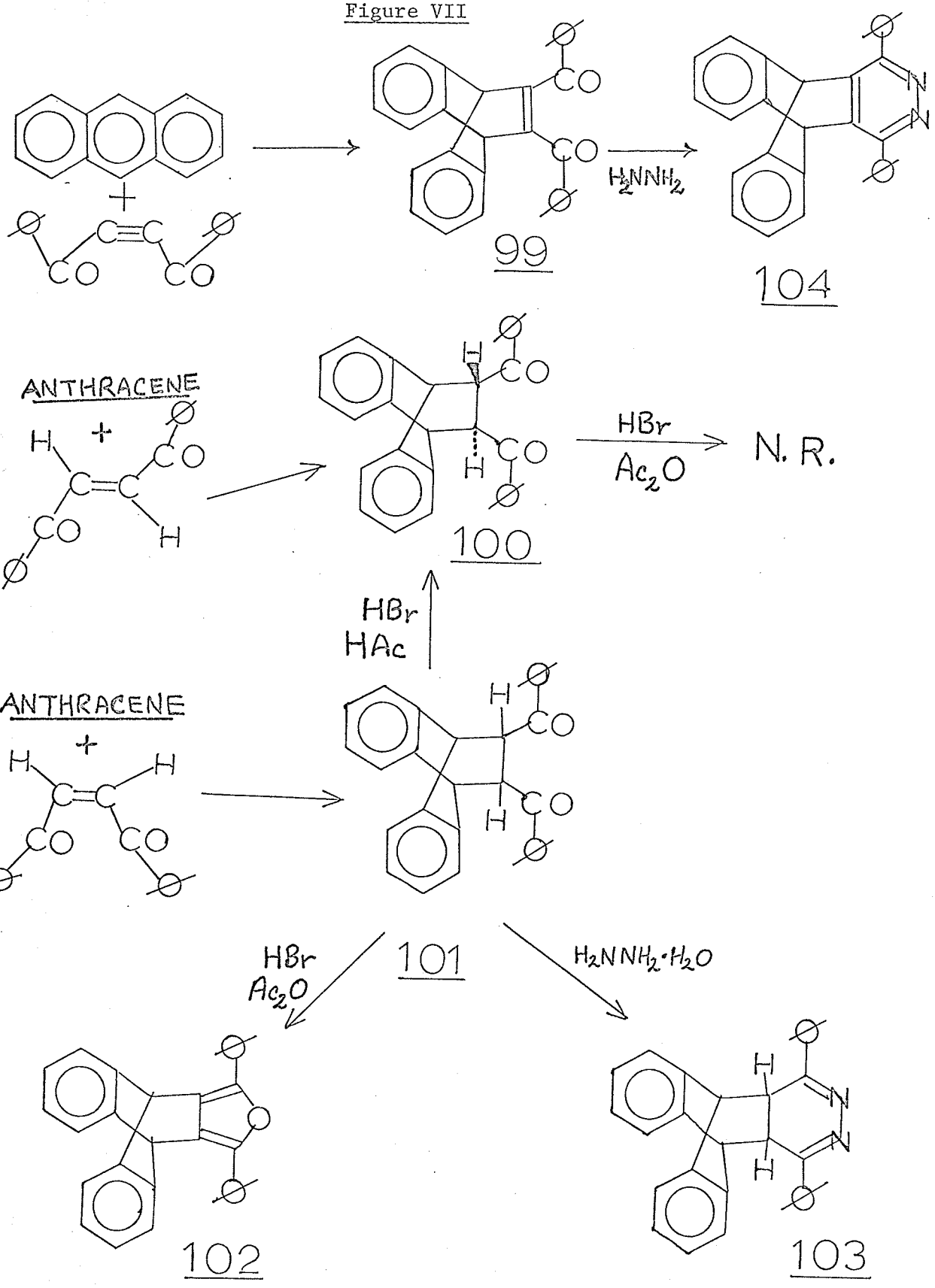
96 97

Azatriptycene (97) was prepared by Wittig and Steinhoff (78) on treatment of 9-(o-chlorophenyl)-9,10-dihydroacridine (96) with KNH_2 in liquid ammonia. They also discovered that Diels-Alder addition of benzyne (88) with acridine (98) failed to yield azatriptycene (97).



98

Figure VII


99
104
ANTHRACENE
100
HBr
Ac2O
N. R.
HBr
HAc
ANTHRACENE
101
HBr
Ac2O
H2NNH2·H2O
102
103

In 1954 Baumgartner et al. (79) fused dibenzoylacetylene or cis or trans-dibenzoylethylene to anthracene at 200°C to give dibenzoyl-dibenzobicyclooctatriene [2,2,2] (99) and cis and trans-dibenzoyl-dibenzobicyclooctadiene [2,2,2] (101) and (100) respectively. On treatment with alcoholic potassium hydroxide or hydrobromic acid with acetic acid, they succeeded in converting the cis adduct 101 to the trans adduct 100. When the cis adduct 101 was refluxed with HBr in acetic anhydride, the dibenzoyl groups cyclised to yield the furan derivative 102. Similar treatment on the trans adduct 100 failed to produce the furan derivative, but gave only anthracene and trans-dibenzoylethylene. Treatment of the cis adduct 101 with hydrazine hydrate in ethanol gave the 2,3-dihydropyridazino derivative 103. The pyridazino derivative of triptycene 104 was obtained by reacting the acetylene adduct 99 with hydrazine hydrate. Apart from these three derivatives, these workers did not attempt to synthesize other heterocyclic analogues by ring closure of the benzoyl groups of the adducts.

Object of Research

As has been stated in the Introduction section, the symmetry of thiathiophthenes 1 has been attributed to:

(a) rapid tautomerism

(b) single bond-no bond resonance

(c) d-orbital participation of the central sulfur atom

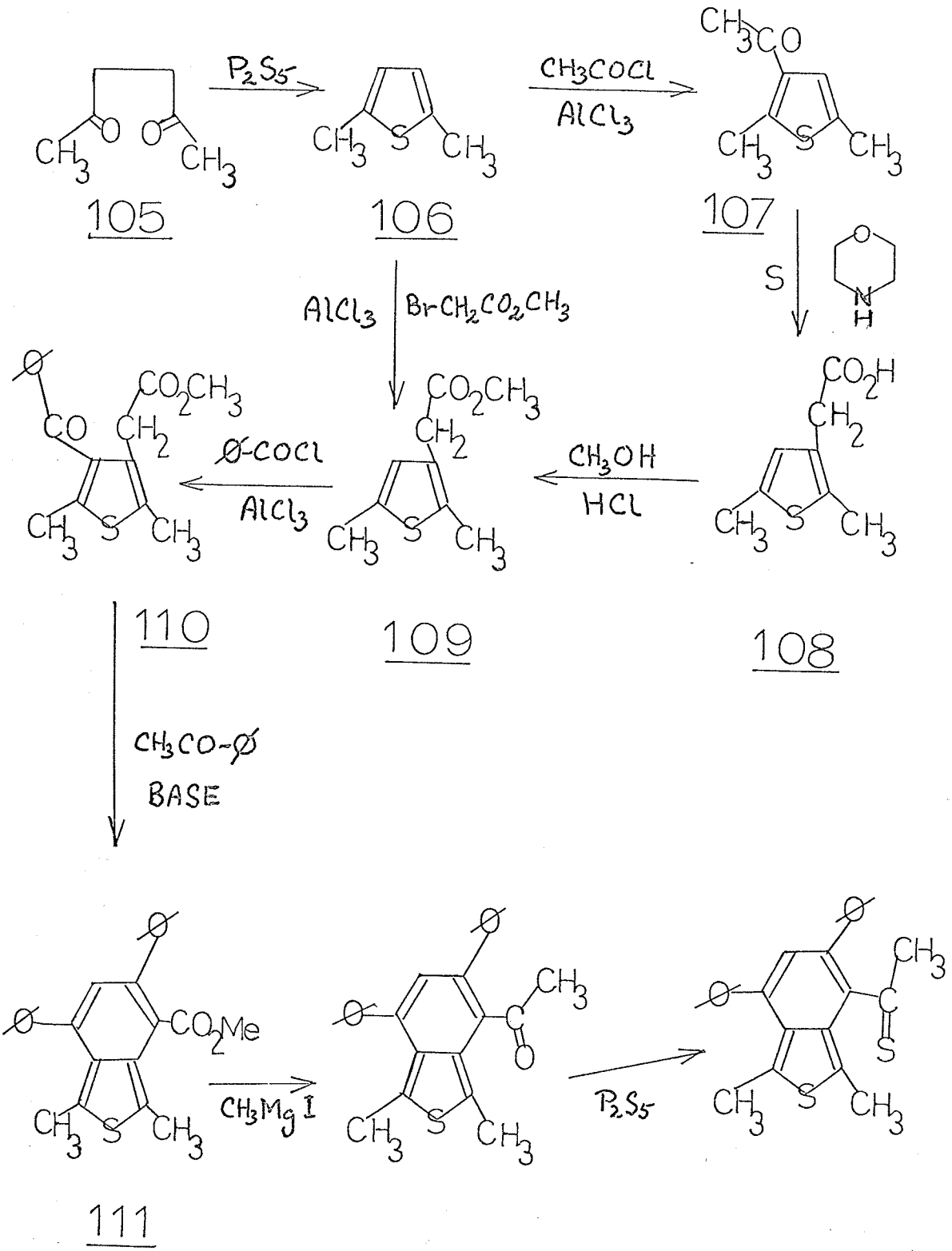
Most evidence seems to indicate hypothesis (c) as providing the most satisfactory explanation of the facts. However, the main object of the present research was to investigate the preparation and properties of related compounds, in which the central atom is incapable of valency shell expansion, to determine to what extent the first two of the above three hypotheses might play a role in thiathiophthenes. Two model systems were selected: the benzo[c]thiophene system and the anthranil system, in which the central sulfur atoms have been replaced by carbon and nitrogen respectively. These two model systems have potential symmetry if either of conditions (a) or (b) holds; and have suitable structures for N.M.R. examination. It was also of interest to extend previous methods of synthesis of benzo[c]thiophenes and anthranils and develop new ones.

The second objective of the investigation was to examine the synthesis and properties of heterocyclic analogues of triptycene. As an extension of the investigation on benzo[c]thiophenes, the major emphasis was on the thiophene derivatives since these contain the benzo[c]thiophene element of structure. It was expected at the outset that these triptycene analogues might have properties similar to

triptycene itself, such as its stability to heat and its inertness to oxidation and SN^1 and SN^2 displacements, of substituents at the bridgehead carbon. These triptycene analogues might also be potential "thiophyne" or dehydrothiophene precursors. Attempts could be made to detect these "thiophyne" intermediates either by mass spectroscopy during the fragmentation process of the molecule or by chemical methods.

DISCUSSION

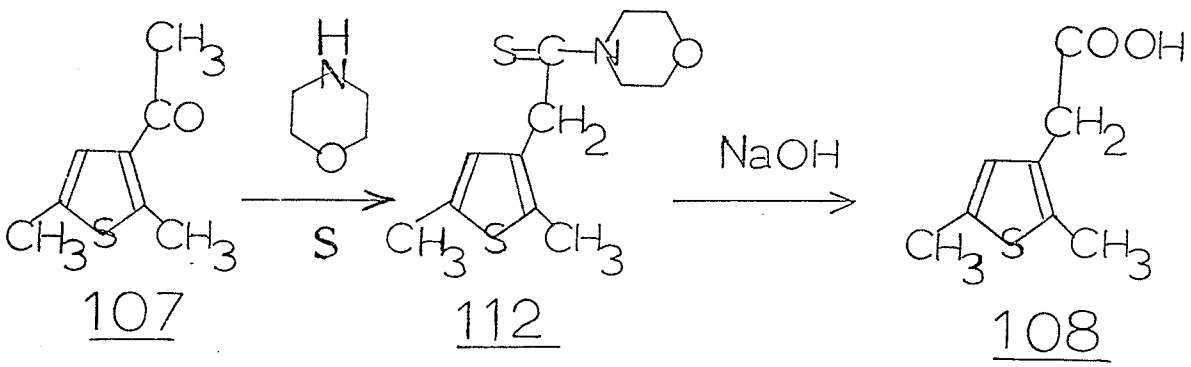
Scheme I


P2S5
CH3COCl
AlCl3
105
106
107
S
AlCl3
BrCH2CO2CH3
CH3OH
HCl
Ø-COCl
AlCl3
110
109
108
CH3CO-Ø
BASE
CH3MgI
P2S5
111

PART A

Discussion on Attempted Synthesis of 4-Thioacetyl or 4-Thiobenzoyl-Benzo[c]thiophenes

Initially, the preparation of 4-thioacetyl-1,3-dimethylbenzo[c]-thiophene was attempted according to Scheme I. The first step involved the acetylation of 2,5-dimethylthiophene (106), which was obtained by heating acetonylacetone (105) with excess phosphorus pentasulfide, to yield 2,5-dimethyl-3-acetylthiophene (107). The acetylation of 2,5-dimethylthiophene was essentially the same procedure which Messina et al. (80) introduced in 1952 in the Friedel-Crafts alkylation of 2,5-dimethylthiophenes. Compound 107 was converted to 2,5-dimethyl-3-thienylacetic acid (108) via the Willgerodt-Kindler method. This consisted of refluxing the ketone 107 with sulfur in morpholine for six hours yielding the amide 112 as an intermediate. Hydrolysis of the amide with sodium hydroxide gave the acid 108. The Willgerodt-Kindler procedure adopted in the present work was under considerably milder conditions than that reported by Blanchette et al. (81) who synthesized 2,5-dimethyl-3-thienylacetamide using sulfur, ammonium hydroxide, and dioxane in a sealed tube under high temperatures. Unfortunately, the yield of the acid 108 was less than 7% and this product could not be successfully purified by crystallization or column chromatography over aluminum oxide. However, the crude acid 108 was successfully converted to the ester 109 in quantitative yield by treatment with anhydrous methanol and gaseous hydrogen chloride.



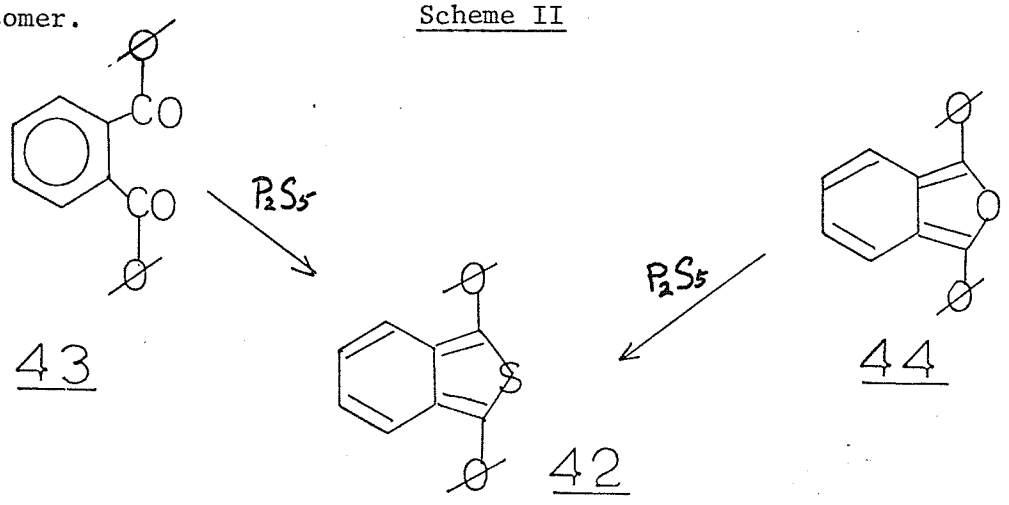
107 112 108

Since both the yield and purity of the acid 108 via the Willgerodt-Kindler reaction were disappointing, attempts were made to convert 2,5-dimethylthiophene (106) directly to the ester 109 by Friedel-Crafts alkylation of the thiophene 106 using methyl bromoacetate and aluminum chloride. This failed. Other attempts using anhydrous stannic chloride, zinc chloride, and boron trifluoride as catalysts, and using anhydrous ether, benzene, nitrobenzene, nitromethane, and carbon disulfide as solvents also failed.

With the small amount of the crude ester 109 from the Willgerodt-Kindler reaction, benzoylation of the ester 109 gave the keto-ester 110. This benzoylation-product was obtained as a dark viscous oil, but its IR spectrum did show absorptions for a benzoyl group and an ester group. When compound 110 is treated with acetophenone in the presence of base, two base-catalysed condensations could occur, producing the cyclised benzo[c]thiophene ester 111. However, the final product isolated was a black viscous oil of which IR spectrum showed no sharp peaks. Thus, after several attempts this scheme had to be abandoned. The failure of Scheme I may be due to the inefficient Willgerodt-Kindler route to the acid 108, and due to the failure to convert the thiophene 106 directly to the ester 109 via the Friedel-Crafts method.

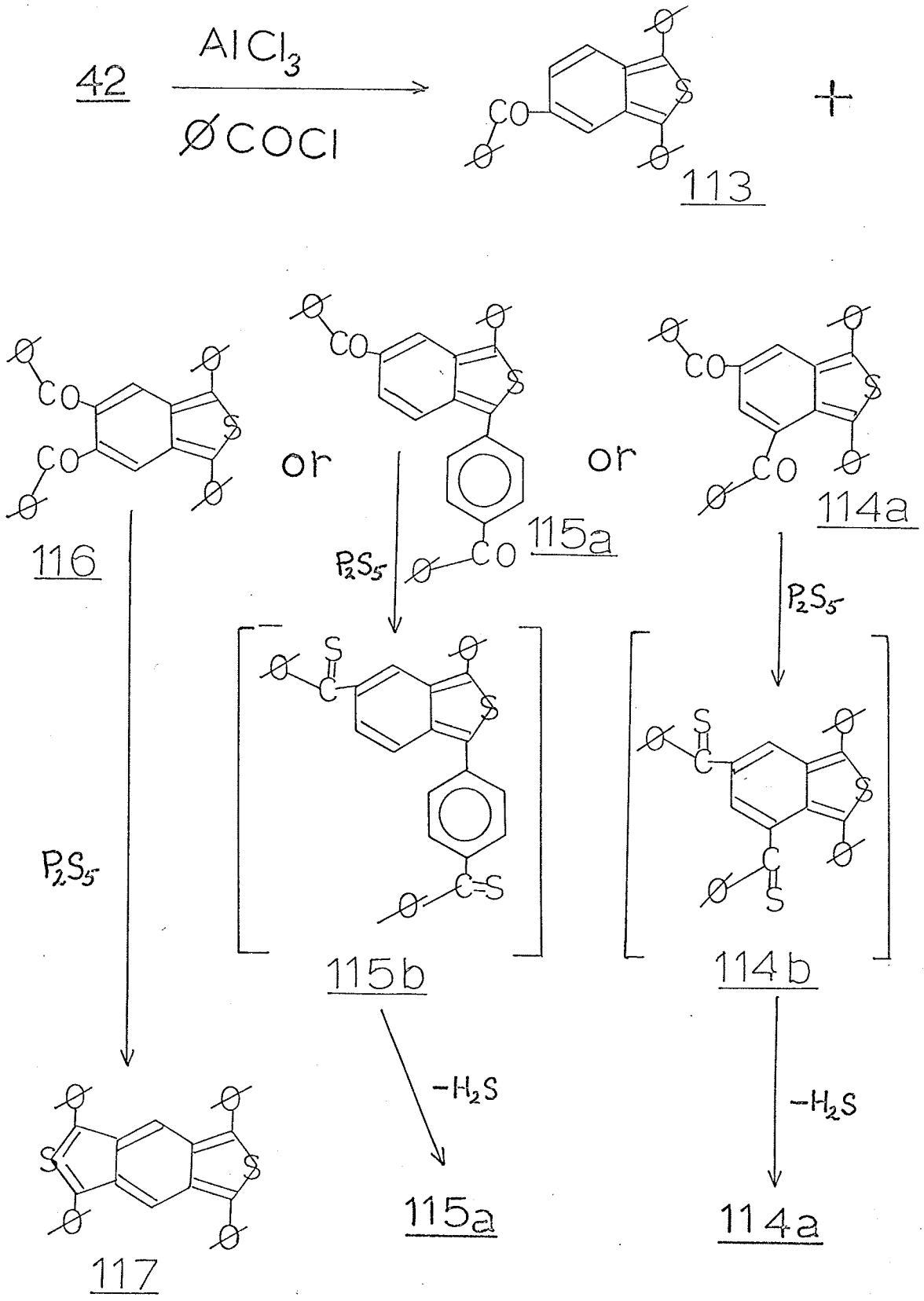
A second series of reactions starting with o-dibenzoylbenzene (43) and 1,3-diphenylbenzo[c]furan (44) were attempted as shown in Scheme II. Treatment of either o-dibenzoylbenzene or 1,3-diphenylbenzo[c]furan with phosphorus pentasulfide in refluxing pyridine gave in excellent yield 1,3-diphenylbenzo[c]thiophene (42) as a yellow solid with a green fluorescence. Friedel-Crafts benzoylation of 42 produced an orange solid, which on separation by thin-layer chromatography showed three fractions. The first band from the top of the plate was the major product, and NMR and IR spectra indicated that it was unchanged starting material. The second band (11% yield) whose elemental analysis and IR spectrum suggested a monobenzoyl product, was first thought to be the 4-benzoylbenzo[c]thiophene. However, electron density calculations by Zahradnik et al. (82) have shown positions 4 and 7 of the benzo[c]thiophene nucleus to be relatively inert to electrophilic substitutions. Hence, the monosubstituted product of the diphenylbenzo[c]thiophene 42 was probably compound 113, substituted at position 5 as shown below. Elemental analysis indicated that the third minor band from the plate was probably a dibenzoyl compound with structural formula similar to 114a, 115a, 116, or some other isomer.

Scheme II

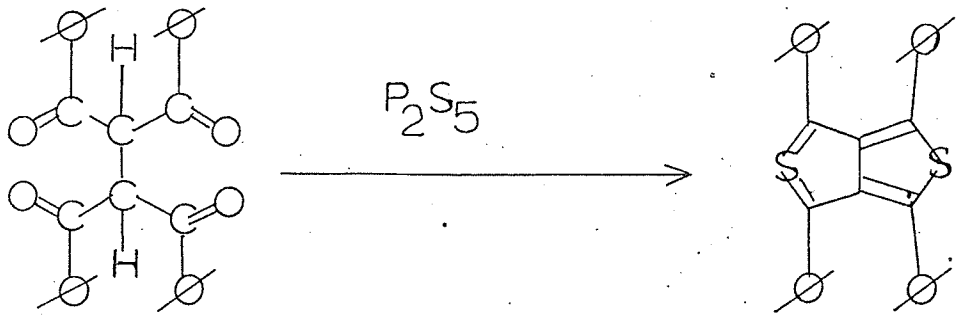


43 42 44

Scheme II continued



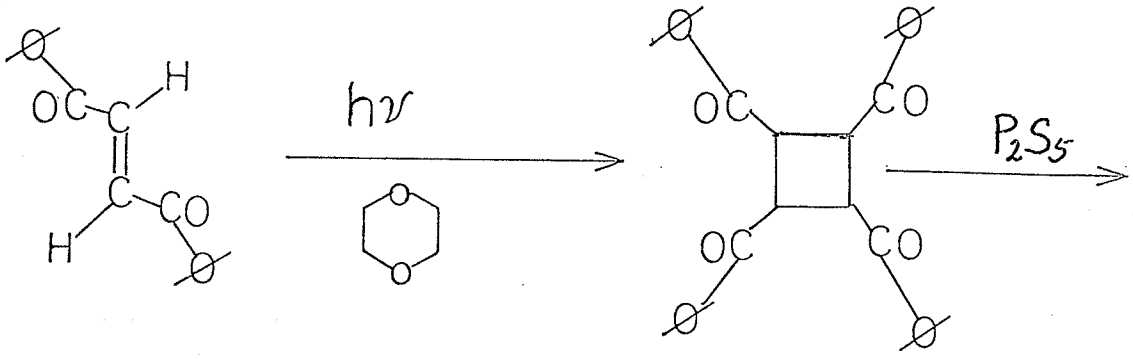
If the dibenzoyl product was 114a or 115a, then sulfurisation of this would give the corresponding thione 114b or 115b, which would hydrolyse back to the starting ketone 114a or 115a. On the other hand, sulfurisation of the dibenzoyl product 116 would produce a 14 π-electron aromatic system 117 containing a tetravalent sulfur. Since compound 117 contains a benzo[c]thiophene element of structure and would represent a rare example of a stable nonclassical thiophene, the investigation of the synthesis of 117 and related compounds became of interest. In 1969 Cava et al.(83) isolated the non-classical thiophene 118 by reacting tetrabenzoylethane (84) with phosphorus pentasulfide. Similarly to compound 117, tetraphenylthieno[3,4c]thiophene (118) is a stable nonclassical thiophene containing a tetravalent sulfur. However, when the dibenzoyl product from Scheme II was treated with phosphorus pentasulfide, the expected thiophene 117 was not detected. But the IR spectrum indicated that the product was unchanged starting material. Thus the dibenzoyl compound was probably 114a, 115a, or some other isomer instead of 116.



118

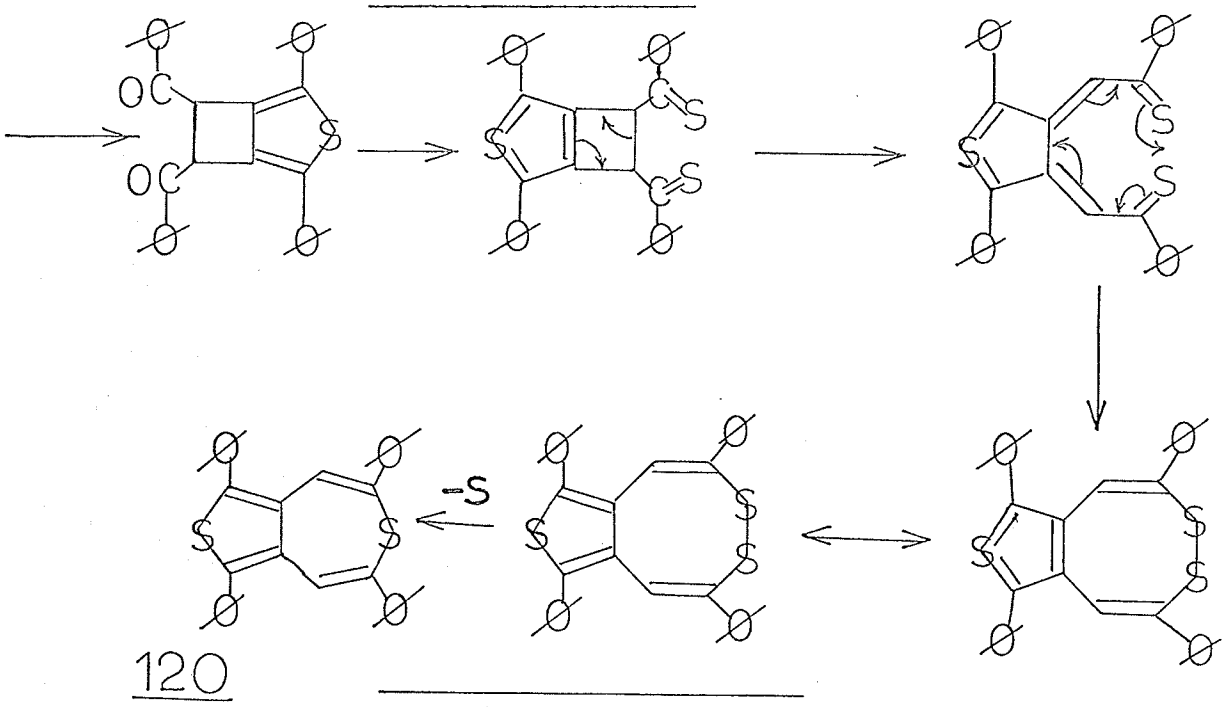
In view of the unsuccessful attempt to obtain compound 117, the preparation of another derivative of 118 was attempted. Irradiation of trans-dibenzoylethylene in dioxane gave in almost quantitative yield a photodimer 119 as white needles. Treatment of the tetrabenzoylcyclobutane (119) with phosphorus pentasulfide in pyridine gave the thienothiepine 120 as a minor product. The structure of 120 was confirmed by elemental analysis and mass spectroscopy. Besides the parent peak and phenyl peak , the mass spectrum of 120 also revealed that the compound readily extrudes sulfur under electron impact. The formation of the thienothiepine 120 from the cyclobutane 119 can be rationalized as possibly involving d-orbital expansion of the sulfur atom and two electrocyclic reactions as illustrated in Scheme III. However, the route from 119 to 120 and the properties of the product require further investigation.

Scheme III

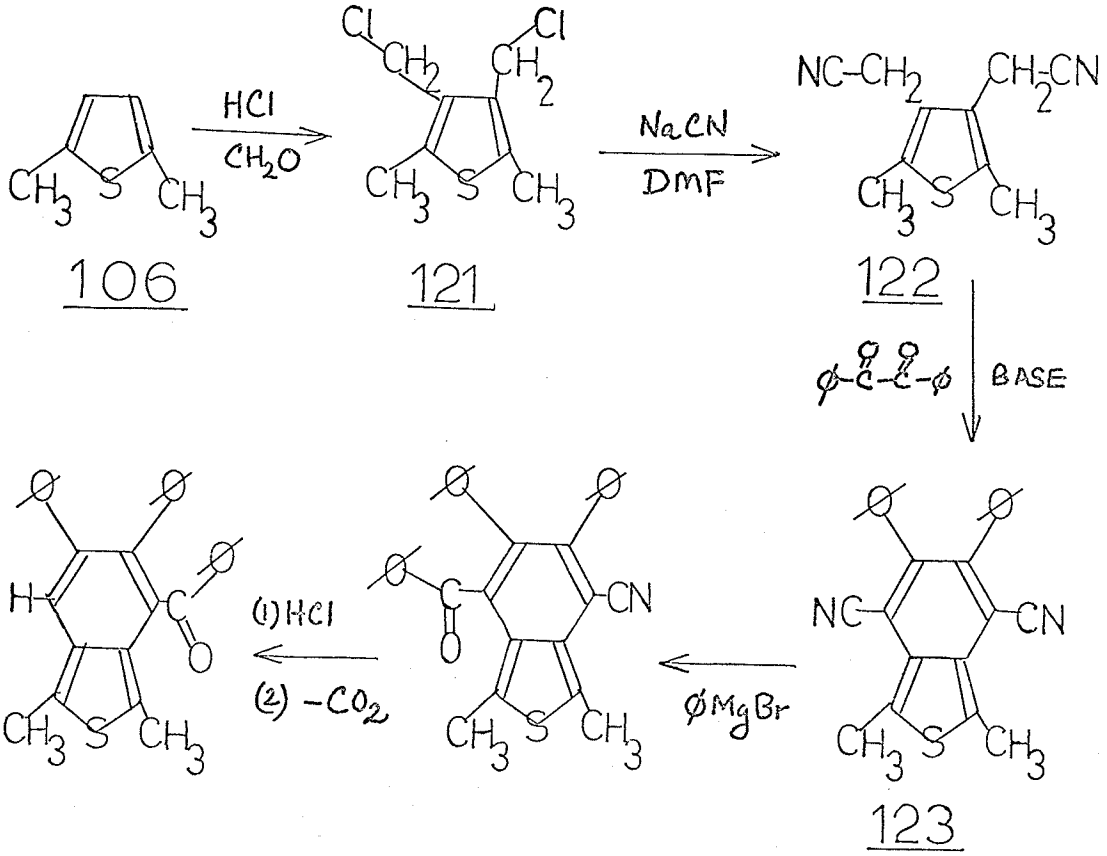


119

Scheme III continued

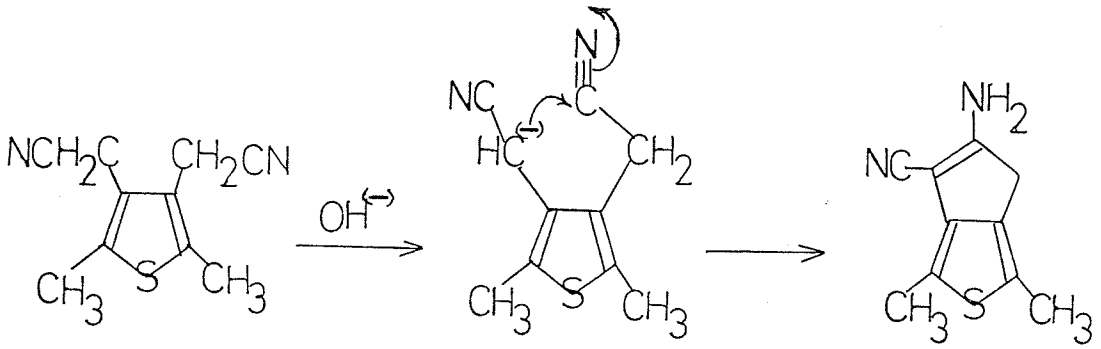


Scheme IV



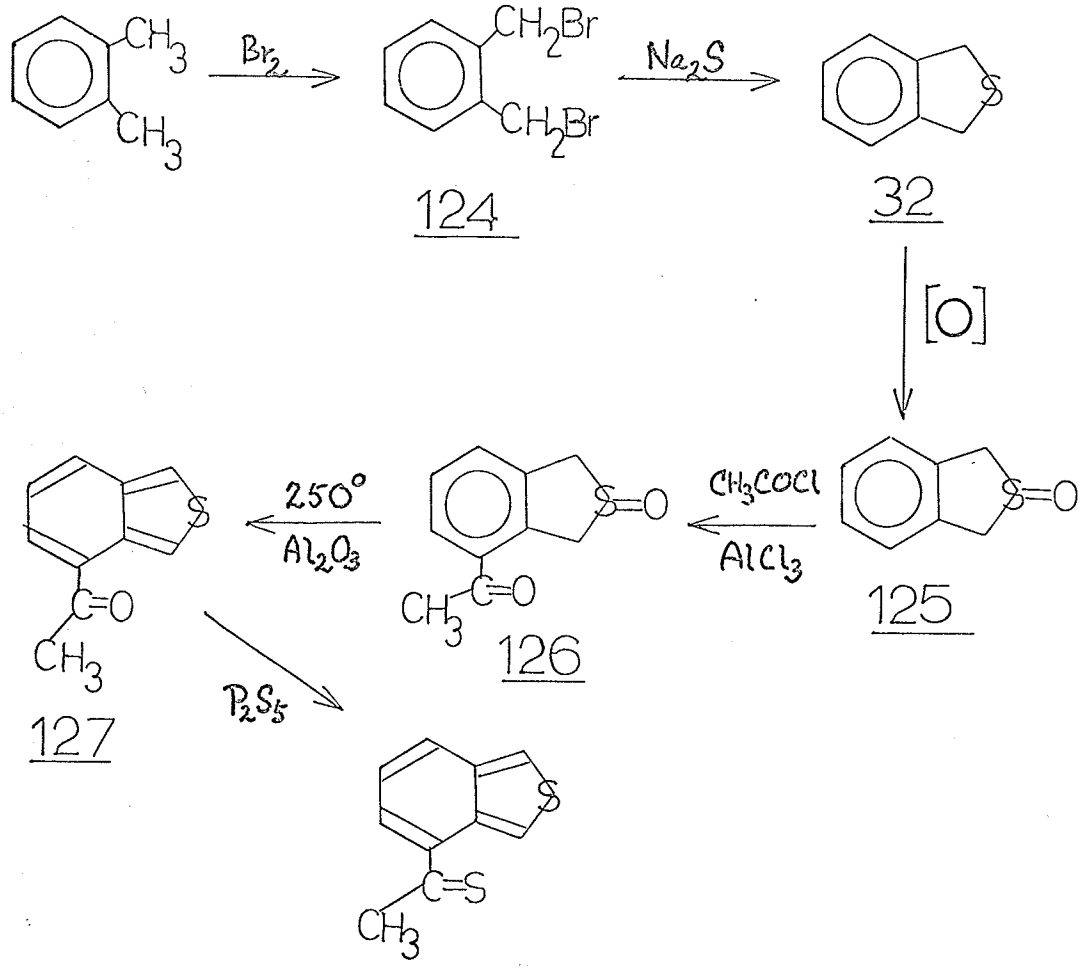
A fairly efficient and simple preparation of monochloromethyl-thiophene and bischloromethylthiophene was introduced by Badger et al. (85) in 1965. This involved the reaction of the thiophene with 40% formalin and hydrogen chloride gas at 50°C for ½ hour. As illustrated in Scheme IV, treatment of 2,5-dimethylthiophene (106) under these conditions yielded 2,5-dimethyl-3,4-bischloromethylthiophene (121) as pale-tan crystals in 78% yield. The conversion of 121 to the corresponding nitrile 122 proceeded smoothly by stirring the chloromethyl product 121 with NaCN in N,N-dimethylformamide. The nitrile 122 should condense with a diketone such as benzil or 2,3-butanedione in the presence of a base to produce the corresponding dicyanobenzo[c]thiophene 123. Unfortunately, compound 123 could not be obtained despite many attempts. Catalysts such as sodium hydride, sodium methoxide, potassium tertiary butoxide, and Hunig bases (triethylamine and di-isopropylethylamine) were tried, and each time a dark brown solid, whose I.R. spectrum showed an amino and a cyano absorption, was noted (7% yield).

The failure of the condensation step may be due to base-catalysed internal tautomerism or internal cyclisation of the nitrile 122 as shown below.



122

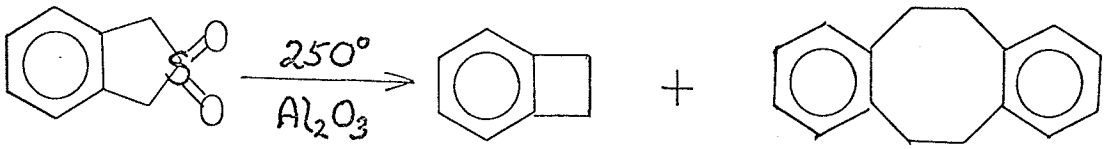
Scheme V



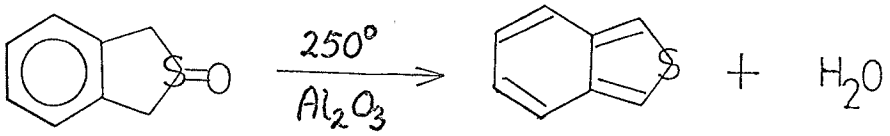
In 1954 Birch et al. (86) reported the synthesis and physical properties of 1,3-dihydrobenzo[c]thiophene (32) and derivatives. Compound 32 was first described by Leser (18) and later by Hjelt (87),who obtained it by the action of potassium sulfide on o-xylylene dibromide (124). The yield by a modified method, using sodium sulfide in ethanol, was 40% according to von Braun et al. (88).

The pyrolysis of 1,3-dihydrobenzo[c]thiophene sulfoxide (125) and 1,3-dihydrobenzo[c]thiophene sulfone (128) was performed by Cava et al. (89). They noted that in the case of the sulfone 128,

treatment of this compound with aluminum oxide at 250°C gave two products, benzocyclobutane (129) and dibenzocyclooctane 130. On the other hand, treatment of the sulfoxide 125 under similar conditions produced benzo[c]thiophene. This latter reaction is actually a dehydration reaction of the sulfoxide.



128 129 130



125 29

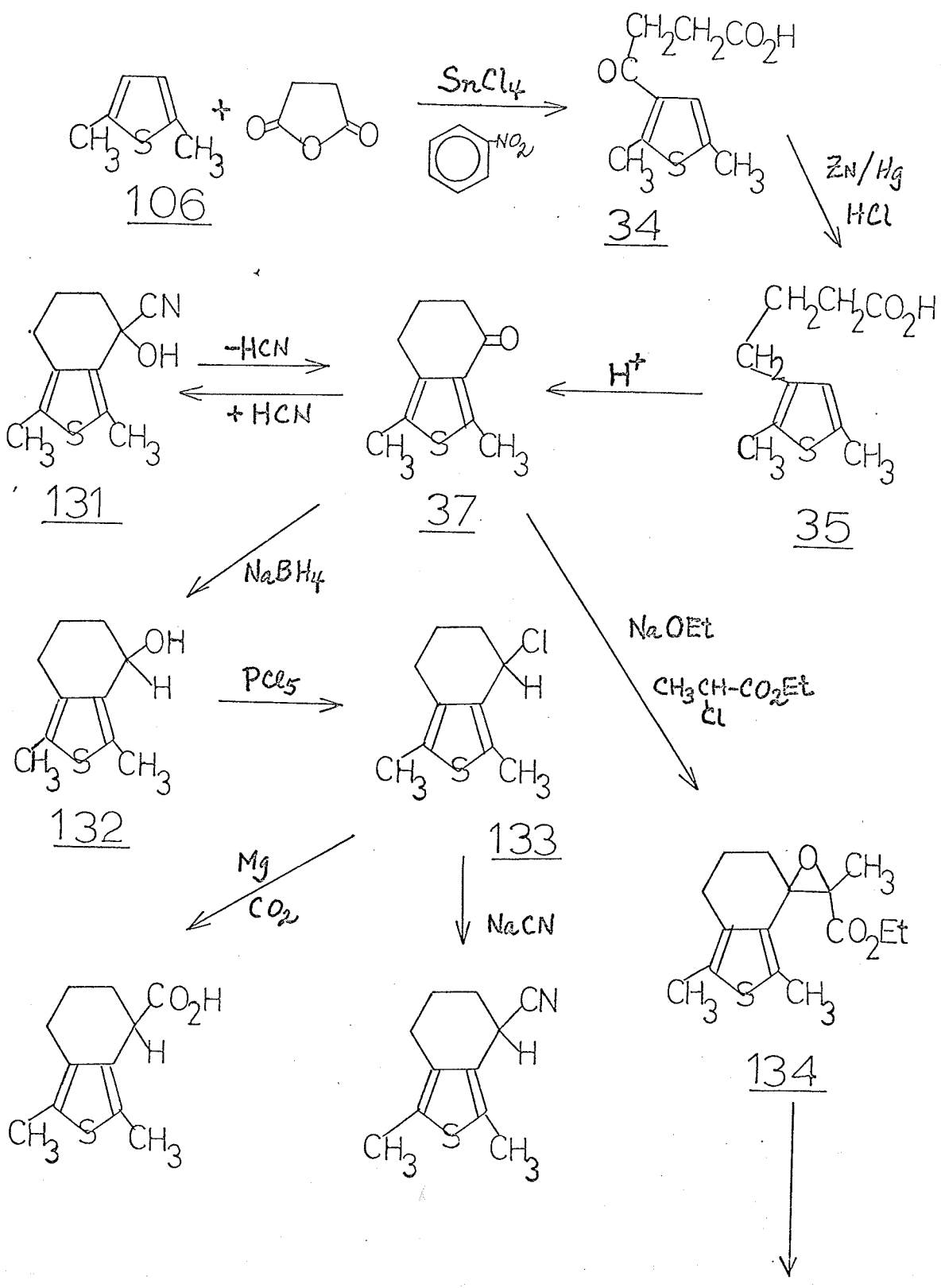
On the basis of the works of the above investigators, Scheme V was developed for the attempted synthesis of the thioacylbenzo[c]thiophene. O-xylylene dibromide (124) was obtained in excellent yield by the bromination of o-xylene according to the method of Atkinson and Thorpe (90). The cyclisation of the dibromide 124 was effected by refluxing this with sodium sulfide for two hours in ethanol to give 32 in 48% yield.

Once the 1,3-dihydrobenzo[c]thiophene was obtained, it was expected to give the sulfoxide 125 on treatment with t-butylhydroperoxide. Then, unlike the substitution problems in Scheme II, acylation of the

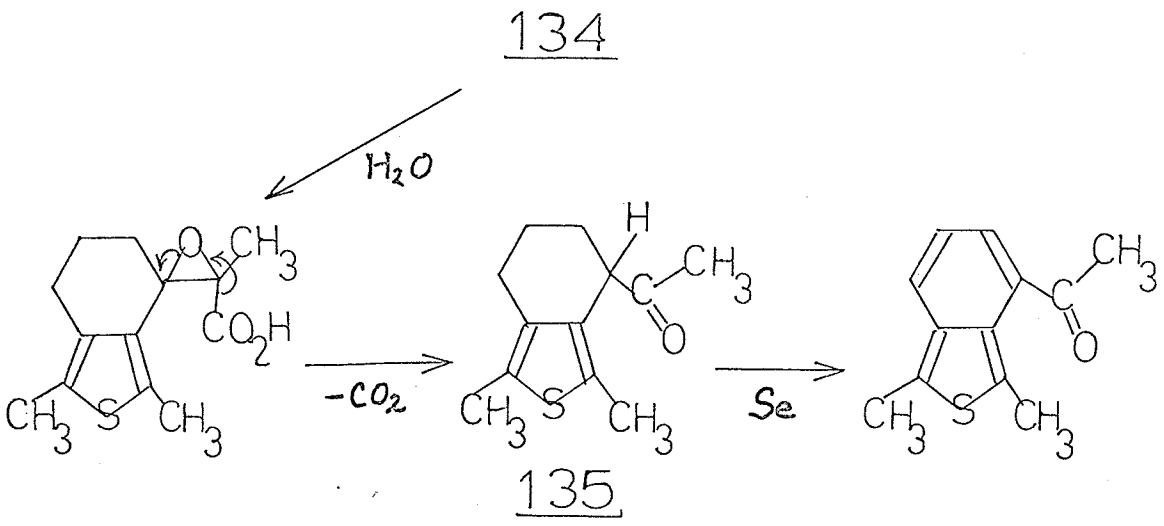
sulfoxide 125 should direct the acyl group to position 4 of the benzo-[c]thiophene nucleus to give 4-acetyl-1,3-dihydrobenzo[c]thiophene sulfoxide (126), along with the 6-acetyl derivative which could be separated. Having obtained 126, it would be relatively easy to pyrolise 126 to 127 utilizing Cava's method. Once the 4-acetylbenzo-[c]thiophene (127) is obtained, its conversion to the 4-thioacetyl product by treatment with phosphorus pentasulfide should present little difficulty.

Once again the sequence of reactions envisaged for Scheme V led to difficulties. Oxidation of 32 with t-butylhydroperoxide gave a product which could not be crystallized to a sharp melting point although the infrared spectrum showed no evidence of a sulfoxide absorption. This unstable product rapidly decomposed on exposure to air by turning into a red oil and then black tar. The oxidation procedure was repeated by using hydrogen peroxide and sodium periodate as oxidizing agents. Similar unstable products were detected. The failure of Scheme V may be caused by the wrong choice of the compound to be oxidized. Instead of trying to oxidize 1,3-dihydrobenzo[c]-thiophene, which itself is unstable, 1,3-diphenyldihydrobenzo[c]thio-phene perhaps would represent a more stable compound. However, using the latter might create problems in the following reaction since acylation may cause substitution in the 1 and 3-phenyl substituents.

Scheme VI


SnCl4
NO2
ZN/Hg
HCl
-HCN
+HCN
H+
NaBH4
PCl5
NaOEt
CH3CH-CO2Et
Cl
Mg
CO2
NaCN
106
34
131
37
35
132
133
134

Scheme VI continued



Using the classical methods developed by Steinkopf et al. (20), the synthesis of 4-acylbenzo[c]thiophene was attempted. Steinkopf et al. had reported the preparation of 1,3-dimethyl-4-keto-5,6,7-trihydrobenzo[c]thiophene (37) from 2,5-dimethylthienyl-3-[γ-butyric acid] (35) and concentrated sulfuric acid at 85°C as shown in Scheme VI. While essentially the same procedure was followed in the present work, a better yield of the ketone 37 was obtained than that previously reported by using nitrobenzene and stannic chloride instead of aluminum chloride and carbon disulfide in the Friedel-Crafts step, and using polyphosphoric acid instead of sulfuric acid in the cyclising of the acid 35 into the ketone 37.

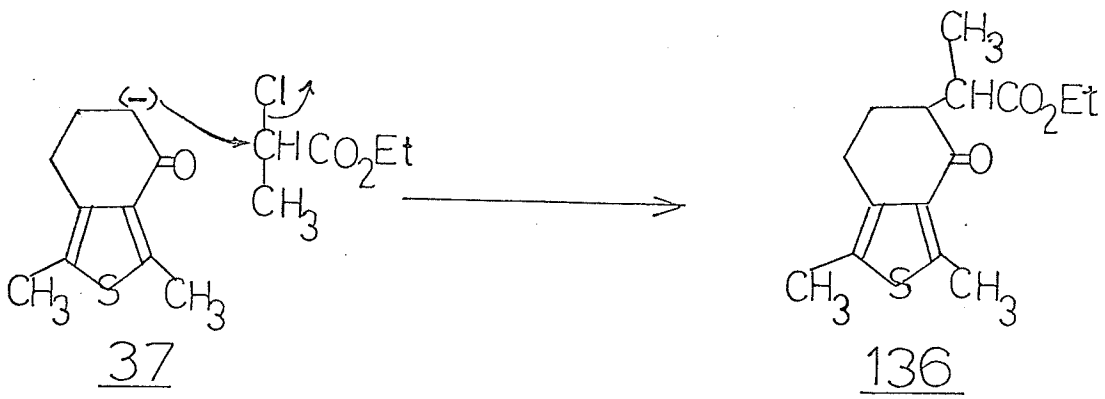
It was hoped that the ketone 37 would be easily converted to the cyanohydrin 131, which then could be hydrolysed to the corresponding acid. However, all attempts to isolate the cyanohydrin 131 failed because it dissociated back to the ketone 37 almost immediately with

hydrogen cyanide given off.

The secondary alcohol 132 was synthesized successfully, but its conversion into the chloride 133 could not be achieved. Each time decomposition products were obtained.

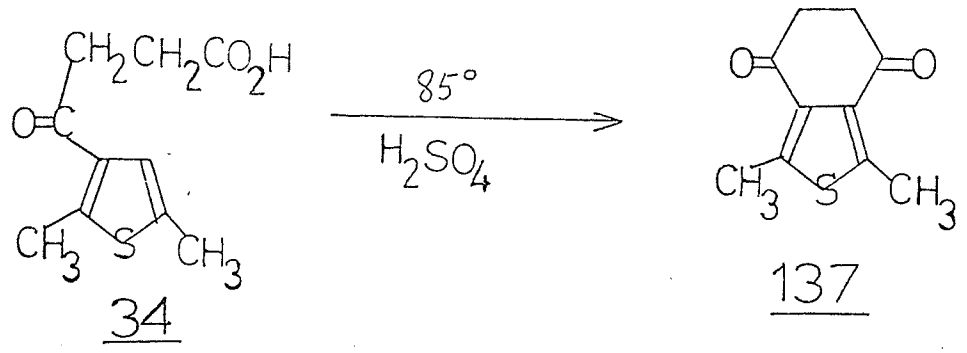
Yarnell et al. (91) had reported the synthesis of certain substituted alicyclic methyl ketones utilizing Darzen's glycidic ester method. Hence, treatment of the ketone 37 with ethyl α-chloropropionate and sodium ethoxide should produce the epoxy ester 134, which can easily be hydrolysed and decarboxylated to the methyl ketone 135. Once the methyl ketone 135 is obtained, its conversion to 4-acetylbenzo[c]thiophene could be conveniently accomplished by heating with selenium.

Contrary to expectations, treatment of the ketone 37 with ethyl α-chloropropionate and sodium ethoxide failed to produce the epoxy ester 134. All spectral data gave no evidence of the formation of the epoxy ester 134 nor the ketone 135. The IR spectrum showed absorptions for a cyclic ketone and an acid or ester group (1695 and 1768 cm^{-1} respectively), indicating that instead of the formation of the glycidic ester, the ketone 37 was condensed with ethyl α-chloropropionate in the presence of a strong base, sodium ethoxide, to give compound 136. The structure of 136 was also supported by NMR evidence.



37 136

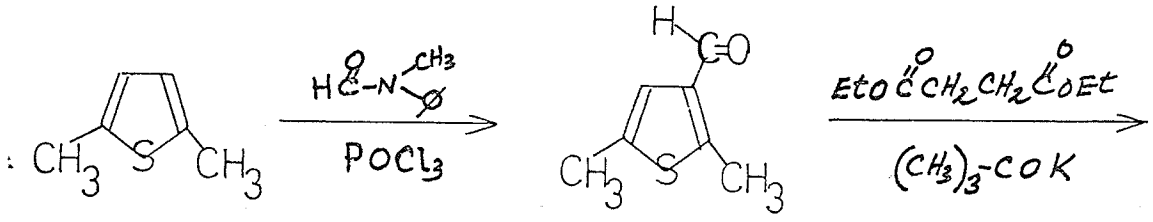
Although the cyanohydrin step and Darzen's glycidic ester synthesis failed, one interesting side reaction from Scheme VI was the cyclisation of the keto-acid 34 to yield 1,3-dimethyl-4, 7-dione-5,6-dihydrobenzo[c]thiophene (137). Cyclisation was effected by stirring the ketoacid 34 with sulfuric acid for 10 minutes at 85°C. The yield (3%) was the same when polyphosphoric acid was utilized as cyclisation agent. The infrared spectrum showed a strong carbonyl absorption at 1690 cm^{-1}, but no evidence of a hydroxy band was detected. The NMR spectrum of 137 showed a four proton singlet at 6.68τ for the two methylene groups and a six proton singlet at 6.83τ for the two methyl groups. In order for the two methylene groups to be equivalent at room temperature, the six-member ring of the compound 137 would have to be: (a) planar and a rigid structure or (b) non-planar with the two methylene groups moving rapidly, analogously to cyclohexane which moves rapidly from chair to boat forms at room temperature. If (b) is the dominant factor, then at low temperatures the two methylene groups of compound 137 should no longer be a singlet, but a multiplet.



34 137

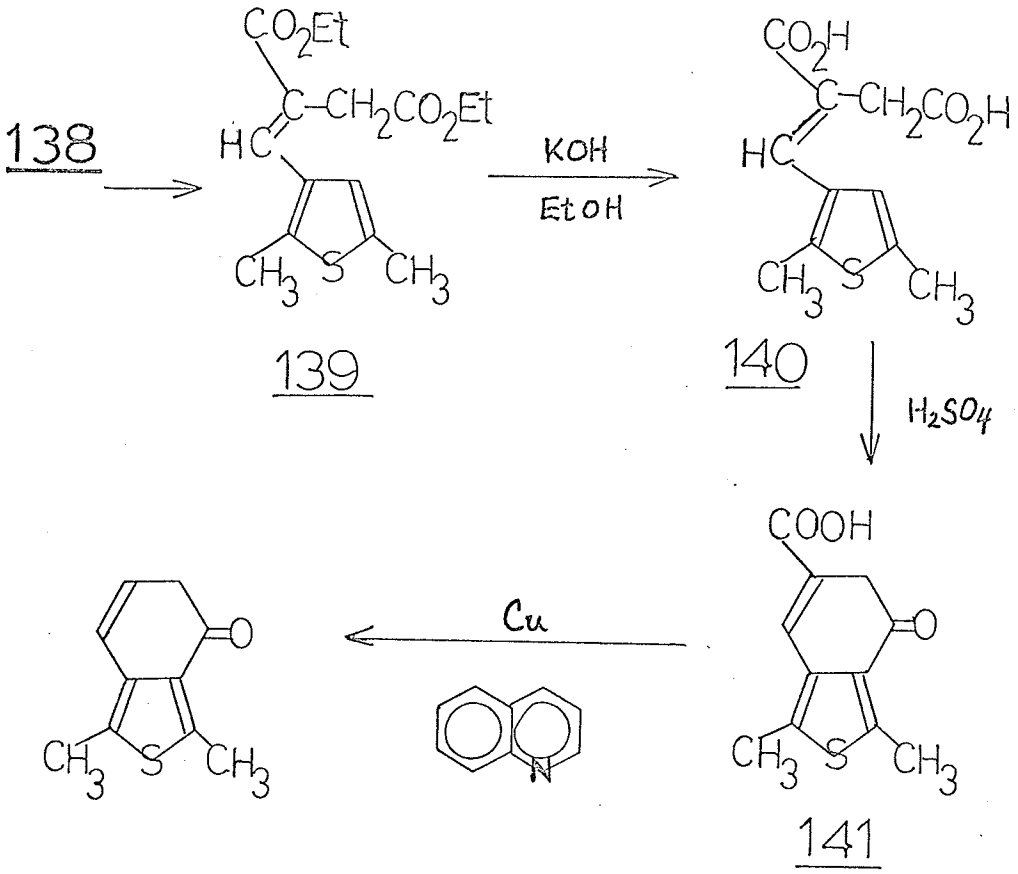
When the NMR spectrum of 137 was run from 0°C to -95°C, the methylene signal remained a singlet and the chemical shift remained at 6.68 τ. The two methylene groups must be equivalent both at room temperature and at -95°C. Hence, the six-member ring of compound 137 must be a rigid planar ring. This would explain why the yield of 137 was so low (3%) because it requires more energy to cyclise the keto-acid 34 into 137 than to cyclise the 2,5-dimethyl-3-[γ-butyric acid] (35) into compound 37.

Scheme VII



106 138

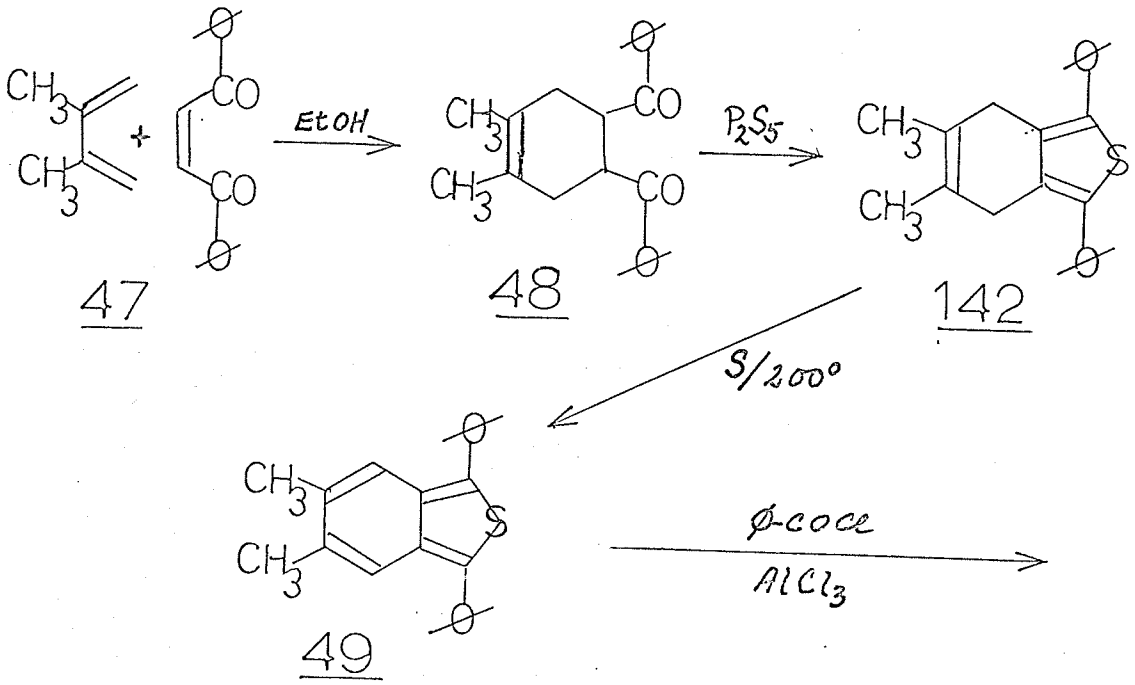
Scheme VII continued



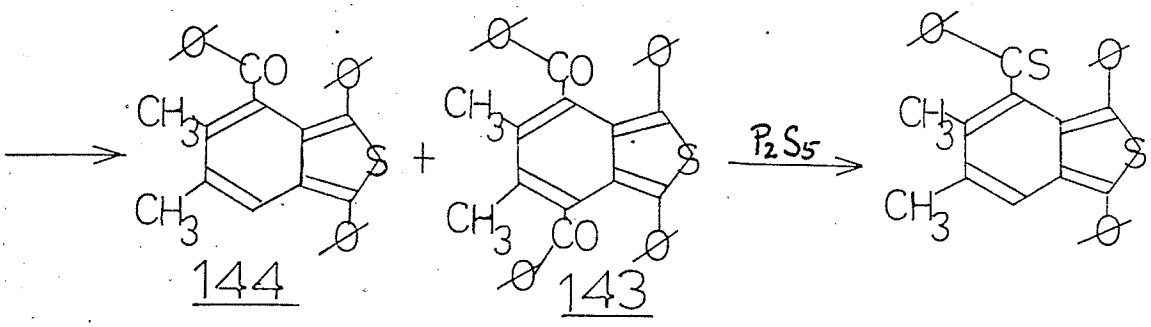
Applications of the Stobbe condensation has proven of considerable interest recently in the preparation of condensed aromatic compounds and heterocyclic compounds. Since Abdel-Wahhab et al. (92) had reported the successful synthesis of phenanthrene derivatives and benzo[b]furan derivatives utilizing the Stobbe condensation, it seemed appropriate to try the Stobbe condensation on thiophene derivatives in our attempted synthesis of 4-acylbenzo[c]thiophene, as described in Scheme VII. The first objective was to formylate 2,5-dimethylthiophene (106) to 2,5-dimethyl-3-formylthiophene (138) in reasonable yields. This was

done via the Vilsmeier method developed by King and Nord (93). By substituting N-methylformanilide for N,N-dimethylformamide in the reaction, the yield was increased from 40% to 68%. Treatment of 138 with diethylsuccinate in the presence of potassium tertiary-butoxide gave the thiophene ester 139, which was characterized by I.R. and N.M.R. Refluxing the ester 139 in potassium hydroxide-ethanol mixture gave the acid 140. Since the acid 140 proved difficult to purify either by recrystallization or column chromatography, the crude product was treated with concentrated sulfuric acid in an attempt to obtain the cyclised ketone 141. The cyclisation step failed. A variety of catalysts such as polyphosphoric acid, acetic anhydride and sodium acetate, and hydrobromic acid were used without any success; each time only decomposition products were obtained. The failure of the cyclisation step meant that Scheme VII had to be abandoned.

Scheme VIII



Scheme VIII continued

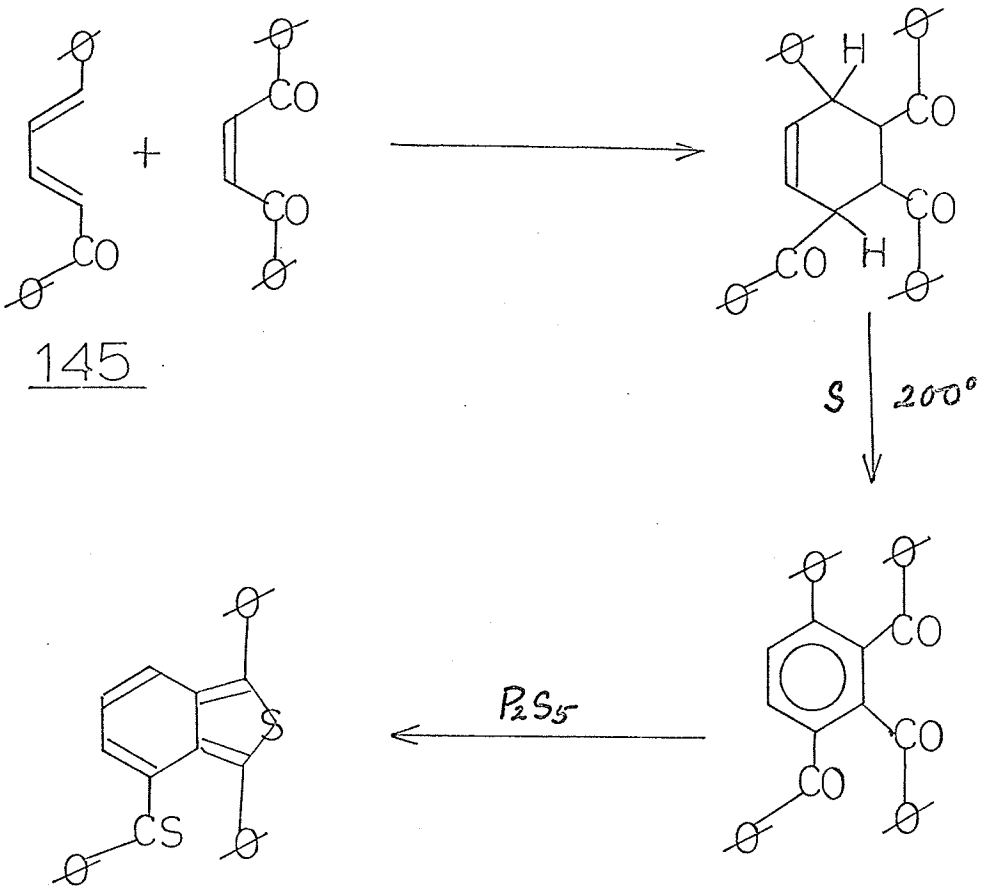


In view of the successful preparation of 1,3-diphenylbenzo[c] thiophene in high yields by the Diels-Alder method (26), it seemed appropriate to attempt to prepare the 4-acylbenzo[c]thiophene derivative by an analogous method described in Scheme VIII. It was found in Scheme II that Friedel-Crafts acylation of the benzo[c] thiophene nucleus would preferably occur at positions 5 and 6. However, if both positions 5 and 6 were blocked by methyl groups, then acylation would be expected to attack positions 4 and 7 to produce both the 4-acyl derivative 144 and the 4,7-diacyl derivative 143 which can easily be separated by thin layer chromatography.

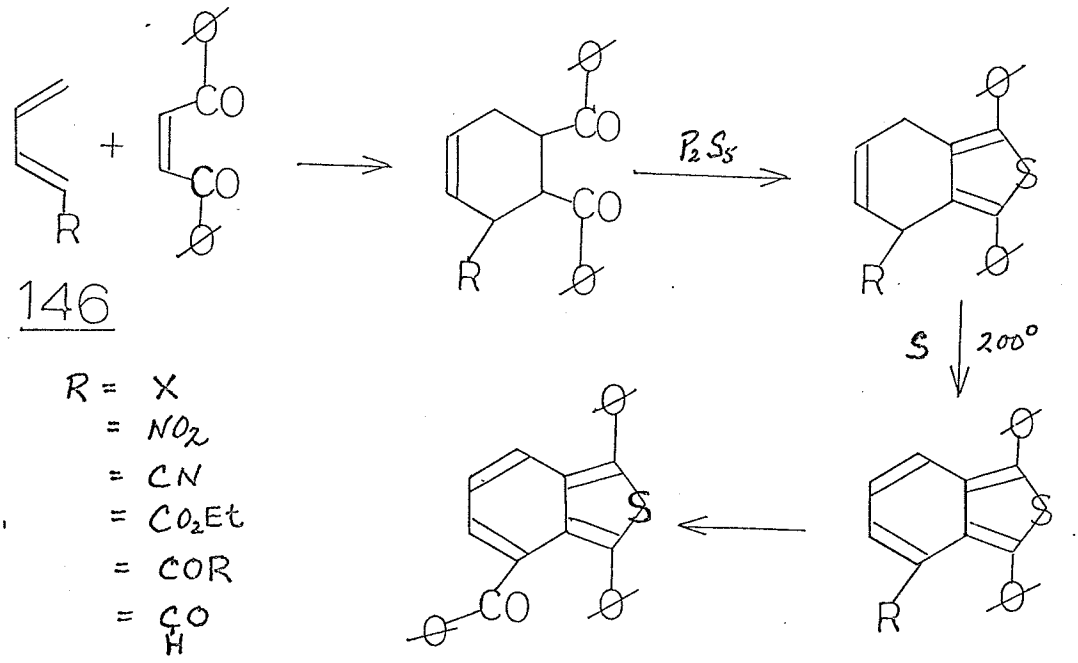
The addition product 48 was made by refluxing equimolar quantities of 2,3-dimethyl-1,3-butadiene and trans-dibenzoylethylene in ethanol for eight hours. Allen et al. (27) had discovered that when the Diels-Alder adduct of 2,3-diphenyl-1,3-butadiene and dibenzoylethylene were heated to 200°C with sulfur, the resulting product, isolated in excellent yield, was 1,3,5,6-tetraphenylbenzo[c]thiophene. Similar treatment with the adduct 48 yielded black tar, not the expected 5,6-dimethyl-1,3-diphenylbenzo[c]thiophene (49). On the basis of these facts, it was decided first to cyclise the adduct 48 to 1,3-diphenyl-4,7-dihydro-5,6-dimethylbenzo[c]thiophene (142) by treatment

with phosphorus pentasulfide in boiling pyridine for 4 hours. Then compound 142 was aromatised by heating with sulfur at 200°C for ½ hour to yield the 5,6-dimethylbenzo[c]thiophene 49 as a green fluorescent solid in 42% yield. Unfortunately, attempts to acylate compound 49 with benzoyl chloride and aluminum chloride, stannic chloride, or zinc chloride failed. The failure may be due to the steric hindrance of positions 4 and 7 of compound 49 to undergo electrophilic substitution.

Scheme IX



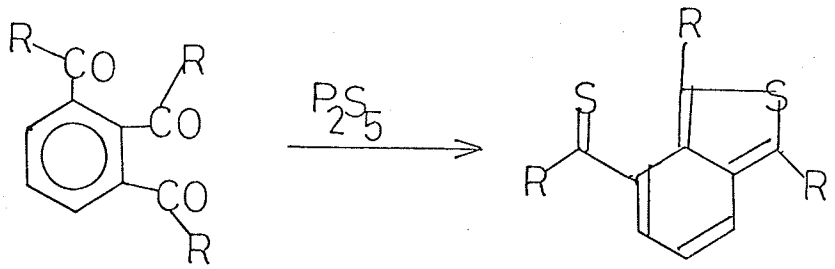
Scheme IX continued



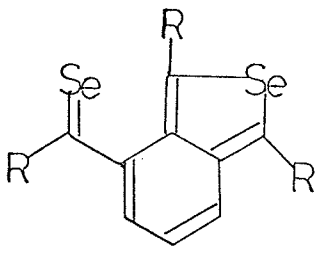
In view of the unsuccessful attempts to acylate the benzo[c]-thiophene nucleus directly, it seemed appropriate to attempt to add dibenzoylethylene directly to 1-acyl-1,3-butadiene 145 or any 1-substituted-1,3-butadienes 146, which can be converted to a ketone after the initial Diels-Alder addition step has been achieved, as illustrated in Scheme IX. Unfortunately, 1-substituted-1,3-butadienes whose substituents are electron withdrawing in character could not be made to react with dibenzoylethylene to form the Diels-Alder adduct. Various solvents such as ethanol, benzene, dioxane, toluene, xylene and nitrobenzene were used; and drastic conditions such as heating the diene and dienophile in a high-pressure bomb up to 300°C were tried. All attempts proved futile. It is probable that electron withdrawing groups attached to positions 1 or 4 of 1,3-butadiene deactivate the diene by conjugative effects.

Attempted Syntheses of a 1,2,3-Triacylbenzene

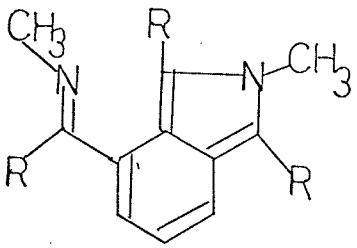
At this point of the investigation, it became apparent that it would be extremely difficult, if not impossible to attempt to attach directly or indirectly a keto side chain to position 4 of the benzo-[c]thiophene nucleus. Hence, it was decided to develop the keto side chain first, before cyclising the benzo[c]thiophene nucleus. A 1,2,3-triacylbenzene 147 seemed to be the ideal precursor to 4-thioacylbenzo-[c]thiophene since refluxing the triketone 147 with phosphorus pentasulfide should yield the sought-after product 25. Up to the present time, the synthesis of a 1,2,3-triacylbenzene has not yet been reported in the published literature. The successful synthesis of the triketone 147 not only would open a direct route to 25, but also would permit the synthesis of the selenium and nitrogen analogues, 148 and 149 respectively.



147 25

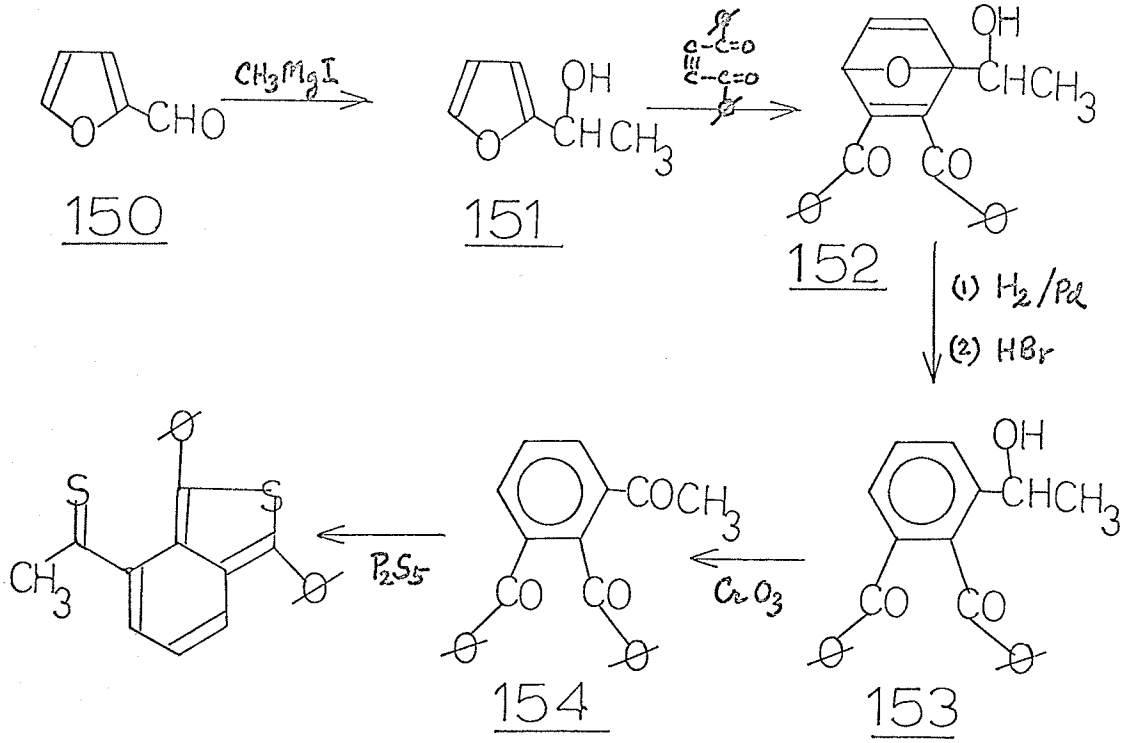


148



149

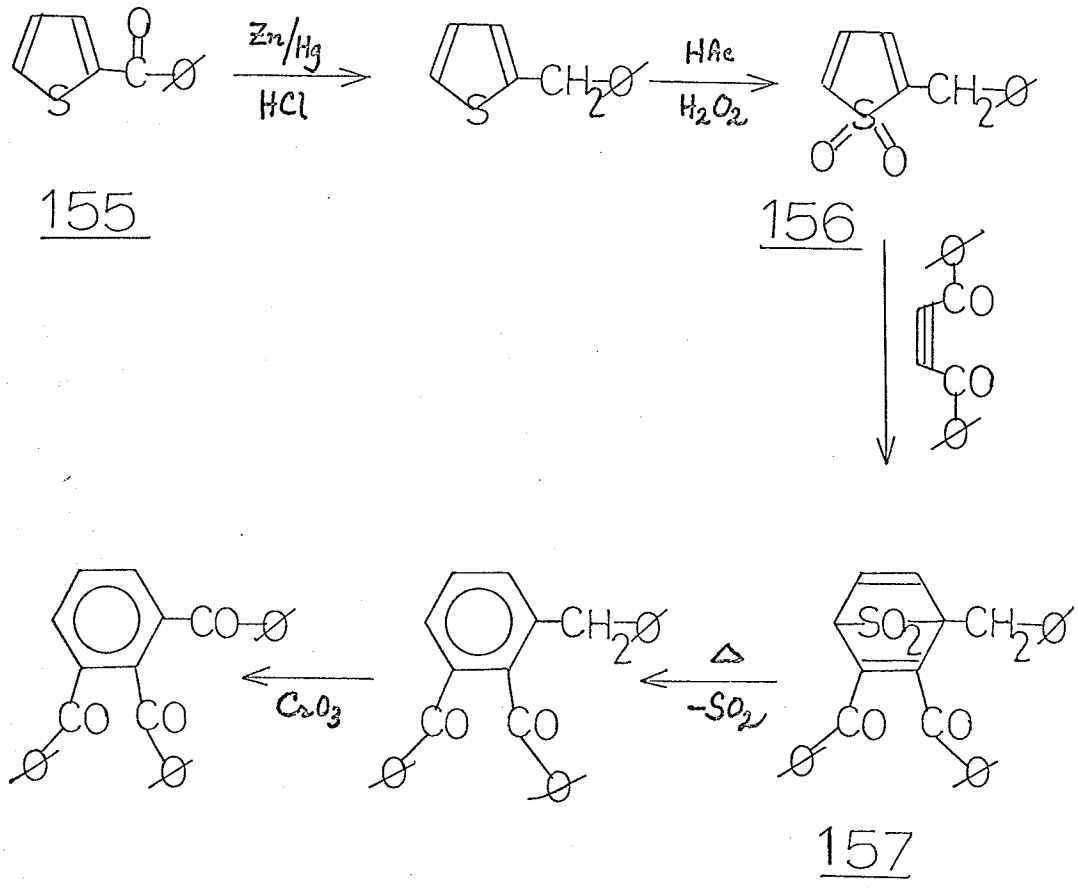
Scheme X



The attempted synthesis of the triketone 154 involved furfural (150) as the starting material. Unlike thiophenes (94) and benzo[c]-thiophenes (23), furans and benzo[c]furans were reported to be excellent dienes for addition to dienophiles in Diels-Alder reactions (95). Because it was discovered in Scheme IX that electron withdrawing substituents of 1,3-butadienes deactivate the dienes in Diels-Alder reactions, it was decided to convert the furfural (150) to the secondary alcohol 151 via Grignard attack of the furfural by methyl magnesium iodide. Then refluxing equimolar amounts of the furan alcohol 151 and dibenzoylacetylene (96) gave in fair yields the adduct 152. Similar attempts to add dibenzoylethylene to the furan alochol 151 failed. Hydrogenation of one of the two C=C bonds of adduct 152 followed by boiling in HBr should aromatise 152 to 153. Then oxidation of the

diketoalcohol 153 would produce the triketone 154. Unfortunately, attempts to aromatise or to break the C-O-C bridge of 152 did not turn out as expected. Each time a dark red oil was noted. Photolysis of 152 gave a red polymer-like product which on examination by t.l.c.showed at least fifteen components. At this point it was obvious to us that Scheme X did not appear too promising as a route to the triketone. Other Diels-Alder reactions involving dibenzoylethylene or dibenzoylacetylene and substituted furans such as furfuryl alcohol and methyl 2-furfuryl ether were attempted without positive results.

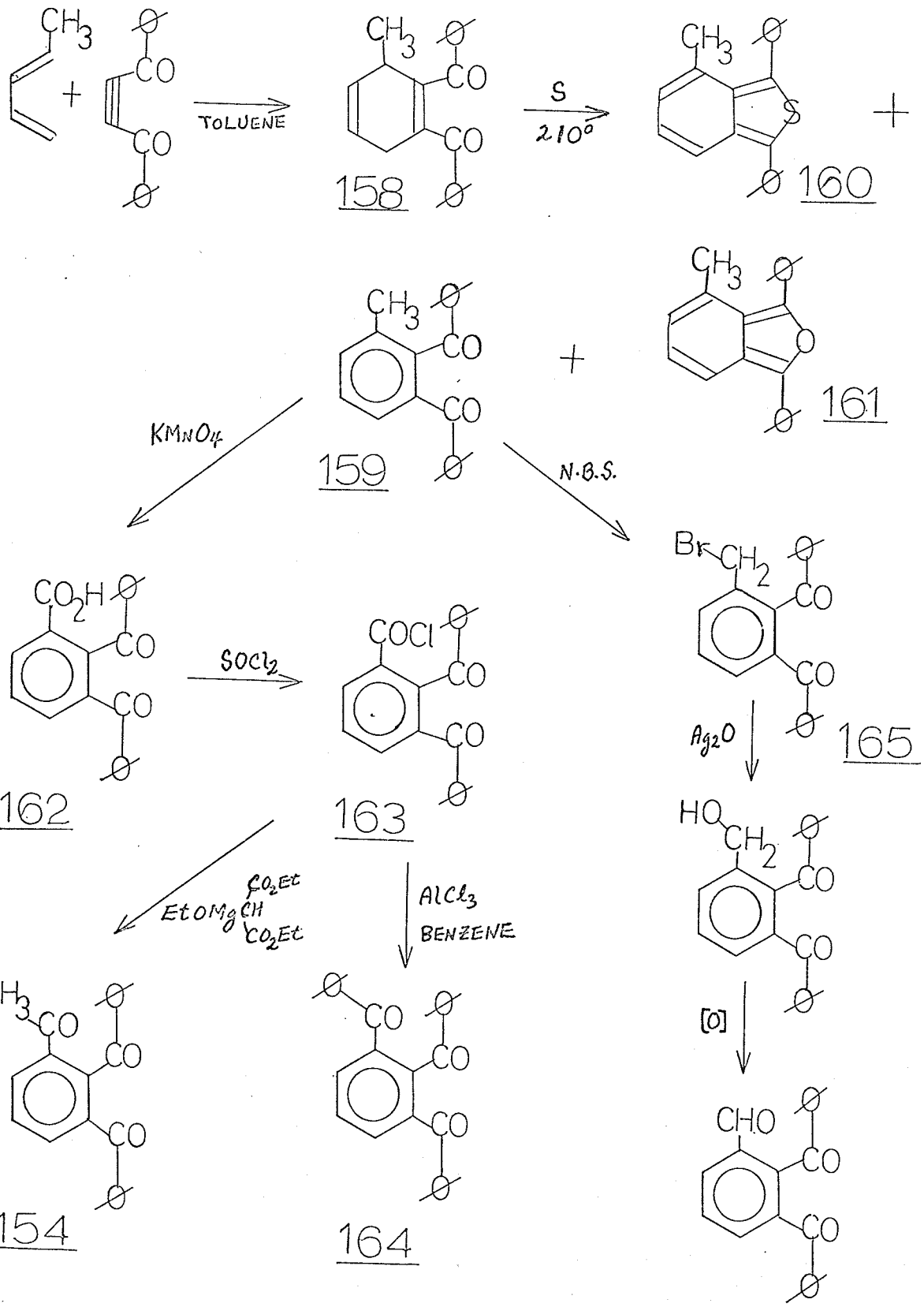
Scheme XI



A second course of reactions starting with 2-benzoylthiophene was attempted as outlined in Scheme XI. At first glance Scheme XI appears to be similar to Scheme X, except that unlike the latter, the aromatisation step should encounter no problems because 157 would be expected to aromatise readily on heating with the loss of SO_2. Two problems not anticipated were the unacceptably low yield of the sulfone 156 and the complete failure of the Diels-Alder step involving dibenzoylacetylene or dibenzoylethylene and the sulfone 156 to give adduct 157. Applying Hinsberg's method (97) which involves hydrogen peroxide in glacial acetic acid gave only 2% yield of 156. Periodate oxidation (98) did not work. Drastic conditions such as heating the sulfone 156 and dibenzoylacetylene up to 300°C in a bomb was unsuccessful.

The third attempt to synthesize 1,2,3-triacylbenzene is outlined in Scheme XII. When 1,3-pentadiene and dibenzoylacetylene were refluxed in toluene for eight hours, it afforded an adduct 158 as a viscous yellow oil. Since the 1,3-pentadiene used contained both the trans and cis isomers, the adduct 158 was not purified but heated with three equivalents of sulfur to yield a brown oil. On separation by column chromatography on alumina, three products were isolated. The major product obtained was 2,3-dibenzoyltoluene (159), which was characterized by NMR, IR, and elemental analysis. The two minor products, both of which exhibited fluorescence under ultraviolet light, were identified as 1,3-diphenyl-4-methylbenzo[c]thiophene (160) and 1,3-diphenyl-4-methylbenzo[c]furan (161). Oxidation of the diketone 159 would be expected to give 2,3-dibenzoylbenzoic acid (162), which could be converted to the acid chloride 163 on treatment with thionyl

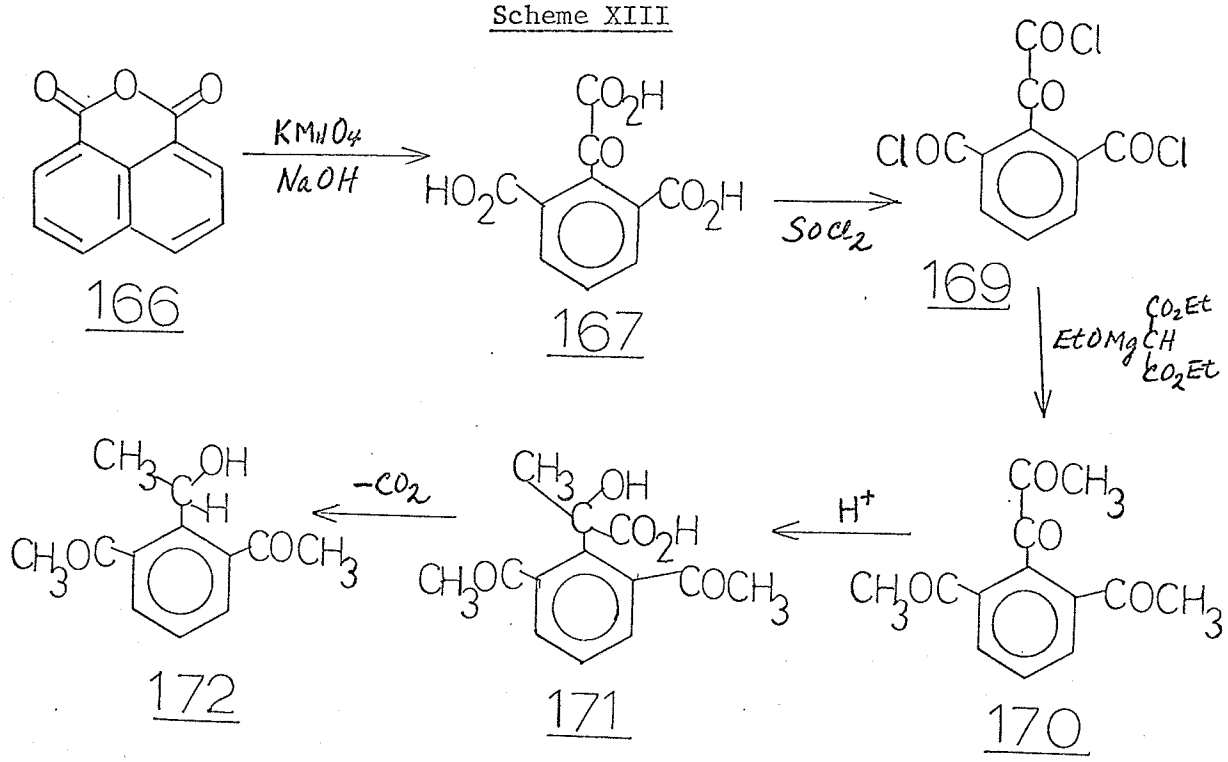
Scheme XII


TOLUENE
158
S
210°
160
159
161
KMnO4
N.B.S.
162
SOCl2
163
165
Ag2O
AlCl3
BENZENE
EtOMgCH(CO2Et)2
[O]
154
164

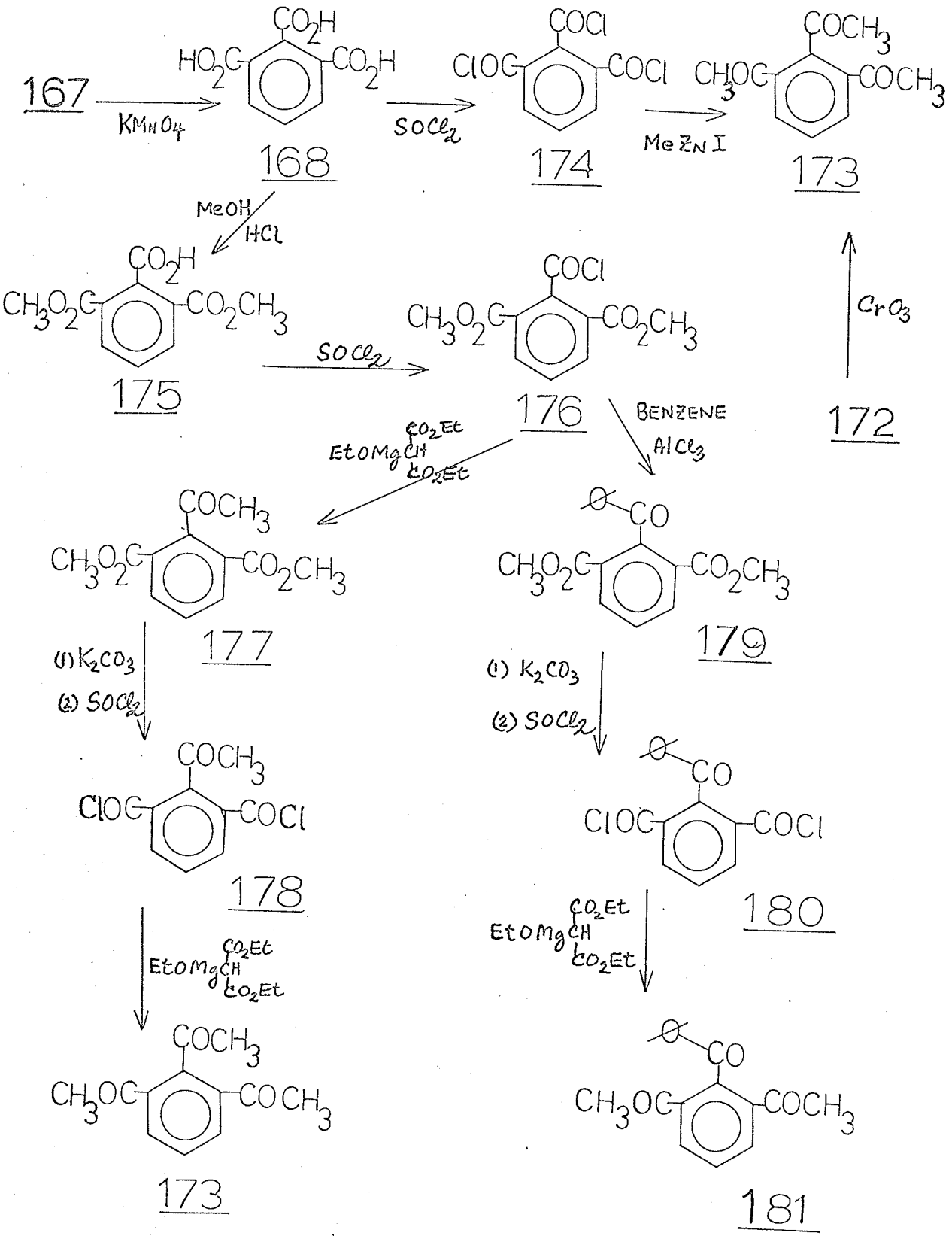
chloride. Once the acid chloride 163 is obtained, its conversion to the triketone 154 on treatment with ethoxymagnesium malonate should present no difficulties. The acid chloride 163, when subjected to Friedel-Crafts acylation with benzene would also be expected to yield 1,2,3-tribenzoylbenzene (164). But when the dibenzoyltoluene 159 was oxidized using first potassium permanganate, then nitric acid, lead tetraacetate, selenium dioxide, or chromium trioxide, the expected product 162 was not obtained. Instead, the only product observed each time was benzoic acid. Evidently the ring is too destabilized by the electron withdrawing substituents and is readily oxidized.

Halogenation of 159 was also attempted by using N-bromosuccinimide, sulfuryl chloride (SO_2Cl_2), or photolytic methods. Such halogenation reactions of toluene derivatives are not uncommon (99,100). However, the formation of 165 was not successful, presumably due to the highly hindered position of the methyl group to free radical attack.

Scheme XIII



Scheme XIII continued



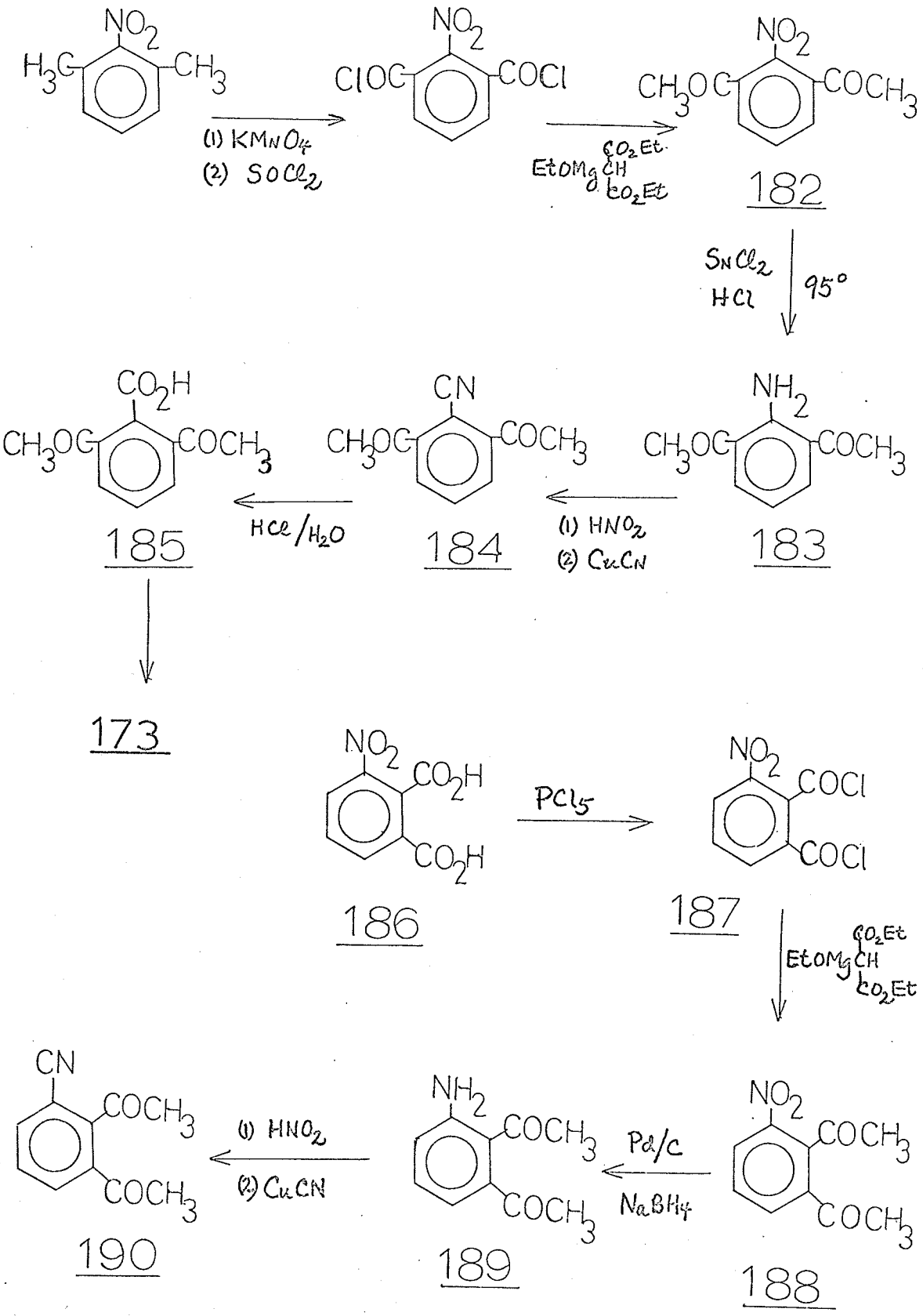
Graebe et al. (101) had reported the preparation of 2,6-dicarboxyphenylglyoxylic acid (167) from naphthalic anhydride (166) as shown in Scheme XIII. While essentially the same procedure was followed in the present work, a better yield of the product 167 was obtained than that previously reported. The acid 167 was refluxed with thionyl chloride in anhydrous benzene to give quantitative yields of the acid chloride 169. This acid chloride was rather unstable, decomposing on exposure to air or on standing overnight. On the basis of the work of Reynolds and Hauser (102), who developed a high yield preparation of o-nitroacetophenone from o-nitrobenzoyl chloride, it seemed reasonable that treatment of the acid chloride 169 with ethoxymagnesiummalonate would produce the corresponding methyl ketone 170. Strong acid or base-catalyzed benzilic acid rearrangement of 170 would produce 171, which would easily decarboxylate into the secondary alcohol 172. Mild oxidation of the alcohol 172 would yield 1,2,3-triacetylbenzene (173). Unfortunately, 170 was not obtained as expected when the acid chloride 169 was treated with ethoxymagnesiummalonate.

Graebe et al. (101) had also reported that 2,6-dicarboxyphenylglyoxylic acid (167) could be further oxidized to 1,2,3-tricarboxybenzene or hemimellitic acid (168) by potassium permanganate treatment. Refluxing the hemimellitic acid (168) with thionyl chloride in benzene gave the corresponding acid chloride 174 in high yield. In 1958 Simmons and Smith (103,104) developed, and Fuson et al. (105) improved on the preparation of methyl zinc iodide (Simmons-Smith Reagent) as an effective reagent for the conversion of acyl halides into the corresponding methyl ketones. But both methyl zinc iodide and ethoxymagnesiummalonate

failed to react with the acid chloride 174 to produce 1,2,3-triacetylbenzene (173).

Since it was found impossible to convert simultaneously the three carboxyl groups of hemimellitic acid (168) into three keto groups directly, it was decided to work on the most hindered or 2-carboxyl group first. After succeeding in transforming the 2-carboxyl group into a ketone, it would be relatively simple to do the same for the unhindered 1 and 3-carboxyl groups. Thus, treatment of hemimellitic acid (168) and anhydrous methanol with hydrochloric acid at $0^{o}C$ gave the diester 175 in 65% yield while performing the same reaction at higher temperatures gave exclusively the triester. Refluxing the diester 175 with thionyl chloride afforded the corresponding acid chloride 176 in quantitative yield. From 176 two routes were available to reach the triketones 173 and 181. Treatment of 176 with ethoxymagnesiummalonate gave 177 in 7% yield, which was characterized by I.R. and N.M.R. The ester 177 was easily hydrolysed to the acid on treatment with potassium carbonate and gave the corresponding acid chloride 178 by refluxing the acid with thionyl chloride. However, when the acid chloride 178 was treated with ethoxymagnesiummalonate, the final product isolated was not the triketone 173, but isophthalic acid. Friedel-Crafts acylation of benzene with the acid chloride 176 and aluminum chloride should produce 179, which would hydrolyse to the corresponding acid on treatment with base. After conversion to the acid chloride 180, the route to the triketone 181 should encounter little difficulty. Contrary to expectations, the Friedel-Crafts acylation of benzene with 176 using first aluminum chloride and then stannic chloride as catalysts, failed------ probably due to the highly hindered position

Scheme XIV


NO2
H3C
CH3
(1) KMnO4
(2) SOCl2
ClOC
COCl
CH3O
COCH3
EtOMgCH(CO2Et)CO2Et
182
SnCl2
HCl
95°
NH2
183
(1) HNO2
(2) CuCN
CN
184
HCl/H2O
CO2H
185
173
186
PCl5
187
188
Pd/C
NaBH4
189
190

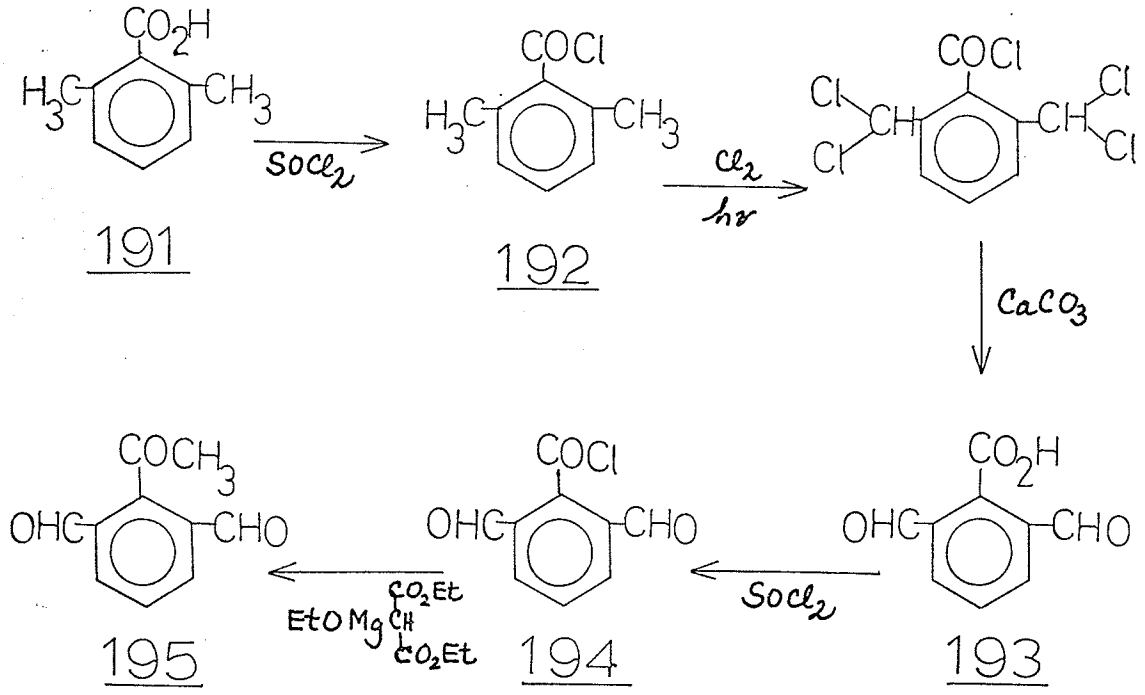
of the acid chloride group of 176. Hence, Scheme XIII had to be abandoned in favour of Scheme XIV.

During the investigation of the synthesis of 7-acetyl-3-methylanthranil, which will be elaborated in a later discussion, 2,6-diacetylaniline (183) was isolated as a minor product. Accordingly, it was decided to utilize 183 in an attempted synthesis of 1,2,3-triacylbenzene. The route to compound 183 is illustrated in Scheme XIV. 2-Nitro-m-xylene was used as starting material since it was readily available. 2,6-Diacetylaniline (183) was obtained in 76% yield on refluxing 2,6-diacetylnitrobenzene (182) with excess stannous chloride in concentrated hydrochloric acid at 90°C for 2½ hours. The structure of the yellow needles isolated was confirmed by I.R., NMR, and elemental analysis. Diazotization of 183, followed by treatment with cuprous cyanide was expected to produce the cyano compound 184, which would hydrolyse to the corresponding acid 185. From here an easy conversion to the triketone 173 seemed reasonable. However, when the Sandmeyer reaction was performed on 183, the expected product 184 was not detected. The failure of the Sandmeyer reaction was probably due to the difficulty of the hindered amino group of 183 to be diazotised and subsequent attack by the cyano anion.

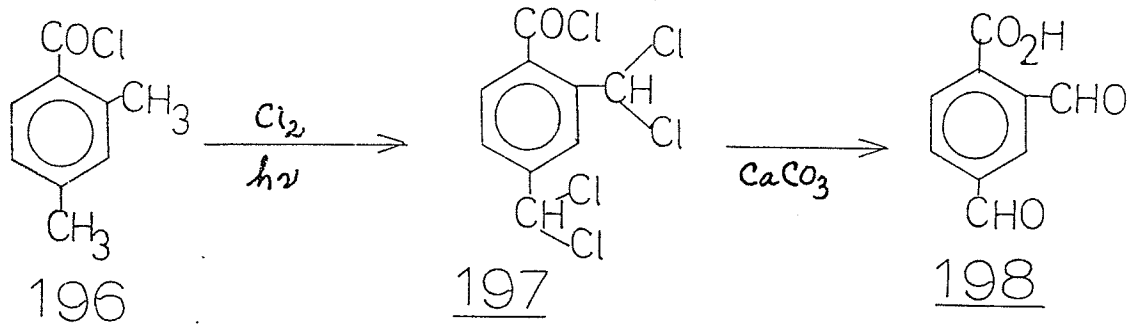
The above reaction scheme was repeated using 3-nitrophthalic acid (186) as the starting material. Since considerable difficulty was experienced in obtaining a fair yield of the acid chloride 187 by using thionyl chloride, the chloride 187 was made by the action of phosphorus pentachloride upon 3-nitrophthalic acid (186) at 140°C (106). Treatment of 187 with ethoxymagnesiummalonate gave 2,3-diacetylnitrobenzene (188) in 8% yield. Reduction of 188 with palladium-charcoal and sodium borohydride

yielded 2,3-diacetylaniline (189), which was confirmed by IR and N.M.R. Unlike 2,6-diacetylaniline (183), the amino group of 189 should be much less hindered to diazotization, and the Sandmeyer reaction should proceed smoothly to yield 190. When the Sandmeyer reaction was performed on the diazotised product of 189, the dark oil obtained showed no CN absorption in the infrared spectrum. Once again, this reaction scheme had to be abandoned.

Scheme XV



During their investigation of the action of halogens on toluene derivatives, Perkin et al. (107) discovered a useful synthesis of aromatic aldehydes. They noted that when 2,4-dimethylbenzoyl chloride (196) was chlorinated at 160-220° in ultraviolet light, one of the products isolated was 2,4-bis(dichloromethyl)benzoyl chloride (197), which gave 2,4-diformylbenzoic acid (198) on treatment with calcium carbonate.



196 197 198

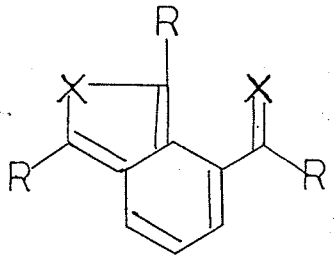
Hence, the light catalysed halogenation of 2,6-dimethylbenzoyl chloride (192) was investigated as a possible route to 2,6-dialdehydoacetophenone (195), as described in Scheme XV. 2,6-Dimethylbenzoyl chloride (192) was prepared in quantitative yield by refluxing 2,6-dimethylbenzoic acid (191) with thionyl chloride for 4 hours. When the chlorination of 192 was carried out in ultraviolet light at 220°C, a yellow oil was obtained. This was not isolated, but probably gave 2,6-dialdehydobenzoic acid (193) after boiling in calcium carbonate solution. After conversion to the acid chloride 194 plus further treatment with ethoxymagnesiummalonate, the expected product 195 was not detected. Careful NMR analysis showed no evidence for any acetyl or aldehyde peaks. The I.R. gave indications of an acid or ester absorption at 1768 cm^{-1}.

Conclusion

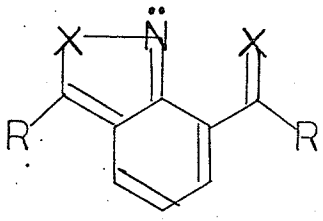
Because of the difficulties encountered in attempts to make the thioacylbenzo[c]thiophenes, approaches to this model compound were abandoned; and work was concentrated on the nitrogen containing model compounds: the acylated anthranils and their thio analogues. As will be seen, conclusions derived from a study of these indicated that such thioacylbenzo[c]thiophenes would be unlikely to be very stable, and would not possess any stabilization due to single bond-no bond resonance or valence tautomerism.

PART B - Discussion on the Preparation of 7-Acetyl-3-Methylanthranil

While the preparation of 4-acylbenzo[c]thiophenes or 4-thioacylbenzo[c]thiophenes was unsuccessful, some of the procedures attempted for these syntheses were useful for the preparation of anthranil and thioanthranil derivatives which had suitable structures for investigation. In some ways, these anthranil nuclei are more suitable for investigation than benzo[c]thiophenes. The unsubstituted compounds are stable at room temperature, in contrast to benzo[c]thiophenes which rapidly decompose at that temperature. Another advantage is that the lone pair of electrons on the nitrogen would offer less steric hindrance to interaction of the isoxazole or isothiazole ring with a thione or ketone group on a side chain than would an alkyl group or even a hydrogen atom at the 3-carbon atom in a benzo[c]thiophene. Rapid tautomerism at least should be easier in the anthranils or thioanthranils.



25

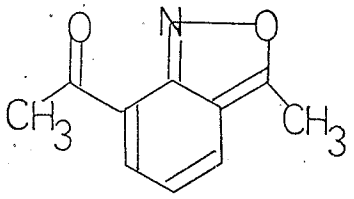


26

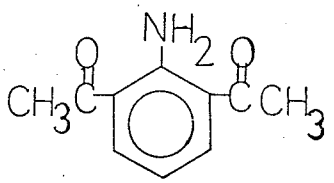
X = O
= S

On the basis of the investigations on the synthesis of benzo[c]-thiophene derivatives, any proposed scheme towards the successful synthesis of 7-acetyl-3-methylanthranil (199) should encompass the fact that it is advisable to develop the keto side chain before cyclising the five-member isoxazole ring. One reason is that the isoxazole ring

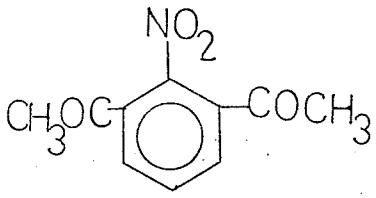
of the anthranil nucleus might cleave under strong oxidation or reduction conditions. Furthermore, similarly to benzo[c]thiophene direct acylation of the anthranil nucleus would probably give the wrong isomer --- the 5-acyl isomer instead of the 7-acyl derivative according to the MO calculations of Berthier et al.(108). Hence, the key towards the synthesis of 199 should involve the preparation of two possible precursors: 2,6-diacetylaniline (183) and 2,6-diacetylnitrobenzene (182).



199



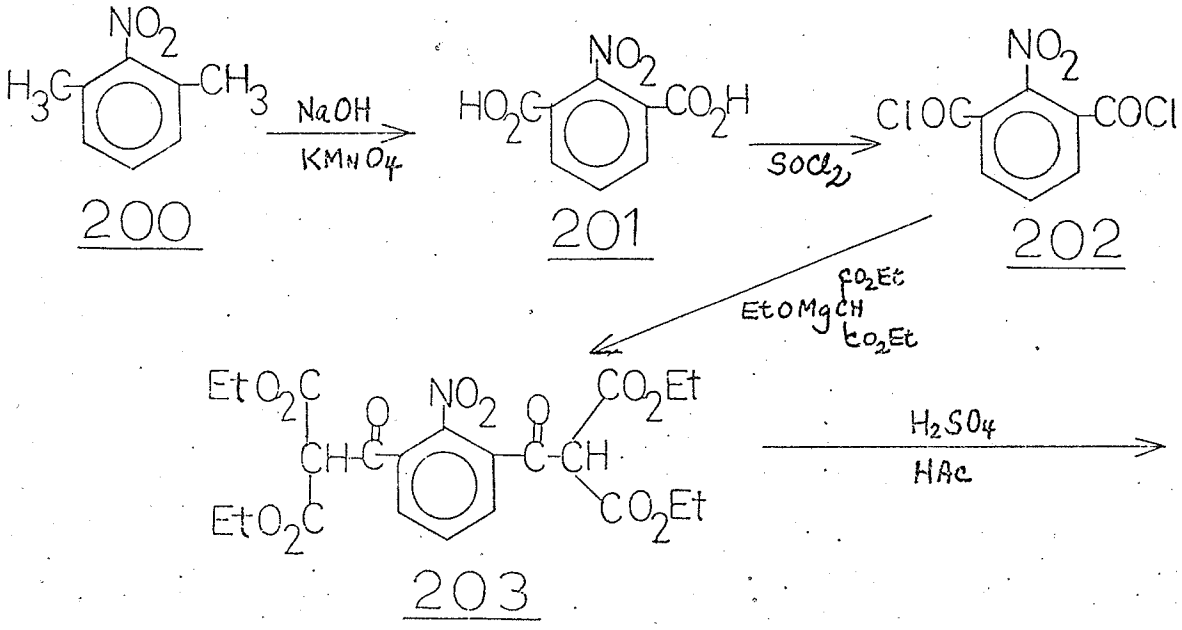
183



182

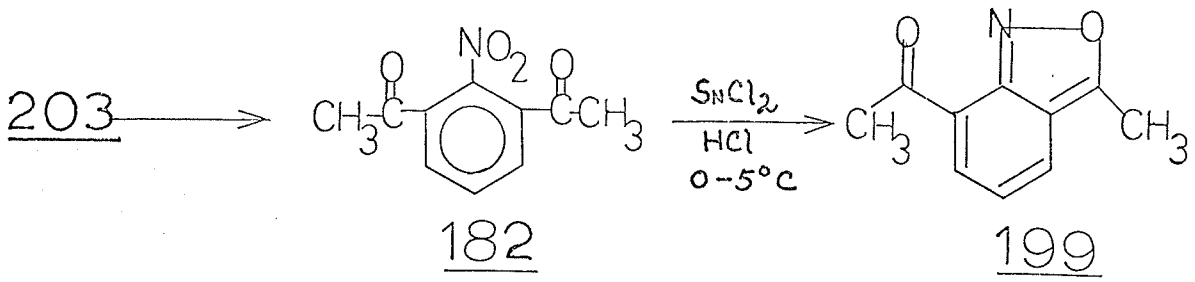
Either the oxidation of 183 or reduction of 182 should produce the product 199. Since the oxidation procedure has rarely been reported in the published literature and might give a lower yield plus many side products, the reduction route involving 182 as the precursor was chosen.

Scheme XVI



200 201 202 203

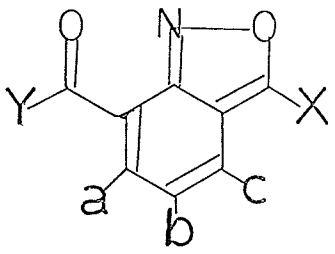
Scheme XVI continued



The complete synthesis of 7-acetyl-3-methylanthranil (199) is illustrated in Scheme XVI. As 2-nitro-m-xylene was readily available, it was used as starting material. Wohl et al. (109) had reported the preparation of 2-nitroisophthalic acid (201) in 52% yield by the oxidation of 2-nitro-m-xylene (200) with potassium permanganate. While essentially the same procedure was followed in the present work, a better yield (72%) of the acid 201 was obtained than that previously reported by using added alkali in the reaction. 2-Nitroisophthaloyl chloride (202) was prepared in quantitative yield by refluxing the acid 201 with excess thionyl chloride. The product was obtained as a white crystalline solid and the infrared (IR) and nuclear magnetic resonance (NMR) spectra were in agreement with the structure 202. 2-Nitroisophthaloyl chloride (202) reacted with ethyl ethoxymagnesium-malonate to provide the tetracarboxylic ester 203 as a viscous oil. This was not isolated but provided, after acid hydrolysis in aqueous sulfuric acid-acetic acid mixture followed by decarboxylation, 2,6-diacetylnitrobenzene (182) in 89% yield. This method, which was developed by Reynolds et al. (102), was reported to be the most satisfactory for the preparation of o-nitroacetophenones. 182 was characterized by elemental analysis, IR, and N.M.R. spectroscopy.

Stannous chloride was readily available, and was reported by previous workers to give a clean reduction product (47,110). Treatment of 182 with stannous chloride in concentrated hydrochloric acid at 5°C for 5 hours gave 7-acetyl-3-methylanthranil (199) as the major product. The product was isolated as colourless needles, and the infrared spectrum, elemental analysis, and N.M.R. spectrum were in agreement with the structure 199. 2,6-Diacetylaniline (183) was also isolated as a minor product after separation by thin-layer chromatography. Furthermore, if the reduction was performed at a higher temperature, the sole product obtained was 2,6-diacetylaniline (183).

NMR Spectroscopy of 7-acetyl-3-methylanthranil



$X = Y = CH_3$

$a = b = c = H$

199

Since 7-acetyl-3-methylanthranil (199) possesses similar electronic and structural features to some benzo-1,2-dithiolium derivatives of the thiathiophthene system (5), it is a suitable compound for NMR examination to test the validity of the three hypotheses, which have been proposed by previous workers, to explain the symmetry of the thiathiophthenes 1 (See Introduction, Part A). Because the central atom of 199 is incapable of valency shell expansion, any symmetry features exhibited by 199 would have to be due to single bond-no bond resonance or rapid tautomerism; and if these processes are important, the NMR spectrum should indicate the equivalence of the two methyl groups and an AB_2 type of pattern for the aromatic protons.

When the ^1H NMR spectrum of 199 was run in deuterochloroform solution at 0^o to 20^o, only one methyl peak was detected at 7.12 τ, indicating that the two methyl groups were equivalent. However, the three aromatic protons (a,b,c), whose chemical shifts gave signals from 1.95 to 3.13 τ suggested an ABX type of pattern. Furthermore, at other temperatures two peaks were observed even though they were only less than 0.06 τ apart at -60^oC as illustrated in Table I. This suggested that the equivalence of the two methyl groups was merely coincidental.

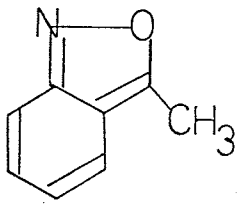
This became apparent when the NMR spectrum was performed in hexadeuterobenzene solution. Because of hexadeuterobenzene's aromatic solvent effects (111, 112, 113), the two methyl groups gave signals which were widely separated (0.77 τ) at probe temperature of 40^oC. Increasing the temperature by 160^o brought these two methyl singlets together by only 0.32 τ, indicating that there is a rather high energy barrier to interconversion of the two identical valency tautomers. Attempts were made to study the NMR of 199 at temperatures above 160^oC but heating the compound at higher temperatures caused decomposition.

Similar results were observed in perdeuterotoluene solution. At 40^oC the two methyl singlets were found to be 0.65 τ units apart. Increasing the temperature by 180^oC brought the two methyl singlets together by 0.37 τ, as shown in Table I. The aromatic protons are not included in Table I but complete spectra of 199 at various temperatures are given in the Experimental section. Under no circumstances were we able to obtain an AB_2 type of pattern from protons on the aromatic ring.

Even when the most extreme case was applied, that of heating the solid melt at 160°C, only an ABX type of pattern was evident for the aromatic protons even though the methyl singlets did coincide perfectly at 7.75 τ.

Table I seems to indicate a linear relationship between temperature and the distance between the two methyl singlets in a plot of T vs (X-Y). As the temperature increases, the methyl signals move closer together, and the aromatic protons tend towards an AB_2 type pattern. Decreasing the temperature induces the two methyl signals to move farther apart and gives rise to a more perfect ABX pattern.

The peaks at higher τ values in deuterobenzene and toluene were assigned to the methyl groups on the heterocyclic ring since an NMR spectrum of 3-methylanthranil (66) in hexadeuterobenzene gave 7.74 τ (3H singlet, methyl group) and 3.55 to 2.42 τ (4H bands, protons on the aromatic ring). The bands at lower τ values were assigned to the acetyl methyl groups because aromatic acetyl groups usually give a signal of 7.10 to 7.35 τ. Hence from Table I the chemical shifts of X refer to the methyl groups on the heterocyclic ring whereas the Y values refer to the acetyl methyls.

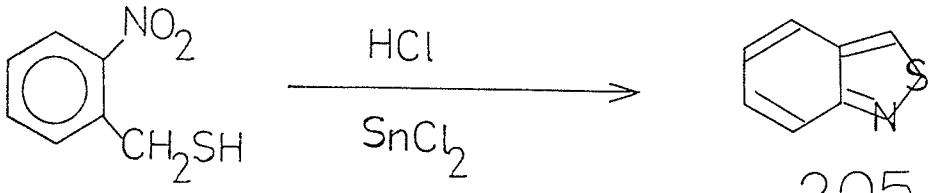


66

Infrared Spectral Properties of 3-Methyl-7-acetylanthranil

The infrared spectrum of 199 was studied at 80°C and -85°C. If there is any interaction between the acetyl oxygen and the nitrogen of 199, i.e.single bond-no bond resonance effect analogous to the thiathiophthenes 1 to give a molecule possessing real or apparent symmetry, the bond lengths and character of the anthranil nucleus would be affected. Hence, the C=O stretch peak of 199 should show a change of either intensity or frequency with temperature. However, when the experiment was performed at 80°C and -85°C, no change in intensity or frequency was observed for the carbonyl peak of 199. This observation reinforces the NMR data which suggests that 199 probably undergoes valency-tautomerism; but this phenomenon is such a slow process that it can not be detected in the NMR time scale. This will be more evident after chemical properties of 199 have been dealt with.

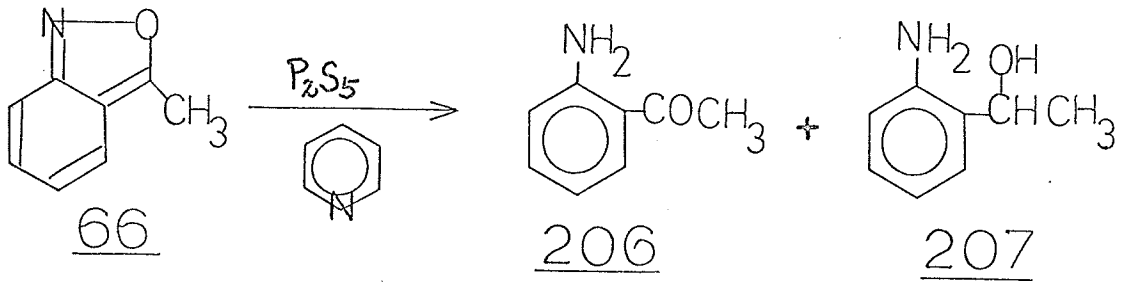
Discussion on the Preparation of 7-acetyl-3-methylthioanthranil



204 205

In 1896 Gabriel et al. (114) had reported the synthesis of thioanthranil (205) by the reduction of o-nitrobenzylmercaptan (204) with stannous chloride in concentrated hydrochloric acid solution. Attempts to prepare 205 by the direct sulfurisation of anthranil with phosphorus pentasulfide failed. When the reaction was performed in carbon disulfide, the starting material, anthranil was recovered unchanged.

Attempted sulfurisation in pyridine caused extensive decomposition. Similar results were observed when 3-methylanthranil (66) was treated under the above conditions. Treating 66 with phosphorus pentasulfide in pyridine for 4 hours resulted in the cleavage of the isoxazole ring of 66. Both I.R. and NMR data suggested that the two major products isolated contained structures similar to 206 and 207.

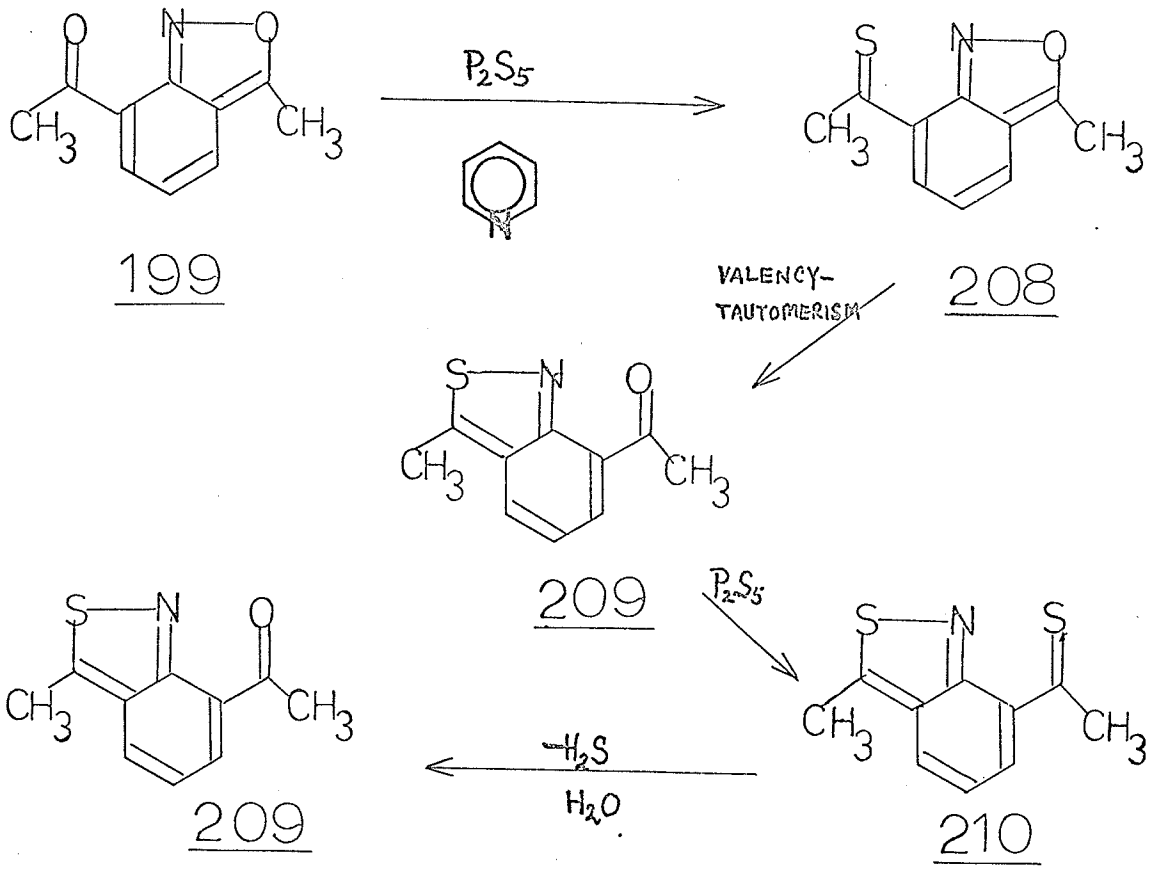


66 206 207

However, when the sulfurisation reaction was extended to include 7-acetyl-3-methylanthranil (199), a different result was noted. Treatment of 199 with phosphorus pentasulfide in either carbon disulfide or pyridine gave another compound in which one oxygen had been replaced with sulfur as confirmed by elemental analysis. Examination of the infrared spectrum showed a strong carbonyl absorption at 1725 cm^{-1}, indicating that the compound is probably 7-acetyl-3-methylthioanthranil (209) rather than the isomeric 7-thioacetyl-3-methylanthranil (208). The isolation of this can be rationalised by initial formation of the thioacetyl compound 208 which under the conditions of the reaction undergoes valency-tautomerism to give the thioanthranil 209. The thioanthranil 209 should be further sulfurised to the corresponding thione 210 since the reaction was performed in excess phosphorus pentasulfide; but this thione was probably readily hydrolysed back to the thioanthranil 209 during the isolation procedure, which involved washing the organic

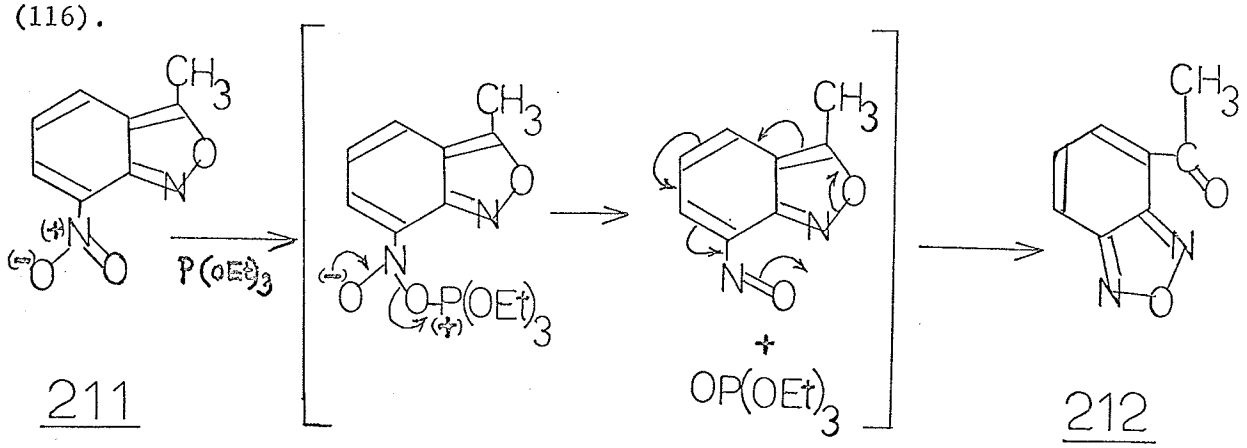
layer with water. This seems reasonable since thiones are generally not stable compounds; certain ones are reported to undergo such hydrolyses as described above (115). The sequence of reactions described above are outlined in Scheme XVII.

Scheme XVII



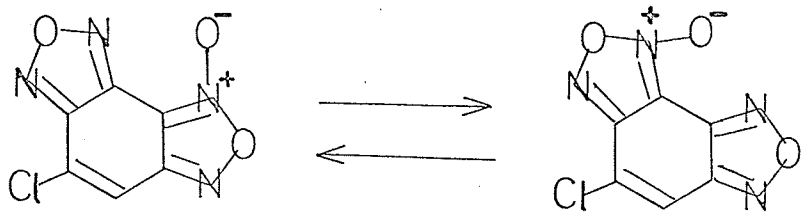
Although NMR evidence indicates that such tautomeric equilibrium as described above is not rapid enough to be detected on the NMR time scale at ordinary temperatures, this is not inconsistent with interconversion under the conditions of the chemical reaction. Evidence to support this is that the anthranils above without substituents capable of interacting with the heterocyclic ring were not sulfurised under the conditions used, eg., compound 66 gave degradation products.

Such interconversions are not uncommon. One related reaction is the conversion of a 2,1-benzisoxazole 211 into an acetylfuroxan 212 (116).



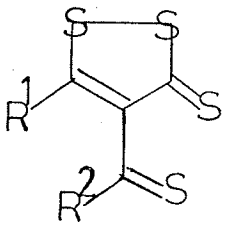
211 212

Other examples are some furoxan interconversions introduced by Boulton et al. in 1967 (117). These workers investigated the synthesis and valency tautomerism of 6- and 7-chlorofurazanobenzofuroxan (213). Similarly to the anthranil 199, they found that attempts to interconvert the two isomers thermally were unsuccessful, and that NMR data showed a rather high energy barrier to interconversion of the two identical valency tautomers. The NMR spectrum of the chlorofurazanobenzofuroxan 213 showed two singlets at 34°C in diglyme solution, indicating that the compound existed as a mixture of two tautomers.



213a 213b

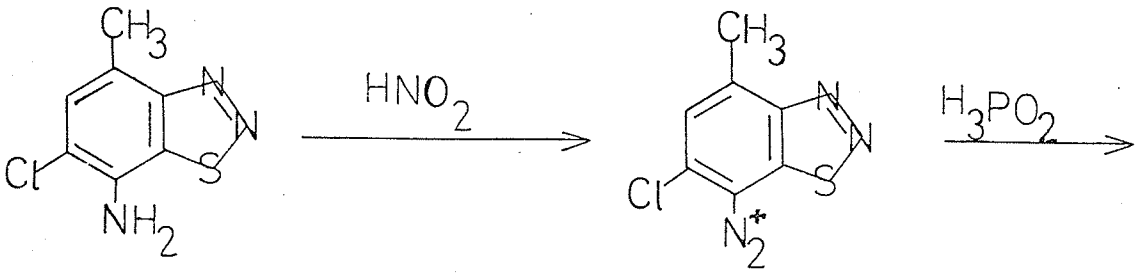
4-Thioacyl-1,2-dithiole-3-thiones 214 have been shown to undergo a similar type of tautomerism by Leaver et al. (5). The NMR spectrum of the 4-thio-p-tolucyl-5-p-tolyl compound 214a contained two methyl singlets, thus showing that the two aryl groups are not rendered equivalent by single bond-no bond resonance. Attempts to prepare the 4-thio-p-toluoyl-5-phenyl 214b and 4-thiobenzoyl-5-p-tolyl compound 214c gave identical mixtures of the two isomeric thioacyl compounds, as shown by the presence of two methyl signals in their NMR spectra. These workers postulated that isomeric thioacyl compounds (214; $R^1 \neq R^2$) are interconvertible but that the tautomeric equilibrium is not rapidly established (on the NMR time-scale) at room temperature.



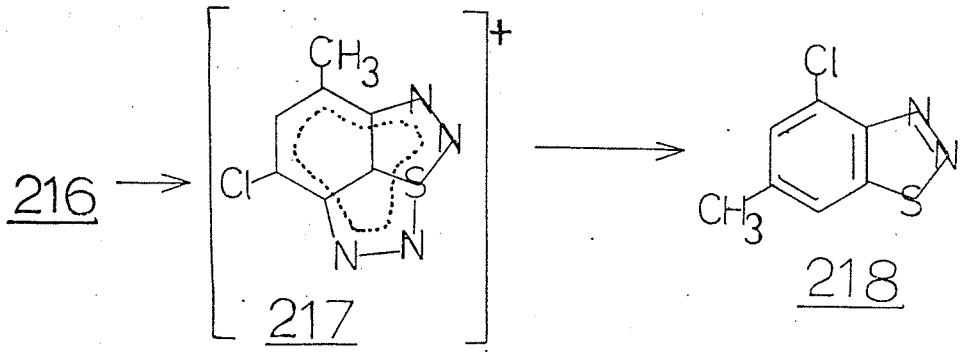
214

	R^1	R^2
(a)	p-MeC_6H_4	p-MeC_6H_4
(b)	Ph	p-MeC_6H_4
(c)	p-MeC_6H_4	Ph

A more recent illustration of such interconversions analogous to the formation of the thioanthranil 209 involved the formation of some rearranged products from a substituted 1,2,3-benzothiadiazole diazonium salt 216.



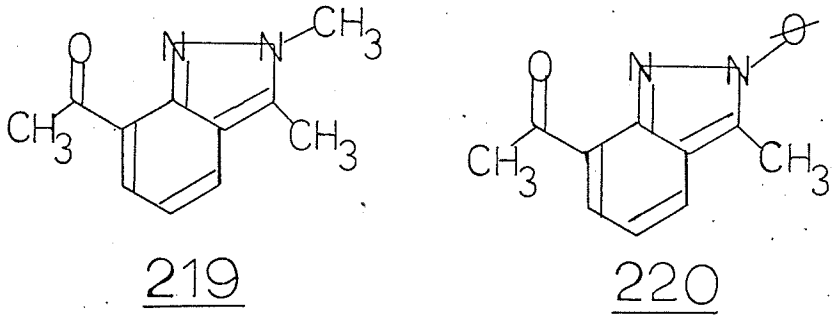
215 216



216 217 218

Haddock (118) discovered that diazotisation of the amino compound 215 followed by removal of the diazonium group of 216 by hypophosphorous acid led to the rearranged benzothiadiazole 218 as the major product. Even though NMR evidence failed to detect the existence of the intermediate 217 these workers postulated that the diazonium salt 216 on contact with hypophosphorous acid undergoes valency tautomerism to the rearranged product 218 by way of the intermediate 217.

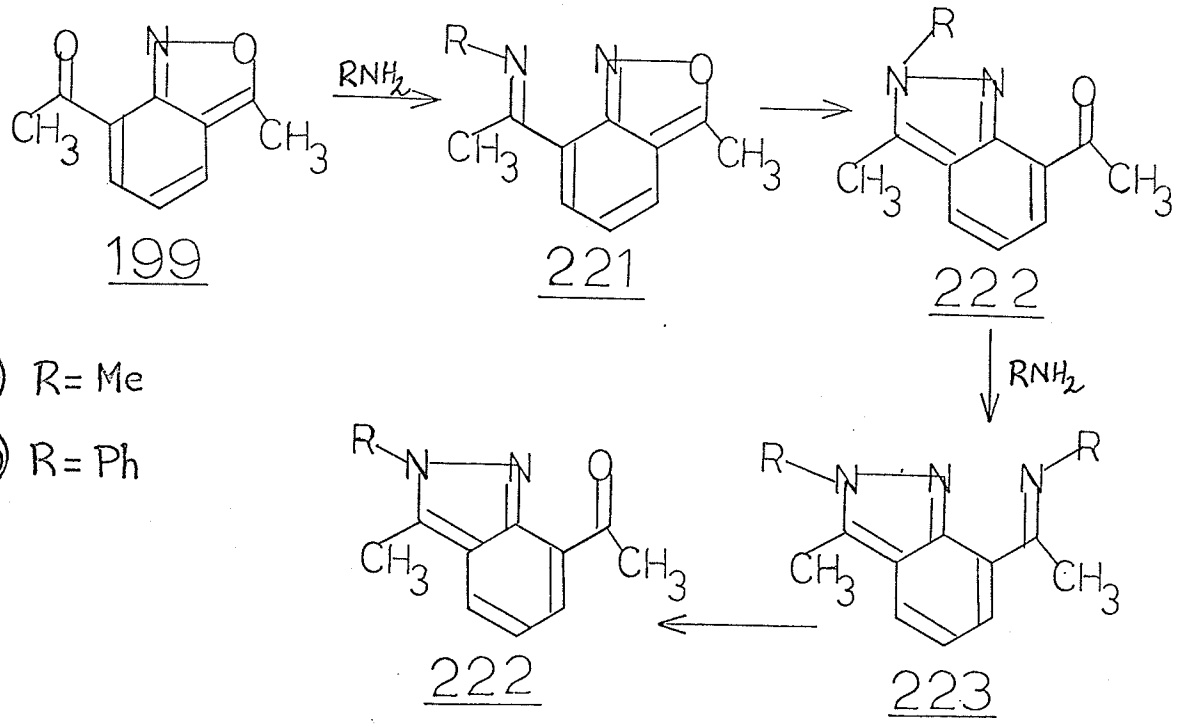
Reaction of 7-acetyl-3-methylanthranil with methylamine and aniline



219 220

Treatment of 7-acetyl-3-methylanthranil (199) with methylamine and aniline provided compounds in which one oxygen had been replaced by a nitrogen as confirmed by elemental analysis. Since these compounds exhibited C=O absorption in the infrared, they were probably benzopyrazoles 219 and 220 respectively, not the corresponding imines 221 (R=Me or Ph). The sequence of reactions resulting in the formation of benzopyrazoles are outlined in Scheme XVIII.

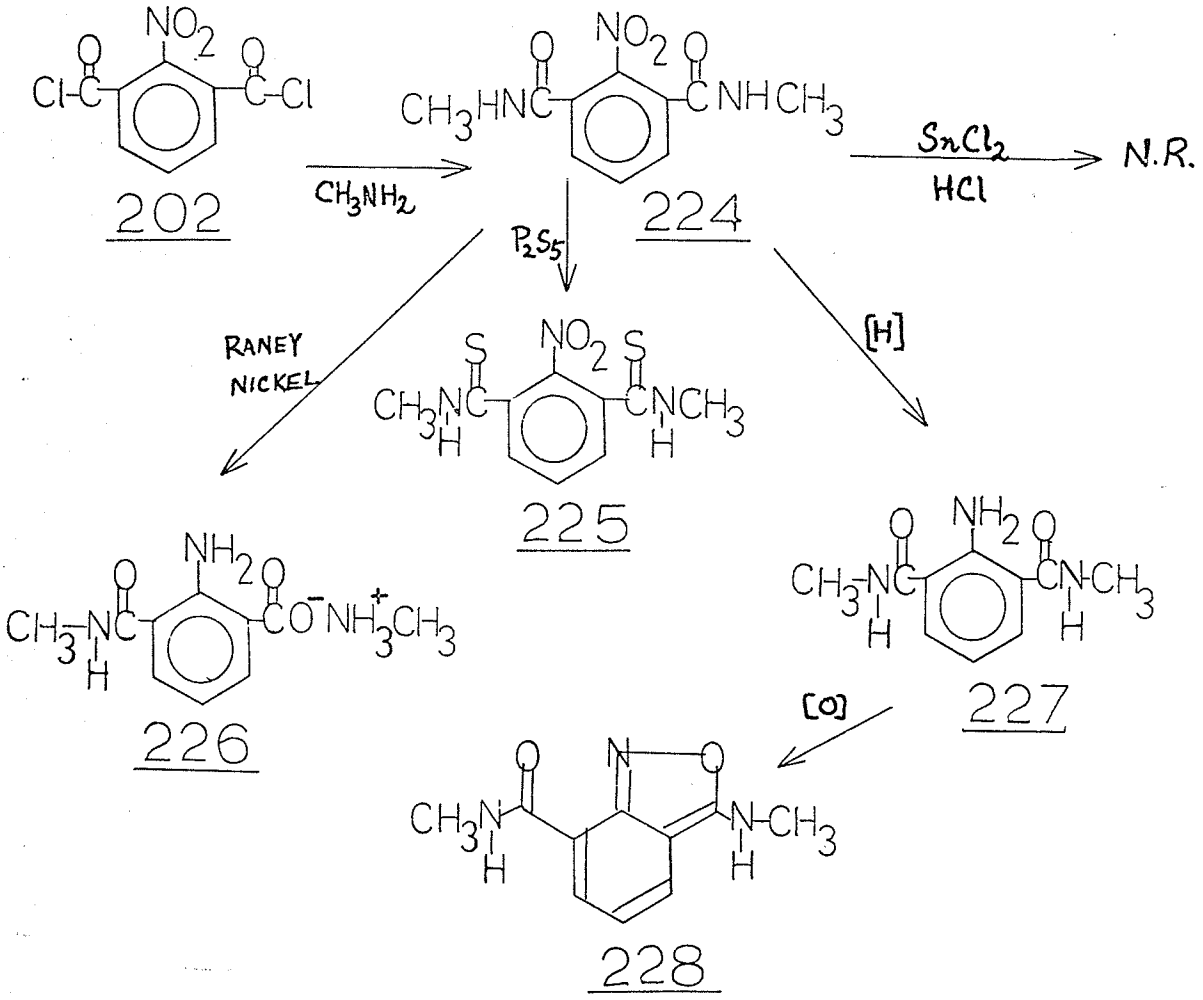
Scheme XVIII



Similarly to the sulfurisation above, reacting 199 with a primary amine probably gave the imine 221 as the initial step. Then the imine 221 underwent valency tautomerism to give the acetylbenzopyrazole 222 as in the case of the thioanthranils. Since the reaction was performed in an excess of amine, 222 might also have reacted with more amine to produce the iminobenzopyrazole 223. However, the imine 223 would be expected to hydrolyse back to the corresponding ketone 222 just as in the case of the thione 210. The fact that these compounds show a strong C=O absorption in the infrared indicates that they exist as acetylbenzopyrazoles rather than the isomeric imino-2,1-benzisoxazoles. It also seems likely from the ready hydrolyses of the thione 210 and the imines 223a,b that such compounds are unlikely to possess resonance stabilization of the single bond-no bond type. If such were the case, they would be expected to be at least capable of isolation.

Attempted Synthesis of a Derivative of 7-Acetyl-3-methyl-anthranil

Scheme XIX



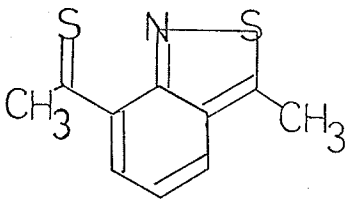
Since the starting material from Scheme XVI was readily available, it seemed appropriate to attempt to synthesize another derivative of 7-acetyl-3-methylanthranil (199) for NMR study using 2-nitroisophthaloyl chloride (202) as starting material. As described in Scheme XIX, 2-nitroisophthaloyl chloride reacted with methylamine to give N,N^{1}-dimethyl-2-nitroisophthalamide (224) in 61% yield. This was readily converted into the bis-thioamide 225, but attempts to cyclise 225 into the corres-

ponding thioanthranil or thioanthranil thione failed. The successful synthesis of the anthranil 199 from its nitro precursor 182 by stannous chloride-hydrochloric acid reduction suggested that similar treatment of 224 would produce the anthranil 228. This failed. Examination of the reduction products by t.l.c. gave only ill-defined bands which could not be properly separated. Using Raney-Nickel as reducing agent proved unproductive also. The product isolated readily dissolved in water and effervesced on treatment with sodium bicarbonate. This product was probably compound 226 in which one amide function had been hydrolysed. The synthetic route via the aminodiamide 227 was attempted, but unexpected difficulties arose in regard to the reduction of the nitro group.

Conclusion

On the basis of the model systems studied in this work, it would appear that two of the three hypotheses, which had been postulated by previous investigators to explain the unique characteristics of the thiathiophthenes, are unsatisfactory in the explanation of these facts. While the chemical properties of 7-acetyl-3-methylanthranil (199) indicate that it undergoes valency-tautomerism, spectroscopic studies indicate that the the tautomeric equilibrium is not rapid enough to be detected in the NMR time-scale at room temperature. The energy barrier is so high that even heating the compound up to 160^{o}C fails to interconvert the two identical valency tautomers at a rate faster than the NMR time-scale. This failure to demonstrate suitable symmetry in 199 suggests that simple valency tautomerism is inadequate in explaining the special properties of symmetry exhibited by the thiathiophthenes.

This leads to the single bond-no bond resonance hypothesis as a possible explanation. However, doubt is also cast on the existence of this phenomenon in the thiathiophthene system. The fact that the attempted syntheses of the thioanthranil thione 210 and the iminobenzopyrazole 223 were unsuccessful practically rules out the single bond-no bond resonance hypothesis as a possible explanation for the special properties of the thiathiophthenes.



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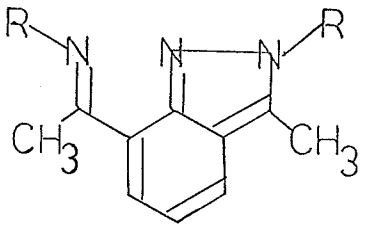
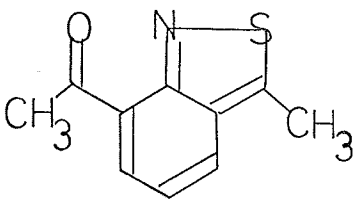


223

If this hypothesis is valid, then 210 and 223 should be stable compounds at room temperature. However, both compounds hydrolyse back to the corresponding ketones 209 and 222 respectively.



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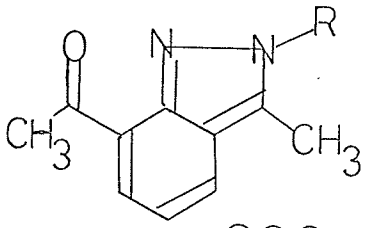
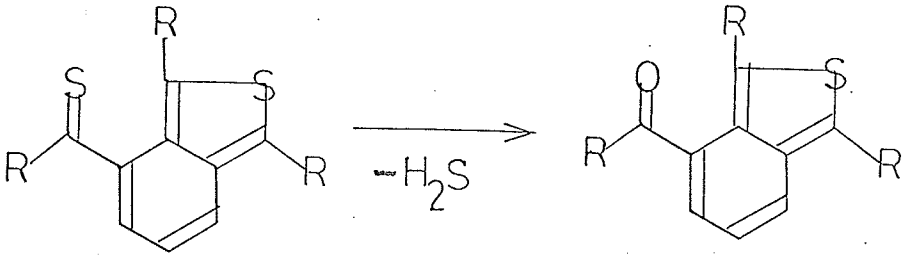


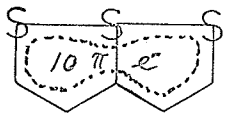
222



25 229

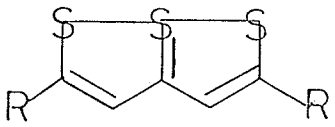
Likewise, even if the preparation of 4-thioacylbenzo[c]thiophene 25 had been successful, it would probably readily hydrolyse back to the ketone 229 similarly to compounds 210 and 223. Compound 25 would only be stable if single bond-no bond resonance occurred. Likewise, doubt is also cast on the stability of the ketone 229 especially if positions 1 and 3 of 229 are not phenyl-substituted. An electron withdrawing group such as an acyl group would normally tend to destabilize the benzo[c]thiophene nucleus. Even if the synthesis of the 1,2,3-triacylbenzene precursor had succeeded, the subsequent sulfurisation step would probably lead to 229, not 25. Many of the difficulties encountered in the synthesis of the benzo[c]thiophene model system can be traced directly to the attempt to attach an unstable side chain to an unstable nucleus. In view of the successful synthesis of the anthranil model system, further examination of the benzo[c]thiophene system appears valueless. However, some of the reactions attempted in the investigation of the benzo[c]thiophene system proved useful in the synthesis of the anthranil model system.

Thus, the theories involving d-orbitals appear to provide the most satisfactory explanation of the special properties of the thiathiophthenes. Invoking the use of sulfur d-orbitals in the bonding of the central sulfur atom giving tetravalent sulfur structures was first proposed by Maeda (11) and developed by Gleiter et al. (12). The MO calculations of Gleiter et al. showed that an electron-rich 3-center bond involving three second row elements could be further stabilized when all three atoms are incorporated in an aromatic 10π-electron system 230.



230

Furthermore, their M.O. calculations showed a clear preference for an unsymmetrical structure when the thiathiophthene system did not utilize 3d orbitals, and a symmetrical structure when 3d orbitals were included. Hence, the thiathiophthenes are better represented by the bicyclic formula 20, which includes a tetravalent sulfur structure, rather than the classical thione formula 1.



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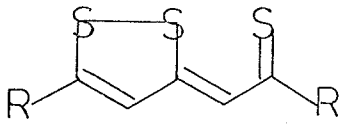
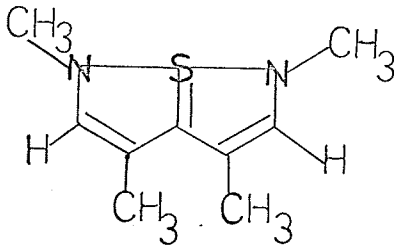
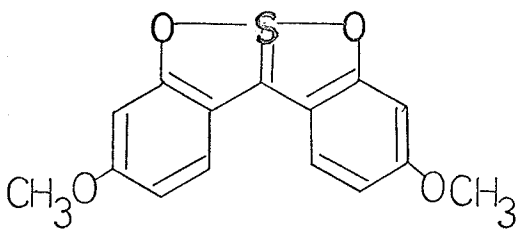


1

The recent acceptance of the bicyclic formula 20 means that the classical nomenclature, "thiathiophthene" is no longer appropriate. The name, 1,6,6,aS(IV)-trithiapentalene, first introduced by Lozac'h and his co-workers (119) is superior to the classical name. Similarly Reid's isothiazole derivative 231 (120) and Pomerantz's benzo-1,2-thioxole derivative 232 (121) are in fact best represented by structures which include a tetravalent sulfur rather than the classical formulae.



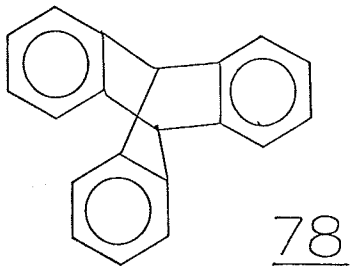
231



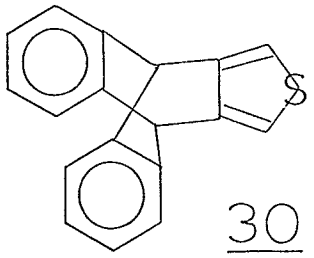
232

PART C Discussion on Heterocyclic Analogues of Triptycene

In connection with the above study on benzo [c] thiophenes, the preparation of some triptycene analogues, especially the thiophene derivatives 30 which contain the benzo [c] thiophene skeleton as an element of structure, was of interest; and it seemed appropriate to investigate the synthesis of some examples of this. Bartlett et al. (61) synthesized the rigid "propeller-like" hydrocarbon, triptycene (78), in 1942. However, only a few heterocyclic analogues, in which one or more of the ortho linked benzene rings of triptycene are replaced by heterocyclic systems, have been reported in the published literature.

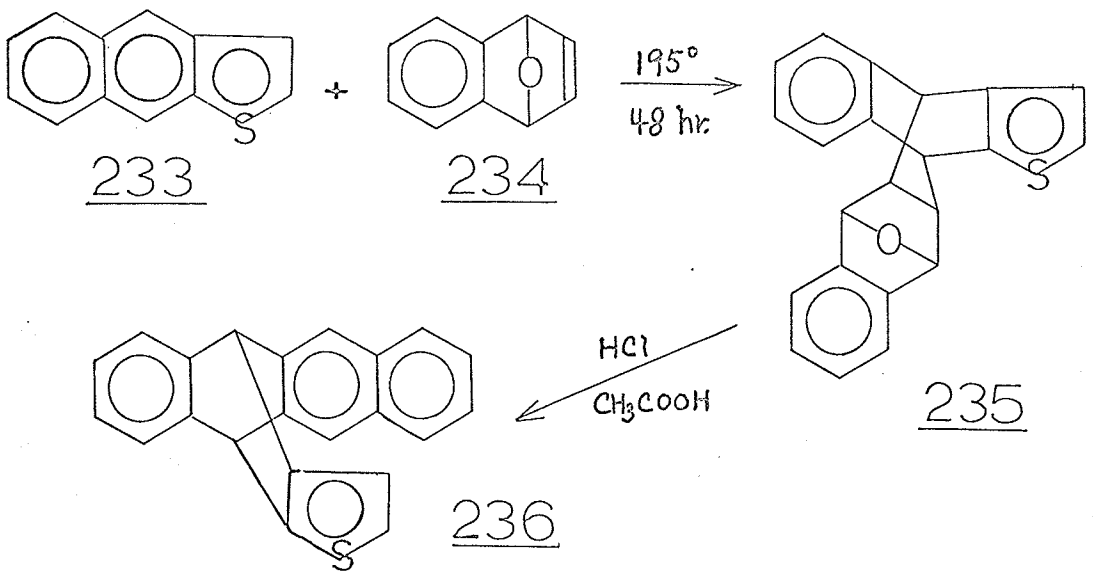


78



30

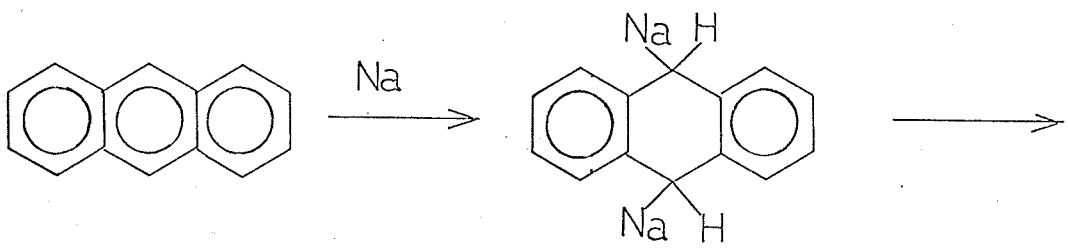
Wittig et al. (78) reported the synthesis of azatriptycene (97) by treating 9-(o-chlorophenyl)-9,10-dihydroacridine (96) with KNH_2 in liquid ammonia. Some 3,4-furano 102 and 4,5-pyridazino 103 analogues have been prepared via the dibenzoylethylene adducts of anthracene (79), (See Introduction; Part D). More recently Wynberg et al. (122) have described the synthesis of a thiophene analogue 236 by Diels-Alder type addition of 1,4-dihydro-1,4-epoxynaphthalene (234) to naphtho [2,3b] thiophene (233) followed by acid-catalysed dehydration of the adduct 235.



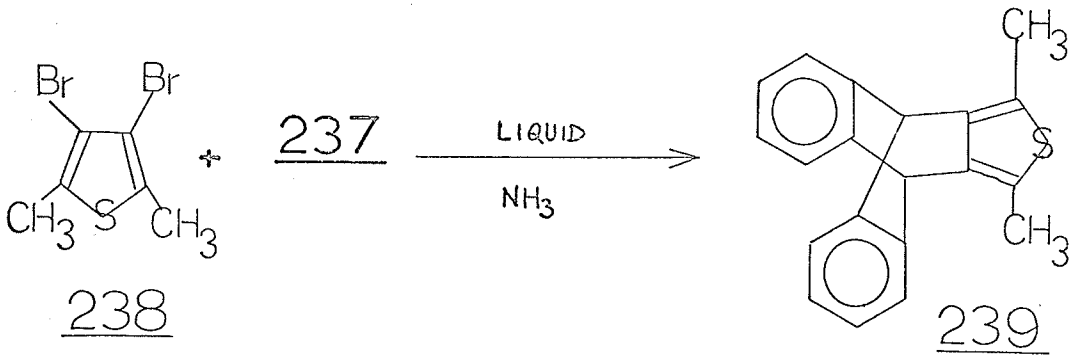
233 234 235 236

Although a few nitrogen analogues have been made to demonstrate that the preparation of these thiophene analogues could be extended to include the nitrogen analogues if desired, the major emphasis was on the thiophene analogues containing the benzo [c] thiophene skeleton.

The initial preparation of a thiophene analogue of triptycene was attempted via the classical route, using 9,10-disodioanthracene (237) as the starting material. Treatment of 237 and 2,5-dimethyl-3, 4-dibromothiophene (238) was expected to yield 239. This procedure failed.



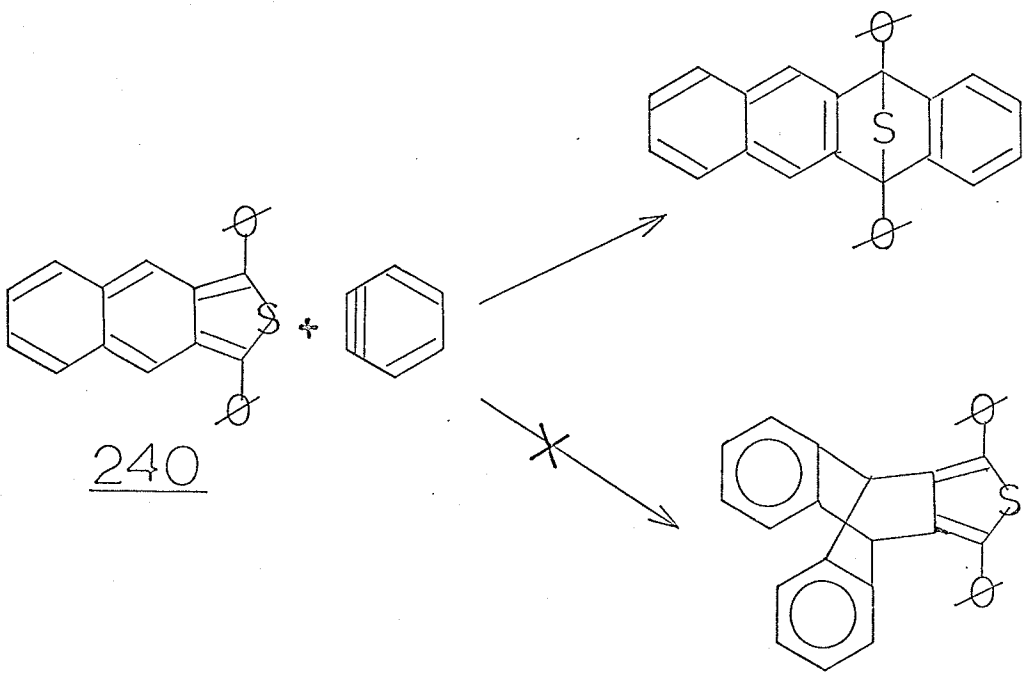
237



238 239

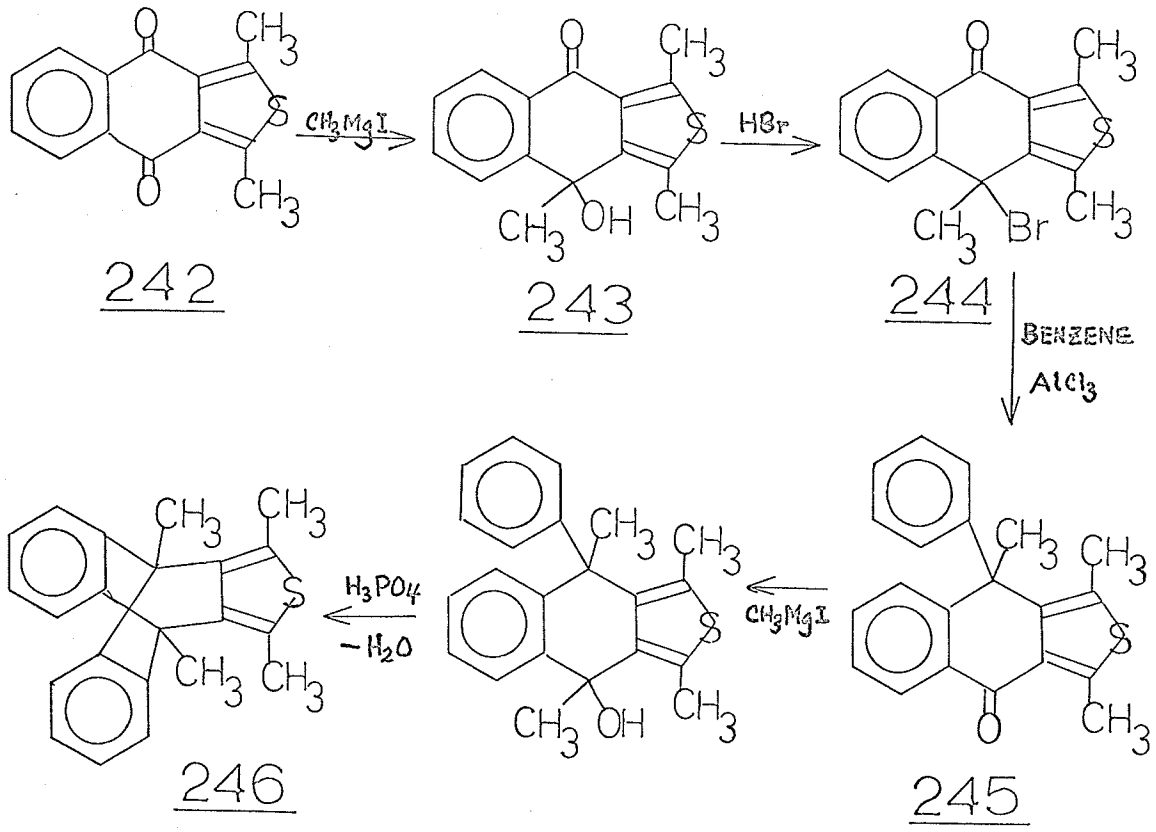
As will be evident in a later discussion, the synthesis of 239 was unsuccessful via a Diels-Alder method.

Another attempt by allowing benzyne to react with 1,3-diphenylnaphtho[2,3-c]thiophene (240) was tried but soon abandoned due to the recent publication of Cava (123), who demonstrated that dienophiles will add to positions 1 and 3 of 240 instead of the desired positions 4 and 9 which would give 241. As will be seen below, another method of preparation of 241 was successful.



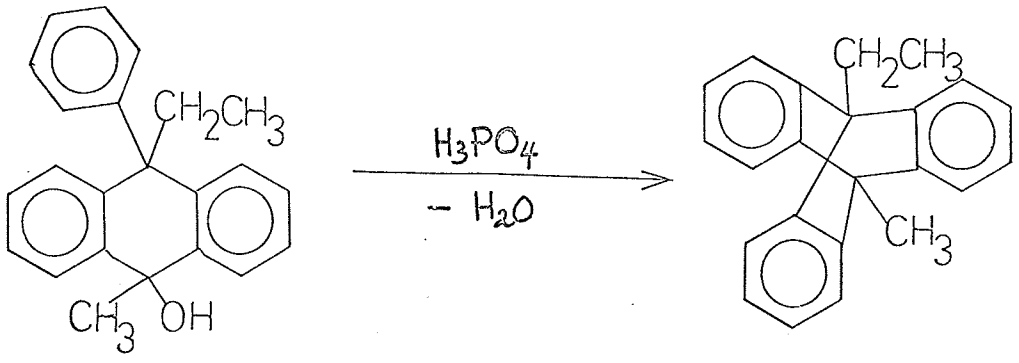
240 241

Scheme XX



242 243 244 245 246

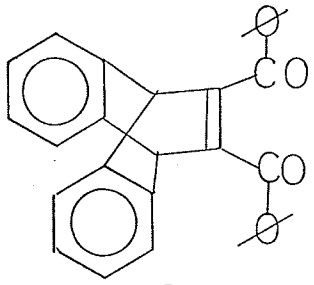
Walborsky et al. (124) reported the preparation of the triptycene 248 by the action of phosphoric acid on 247.



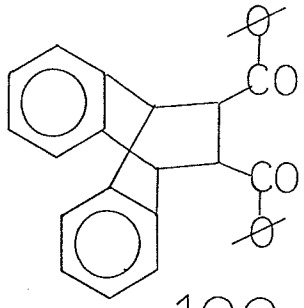
247 248

By an analogous procedure, an attempt was made to obtain the triptycene analogue 246 starting with the quinone 242 as illustrated in Scheme XX. The starting material 242 was made essentially according to the work of Steinkopf et al. (125). Treatment of the quinone 242 with one equivalent of methylmagnesium iodide produced 243 in 18% yield. When the compound 243 was boiled with hydrobromic acid, the subsequent bromide 244 was obtained as a dark oil which could not be made to crystallize. The Friedel-Crafts step involving the bromo compound 244 and benzene failed to yield the product 245. Consequently, this scheme had to be abandoned.

Careful examination of the literature has revealed that the most efficient preparation of triptycene and substituted triptycenes have been limited to the use of Diels-Alder type additions using benzyne intermediates as the dienophiles and anthracenes as the dienes. Consequently, analogous procedures involving anthracene derivatives as dienes and suitable ketodienophiles such as dibenzoylethylene, which can be cyclised to form heterocycles, were investigated as possible routes to the formation of the triptycene analogues. Even though anthracenes were found to be poor dienes in Diels-Alder additions in comparison to aliphatic dienes such as 1,3-butadiene (77), Baumgartner et al. (79) did obtain acceptable yields of the Diels-Alder adducts, dibenzoyldibenzo[2,2,2]-bicycloocta-triene (99) and dibenzoyldibenzo[2,2,2]-bicyclooctadiene (100), by fusing dibenzoylacetylene and dibenzoylethylene, respectively, with anthracene at 200°C.

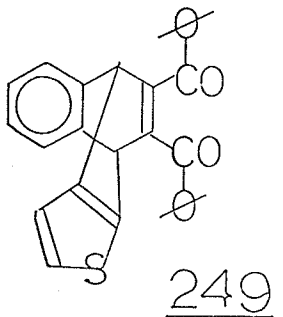


99

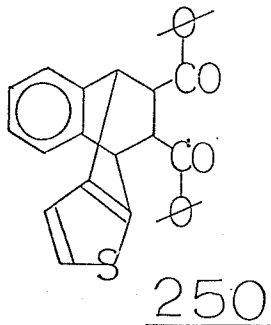


100

In the present investigation on benzo[c]thiophenes, an ortho diketone, o-dibenzoylbenzene (43), was discovered to undergo ring cyclisation readily on treatment with phosphorus pentasulfide to produce benzo[c]thiophene in excellent yield. White and Mann (126) extended this procedure to include the benzo[c]furans and benzo[c]-pyrroles on treating o-dibenzoylbenzene with acetic anhydride and ammonium acetate, respectively. Hence similar ring cyclisation of the anthracene adducts 99 and 100 would produce heterocyclic analogues of triptycene in which one ortho linked benzene ring has been replaced by a five member heterocyclic system. Furthermore, preparation of analogues in which two ortho linked benzene rings are replaced by heterocyclic systems should also be feasible by ring cyclisation of the naphtho[2,3-b]thiophene adducts 249 and 250 if these adducts can be obtained in acceptable yields.

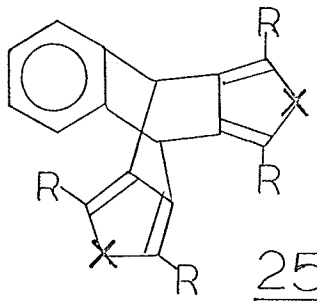


249



250

Unfortunately, dienophiles will add to positions 1 and 3 of naphtho-[2,3-c]thiophene (240) instead of positions 4 and 9 (123), which would have permitted the synthesis of more symmetrical analogues such as 251.



251

X = O
= NH
= S

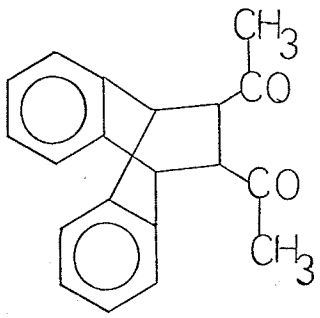
Thus, the preparation of these heterocyclic analogues of triptycene involves essentially two stages:

(a) Diels-Alder type additions to yield substituted bicyclooctatrienes and bicyclooctadienes

(b) Ring closure of these adducts to give derivatives of benzenonaphtho[c]thiophenes, which are thiophene analogues of triptycene.

Preparation of Substituted Bicyclooctadienes and Bicyclooctatrienes

Dibenzoylacetylene, trans-dibenzoylethylene, and diacetylethylene reacted with a variety of substituted anthracenes to give the corresponding dibenzoyldibenzo[2,2,2]bicyclooctatriene (99), dibenzoyldibenzo[2,2,2]-bicyclooctadiene (100), and diacetyldibenzo[2,2,2]bicyclooctadiene (252), respectively.



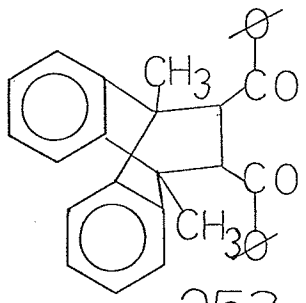
252

The above dienophiles, which were chosen to react with a variety of substituted anthracenes, are readily prepared (96,127) and are highly reactive dienophiles (79,126,128,129).

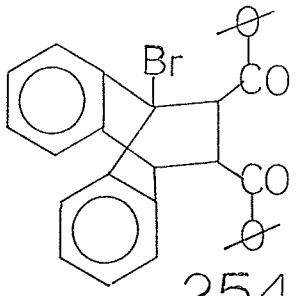
(1) Dibenzoylethylene

Three procedures are applicable in the preparation of Diels-Alder adducts 100 from substituted anthracenes and dibenzoylethylene. In accordance with Diels and Alder's method (76), dibenzoyldibenzo [2,2,2]-bicyclooctadiene (100) can be obtained by fusing a mixture of anthracene and trans—— or cis——dibenzoylethylene just below 260°C. The adduct 100 can also be obtained by heating a solution of the two compounds in a suitable solvent (130). The third method involves catalysis by strong Lewis acids such as aluminum chloride or stannic chloride. In the present investigation, the second method of performing the Diels-Alder addition in a suitable solvent was employed in a majority of cases, because this procedure usually gives a clean reaction product and a more acceptable yield.

On heating a mixture of equimolar proportions of dibenzoylethylene and anthracene in xylene at the boiling point of the solution for 24 hours, a 56% yield of the adduct 100 was obtained. Heating equimolar proportions of 9,10-dimethylanthracene and dibenzoylethylene in ethanol for eight hours yielded the adduct 253. Similarly, 9-methylanthracene, 2-methylanthracene, 9-methoxyanthracene, and naphthacene reacted readily to give the adducts in fair to excellent yields. A summary of the dibenzoylethylene adducts is outlined in Table II.



253



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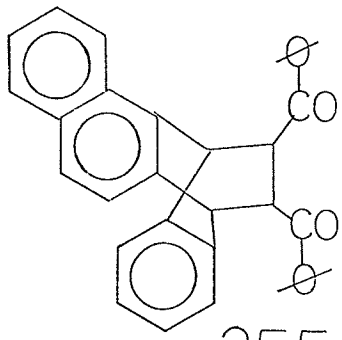


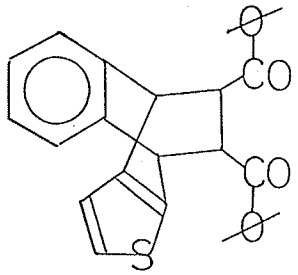
255

Attempts to prepare the adduct 255 by heating equimolar quantities of 1,2-benzanthracene and dibenzoylethylene in a variety of solvents such as benzene, toluene, and xylene were unsuccessful. Each time starting materials were recovered unchanged. Solvents whose boiling points are higher than that of xylene were not used since overheating usually results in retro Diels-Alder reactions, e.g., the reverse reaction in which the adducts are broken down into the diene and dienophile (77). However, a small yield (19%) of the adduct 255 was isolated when the reaction was performed with a Lewis acid catalyst, e.g., anhydrous aluminum chloride, at room temperature.

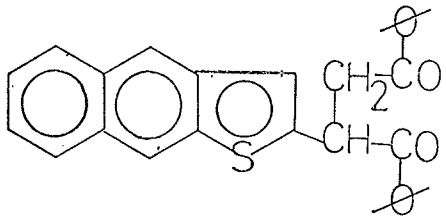
When excess quantities of the dienophile and 9-bromoanthracene were refluxed in toluene for 48 hours, only a small yield (12%) of the adduct 254 was isolated. Utilizing more vigorous reaction conditions did not increase the yield. The low yield of the adduct 254 may be due to the electron withdrawing character of the bromine which deactivates position 9 of 9-bromoanthracene .

According to the localization energy calculations of Dewar (131) and Brown (132), the Diels-Alder reactivity of naphtho [2,3-b] thiophene (233) is a great deal less than that of anthracene. Hence, it was not surprising to observe that when the reaction was carried out in boiling xylene for 48 hours, only an extremely poor yield of the adduct 250

was detected (2½%). Catalysis by a Lewis acid did not give the expected adduct 250, but a yellow non-crystalline oil which was characterized to have a molecular structure similar to 256 by NMR and mass spectral evidence. Although Carruthers (133) did obtain a small yield of the maleic anhydride adduct with naphtho [2,3-b] thiophene under forcing conditions, similar treatment using dibenzoylethylene as the dienophile gave only coloured intermediates, but no adduct 250 could be isolated. Even when a large excess of dibenzoylethylene and the no-solvent fusion technique were used the Diels-Alder reaction did not work.



250



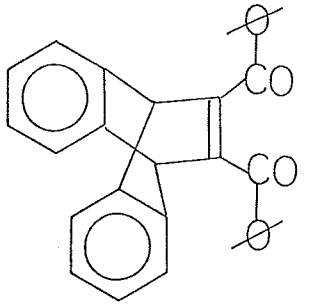
256

The presence of methyl groups in the meso-positions of anthracene greatly facilitated the Diels-Alder reactions. Thus, 9-methylanthracene reacted much faster with dibenzoylethylene than anthracene. Furthermore, the Diels-Alder addition between dibenzoylethylene and 9,10-dimethylanthracene was so efficient that the yield was found to be almost quantitative. On the other hand, the presence of phenyl groups in the meso-positions slowed up the reaction enormously. As a result, even after days of boiling in xylene no adduct between dibenzoylethylene and 9-phenylanthracene or 9,10-diphenylanthracene was detected. The reaction was also slow when benzo groups are present in the 1,2- and 5,6- positions of anthracene. Cook (134) reported that the meso additive

power of 1,2,5,6-dibenzanthracene is less than that of anthracene, and correlated this property with the greater aromaticity of the anthracene molecule containing benzene rings condensed in the angular positions. 2,3-Benzanthracenes or tetracenes, on the other hand, were found to be more reactive than anthracene and 1,2- and 5,6-benzanthracenes. This indicates that anthracenes with linearly-fused benzo rings contain more diene character than angularly-fused anthracenes, and thus the former should be more reactive than the latter. Acridine was also treated with dibenzoylethylene in an attempt to make a precursor of an azatriptycene, but no adduct could be isolated. This may be due to the fact that a nitrogen replacing a carbon at position-9 of anthracene has the same effect as an electron withdrawing 9-substituent, which increases the aromaticity and decreases the diene character of the molecule.

(2) Dibenzoylacetylene

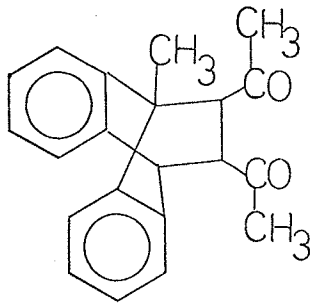
Likewise, dibenzoylacetylene reacted with anthracenes to give dibenzoyldibenzo [2,2,2] bicyclooctatrienes (99). Generally, yields of these were better, in accord with the enhanced dienophilic properties compared to dibenzoylethylene. As will be evident in a later discussion, since these octatrienes did not prove to be suitable precursors of thiophene analogues of triptycene, the preparation of some substituted octatrienes was limited to the addition involving a few reactive anthracenes and dibenzoylacetylene, as summarized in Table II.



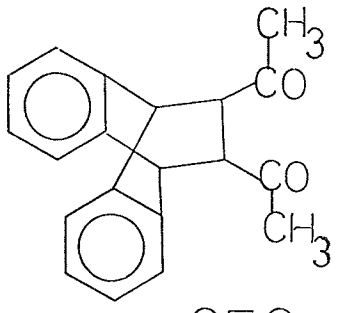
99

(3) Diacetylethylene

Attempts were also made to produce analogues without the bulky phenylsubstituents on the thiophene ring, since the deshielding effect of these phenylsubstituents shifts the methine signals to a lower field in the NMR spectra, and the phenyls also distort the A_2B_2 splitting pattern of other aromatic protons. Thus, refluxing equimolar quantities of 9-methylanthracene and diacetylethylene in toluene for 12 hours afforded the adduct 257 in excellent yield. Similar treatment extended to anthracene in boiling xylene produced the adduct 252. Diels-Alder adducts involving diacetylethylene and other anthracene derivatives were not prepared due to the difficulties encountered in attempting to obtain diacetylethylene in acceptable yields.



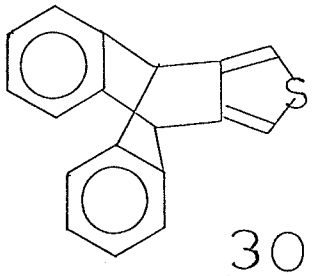
257



252

An attempted Diels-Alder reaction involving anthracene and 2,5-dimethoxy-2,5-dihydrofuran, which would have permitted synthesis of

compounds without substituents in the thiophene ring, was unsuccessful even under forcing conditions. This thiophene analogue 30 would have been an ideal compound for NMR analysis.

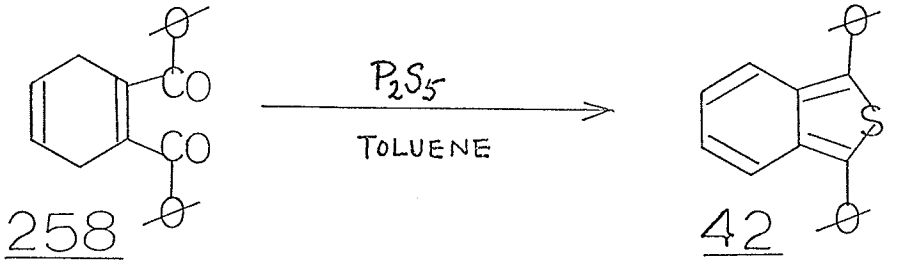


30

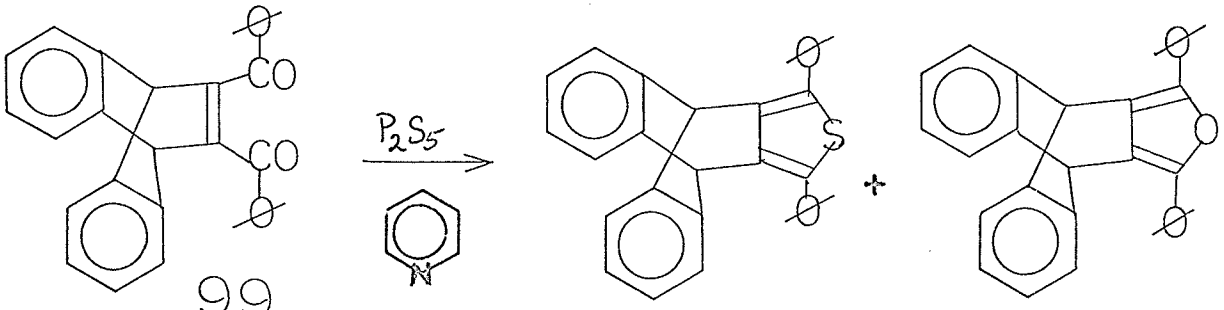
Ring Cyclisation of the adducts to form substituted 4,9-dihydro-4,9-0-benzenonaphtho[2,3-c]thiophenes

On the basis of the work of White et al. (126), who converted 1,2-dibenzoylcyclohexa-1,4-diene (258) into the corresponding benzo[c]thiophene 42 by treatment of 258 with phosphorus pentasulfide in toluene, similar treatment extended to 99 and 100 should give the thiophene analogue of triptycene 241. In the case of dibenzoyldibenzo[2,2,2]bicyclooctadiene (100), treatment of this with phosphorus pentasulfide in pyridine gave the thiophene 241 in 59% yield. When sulfurisation was attempted in other solvents, only retro Diels-Alder products were obtained. The structure of the sulfurised product 241 was characterized by elemental analysis and mass spectral and NMR data. Compound 241 is the thiophene analogue of triptycene, in which one of the ortho linked benzenes has been replaced by a five-member thiophene ring. The sulfurised product is best named as a derivative of naphtho[2,3-c]thiophene, although similar compounds have been named as substituted bicycloctatrienes (79) or as derivatives of the corresponding polynuclear

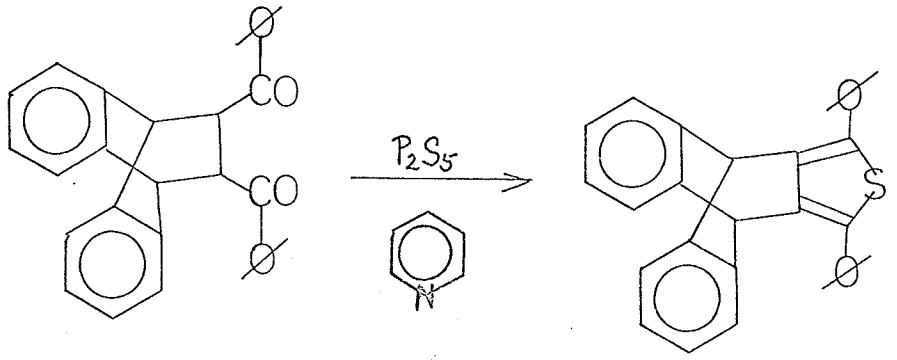
hydrocarbon (122). Thus compound 241 would be named 1,3-diphenyl-4,9-dihydro-4,9-o-benzenonaphtho[2,3-c]thiophene. The sulfurisation of the dibenzoylethylene adducts of a variety of substituted anthracenes to give the corresponding o-benzenonaphtho[2,3-c]thiophenes are summarized in Table III. In instances where the three rings attached to the central methine carbon atoms are different, the compounds obtained will be a mixture of enantiomers. But these enantiomers will not be separable by thin-layer chromatography.



258 42



99 241 102

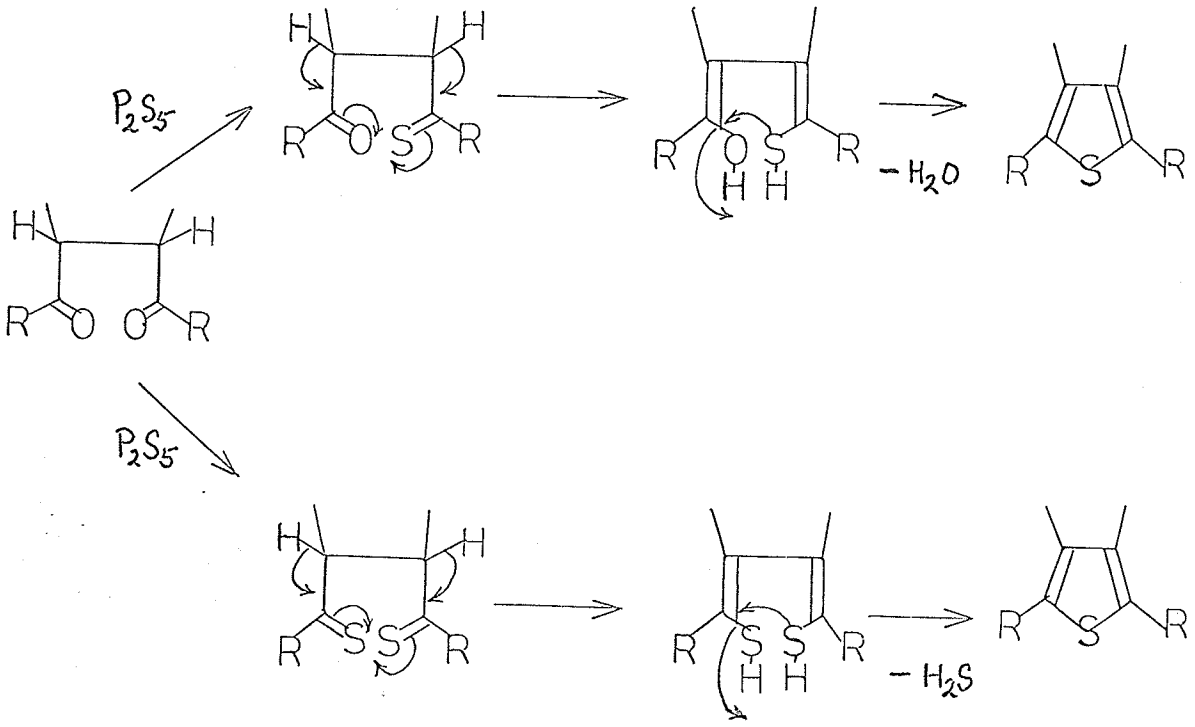


100 241

Sulfurisation of the acetylene adduct 99 in toluene did produce the expected retro Diels-Alder products; but performing the reaction in pyridine did not give solely the desired thiophene 241. Instead, the product isolated was a mixture of the desired thiophene 241 and the corresponding furan 102. The existence of this mixture was confirmed by elemental analysis and mass spectral data, which clearly indicated the presence of the furan 102 in addition to the thiophene 241. These could not be separated by t.l.c. The ratio of thiophene to furan present would probably depend on the amount of phosphorus pentasulfide used and the length of time of sulfurisation, although it depends on the detailed mechanism.

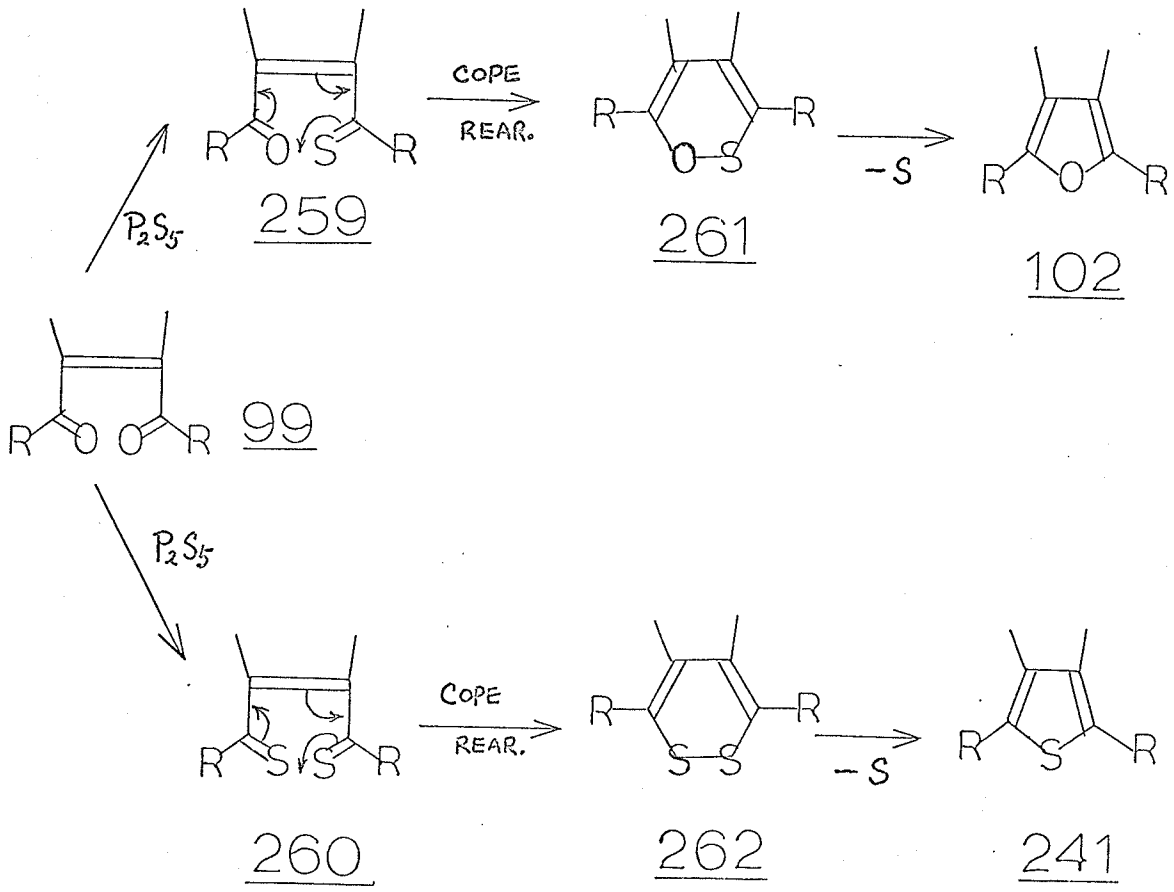
The conversion of the ethylene adducts to the corresponding thiophenes corresponds to a simple well-known thiophene synthesis, probably via the mechanism outlined in Scheme XXI.

Scheme XXI

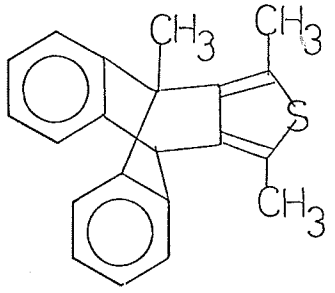


On the other hand, sulfurisation of the acetylene adducts 99 to form the furan 102 and the thiophene 241 can be rationalized as proceeding via a Cope-type rearrangement as illustrated in Scheme XXII. In the first step the acetylene adduct 99 is sulfurised (partially or completely) to form a mixture of the intermediates 259 and 260 respectively. Next the intermediates 259 and 260 proceed via Cope-type rearrangements to a 1,2-thioxin 261 and a 1,2-dithiin 262 respectively. Schroth et al. (135) had postulated that dithiins readily split off sulfur, especially rapid on heating to form 2,5-disubstituted thiophenes. Since the sulfurisations were carried out over an extensive period (6½ days), it seems reasonable to postulate that both the thioxin 261 and the dithiin 262 extrude sulfur to give the furan 102 and thiophene 241 respectively.

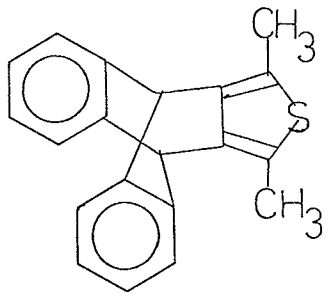
Scheme XXII



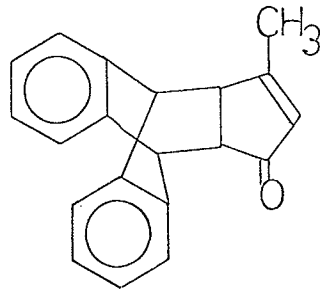
The diacetylethylene adducts 257 and 252 proceeded smoothly to the respective thiophenes 263 and 239 on refluxing the adducts with phosphorus pentasulfide in toluene. It was noted that in the previous cases carrying out the sulfurisation in toluene gave a poorer yield than in pyridine, probably because of competing retro Diels-Alder reactions. But here pyridine was not used because the acetyl methyls of the diacetylethylene adducts can easily undergo internal cyclisations in the presence of a base to produce cyclopentenone derivatives such as 264. Both 263 and 239 are better compounds for NMR study than the ones with bulky phenyl-substituents on the thiophene ring. The thiophenes 263 and 239 are best named as 1,3-dimethyl-4-methyl-4,9-dihydro-4,9-o-benzenonaphtho-[2,3-c]thiophene and 1,3-dimethyl-4,9-dihydro-4,9-o-benzenonaphtho-[2,3-c]thiophene, respectively.



263



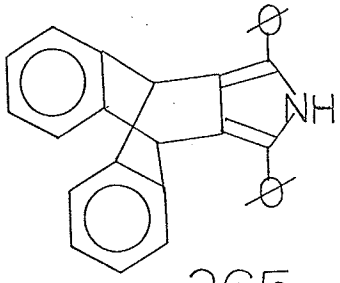
239



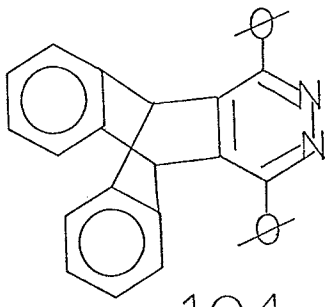
264

Reaction of the dibenzoylethylene adduct 100 with ammonium acetate in glacial acetic acid gave the pyrrole derivative 265 in excellent yield. 1,3-Diphenyl-4,9-dihydro-4,9-o-benzenonaphtho[2,3-c]pyrrole (265) was made to confirm the structures of the initial dibenzoylethylene adducts and to demonstrate that other ethylene adducts listed in Table II could be converted to the corresponding pyrroles if desired. Compound 265

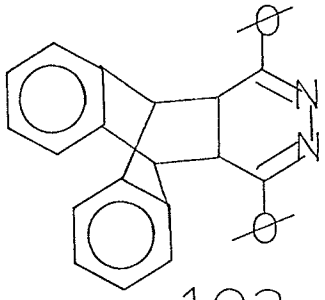
is probably formed by a mechanism corresponding to a Paal-Knorr synthesis (136,137). The Paal-Knorr synthesis is a general procedure whereby an enolizable 1,4-dicarbonyl compound is heated with a dehydrating agent, ammonia or a primary amine, or an inorganic sulfide. The mechanistic aspect of the formation of 265 is suggested in Scheme XXIII below. Nowlin (138) suggested that the driving force behind the Paal-Knorr synthesis results from the stabilization gained in formation of the aromatic heterocycle.



265

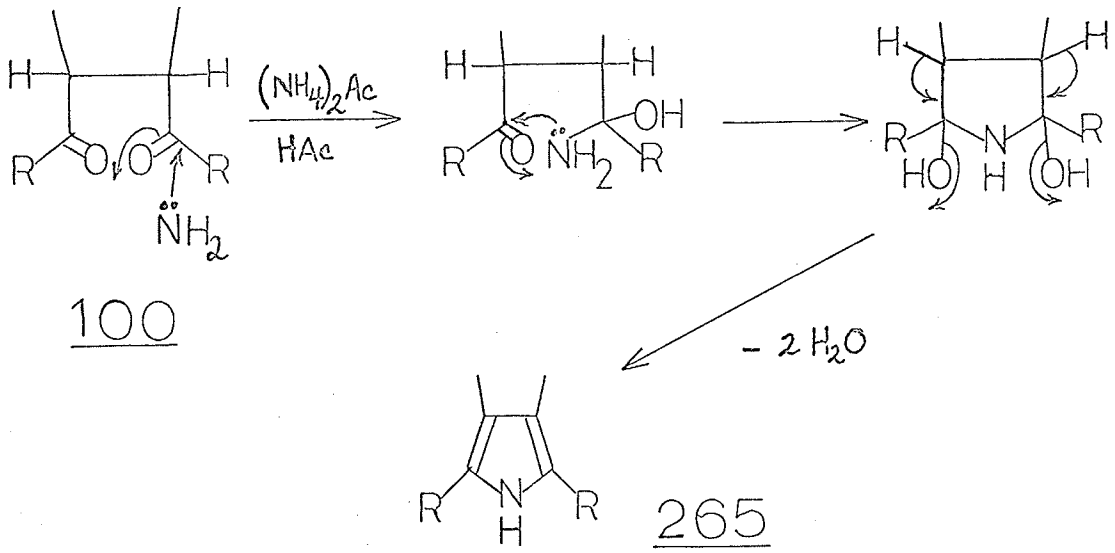


104



103

Scheme XXIII



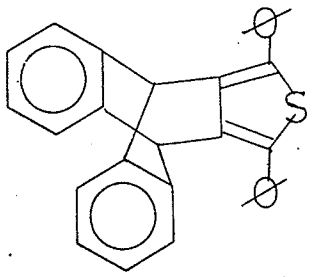
100

265

Reaction of the acetylene adduct 99 and ethylene adduct 100 with hydrazine gave the pyridazino compound 104 and the 2,3-dihydropyridazino compound 103, respectively. These compounds were originally prepared by Baumgarter and Hugel (79) using different reaction conditions.

NMR Spectroscopy of the Triptycene Analogues

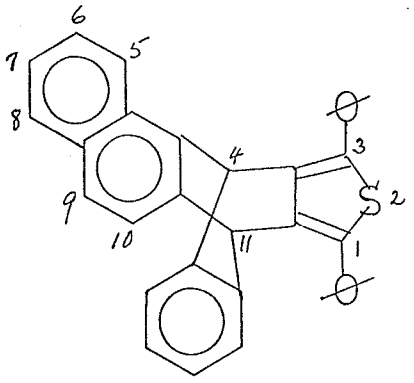
The NMR spectra of these heterocyclic analogues of triptycene are consistent with the assigned structures, elemental analyses, and properties. In general, the aromatic peaks in these compounds are rather complex, giving signals from 1.80 τ to 3.29 τ. On the other hand, the methine protons give sharp singlets with chemical shifts varying from 4.40 τ to 4.54 τ. These NMR spectra are illustrated in the Experimental section.



241

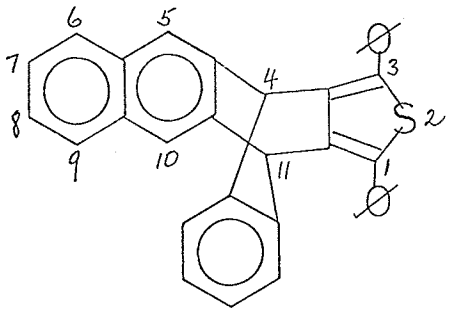
In the parent compound 241 the chemical shift of the methine proton occurs at 4.52τ in deuterochloroform with the complex aromatic protons giving signals from 2.51 τ to 3.26 τ. The methine signal of 241 falls within a similar range to that of triptycene itself (74, 139) and Wynberg's thiophene analogue (122). In the case of triptycene and Wynberg's thiophene 236, the methine protons are scarcely

influenced by any neighbouring groups whereas in compound 241 the methine protons come into the deshielding range of the two phenyls at positions 1 and 3. Hence, it is not too surprising to find that the methine values of the phenyl compounds are, indeed, at slightly lower field due to deshielding effects of the phenyl substituents on the thiophene ring.



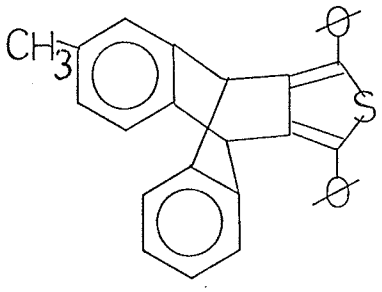
266

With reference to the phenanthro compound 266, two singlets are observed for the methine protons, at 3.74 τ and 4.35 τ. Because of the steric effect caused by interference of the 4-methine proton with the 5-aromatic proton, the chemical shift of the 4-methine proton is expected to occur at a lower field than that for the 11-methine proton. Furthermore, the 4-methine proton also comes into the deshielding range of the angularly-fused aromatic ring. Similar effects have been used to explain the low field absorption of the 4,5-protons in phenanthrene (140,141). Thus, it seems reasonable to assign the signal at 3.74 τ to the 4-methine proton and the signal at 4.35 τ to the 11-proton. The latter falls within the same range as that for the parent compound 241.



267

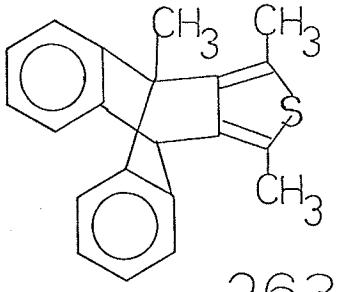
Another interesting compound is 1,3-diphenyl-4,11-dihydro-4,11-o-benzenoanthra[2,3-c]thiophene (267). The two methine protons give a sharp singlet at 4.40τ, which is comparable to the parent compound 241. But a sharp singlet for the 5,10-aromatic protons was observed at 2.40τ in addition to the expected complex aromatic signals covering the region between 2.40τ and 3.19τ. The 5,10-protons are uncoupled to the other aromatic protons. In connection with their investigations on the NMR of polycyclic aromatic hydrocarbons, Martin et al. (142) and Jonathan et al. (140) discovered similar results for the corresponding protons in anthracene and naphthacene.



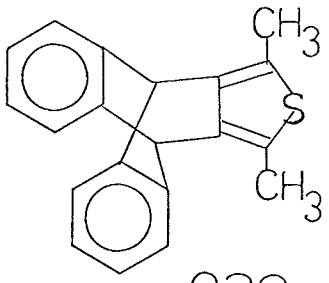
268

In the case of the thiophene 268, it seems reasonable to suspect that because the environments of the 4 and 9-methine protons are different due to the presence of the 6-methyl substituent, the chemical

shifts of these two methine protons should be different. However, the NMR of 268 gives only a singlet at 4.47τ for the two methine protons. This suggests that the methyl substituent is too far away to affect the environment of the 4-proton as compared to the 9-proton.



263



239

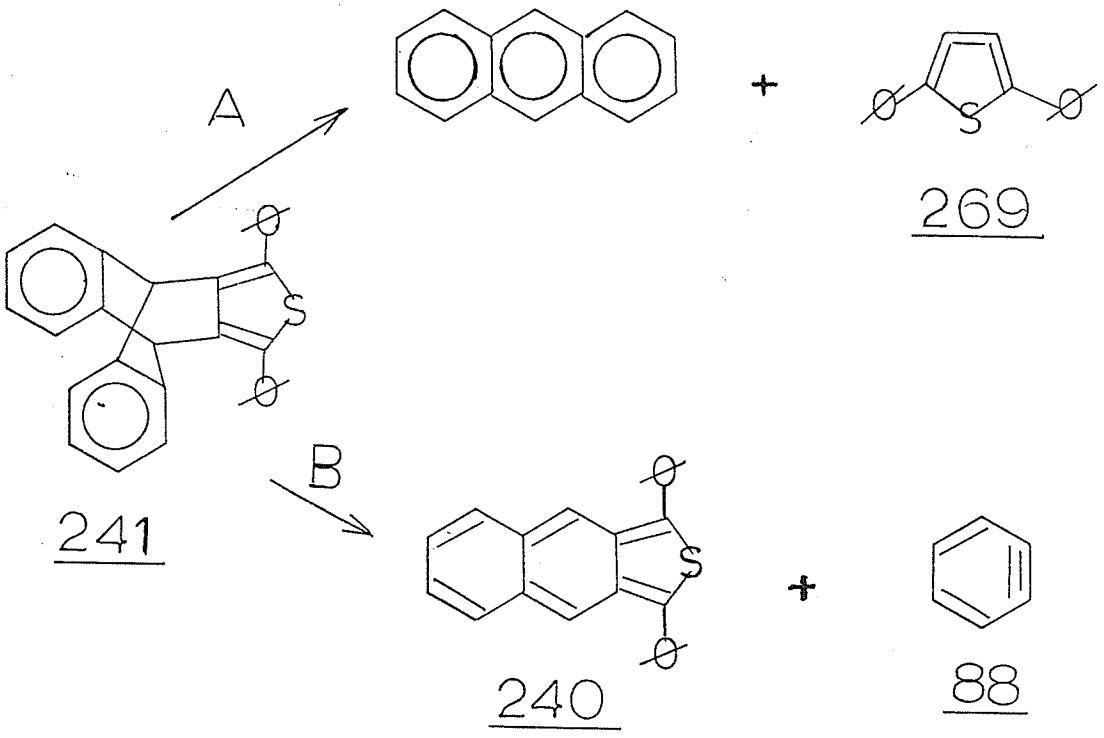
Analysis of the NMR spectra of the 1,3-dimethyl compounds 263 and 239 leads to the same conclusions about the deshielding effect of the 1,3-diphenyls in contrast to the 1,3-dimethyls. The NMR spectrum of 1,3-dimethyl-4 methyl-4,9-dihydro-4,9-o-benzenonaphtho [2,3-c] thiophene (263) exhibits a singlet at 7.72τ for (3H) 4-methyl, a singlet at 7.68τ for (6H) the 1,3-dimethyls, a singlet at 4.96τ for (H) methine proton, and multiplets from 2.71 to 3.22τ for the (8H) aromatics. The NMR spectrum of 1,3-dimethyl-4,9-dihydro-4,9-o-benzenonaphtho [2,3-c]-thiophene (239) shows a sharp singlet at 7.72τ for (6H) the 1,3-dimethyls, a singlet at 4.95τ for (2H) methine protons, and multiplets from 2.73τ to 3.22τ for the (8H) aromatics. Because compounds 263 and 239 contain no deshielding phenyls, the chemical shifts of the methine protons of these compounds should move up-field. In agreement with this argument, the chemical shifts of the methine protons of 263 and 239 are observed to be approximately 0.43 p.p.m. higher than for the 1,3-diphenyl

parent thiophene 241. Thus, the shift difference between 239 and 241 gives the approximate magnitude of the deshielding effects of the 1,3-diphenyls on the thiophene ring. Furthermore, unlike the complex aromatic region exhibited by the 1,3-diphenyl analogues, the aromatic regions of 263 and 239 exhibit more analytical A_2B_2 type of splitting patterns similarly to triptycene.

Mass Spectral Properties

Since the preparation and detection of 3,4-dehydrothiophenes have not yet been reported in the published literature, the possibility that these thiophene analogues of triptycene might be precursors to the formation of dehydrothiophenes became of interest. Retro Diels-Alder reactions of thiophene 241 can proceed via two pathways illustrated in Scheme XXIV.

Scheme XXIV



Route A might provide anthracene and 3,4-dehydrothiophene 269 as retro Diels-Alder products. Although the preparation of 2,3-dehydrothiophenes has been demonstrated by applying procedures analogous to the preparation of dehydrobenzenes, similar attempts on the 3,4-dehydrothiophenes led to rearranged intermediates (143). Such rearrangements would be unlikely with a 2,5-diphenyl intermediate 269 such as in route A. If the retro Diels-Alder route proceeds via the B pathway, the resultant products are Cava's 1,3-diphenylnaphtho [2,3-c]-thiophene (240) and dehydrobenzene (88). This is similar to Wynberg's thiophene 236 (122), which showed a base peak at m/e 184 for naphtho-[2,3-b] thiophene 233 and another peak for 2,3-dehydronaphthalene in the mass spectrum. The dehydrobenzene formed via route B would have to be trapped by some suitable diene. Otherwise, the dehydrobenzene may add to the naphtho [2,3-c] thiophene at positions 1 and 3 with eventual formation of a tetracene derivative as proposed by Cava et al. (123). The problems are to induce the retro Diels-Alder reaction and then to detect the intermediates formed by some suitable methods. One method involves the pyrolysis of the thiophene 241 with a heat-stable, very reactive diene such that the dehydrobenzene or dehydrothiophene formed could be trapped by this diene. Another method would be to subject compound 241 under electron impact in the mass spectrometer to determine if ions with masses corresponding to either dehydrobenzene or dehydrothiophene could be detected.

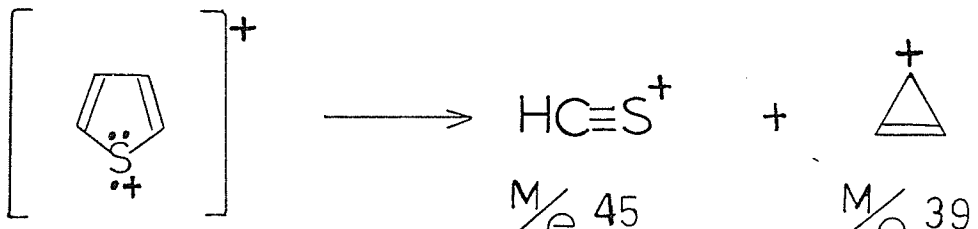
However, heating a mixture of the thiophene 241 with 9-methylanthracene above the melting point of 241 gave mainly unchanged starting materials along with small traces of unknown material. This indicates

that these thiophene analogues of triptycene are very stable even under drastic conditions.

Examination of the mass spectra indicates that the fragmentation patterns of the 1,3-diphenylthiophenes and 1,3-dimethylthiophenes listed in Table III are very similar. The mass spectra of all these thiophenes show three intense molecular ions. Apart from the parent peaks, there are large peaks corresponding to m/e 121 for the 1,3-diphenylthiophenes and m/e 59 for the 1,3-dimethylthiophenes. These masses are probably $Ph\text{-}C{\equiv}S^+$ and $CH_3C{\equiv}S^+$ groups, respectively. The losses of thiobenzoyl and thioacetyl fragments under electron impact are analogous to the loss of $HC{\equiv}S^+$ from Wynberg's compound 236 and from other thiophenes (144,145,146). The third abundant peak, common to all the thiophenes investigated, is the intense molecular ion at m/e ($M^+ - PhC{\equiv}S^+$) for the 1,3-diphenylthiophenes and at m/e ($M^+ - CH_3C{\equiv}S^+$) for the 1,3-dimethylthiophenes arising from cleavage of thiobenzoyl and thioacetyl groups from the respective parent ions.

The remaining ions in the mass spectra of these thiophenes appear to result from complex fragmentations. For example, one possible route is illustrated in Scheme XXV for the fragmentation patterns of 1,3-diphenyl-4-methyl-4,9-dihydro-4,9-o-benzenonaphtho[2,3-c]thiophene (270), but other routes can also be written. The ions at m/e 411 and 334 show that substituents at positions 1,3,4 and 9 of 270 are readily lost under electron impact. This was found to be the case with regard to the other thiophenes also. Thus, the formation of the ion at m/e 411 presumably results from the loss of the 4-methyl. As shown in Scheme XXV, this ion can be written in three resonance forms. Cleavage

of the methyl and phenyl groups gives rise to the peak at m/e 334. These peaks in general are small. However, the major fragmentation route goes via the formation of the cyclopropene intermediate at m/e 305 with cleavage of the fragment $PhC{\equiv}S^+$ (m/e 121). The cyclopropene intermediate can be postulated in view of the fact that the fragmentation mode of thiophene itself yields a $HC{\equiv}S^+$ ion plus a cyclopropene intermediate 271 (144).

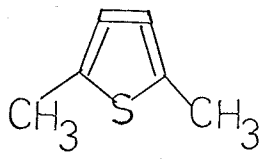


271

The cyclopropene intermediate at m/e 305 has three resonance structures. Loss of CH_4 gives rise to the ion at m/e 289. After this, the fragmentation pattern becomes more complex. No overall scheme can be postulated to account for the further breakdown of ion at m/e 289 that is common to all the thiophene analogues investigated.

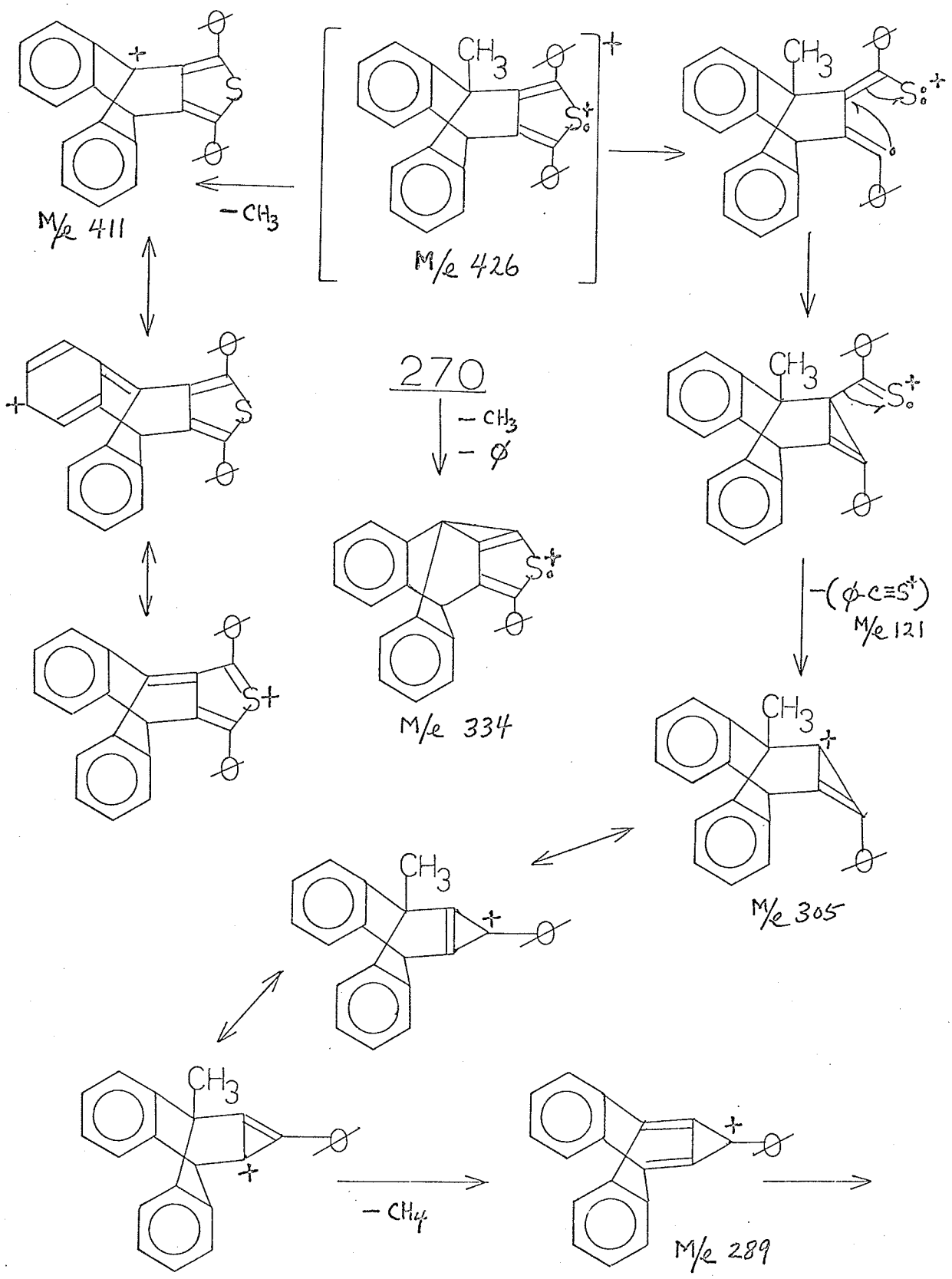
At first sight, the most interesting feature of the spectra of all the thiophene analogues of triptycene is their overall similarity. They all show three comparatively large peaks (above 50% of the base peak). No significant peaks at m/e 76 or m/e 77 were detected. This rules out the formation of dehydrobenzenes or phenyls. The ion at m/e 350, which would indicate the existence of 1,3-diphenylnaphtho-[2,3-c] thiophene (240), was absent in all the spectra. The fragmentation modes of the 1,3-diphenyl analogues gave no evidence for the formation

of either 2,5-diphenyl-3,4-dehydrothiophenes (269) or anthracenes. Yet, the mass spectrum of 1,3-dimethylthiophene 263 indicated an ion at m/e 110, which would correspond to 2,5-dimethyl-3,4-dehydrothiophene (272). But the low intensity of the m/e 110 peak suggests that the fragmentation mode via the dehydrothiophene 272 is probably insignificant. It seems appropriate to conclude that these proposed retro Diels-Alder reactions are unimportant. The fact that cleavage at the 4 and 9 bridgehead carbons did not take place even under drastic reaction conditions and electronic impact suggests that these thiophenes have strong molecular lattice structures.



272

Scheme XXV



Conclusion

A number of thiophene analogues of triptycene, in which one of the ortho linked benzene rings is replaced by a heterocyclic system, have been successfully prepared by sulfurisation of substituted bicyclo-octadienes. These bicyclooctadienes are Diels-Alder type adducts of the substituted anthracenes and dibenzoylethylene or diacetylethylene. These Diels-Alder experiments reveal that 9 and 10-methyl or methoxy anthracenes and linearly-fused benzo derivatives of anthracene are the best dienes for Diels-Alder type additions. Other anthracene derivatives and, in particular, angular-fused benzo derivatives are generally poor dienes. In fact, 9,10-diphenylanthracene and naphtho-[2,3-b]thiophene are inert to dienophiles even under drastic conditions. These findings coincide with Sauer's hypothesis (147) that Diels-Alder reactions normally proceed most readily when one component is electron rich and the other electron deficient.

Dibenzoylacetylene adducts of substituted anthracenes have also been prepared. But attempted sulfurisations of these adducts gave mixtures of the thiophenes and the corresponding furans.

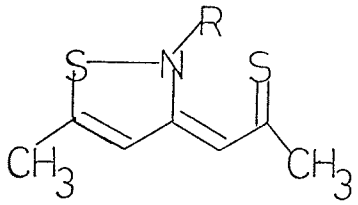
Attempted synthesis of thiophene analogues of triptycene, in which two ortho linked benzene rings are replaced by heterocyclic systems, failed. This may be due to the fact that naphtho[2,3-b]-thiophene, which has more aromatic character than diene character, failed to react with dibenzoylethylene even under very drastic conditions. In the case of naphtho[2,3-c]thiophene, positions 4 and 9 are not labile enough to permit its addition to dibenzoylethylene.

Interpretation of the mass spectral data leads to the conclusion that the retro Diels-Alder reactions of these thiophenes are unimportant. Neither dehydrobenzene nor 2,5-diphenyl-3,4-dehydrothiophene is generated in these reactions. However, there is evidence for the formation of 2,5-dimethyl-3,4-dehydrothiophene although these ions are not abundant in the mass spectra.

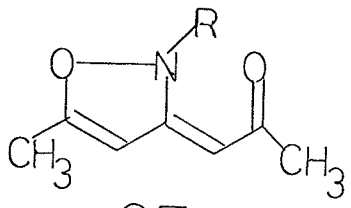
In general, these thiophenes are colourless or pale yellow solids, and are extremely soluble in most organic solvents. Most of these compounds have high melting points analogous to triptycene; and are extremely stable at high temperatures. Similarly to triptycene, substituents at positions 4 and 9(bridgehead carbons) of these thiophenes should be stable to oxidation and displacement reactions of the SN^1 and SN^2 type.

PART D Suggestions for Future Work

While the attempted synthesis of the benzo[c]thiophene model failed, the successful preparation and subsequent investigation of the anthranil model system did provide some insight with regard to the special properties of the thiathiophthenes. Evidence from the present investigation and from the latest published literature appears to favour the hypothesis that invokes the use of d-orbitals in the bonding of the central sulfur atom, which would lead to the bicyclic structure for thiathiophthenes. This bicyclic structure would contain a tetravalent sulfur. To gain further insight on the thiathiophthenes, the next step would be to investigate the synthesis and properties of model compounds with structures identical to thiathiophthenes, but containing no central sulfur atom such as 273 and 274. Another model compound worth investigating is 276, which can be prepared by direct sulfurization of the precursor, 3,4,5-tribenzoylpyrazole (275) (148).



273



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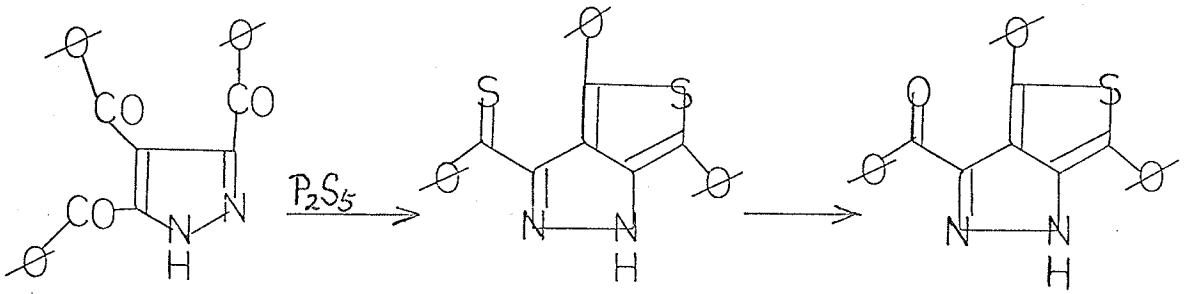

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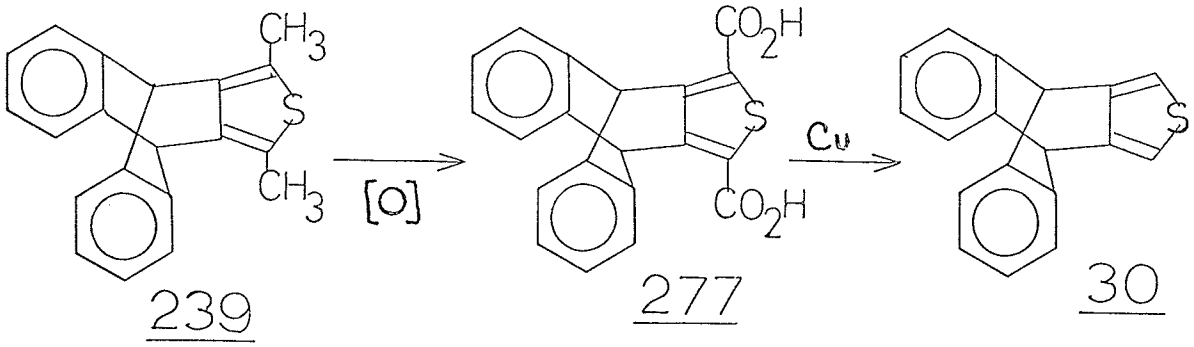
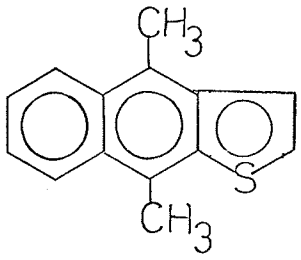


239 277 30

Various thiophene analogues of triptycene, in which one ortho linked benzene ring has been replaced by a heterocyclic system, have been prepared successfully even though the yields for some derivatives are very low. Unfortunately, the retro Diels-Alder reactions of the majority of these thiophenes did not emit thiophyne or benzyne intermediates as anticipated. This undoubtedly reveals the stability and strong lattice structures of these thiophenes. One interesting possibility for future work involves the preparation of thiophenes without 1 and 3 substituents such as 30. This may be



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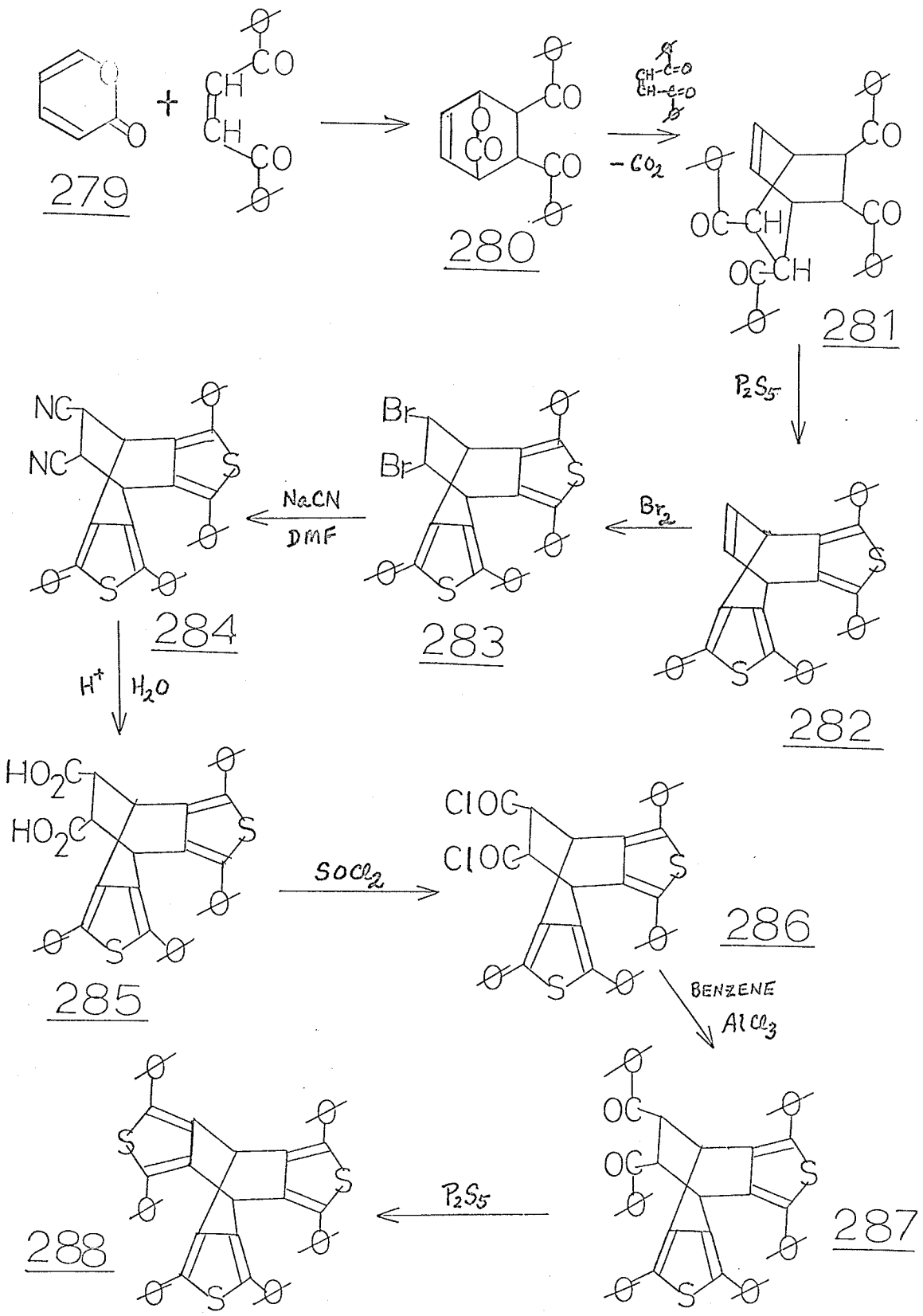
accomplished by oxidizing the methyls of 239 with potassium ferricyanide followed by decarboxylation of the acid 277 with copper powder in quinoline.

The photochemical reactions of these thiophene analogues should be investigated since interesting rearrangements might result.

Attempts to synthesize thiophene analogues, in which two ortho linked benzene rings are replaced by heterocyclic systems, failed because the Diels-Alder addition involving dibenzoylethylene and naphtho [2,3-b] thiophene was unsuccessful. The emphasis should be on the preparation of a more reactive derivative of naphtho [2,3-b] thiophene such as 278. Similarly to 9,10-dimethylanthracene, 4,9-dimethylnaphtho [2,3-b] thiophene (278) should readily react with dibenzoylethylene.

Finally, an interesting possibility for future work involves the synthesis of a heterocyclic analogue of triptycene in which all three ortho linked benzene rings are replaced by heterocyclic systems. A possible route is outlined below in Scheme XXVI. The starting material would be α-pyrone (279). If the Diels-Alder reaction involving α-pyrone and dibenzoylethylene is successful, then the monoadduct 280 would be obtained. Fusion of this monoadduct with excess dibenzoylethylene followed by extrusion of carbon dioxide would give the diadduct 281. Sulfurization of 281 would yield the bicyclooctatriene system 282. First bromination of the C=C bond then treatment of the resulting bromine compound 283 with sodium cyanide should produce the nitrile 284, which would easily hydrolyse to the acid 285. After conversion of the acid to the acid chloride 286, a double Friedel-Crafts reaction would be performed with benzene giving the dibenzoyl precursor 287. Compound 287 could easily be converted to the product 288 on sulfurization. The critical step in this scheme is the formation of the diadduct 281. Failure to obtain this diadduct would mean the abandonment of this entire scheme.

Scheme XXVI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P_2S_5
Br_2
NaCN
DMF
H^+
H_2O
$SOCl_2$
BENZENE
$AlCl_3$
$-CO_2$

EXPERIMENTAL PROCEDURES AND RESULTS

Experimental Procedures and Results

The infrared (IR) spectra were performed on a Perkin-Elmer model 337 spectrophotometer in liquid paraffin mulls. Nuclear Magnetic Resonance spectra were obtained on a Varian model 56/60A spectrometer and, unless otherwise stated, in deuterochloroform at 40°C, using tetramethylsilane as an internal standard. Chemical shifts are given in τ units. The mass spectra were obtained on a Hitachi Perkin-Elmer RMU-6D model and Finnigan 1015 model mass spectrometers. Melting points (m.p.) were obtained on a calibrated Fisher-Johns melting point apparatus. Thin-layer chromatography (t.l.c.) was performed using "Camag" silica-gel type DSF5 supplied by Mondray Ltd. Development of plates, unless otherwise stated, was carried out using benzene as standard with increasing proportions of chloroform added when necessary. The elemental analyses were done by Alfred Bernhardt Microanalytical Laboratory, 5251 Elbach uber Engelskirchen, West-Germany.

Part A Attempted Syntheses of 4-Thioacylbenzo[c]thiophene

Preparation of 2,5-dimethylthiophene (106)

This was prepared by vigorously stirring a mixture of acetonylacetone (285g) and phosphorus pentasulfide (220g) for ½ hour according to reference (149). After the initial intensive reaction had subsided, the mixture was heated in an oil bath for 1½ hours. The material was distilled, and the fraction boiling at 134-135°C was collected; B.P. = 136-137°C; yield = 87%.

Preparation of 3-acetyl-2,5-dimethylthiophene (107)

Acetylation of the thiophene 106 was carried out similarly to Messina's method of alkylation of 2,5-dimethylthiophene (80). To a well stirred suspension of 350 ml of carbon disulfide and 67g of aluminum chloride, cooled in ice, there was added dropwise a mixture of 2,5-dimethylthiophene (56g) and acetyl chloride (39g). After standing in the cold for ten hours, the dark-brown mixture was treated with hydrochloric acid and ice. The carbon disulfide layer was separated and the aqueous layer was extracted three times with 50ml. aliquots of ether. The combined ether extracts and carbon disulfide layer were washed with water, 10% sodium carbonate solution, and water; and dried over sodium sulfate. Fractional distillation gave the product as a colourless oil. B.P. = 224°C

Yield = 78%

Preparation of 2,5-dimethyl-3-thienylacetic acid (108)

The method of Blanchette (81) was modified in the following way. 2,5-Dimethyl-3-acetylthiophene (4 g) and sulfur (1 g) in morpholine (20 ml) were refluxed for 6 hours. The dark oil was poured into water and ethanol was added until the solution became clear. After standing for two days, the precipitated solid was filtered off and hydrolysed with sodium hydroxide by refluxing the mixture for 6 hours. After cooling, the mixture was acidified with dilute hydrochloric acid, and the product was extracted with three 50 ml aliquots of ether. The combined ether extracts were dried with anhydrous sodium sulfate and evaporated to give a dark brown oil which could not be made to crystallize. Yield = 7%.

Preparation of methyl 2,5-dimethyl-3-thienylacetate (109)

The crude acid 108 from above was added to 50 ml. of anhydrous methanol. This solution was saturated with gaseous hydrochloric acid and allowed to stand at room temperature for 24 hours. Then the mixture was poured into ice, extracted with ether, washed with dilute sodium carbonate, and dried with sodium sulfate. Evaporation of the combined ether extracts gave a black oil, which was fractionally distilled to yield a yellow oil. B.P. = 250°C

Yield = 98%

Attempted preparation of methyl 2,5-dimethyl-3-thienylacetate (109) from Friedel—Crafts acylation of 2,5-dimethylthiophene

The method of Stadnikoff and Goldfarb (150) was modified in the following way. In a 250 ml round-bottomed, three-necked flask provided with a thermometer, dropping funnel, and a mechanical stirrer, were

placed 2,5-dimethylthiophene (5 g), methyl bromoacetate (6 g), and carbon disulfide (100 ml). The solution was cooled to 0°C, and anhydrous stannic chloride (10 ml) was added dropwise with efficient stirring during the course of about 40 minutes. The mixture was stirred at room temperature overnight. The resulting thick mass was decomposed with 50 g ice and 30 ml of dilute hydrochloric acid. The carbon disulfide layer was separated, washed with 25 ml of water, and dried over 5 g of anhydrous sodium sulfate. Distillation gave a brown oil. An infrared spectrum of this oil showed that starting materials were recovered unchanged.

Attempted acylation of methyl 2,5-dimethyl-3-thienylacetate

The method of Stadnikoff and Goldfarb (150) was modified as described above. The calculated quantities of benzoyl chloride, aluminum chloride, and methyl 2,5-dimethyl-3-thienylacetate were used. No product could be isolated on work up.

Preparation of 1,3-diphenylbenzo[c]thiophene (42)

The method of Dufraisse and Daniel (23) was modified in the following way. o-Dibenzoylbenzene (1 g) or 1,3-diphenylbenzo[c]furan (1 g) and phosphorus pentasulfide (1 g) in 50 ml of pyridine were refluxed with stirring for 24 hours. After cooling, the mixture was thrown into ice and the inorganic solids were filtered off. The mixture was extracted with three 50 ml aliquots of ether. The combined ether extracts were washed with dilute hydrochloric acid, dried with sodium sulfate, and evaporated off to yield a yellow solid with green fluorescence. Purification by column chromatography (alumina) gave bright yellow needles; m.p. = 120°C, Lit. (23) = 118°C; Yield = 78%.

Friedel-Crafts acylation of 1,3-diphenylbenzo[c]thiophene

1,3-Diphenylbenzo[c]thiophene (0.5 g) was added to anhydrous aluminum chloride (0.5 g) in 50 ml of carbon disulfide. The mixture was cooled to 0-5°C in an ice bath. Benzoyl chloride (0.3 g) in 10 ml of carbon disulfide was added dropwise to the mixture with stirring. The mixture was stirred overnight at room temperature. Then it was poured into water and extracted with benzene (3 x 30 ml). The combined extracts were washed with water (2 x 40 ml), dried, and evaporated to give an orange solid. This solid was further purified by thin layer chromatography using benzene as a developing solvent. Three major bands were observed on the plate.

An infrared spectrum of the compound from the top band of the plate suggested that it was 1,3-diphenylbenzo[c]thiophene.

The mass spectrum of the compound from the second band contained a peak at m/e 390. This suggested that the compound was a monoacylated product, probably compound 113; m.p. = 184°C (11%).

Anal. calculated for $C_{27}H_{18}O_1S$; C,83.15; H,4.63; S,8.25

Found. C, 82.96; H, 4.46; S, 8.25

The mass spectrum of the compound from the third band showed the parent peak at m/e 494. This suggested a diacylated product, probably compound 114a or 115a; m.p. = 132°C.

Yield = 3%

Anal. calculated for $C_{34}H_{22}SO_2$; C, 82.59; H, 4.45; S,6.48

Found. C, 82.30; H, 4.39; S, 6.15

Preparation of tetrabenzoylcyclobutane (119)

Trans-dibenzoylethylene (18 g) in 250 ml dioxane was irradiated for 24 hours with a Hanovia Quartz ultraviolet No. 30620 - Lamp. The mixture was concentrated to 50 ml and 25 ml of carbon tetrachloride were added. Cooling afforded the cyclobutane as colourless needles; m.p. = 139°C (68%).

Anal. calculated for $C_{32}H_{24}O_4$; C, 81.36; H, 5.08

Found, C, 81.22; H, 5.17

The IR spectrum, 1713 cm^{-1} (C=O)

Preparation of tetraphenylthieno[c]thiepine (120)

The tetrabenzoylcyclobutane (100 mg) in pyridine (35 ml) was refluxed with phosphorus pentasulfide (300 mg) for 8 hours. The mixture was cooled, poured into water, and extracted with chloroform (3 x 50 ml). The extract was washed with water (5 x 30 ml), dried, and evaporated to give a yellow oil which was purified by thin-layer chromatography using 25% benzene -petroleum ether as a developing solvent. Colourless crystals were obtained; m.p. 146°C; yield = 29%.

Anal. calculated for $C_{32}H_{22}S_2$; C, 81.70; H, 4.68; S, 13.62

Found, C, 81.53; H, 4.75; S, 13.70

Mass spectrum: m/e 470, 438(M^+-32),

possibly for tetraphenylbenzo[c]thiophene.

Preparation of 2,5-dimethyl-3,4-bischloromethylthiophene (121)

A stream of hydrogen chloride gas was added to a stirred solution of 37% formalin (50 ml) and 20 ml of concentrated hydrochloric acid, allowing the temperature to rise to 50-60°C until the solution was saturated. The mixture was then cooled to 30°C whereupon 19 g of

2,5-dimethyl-thiophene was added dropwise with stirring. After the mixture had been stirred for 20 minutes, the oily lower layer was separated and washed with water (5 x 100 ml). The oil was refrigerated overnight and recrystallized from hexane-petroleum ether to give pale-tan crystals; m.p. = 64°C; yield = 78%. The compound turned black on prolonged exposure to air and light.

Anal. calculated for $C_8H_{10}Cl_2$; C, 45.95; H, 4.80; S, 15.32; Cl, 33.95.

Found, C, 46.13; H, 4.84; S, 15.47; Cl, 33.56

The NMR spectrum, 7.72 τ (6H, two equivalent methyls), 5.55 τ (4H, methylene protons).

Preparation of 2,5-dimethyl-3,4-biscyanomethylthiophene (122)

Freshly distilled 2,5-dimethyl-3,4-dichloromethylthiophene (20 g) was added portion-wise over 10 minutes to a stirred mixture of sodium cyanide (27 g) in anhydrous N,N-dimethylformamide (200 ml). Cooling was applied to keep the temperature below 90°C. Then the mixture was stirred at room temperature for 2 hours. Chloroform was added, and the mixture was poured into 200 ml of saturated sodium chloride solution. The chloroform extract was washed with water (3 x 50 ml), dried with sodium sulfate, and evaporated to give a pale yellow solid. Recrystallization from anhydrous ethanol gave white needles; m.p. = 121°C; yield = 34%.

Anal. calculated for $C_{10}H_{10}N_2S$; C, 63.15; H, 5.26; S, 16.84; N, 14.75

Found, C, 63.05; H, 5.18; S, 16.69; N, 15.08

The IR spectrum, 2280 cm^{-1} (C≡N)

The NMR spectrum, 7.63 τ (6H singlet, equivalent methyls), 6.40 τ (4H singlet, methylene protons)

Attempted condensation of 2,5-dimethyl-3,4-dicyanomethylthiophene with benzil

A solution of potassium tertiary butoxide in tertiary butyl alcohol was prepared according to the method of Johnson and Schneider (151), using anhydrous t-butyl alcohol (10 ml) and potassium (0.43 g). To this freshly-prepared basic mixture was added portionwise 2,5-dimethyl-3,4-dicyanomethylthiophene (2.85 g). The mixture was refluxed for 2 hours; then it was cooled to room temperature. Benzil (2.10 g) in t-butyl alcohol (10 ml) was added dropwise to the mixture. The mixture was refluxed for another 3 hours. After cooling the mixture, it was poured into ice and extracted with benzene (3 x 40 ml). The benzene extracts were washed with water, dried, and evaporated to give a black solid. The infrared spectrum showed an amino absorption (3420 cm^{-1}) and a cyano absorption (2270 cm^{-1}).

The reaction was repeated using 2,3-butanedione instead of benzil. The expected condensation product was not detected.

Preparation of 1,3-dihydrobenzo[c]thiophene (32)

Preparation of this compound was carried out in accordance with the method of Birch et al. (86).

Yield = 67%.

Attempted preparation of 1,3-dihydrobenzo[c]thiophene sulfoxide (125)

A solution of t-butylhydroperoxide (5 ml) in t-butyl alcohol (5 ml) was added dropwise to a cooled solution of 1,3-dihydrobenzo[c]thiophene (5 g) in glacial acetic acid (15 ml). Removal of the solvent and distillation of the residual oil gave a red liquid which later turned black.

Preparation of 2,5-dimethylthenoyl-3-[β-propionic acid] (34)

The method of Steinkopf et al. (20) was modified by the use of stannic chloride instead of aluminum chloride as the catalyst; m.p. = 109°C, Lit. (20) = 112°C; yield = 49%.

Preparation of 2,5-dimethylthienyl-3-[γ-butyric acid] (35)

The Clemmensen reduction was carried out in accordance with the method of Steinkopf et al. (20).

Yield = 71% .

Preparation of 1,3-dimethyl-4-keto-5,6,7-trihydrobenzo[c]thiophene (37)

The method of Steinkopf et al. (20) was modified in the following way. 2,5-Dimethylthienyl-3-[γ-butyric acid] (4 g) and polyphosphoric acid (25 ml) were stirred at 85°C for 10 minutes. After cooling, the mixture was poured into ice. The white precipitate was filtered off and recrystallized from petroleum ether-ethanol. White needles; m.p. = 40°C, Lit. (20) = 41° ; yield = 42%.

Preparation of 1,3-dimethyl-4,7-diketo-5,6-dihydrobenzo[c]thiophene (137)

2,5-Dimethylthenoyl-3-[β-propionic acid] (4 g) was added portion-wise to 25 ml of concentrated sulfuric acid. The mixture was heated to 85°C with stirring. After 5 minutes the mixture was cooled down to 10°C and poured into ice. The aqueous mixture was made basic with ammonium hydroxide and extracted with ether (3 x 50 ml). The ether extracts were washed with water, dried, and evaporated off to give a solid. Recrystallization from petroleum ether afforded white needles; m.p. = 118°C; yield = 6%.

Anal. calculated for $C_{10}H_{10}SO_2$; C, 61.86; H, 5.11; S, 16.49

Found, C, 61.73; H, 5.09; S, 16.38

The IR spectrum, 1690 cm^{-1} (C=O)

The NMR spectrum, 6.83τ(6H, methyls), 6.68τ(4H, methylene protons)

Preparation of 1,3-dimethyl-4-hydroxy-4,5,6,7-tetrahydrobenzo[c]thiophene (132)

1,3-Dimethyl-4-keto -5,6,7-trihydrobenzo[c]thiophene (4 g) was dissolved in 50 ml of methanol. The solution was cooled to 5°C. Sodium borohydride (0.6 g) was added portionwise with stirring to the cooled solution. The mixture was stirred overnight at room temperature. The white crystals formed were filtered off and washed with petroleum ether; m.p. = 110°C ; yield = 79%.

Anal. calculated for $C_{10}H_{14}OS$; C, 65.94; H, 7.69; S, 17.58

Found, C, 66.03; H, 7.59; S, 17.65

The IR spectrum, 3310 cm^{-1} (OH)

Attempted reaction of 1,3-dimethyl-4-keto-5,6,7-trihydrobenzo[c]thiophene with sodium cyanide

The keto-thiophene (5 g) and sodium cyanide (1 g) in 60 ml of water were stirred vigorously at 0° - 5°C according to reference (152). Then 40% sulfuric acid (10 ml) was added dropwise over a period of 1 hour with the temperature kept between 10° and 20°. Water was added and the product was extracted with ether (3 x 30 ml). The combined ether extracts were washed with water (3 x 50 ml), dried, and evaporated to give a brown oil which solidified on standing. The IR spectrum showed that unchanged starting material was recovered.

Attempted reaction of 1,3-dimethyl-4-hydroxy-4,5,6,7-tetrahydrobenzo-[c]-thiophene with phosphorus pentachloride

In accordance with the general method of Lutz et al.(153), the hydroxy compound (1 g) was dissolved in chloroform (50 ml). Then phosphorus

pentachloride (0.5 g) was added portionwise with stirring. The excess phosphorus pentachloride was filtered off; and the filtrate washed with water (3 x 50 ml), dried, and evaporated to give an oil. This oil rapidly decomposed on exposure to air.

Darzen's Glycidic Ester Condensation of ethyl α-chloropropionate and 1,3-dimethyl-4-keto-5,6,7-trihydrobenzo[c]thiophene

In accordance with Yarnell and Wallis's general preparation of alicyclic methyl ketones (91), a solution of 1.6 g of the ketone and 1.2 ml of ethyl α-chloropropionate in 150 ml of dry ether was cooled to $-80^{\circ}C$, and to it was added the powdered sodium ethoxide made from 0.58 g of sodium. After the mixture had come to room temperature, it was refluxed for 60 hours in an atmosphere of nitrogen. The ether was then evaporated, and the residue was refluxed for 2 hours with a solution of 120 ml of 90% ethanol, which contained 4 g of sodium hydroxide. The cold solution was diluted with water and extracted with ether which was discarded. The alkaline aqueous layer was acidified with dilute acid and again extracted with ether (3 x 50 ml). This latter ether extract was washed with water, dried, and evaporated to give a brown oil. The IR spectrum showed absorptions for a cyclic ketone and an acid or ester group ($1695cm^{-1}$ and $1768cm^{-1}$ resp.). The NMR evidence also suggested that the product had structure similar to 136. The NMR spectrum, 8.22 τ, 8.33 τ (3H doublet, methyl attached to α-carbon), 8.70 τ, 5.75 τ (3H triplet, 2H quartet, ethyl group), 7.56 τ, 7.63 τ (6H singlets, 1,3-dimethyls), 5.53 τ (1H quartet, α-methine proton), 5.40 τ (1H, methine proton), 5.89 to 6.39 τ (6H bands, methylene protons).

Preparation of 2,5-dimethylthiophene-3-aldehyde (138)

The method of King and Nord (93) was modified in the following way. 2,5-Dimethylthiophene (¼ mole), phosphorus oxychloride (0.31 mole), and N-methylformanilide (0.32 mole) were heated cautiously on the steam bath until hydrogen chloride gas evolved. At this point, heating was discontinued and cooling immediately applied to prevent excessive decomposition. After the initial reaction has subsided, the reaction mixture was heated for twenty minutes on a steam bath to complete the reaction. At the end of this period, cooling was again applied and the contents of the flask carefully neutralized with excess sodium acetate. The mixture was then steam distilled; the distillate was extracted with ether (3 x 50 ml); and the extract was washed with first dilute 6N HCl and then 5% sodium bicarbonate, dried, and evaporated to give a brown oil. Fractional distillation gave a colorless liquid (17 g or 46 % yield). B.P. = 79° - 83°C, Lit.(93) 84°C.

Attempted condensation of 2,5-dimethylthiophene-3-aldehyde and diethyl-succinate

A mixture of 2,5-dimethylthiophene-3-aldehyde (10 g) and diethyl-succinate (13 g) in 15 ml of t-butyl alcohol was added dropwise during 45 minutes to a heated solution of potassium t-butoxide (from potassium (5.8 g) and t-butyl alcohol (85 ml) at 60 - 70°C. This temperature was maintained for a further 75 minutes. After cooling, the mixture was poured into water and extracted with ether (3 x 40 ml). The ether extracts were washed with water, dried, and evaporated to give a brown oil (8 g or 39%).

The brown oil was not isolated but refluxed for 2 hours with potassium hydroxide solution to give an orange liquid, which could not be made to crystallize.

The NMR spectrum, 7.57 τ and 7.63 τ (6H, methyl singlets), 6.32 τ (2H, methylene protons), 4.44 τ (1H, vinyl singlet), 3.40 τ (1H, aromatic) and -1.5 τ (2H, acidic protons).

The IR spectrum, 1720 cm^{-1} (COOH), 1640 cm^{-1} (C=C)

Attempted Cyclisation of the Stobbe condensation product 140

The crude acid 140 from above was treated with concentrated sulfuric acid at 85°C for 20 minutes. After cooling, the dark viscous mixture was thrown into ice. The product was extracted with ether (3 x 30 ml). Working up gave only black decomposition materials.

The procedure was repeated by substituting sulfuric acid with other catalysts such as acetic anhydride and sodium acetate, and polyphosphoric acid. The expected product was not detected.

Preparation of 1,2-dibenzoyl-4,5-dimethylcyclohex-4-ene (48)

This was made by the method of Adams and Gold (26). Equimolar ratios of 2,3-dimethyl-1,3-butadiene and trans-dibenzoylethylene were refluxed in 95% ethanol for 6 hours. Yield = 88%.

Preparation of 1,3-diphenyl-4,7-dihydro-5,6-dimethylbenzo[c]thiophene (142)

The adduct 48 (2 g) and phosphorus pentasulfide (2 g) in 50 ml of pyridine were refluxed for 4 hours. After cooling, the mixture was thrown into ice. The bright yellow precipitate was then filtered off and washed with dilute sodium hydroxide solution. Purification by column chromatography on alumina gave yellow needles with green

fluorescence; m.p. = 168°C; yield = 74%.

Anal. calculated for $C_{22}H_{20}S$; C, 83.58; H, 6.30; S, 10.12

Found, C, 83.94; H, 6.19; S, 9.93

The NMR spectrum, 8.32 τ (6H methyl singlet), 6.21τ(4H,methylene protons) and 2.22 τ to 2.83 τ (10H, aromatic protons).

Preparation of 1,3-diphenyl-5,6-dimethylbenzo[c]thiophene (49)

1,3-Diphenyl-4,7-dihydro-5,6-dimethylbenzo[c]thiophene (2 g) and sulfur (0.5 g) were heated for one-half hour at 200-220°C. Purification by thin-layer chromatography with 50% benzene-petroleum ether as developing solvent gave yellow needles with green fluorescence; m.p. = 183°C; yield = 42%.

Anal. calculated for $C_{22}H_{18}S$; C, 84.07; H, 5.73; S, 10.19

Found, C, 83.94; H, 5.93; S, 10.36

The NMR spectrum, 7.68τ(6H, methyl singlet), 2.20τ to 2.80τ (12H, aromatic bands).

Attempted Friedel-Crafts acylation of 1,3-diphenyl-5,6-dimethylbenzo-[c]-thiophene (49)

The thiophene (1 g) was added to anhydrous aluminum chloride (1 g) in 50 ml of carbon disulfide. The mixture was cooled to 0° - 5°C in an ice bath. Benzoyl chloride (0.6 g) in 10 ml of carbon disulfide was added dropwise to the mixture with stirring. The mixture was stirred overnight at room temperature, then it was poured into water and extracted with benzene (3 x 30 ml). The combined extracts were washed with water (2 x 40 ml), dried, and evaporated to give an orange solid. Purification by t.l.c. indicated that the major product isolated was unchanged starting material with small traces of benzoic acid detected.

Attempted reaction of 1-benzoyl-4-phenyl-1,3-butadiene (145) with dibenzoylethylene

(a) Equimolar ratios of the diene and dibenzoylethylene were refluxed for 48 hours in the following solvents; ethanol, benzene, dioxane, toluene, xylene, and nitrobenzene. Each time the starting materials were recovered unchanged.

(b) One equivalent of the diene and 30 equivalents of dibenzoylethylene in a high pressure bomb were heated up to 300°C for 12 hours. Working up according to the usual method gave only unknown coloured materials.

Preparation of dibenzoylacetylene

47.2 g of the dibenzoylethylene were converted to its bromide by the usual method (using bromine in chloroform). 25 g of this were then converted to dibenzoylacetylene by the method of Lutz and Smithy (96).

Preparation of α-furylmethylcarbinol (151)

This was made by the method of Duveen and Kenyon (154) using furfural and methylmagnesiumiodide as starting materials; yield = 50%.

Reaction of α-furylmethylcarbinol and dibenzoylacetylene

Equimolar amounts of α-furylmethylcarbinol and dibenzoylacetylene in 50 ml of benzene were refluxed for 12 hours. After cooling to room temperature, 10 ml of ethanol were added. The white precipitate formed was filtered off and recrystallized from petroleum ether-methanol to give white platelets; m.p. = 138°C; yield = 43%.

Anal. calculated for $C_{22}H_{18}O_4$; C, 76.30; H, 5.20

Found, C, 76.19; H, 5.23

The IR spectrum 3440 cm^{-1} (OH), 1645 cm^{-1} (C=O str.) The NMR spectrum, 8.60 τ, 8.71 τ (3H, methyl singlets) 6.54 τ (1H, broad methine singlet), 5.23 τ to 5.63 τ (1H, methine quartet), 4.08 τ, 4.12 τ (2H, vinyl singlets), and 2.54 τ to 2.95 τ (10H, aromatics).

Attempted aromatisation of the adduct 152

(a) The adduct (2 g) 152 suspended in methanol (50 ml) was hydrogenated over palladium-charcoal at 600 p.s.i. at 60° for 24 hours in a pressure vessel with a glass liner. An orange solution was obtained which on evaporation gave a yellow-brown oil. This was not purified but boiled with 1 ml of hydrobromic acid in 50 ml of dioxane for 15 minutes. Working up according to the usual method gave an unknown red oil which showed broad absorption bands in the IR spectrum.

(b) The adduct 152 (1 g) in 50 ml. of carbon tetrachloride was irradiated for 24 hours with a Hanovia Quartz U.V. Lamp, model: 30620. The solvent was evaporated off and the red oil on examination by t.l.c. showed at least 15 components.

Attempted reaction of methyl 2-furfuryl ether with dibenzoylethylene

(a) Equimolar ratios of the ether and dibenzoylethylene were refluxed for 24 hours in the following solvents: ethanol, benzene, toluene, xylene, and hexachloro-1,3-butadiene. Each time unchanged starting materials were recovered.

(b) Equimolar ratios of the ether and dibenzoylethylene plus 1/10 equivalent of aluminum chloride in 50 ml of anhydrous methylene chloride were stirred at room temperature for 72 hours. Water was added and the product was extracted with ether (3 x 30 ml). Evaporation of the ether extracts gave black decomposition products .

Preparation of 2-benzylthiophene

This was made by the Clemmensen reduction of 2-benzoylthiophene according to the general reduction method of Steinkopf et al.(20); m.p. = 127°C, Lit. (155) 129° - 135°C; yield 23%.

Attempted oxidation of 2-benzylthiophene to produce 2-benzylthiophene-S,S-dioxide (156)

(a) In accordance with Hinsberg's method (97), 10 ml of hydrogen peroxide were added to 25 ml of glacial acetic acid and the solution was cooled to 0° - 5°C. To this were added 4 g of 2-benzylthiophene. The mixture was refrigerated for 48 hours and thrown into ice. The product was extracted with ether (3 x 40 ml). The ether extracts were washed with water (5 x 20 ml) and with dilute sodium carbonate solution, dried, and evaporated to give a yellow oil (2% yield). This crude oil was reflux with dibenzoylacetylene for 8 hours in 50 ml of toluene. However, working up gave only dibenzoylacetylene and some decomposed materials. Thus, the yellow oil from above was probably not the expected product.

(b) The oxidation procedure was repeated by using Leonard and Johnson's periodate method (98). Again the expected S,S-dioxide 156 was not detected.

Preparation of the Diels-Alder adduct of piperylene and dibenzoylacetylene

In accordance with Dupont and Paquot's method (156) equimolar quantities of piperylene and dibenzoylacetylene were refluxed for 8 hours in toluene to give 1-methyl-2,3-dibenzoylcyclohexa-2,5-diene (158) as a yellow oil. Yield = 68% .

Preparation of 2,3-dibenzoyltoluene (159)

1-Methyl-2,3-dibenzoylcyclohexa-2,5-diene (5 g) and sulfur (1.6 g) were heated at 220°C for ½ hour. The product was purified by column chromatography on alumina to give white prisms; m.p. = 125°C; yield = 37%.

Anal. calculated for $C_{21}H_{16}O_2$; C, 84.00; H, 5.33;

Found C, 83.88; H, 5.45

The IR spectrum, 1647 cm^{-1} (C=O)

The NMR spectrum, 7.82 τ (3H, methyl singlet), 2.27 τ to 3.38 τ (13 H, aromatics).

Preparation of 1,3-diphenyl-4-methylbenzo[c]thiophene (160)

The 2,3-dibenzoyltoluene (1 g) in toluene (80 ml) was refluxed with phosphorus pentasulfide (1.5 g) for 8 hours. The mixture was cooled, and inorganic solids were filtered off. The filtrate was washed with dilute acid and dilute sodium bicarbonate, dried, and evaporated to give a yellow oil which crystallized on standing, and was further purified by thin layer chromatography using benzene as a developing solvent; m.p. = 96 - 108°C; yield = 17%.

Anal. calculated for $C_{21}H_{16}S$, C, 84.00; H, 5.33; S, 10.67

Found, C, 83.92; H, 5.47; S, 10.55

The NMR spectrum, 7.80 τ (3H, methyl singlet), 2.18 τ to 3.35 τ (13H, aromatics).

Oxidation of 2,3-dibenzoyltoluene (159)

2,3-Dibenzoyltoluene (5 g), potassium permanganate (7 g), and sodium hydroxide (1 g) in 300 ml of water were refluxed for 24 hours. The manganese dioxide was filtered off and the filtrate was treated with sodium bisulfite to destroy the excess permanganate. The aqueous

solution was acidified with acid and extracted with ether. Evaporation of the ether extract gave a white solid which was purified by t.l.c. The IR spectrum showed that the product was not 2,3-dibenzoylbenzoic acid, but benzoic acid instead.

Attempted reaction of 2,3-dibenzoyltoluene with N-bromosuccinimide

Equimolar quantities of 2,3-dibenzoyltoluene and N-bromosuccinimide, and 0.05 g of benzoyl peroxide in 100 ml of carbon tetrachloride were refluxed for 5 hours. The end of the reaction was indicated by the disappearance of N-bromosuccinimide from the bottom of the flask and accumulation of succinimide at the top of the reaction mixture. The succinimide was filtered off and the carbon tetrachloride was evaporated to give a brown solid which was recrystallized from cyclohexane. The IR spectrum showed that the product was unchanged 2,3-dibenzoyltoluene.

Preparation of 2,6-dicarboxyphenylglyoxylic acid (167)

The method of Graebe et al, (101) was modified in the following way. Naphthalic anhydride (30 g) was added to a solution of sodium hydroxide (12 g) in water (150 ml). To this mixture was added portionwise a concentrated boiling solution of potassium permanganate (150 g) in the minimum amount of water. The mixture was refluxed 16 hours. The manganese dioxide was filtered off, and the filtrate was treated with 100 ml ethanol to destroy the excess permanganate. The aqueous solution was concentrated to 150 ml. After acidification with HCl, the aqueous solution was extracted with ether (3 x 50 ml). The ether extract was dried and evaporated to give white needles; yield = 38%; m.p. = 238°C; Lit. (101) 239°C.

Preparation of hemimellitic acid (168)

This was made by the method of Graebe and Bossel (101); m.p. = 197°C ; yield = 27%.

Preparation of 2,6-dicarbomethoxybenzoic acid (175)

This was made by the method of Meyer (159); m.p. = 149°C ; yield = 72%.

Preparation of 2,6-dicarbomethoxybenzoyl chloride (176)

This was made by the method of Meyer (159); m.p. = 85% ; yield = 93%.

Attempted Friedel-Crafts reaction of 2,6-dicarbomethoxybenzoyl chloride and benzene

Anhydrous benzene (20 ml) was added to anhydrous aluminum chloride (3 g) in 100 ml of carbon disulfide. The mixture was cooled to 5°C in an ice bath and 2,6-dicarbomethoxybenzoyl chloride (5.4 g) in carbon disulfide (10 ml) was added dropwise to the mixture with stirring. The mixture was stirred for 6 hours longer at room temperature. Then dilute hydrochloric acid (100 ml) was added to decompose the thick mixture and the product was extracted with benzene (3 x 50 ml). The benzene extracts were washed with water, dried, and evaporated to give a brown solid. Examination by IR spectroscopy showed that the product was hemimellitic acid.

Reaction of ethyl ethoxymagnesiummalonate with 2,6-dicarbomethoxybenzoyl chloride.

Ethyl ethoxymagnesiummalonate was prepared according to the procedure of Reynolds and Hauser (102). The compound (8 g) was treated with 2,6-dicarbomethoxybenzoyl chloride (8.5 g). The reaction was stirred

overnight at 40°C. The cooled reaction mixture was treated with dilute sulfuric acid and the mixture extracted with ether. The dried extract on evaporation was refluxed 4 hours with a mixture of glacial acetic acid (60 ml), sulfuric acid (7 ml), and water (40 ml). The cooled mixture was thrown on ice, and the colourless precipitate was washed with water. The IR spectrum of this solid was found to be identical to that of isophthalic acid.

The aqueous filtrate from above was extracted with ether and the ether extracts were washed with water (5 x 20 ml), dried, and evaporated to give a yellow oil; yield = 7%. The NMR spectrum, 7.63 τ (3H singlet, methyl), 6.12 τ (6H singlet, equivalent methoxy groups), from 2.82 τ to 2.34 τ (3H bands, three aromatic protons, AB_2 pattern).

Attempted preparation of 2-acetylisophthaloyl chloride

The crude 2,6-dicarbomethoxyacetophenone from above was first hydrolysed to 2-acetylisophthalic acid by boiling with 50% potassium carbonate solution for 2 hours. However, when the acid was treated with either thionyl chloride or phosphorus pentachloride, black tar resulted.

Attempted preparation of 1,2,3-triacetylbenzene from hemimellitic acid

Hemimellitic (5 g) acid was suspended in benzene (50 ml) and treated with excess thionyl chloride (6 ml). The mixture was refluxed until homogeneous then evaporated under reduced pressure. The crude material was recrystallized from benzene and was used without further purification. Yield was almost quantitative.

This crude acid chloride (5 g) was treated with methyl zinc iodide made from zinc (6 g) and methyl iodide (13 g) according to the method of Simmons and Smith (103,104). Working up gave traces of unknown material.

The expected product, 1,2,3-triacetylbenzene, was not detected.

Reaction of 2,6-dicarboxyphenylglyoxylic acid with thionyl chloride

The acid (5 g) was suspended in benzene (50 ml) and treated with excess thionyl chloride (7 ml). The mixture was refluxed until homogeneous, then evaporated under reduced pressure. The crude acid chloride was used without further purification. Yield was almost quantitative.

Reaction of ethyl ethoxymagnesiummalonate with the triacid chloride (169)

The crude acid chloride from above was treated with ethyl ethoxymagnesiummalonate, made according to the method of Reynolds and Hauser (102). Working up as described above did not give the expected product 170.

Attempted Sandmeyer reaction involving cuprous cyanide and 2,6-diacetylaniline (183)

2,6-Diacetylaniline (3 g) was dissolved in hydrochloric acid (4.4 ml) and water (50 ml). To this cooled solution was added with stirring sodium nitrite (1.3 g) solution according to reference (158). The diazonium solution was neutralized with sodium carbonate before treatment with cuprous cyanide solution (8 g in 10 ml of water) so that the liberation of hydrogen cyanide was avoided. Working up by the usual method (158) gave unchanged starting materials.

Preparation of 3-nitrophthalyl chloride (187)

In accordance with Chambers' method (106), the chloride was made by the action of phosphorus pentachloride upon 3-nitrophthalic acid; m.p. = 78°C ; yield = 53%.

Preparation of 2,3-diacetylnitrobenzene (188)

Ethyl ethoxymagnesiummalonate was prepared from magnesium (1.2 g), ethyl malonate (8 g), and ethanol (10 ml) according to reference (102). This was treated with 3-nitrophthalyl chloride (6 g). Working up by the usual method gave a yellow oil which was refluxed for 4 hours with a mixture of glacial acetic acid (60 ml), sulfuric acid (7 ml), and water (40 ml). The cooled mixture was thrown on ice, and the product was extracted with ether (3 x 30 ml). The ether extracts were dried and evaporated to give a brown oil; yield = 8%. The IR spectrum, 1700 cm^{-1} (C=0), 1550 cm^{-1} and 1375 cm^{-1} (NO_2). The NMR spectrum, 7.60 τ , 7.69 τ (6H singlets, two acetyl methyls), 2.43 τ to 2.90 τ (3H bands, three aromatic protons, ABX pattern).

Reduction of 2,3-diacetylnitrobenzene (188)

The crude 2,3-diacetylnitrobenzene from above was added to a mixture of 0.2 g of palladium-charcoal and sodium borohydride (0.3 g) in water (100 ml). The mixture was cooled to 5°C and stirred for ½ hour at this temperature. Then sodium borohydride (0.5 g) was added and the mixture was stirred for another hour. The palladium charcoal was first filtered off and the filtrate was extracted with ether (3 x 30 ml). The ether extracts were dried and evaporated to give an orange oil which could not be made to crystallize. Examination by t.l.c. showed 5 bands on the plate. The major product (3% yield) was a yellow oil, whose IR spectrum showed absorptions at 3315 cm^{-1} and 3480 cm^{-1} (NH_2) and at 1679 cm^{-1} (C=0 str.)

Attempted preparation of 2,3-diacetylbenzonitrile (190)

The general procedure of Clark and Read (158) for a Sandmeyer reaction was performed on the crude reduction product of 2,3-diacetylnitrobenzene. Working up gave unknown coloured products of which IR spectra

showed broad peaks.

Preparation of 2,6-dimethylbenzoylchloride (192)

The method of Bull and Fuson (159) gave the acid chloride in nearly theoretical amounts. The crude acid chloride (a yellow liquid) was used without further purification.

Attempted preparation of 2,6-diformylbenzoic acid (193)

2,6-Dimethylbenzoyl chloride (5 g) in hexachloro-1,3-butadiene (50 ml) was chlorinated at 210°C in ultraviolet light from a Hanovia Quartz U.V. Lamp, model # 30620 until the increase in weight corresponded with the introduction of 4 atoms of chlorine. Fractional distillation gave the 2,6-di(dichloromethyl)benzoyl chloride as a brown viscous oil. This was not isolated, but boiled with calcium carbonate (5 g) and water (50 ml) for 2 hours to give a yellow oil which could not be made to crystallize. The IR and NMR spectra showed that the product was not 2,6-diformylbenzoic acid yield = 11%.

PART B Anthranils

Preparation of 2-nitroisophthalic acid (201)

The method of Wohl (109) was modified in the following way. 2-Nitro-m-xylene (20 g), potassium permanganate (160 g), and sodium hydroxide (13 g) in 2½ litre of water were refluxed overnight. After cooling, the manganese dioxide was filtered off. After destroying the excess permanganate with sodium bisulfite, the filtrate was acidified with hydrochloric acid. The white precipitate was separated and recrystallized from ethanol to give white needles; m.p. = 300°C, Lit. (109) 300°C; yield = 72%.

Preparation of 2-nitroisophthaloyl chloride (202)

2-Nitroisophthalic acid (25 g) was suspended in benzene (100 ml) and treated with thionyl chloride (30 ml). The mixture was refluxed until homogeneous then evaporated under reduced pressure. The crude material was recrystallized from benzene and was used without further purification. Yield was almost quantitative.

Preparation of 2,6-diacetylnitrobenzene (182)

Magnesium turnings (9.3 g), in a three-necked flask equipped with magnetic stirrer and a reflux condenser, were treated with a mixture of anhydrous ethanol (10 ml) and carbon tetrachloride (1 ml). The mixture was warmed gently to start the reaction; then anhydrous ether (300 ml) was added. A mixture of anhydrous ether (50 ml), ethyl malonate (60 g) and anhydrous ethanol (100 ml) was added at such a rate that rapid boiling was maintained. The mixture was heated under reflux for 3 hours, when all the magnesium had dissolved.

To the solution was added dropwise over 15 minutes a solution of 2-nitroisophthaloyl chloride (45 g) in anhydrous ether (100 ml). Reflux was maintained for 4 hours until the mixture became too viscous to stir. The cooled reaction mixture was treated with dilute sulfuric acid and the mixture extracted with ether. The dried extract on evaporation gave the tetracarboxylic ester as a viscous yellow oil. This was refluxed 4 hours with a mixture of glacial acetic acid (120 ml), concentrated sulfuric acid (15 ml), and water (80 ml). The cooled mixture was thrown on ice, and the colourless precipitate was washed with water and recrystallized from ethanol; m.p. = 160°C; yield = 89%.

Anal. calculated for $C_{10}H_9NO_4$; C, 57.97; H, 4.35; N, 6.76

Found, C, 57.87; H, 4.54; N, 6.86

The IR spectrum, 1700 cm^{-1} (C=0), 1555 cm^{-1}, 1370 cm^{-1} (NO_2)

The NMR spectrum 7.68 τ (6H singlet, two equivalent CH_3 groups), 2.84 τ, 2.75 τ, 2.63 τ, 2.50 τ (3H bands, three aromatic protons, AB_2 pattern)

Preparation of 7-acetyl-3-methylanthranil (199)

2,6-Diacetylnitrobenzene (2.1 g) was added to a stirred solution of stannous chloride (8.2 g) in concentrated hydrochloric acid (21 ml) at 5°C. A pale yellow ppt. was initially formed, but dissolved after 3 hours. After 5 hours, the mixture was diluted with water (100 ml) and extracted with ether (3 x 50 ml). The dried ether extracts on evaporation gave a pale tan solid, which was examined by t.l.c. Three bands were evident under U.V. examination:

(a) The first on elution gave 2,6-diacetylaniline as bright yellow needles; m.p. = 144°C; yield = 8%.

Anal. calculated for $C_{10}H_{11}NO_2$; C, 67.79; H, 6.22; N, 7.91

Found, C, 67.73; H. 6.36; N, 8.09

The IR spectrum, 1668 cm^{-1} (C=0) 3310 cm^{-1}, 3450 cm^{-1} (NH_2)

The NMR spectrum, 7.48 τ (6H singlet, two equivalent CH_3 singlets), 2.01 τ, 2.18 τ, 3.37 τ, 3.48 τ, 3.60 τ (3H bands, protons on aromatic ring, AB_2 pattern). A better synthesis of this compound is described below:

(b) The second band on elution gave the 7-acetyl-3-methylanthranil (199) as colourless needles; m.p. = 97°C; yield = 38%.

Anal. calculated for $C_{10}H_9NO_2$; C, 68.77; H, 5.15; N, 8.00

Found, C, 68.37; H, 5.04; N, 7.94

The IR spectrum, 1650 cm^{-1} (tentatively C=N), 1695 cm^{-1} (C=0)

The NMR spectrum in deuterochloroform at 20°C, 7.13 τ (6H singlet, two superimposed singlets), 3.11 τ to 1.83 τ (3H bands, protons on the aromatic ring, ABX pattern). The NMR data of this compound at other temperatures and in other solvents are summarized in Table I

(c) The third band on elution gave only traces of coloured material and was not further examined.

Preparation of 2,6-Diacetylaniline (183)

2,6-Diacetylnitrobenzene (7.24 g), stannous chloride (30.00 g) and conc. hydrochloric acid (80 ml) were heated at 90°C for 2½ hour with stirring. The orange mixture was neutralized with solid sodium carbonate and extracted with ether (3 x 100 ml). The ether extracts were washed with dilute sodium carbonate, with water, and dried over sodium sulfate. Evaporation gave a yellow powder which was recrystallized from hexane as yellow needles; m.p. = 144°C; yield = 76%.

Preparation of 7-acetyl-3-methylthioanthranil (209)

7-acetyl-3-methylanthranil (5 g) in pyridine (80 ml) was refluxed with phosphorus pentasulfide (8 g) for 8 hours. The mixture was cooled, poured into water, and extracted with chloroform (3 x 50 ml). The extract was washed with water (5 x 20 ml), dried, and evaporated to give a yellow oil which crystallized on standing, and was further purified by thin-layer chromatography using chloroform as a developing solvent. Yellow crystals were obtained; m.p. = 79°C; yield = 75%.

Anal. calculated for $C_{10}H_9NOS$; C,62.83; H, 4.71; N, 7.33; S, 16.76

Found, C, 62.67; H, 4.84; N, 7.15; S, 16.76

The IR spectrum, 1725 cm^{-1} (C=O), 1635 cm^{-1} (tentatively C=N)

The NMR spectrum 7.15 τ, 7.17 τ (6H, two methyl singlets) 1.80 τ to 3.12 τ (3H bands, protons on the aromatic ring)

Similar results, but with lower yields (~15%) were obtained when sulfurization was performed in carbon disulfide.

Preparation of 7-acetyl-3-methyl-2-phenylbenzo[c]pyrazole (222 b)

The anthranil (0.5 g) and aniline (0.6 g) in glacial acetic acid (50 ml) were refluxed for 16 hours. The mixture was poured into ice and extracted with ether (3 x 50 ml). The ether extracts were washed with saturated sodium carbonate solution and with water, and dried over anhydrous sodium sulfate. Evaporation gave a crude solid which was purified by t.l.c. using a 5% solution of diethyl ether in chloroform as a developer. A band with a blue fluorescence in the ultraviolet was eluted and gave a pale yellow solid on evaporation; m.p. = 120 - 122°C; yield = 27%.

Anal. calculated for $C_{16}H_{14}N_2O$; C,76.80; H, 5.60; N, 11.20

Found C, 76.93; H, 5.75; N, 11.00

The IR specturm, 1698 cm^{-1} (C=0 str.)

The NMR spectrum, 7.31 τ(3H singlet, methyl on the heterocyclic ring), 7.00 τ(3H singlet, methyl on acetyl group), 2.42 τ(5H singlet, protons on phenyl group), 1.81 τ to 2.98 τ (3H bands, protons on the benzo ring, ABX pattern).

Preparation of 7-acetyl-2,3-dimethylbenzo[c]pyrazole (222 a)

The 7-acetyl-3-methylanthranil (0.5 g) and 40 % aqueous methylamine solution (10 ml) in methanol (15 ml) were refluxed for 16 hours. The mixture was poured into ice, and extracted with ether (3 x 25 ml). The combined ether extracts were washed with water, dried, and evaporated to give a solid product. Purification was effected by t.l.c. using 16% diethyl ether in chloroform as a developer. A band with a blue fluorescence in the U.V. was eluted and gave on evaporation pale yellow crystals; m.p. = 110 - 114°C; yield = 34%.

Anal. calculated for $C_{11}H_{12}N_2O$; C, 70.21; H, 6.38; N, 14.89

Found, C, 69.97; H, 6.60; N, 14.67

The IR spectrum, 1701 cm^{-1} (C=O str.)

The NMR spectrum, 7.35 τ (3H singlet, methyl group on the heterocyclic ring), 7.09 τ (3H singlet, methyl on acetyl group), 5.82 τ (3H singlet, methyl on 2-nitrogen), 1.92 τ - 3.01 τ (3H bands, protons on the aromatic ring, ABX pattern).

Preparation of N,N^1-Dimethyl-2-nitroisophthalamide (224)

2-Nitroisophthaloyl chloride (16 g) in benzene (100 ml) was treated with 40% methylamine solution in water (200 ml). After the immediate vigorous reaction the mixture was allowed to stand 1 hour, then filtered. The precipitate was washed with cold water, dried, and recrystallized from dimethylformamide. Small colourless prisms were obtained; m.p. = 273 - 275°C, subliming above 250°C; yield = 61%.

Anal. calculated for $C_{10}H_{11}N_3O_4$; C, 50.61; H, 4.64; N, 17.72

Found, C, 50.85; H, 4.61; N, 17.62

The IR spectrum, 16 70 cm^{-1} (C=O), 3205 cm^{-1} (NH str.)

N,N^1-Dimethyl-2-nitroisothiophthalamide (225)

N,N^1-Dimethyl-2-nitroisophthalamide (5 g) in pyridine (60 ml) was refluxed with phosphorus pentasulfide (15 g) for 3 hours. The mixture was poured into water and extracted with benzene (3 x 150 ml). The dried benzene extracts on evaporation gave a yellow oil which crystallized from methanol as lemon-yellow prisms; m.p. = 204 - 206°C; yield = 81%.

Anal. calculated for $C_{10}H_{11}N_2O_2S_2$; C, 44.65; H, 4.09; N. 16.61; S, 23.83

Found, C, 44.90; H, 4.36; N, 16.29, S, 23.93

The IR spectrum, 1193 cm^{-1} (tentatively C=S), 3191 cm^{-1} (NH str)

Reduction of N,N^1-dimethyl-2-nitroisophthalamide

The amide (2 g) suspended in methanol (50 ml) was hydrogenated over Raney Nickel (0.5 g) at 600 p.s.i. at 60°C for 48 hours in a pressure vessel with a glass liner. A yellow solution was obtained which on evaporation gave a yellow solid, which was crystallized from methanol. Colourless needles with a blue fluorescence in the U.V. were obtained. The compound partly melted at 158°C, resolidified about 180°C, and completely melted at 212°C.

Anal. calculated for $C_{10}H_{15}N_3O_4$; C, 53.22; H, 6.66; N, 18.12

Found, C, 53.21; H, 6.71; N, 18.47

Hydrogenation at lower temperatures, pressures, or shorter times gave erratic yields and products were contaminated with starting materials. Other methods of reduction, eg. dissolving metal, hydride, were also tried but the extreme solubility of the products in polar or aqueous solvents made isolation unsatisfactory.

Attempted sulfurization of 3-methylanthranil (66)

3-Methylanthranil (1 g) and phosphorus pentasulfide (5 g) in carbon disulfide were refluxed for 6 hours. Work up provided only starting material.

When the reaction was performed in pyridine, extensive decomposition was evident. Examination of the products by t.l.c. gave only ill-defined bands which could not be properly separated.

PART C Heterotriptycenes

Preparation of diacetylethylene

In accordance with Armstrong and Robinson's method (127), acetonylacetone was oxidized by selenious acid. The product was isolated by steam distillation followed by ether extractions; m.p. = 78°C; yield = 9½%.

Preparation of naphthacene

Naphthacene was prepared by the methods of Schroeter (160) and Clar (161). The overall yield was 31%; m.p. = 357°C (literature).

Preparation of naphtho[2,3-b]thiophene

The method of Carruthers et al. (162) was modified in the following way. The Friedel-Crafts reaction between thiophene and phthalic anhydride was performed in nitrobenzene instead of carbon disulfide; m.p. = 197°C, Lit. (162) 198°C; yield = 11%.

Preparation of 9-bromoanthracene

9-Bromoanthracene was made by the method of de Barry Barnett and Cook (163). Yield = 88%.

Preparation of 2-methylanthracene

This was made by the method of Bapat et al. (164). To a stirred suspension of 2-methylanthraquinone (2 g) in diglyme (10 ml) a solution of sodium borohydride in diglyme (10 ml of 1M solution) was added. The flask was cooled to 20°C and a solution of boron trifluoride-etherate in diglyme (5 ml of 2M solution) was slowly added during 5 minutes. The mixture was magnetically stirred for 2 hours at 25°C. The yellow precipitate was separated and recrystallized from ethanol; m.p. = 207°C; yield = 65%.

Preparation of 9-methoxyanthracene

In accordance to the method of Meyer et al.(165), 9-methoxyanthracene was made by treating anthrone with dimethylsulfate in dilute sodium hydroxide solution; m.p. = 95°C; yield 71%.

Attempted reaction of 9,10-disodioanthracene with 2,5-dimethyl-3,4-dibromothiophene

Liquid ammonia (100 ml) and sodium (1.3 g) were stirred for 15 minutes with a magnetic stirrer. To this mixture was added portionwise 2,5-dimethyl-3,4-dibromothiophene (7.6 g). The mixture was stirred overnight until all the ammonia was evaporated. Ice was added and the product was extracted with ether (3 x 50 ml). The ether extracts were washed with water, with dilute acid, dried, and evaporated to give a brown solid. Separation by t.l.c. showed that the starting materials were recovered unchanged.

Preparation of 2-(2,5-dimethyl-3-thenoyl)benzoic acid

The method of Steinkopf et al. (125) was modified in the following way. Stannic chloride and carbon disulfide were used instead of aluminum chloride and nitrobenzene; m.p. = 129°C; Lit.(125) 129°C; yield = 70%.

Preparation of 2,7-dimethyl-β-thiophanthraquinone (242)

The method of Steinkopf et al. (125) was modified in the following way. 2-(2,5-Dimethyl-3-thenoyl) benzoic acid (2 g) and concentrated sulfuric acid (6 ml) were stirred at 85°C for 5 minutes and at room temperature for ½ hour. The dark viscous mixture was poured into ice. The white precipitate was collected and recrystallized from ethanol; m.p. = 177°C, Lit. (125) 178°C; yield = 24%.

Attempted preparation of 1,3-dimethyl-4-keto-9-phenyl-9-methylnaphtho [2,3-c] thiophene (245)

2,7-Dimethyl-β-thiophanthraquinone (5 g) was treated with 1 equivalent of methyl magnesium iodide, made from 0.5 g of magnesium and 2.9 g of methyl iodide. The mixture was stirred at 40°C for 8 hours. Water was added and the product was extracted with ether (2 x 40 ml). The ether extracts were washed with water, dried, and evaporated to give a yellow oil. This was not purified but boiled for ½ hour with hydrobromic acid (10 ml) to give a brown oil which could not be made to crystallize. However, when this was treated with calculated quantities of aluminum chloride and benzene in carbon disulfide solution, the resultant product was black tar.

Reactions of anthracenes with dibenzoylacetylene to form substituted dibenzoyldibenzo [2,2,2] bicyclooctatrienes

Unless stated otherwise, equimolar quantities of the anthracene and dibenzoylacetylene were refluxed together in a suitable solvent for specific times. The solvents were removed, and the crude products purified by thin-layer chromatography using chloroform as developing solvents. The results are summarized below.

Reaction of anthracene with dibenzoylacetylene 99

Anthracene (2 g) and dibenzoylacetylene (2.6 g) in 50 ml of xylene were refluxed for 12 hours. Working up as described above gave an oil which formed white needles in light petroleum; m.p. = 207-208°C; yield = 87%.

Anal. calculated for $C_{30}H_{20}O_2$; C, 87.38; H, 4.85

Found, C, 87.27; H, 5.01

The Ir spectrum, 1670 cm^{-1} (C=O str.)

Reaction of 9,10-dimethylanthracene with dibenzoylacetylene

9,10-Dimethylanthracene (0.25 g) and dibenzoylacetylene (0.28 g) in 50 ml benzene were refluxed for 14 hours. Working up gave white needles; recrystallized from methanol; m.p. = 261-264°C; yield = 96%.

Anal. calculated for $C_{32}H_{24}O_2$; C, 87.27; H, 5.45

Found, C, 87.14, H, 5.41

The IR spectrum, 1675 cm^{-1} (C=O str)

Reaction of 9-methylanthracene with dibenzoylacetylene

9-Methylanthracene (0.52 g) and dibenzoylacetylene (0.62 g) in 50 ml benzene were refluxed for 14 hours. Working up gave white needles; recrystallized from petroleum ether; m.p. = 179°C; yield = 91%.

Anal. calculated for $C_{31}H_{22}O_2$; C, 87.33; H, 5.17

Found, C, 87.18; H, 5.26

The IR spectrum, 1674 cm^{-1} (C=O str)

Reaction of 2-methylanthracene with dibenzoylacetylene

2-Methylanthracene (0.50 g) and dibenzoylacetylene (0.62 g) in 50 ml toluene were refluxed for 48 hours. Working up gave white prisms; recrystallized from petroleum ether; m.p. = 223°C; yield = 88%.

Anal. calculated for $C_{31}H_{22}O_2$; C, 87.33; H, 5.17

Found, C, 87.13, H, 5.28

The IR spectrum, 1680 cm^{-1} (C=O)

Reactions of anthracenes with dibenzoylethylene to form substituted dibenzoyldibenzo[2,2,2]bicyclooctadienes

Unless stated otherwise, equimolar quantities of the anthracene and dibenzoylethylene were allowed to react together in a suitable solvent for specific times, and at a suitable

temperature. In some cases, Lewis acid catalysts were necessary. The solvents were removed and the crude products purified by t.l.c. using chloroform as a developing solvent. The results are summarized below.

Reaction of anthracene with dibenzoylethylene 100

Anthracene (0.50 g) and trans-dibenzoylethylene (0.67 g) in 50 ml of xylene were refluxed for 24 hours. Working up gave white prisms; recrystallized from petroleum ether; m.p. = 165°C; yield = 56%.

Anal. calculated for $C_{30}H_{22}O_2$; C, 86.96; H, 5.31

Found, C, 86.87; H, 5.24

The IR spectrum, 1676 cm^{-1} (C=O str.)

Reaction of 9,10-dimethylanthracene and dibenzoylethylene 253

9, 10-Dimethylanthracene (0.30 g) and dibenzoylethylene (0.34 g) in 40 ml of ethanol were refluxed for 8 hours. The pale yellow precipitate formed were filtered off and recrystallized from hexane; m.p. = 195°C; yield = 98%.

Anal. calculated for $C_{32}H_{26}O_2$; C, 86.88; H, 5.88

Found, C, 86.81; H, 6.00

The IR spectrum, 1700 cm^{-1} (C=O str)

Reaction of 9-Methylanthracene and dibenzoylethylene 289

9-Methylanthracene (0.50 g) and dibenzoylethylene (0.62 g) in 50 ml of ethanol were refluxed for 24 hours. The white powdery solid formed were filtered off and recrystallized from petroleum ether; m.p. = 92°C; yield = 88%.

Anal. calculated for $C_{31}H_{24}O_2$; C, 86.92; H, 5.61

Found, C,86.81, H, 5.77

The IR spectrum, 1710 cm^{-1} (C=O str.)

Reaction of 2-methylanthracene and dibenzoylethylene 290

2-Methylanthracene (0.50 g) and dibenzoylethylene (0.62 g) in 50 ml of toluene were refluxed for 12 hours. Working up gave white needles; recrystallized from petroleum ether; m.p. = 112°C; yield = 70%.

Anal. calculated for $C_{31}H_{24}O_2$; C, 86.92; H, 5.61

Found, C, 86.77; H, 5.46

The IR spectrum, 1690 cm^{-1} (C=O str)

Reaction of 1,2-benzanthracene and dibenzoylethylene 255

1,2-Benzanthracene (0.30 g) and dibenzoylethylene (0.36 g) in 50 ml of anhydrous methylene chloride were stirred at 0°C for 5 minutes. The aluminum chloride (0.1 g) was added to the mixture with stirring. The mixture was stirred one hour longer at 0°C and at room temperature for 5 days. The mixture was thrown into ice and extracted with chloroform (3 x 30 ml). The chloroform extracts were washed with water (3 x 50 ml), dried with sodium sulfate, and evaporated off to give a brown solid which was purified by t.l.c., using 50% benzene-chloroform solution as a developing solvent; m.p. = 116°C; yield = 19%.

Anal. calculated for $C_{34}H_{24}O_2$; C, 87.93; H, 5.17

Found, C, 87.61; H, 5.26

The IR spectrum, 1685 cm^{-1} (C=O str.)

Reaction of 9-bromoanthracene with dibenzoylethylene 254

9-Bromoanthracene (0.30 g) and three and one-half equivalents of dibenzoylethylene (1.00 g) in 40 ml of toluene were refluxed for 48 hours. Working up gave an oil which formed white prisms in petroleum ether;

m.p. = 98°C; yield = 12%.

Anal. calculated for $C_{30}H_{21}BrO_2$; C, 73.02; H, 4.26; Br, 16.23

Found, C, 72.97; H, 4.44; Br, 16.05

The IR spectrum, 1695 cm^{-1} (C=0 str.)

Reaction of 9-methoxyanthracene with dibenzoylethylene 291

9-Methoxyanthracene (0.40 g) and dibenzoylethylene (0.49 g) in 50 ml of methanol were refluxed for 48 hours. Working up gave pale yellow prisms; m.p. = 180°C; yield = 43%.

Anal. calculated for $C_{31}H_{24}O_3$; C, 83.78; H, 5.41

Found, C, 83.43; H, 5.53

The IR spectrum, 1680 cm^{-1} (C=0 str.)

Reaction of naphthacene and dibenzoylethylene 292

Naphthacene (0.12 g) and dibenzoylethylene (0.13 g) in 30 ml of toluene were refluxed for 12 hours. Working up gave white prisms; m.p. = 133°C; yield = 67%.

Anal. calculated for $C_{34}H_{24}O_2$; C, 87.93; H, 5.17

Found, C, 87.82; H, 5.34

The IR spectrum, 1680 cm^{-1} (C=0 str.)

Reaction of anthracenes with diacetylethylene to form substituted diacetyldibenzo [2,2,2] bicyclooctadienes

Equimolar quantities of the anthracene and diacetylethylene were refluxed together in suitable solvents for specific times. The solvents were removed and the crude products purified by t.l.c. using 50% benzene-chloroform solution as the developing solvent. The results are summarized below.

Reaction of anthracene and diacetylethylene 252

Anthracene (0.57 g) and diacetylethylene (0.35 g) in 30 ml of xylene were refluxed for 48 hours. Working up gave white prisms; m.p. = 182°C; yield = 41%.

Anal. calculated for $C_{20}H_{18}O_2$; C, 82.75; H, 6.20

Found, C, 82.67; H, 6.22

The IR spectrum, 1725 cm^{-1} (C=O str.)

Reaction of 9-methylanthracene with diacetylethylene 257

9-Methylanthracene (0.5 g) and diacetylethylene (0.3 g) in 30 ml of toluene were refluxed for 12 hours. Working up gave white prisms; m.p. = 188°C; yield = 55%.

Anal. calculated for $C_{21}H_{20}O_2$; C, 82.89; H, 6.58

Found, C, 82.70; H, 6.63

The IR spectrum, 1725 cm^{-1} (C=O str.)

Attempted reactions of naphtho[2,3-b]thiophene with dibenzoylethylene

(a) One equivalent of naphtho[2,3-b]thiophene (0.40 g) and three equivalents of dibenzoylethylene (1.56 g) in 50 ml of xylene were refluxed for 60 hours. Working up gave unchanged starting materials.

(b) Equimolar quantities of naphtho[2,3-b]thiophene (0.28 g) and dibenzoylethylene (0.36 g) in anhydrous methylene chloride with 0.10 g of aluminum chloride were stirred at 0°C for 2 hours, and at room temperature for 48 hours. The mixture was poured into ice and extracted with chloroform (3 x 30 ml). Evaporation of the organic extracts gave a crude brown solid which was purified by t.l.c. The major product isolated, a yellow oil, was not the Diels-Alder adduct, but probably compound 256 according to

spectral evidence.

Sulfurization of the substituted dibenzoyldibenzo[2,2,2]bicyclooctadienes to form the 1,3-diphenylthiophene analogues of triptycene

The bicyclooctadienes were refluxed with two and one-half equivalents of phosphorus pentasulfide in pyridine for varying times. The mixtures were poured into water and extracted with chloroform (3 x 30 ml). The combined chloroform extracts were washed with water (3 x 50 ml), with dilute hydrochloric acid (4 x 50 ml), dried, and evaporated to give crude products, which were purified by t.l.c. using 20% benzene in petroleum ether as developing solvent. Sulfurization in other solvents tried gave either retro Diels-Alder reaction or did not give satisfactory sulfurization. The results are summarized below.

1,3-Diphenyl-4,9-dihydro-4,9-o-benzenonaphtho[2,3-c]thiophene (241)

This was prepared by sulfurization of adduct 100 for 4 days. The product was purified by t.l.c. using 20% benzene in petroleum ether solution and crystallized from petroleum ether. Colourless needles; m.p. = 236°C; yield = 59% were obtained.

Anal. calculated for $C_{30}H_{20}S$; C, 87.38; H, 4.85; S, 7.77

Found, C, 87.20; H, 4.98; S, 7.87

The NMR spectrum, 4.52 τ (2H singlet, two equivalent methine protons), 2.51 τ to 3.26 τ (18H bands, protons on the aromatic rings).

The mass spectrym m+/e 412(parent peak), 291 (M^+-PhCS), 121 ($PhCS^+$)

The NMR spectrum (in carbon disulfide solution) showed the methine protons as a singlet at 4.67 τ .

1,3-Diphenyl-4,9-dimethyl-4,9-dihydro-4,9-o-benzenonaphtho[2,3-c]thiophene

This was prepared by sulfurization of adduct 253 for 2 days. The product was isolated as described above and crystallized from petroleum ether. White needles, m.p. = 246-248°C, were obtained; yield = 48%.

Anal. calculated for $C_{32}H_{24}S$; C, 87.27; H, 5.45; S, 7.28

Found, C, 87.11; H, 5.60; S, 7.15

The NMR spectrum, 8.10 τ (6H singlet, 2 equivalent methyls), 2.43 τ to 3.05 τ (18H bands, protons on the aromatic ring)

The mass spectrum, M^+/e 440 (parent peak), 319(M^+-PhCS), 121($PhCS^+$)

1,3-Diphenyl-4-methyl-4,9-dihydro-4,9-o-benzenonaphtho[2,3-c]thiophene

This was prepared by sulfurization of adduct 289 for 2 days. Working up gave colourless needles; M.P. = 147°C; yield = 27%.

Anal. calculated for $C_{31}H_{22}S$; C, 87.32; H, 5.17; S, 7.50

Found, C, 87.14; H, 5.36; S, 7.30

The NMR spectrum, 8.08 τ (3H singlet, methyl group), 4.45 τ (1H singlet, methine proton), 2.47 -3.12 τ (18H bands, protons on the aromatic rings)

The mass spectrum, m^+/e 426 (parent peak), 305 (M^+-PhCS), 121($PhCS^+$)

1,3-Diphenyl-6-methyl-4,9-dihydro-4,9-o-benzenonaphtho[2,3-c]thiophene (268)

This was prepared by sulfurization of adduct 290 for 3 days. The product was purified by t.l.c. and crystallized from petroleum ether. Colourless needles, m.p. = 209°C, were obtained; yield = 67%.

Anal. calculated for $C_{31}H_{22}S$; C, 87.33; H, 5.17; S, 7.50

Found, C, 87.22; H, 5.31; S, 7.34

The NMR spectrum, 7.75 τ (3H singlet, methyl group), 4.47 τ (2H singlet, methine protons), 2.38 τ to 3.29 τ (17H bands, protons on the

aromatic rings). The mass spectrum, m^+/e 426 (parent peak), 305 (M^+-PhCS), 121 ($PhCS^+$)

1,3-Diphenyl-4,11-dihydro-4,11-o-benzenophenanthro[2,3-c]thiophene (266)

This was prepared by sulfurization of adduct 255 for 2 days. Working up gave white prisms; m.p. = 161°C; yield = 71%.

Anal. calculated for $C_{34}H_{22}S$; C, 88.31; H, 4.76; S, 6.93

Found, C, 88.06; H, 4.66; S, 7.09

The NMR spectrum, 3.74 τ (1H singlet, 4-methine proton), 4.35 τ (1H singlet, 11-methine proton), 1.80 τ to 3.21 τ (20H bands, protons on the aromatic rings)

The mass spectrum, M^+/e 462 (parent peak), 341 (M^+-PhCS), 121 ($PhCS^+$)

1,3-Diphenyl-4-bromo-4,9-dihydro-4,9-o-benzeno-naphtho[2,3-c]thiophene

This was prepared by sulfurization of adduct 254 for 2 days. Working up gave pale yellow prisms; m.p. = 142°C; yield = 77%.

Anal. calculated for $C_{30}H_{19}SBr$; C, 73.32; H, 3.87; Br, 16.29 S, 6.52

Found, C, 73.24; H, 3.80; Br, 15.81; S, 6.62

The NMR spectrum, 4.54 τ (1H singlet, methine proton)

2.22 - 3.09 τ (18H bands, protons on the aromatic rings).

The mass spectrum, M^+/e 491 (parent peak), 411 (M^+-Br), 370 (M^+-PhCS), 121 ($PhCS^+$)

1,3-Diphenyl-4-methoxy-4,9-dihydro-4,9-o-benzenonaphtho [2,3-c] thiophene

This was prepared by sulfurization of adduct 291 for 2 days. Working up gave pale yellow needles; m.p. = 137°C; yield = 47%.

Anal. calculated for $C_{31}H_{22}OS$; C, 84.16; H, 4.98; S, 7.24

Found, C, 84.01; H, 4.79; S, 7.17

The NMR spectrum, 6.16τ(3H singlet, methoxy protons), 4.45τ (1H singlet, methine proton), 2.17-3.15τ(18H bands, protons on the aromatic rings).

The mass spectrum, M^+/e 442(parent peak), 411(M^+-OCH_3) 321 (M^+-PhCS), 121($PhCS^+$)

1,3-Diphenyl-4,11-dihydro-4,11-o-benzenoanthra [2,3-c] thiophene (267)

This was prepared by sulfurization of adduct 292 for 3 days. Working up gave white prisms; m.p. = 177°C; yield = 58%.

Anal. calculated for $C_{34}H_{22}S$; C, 88.31; H, 4.76; S, 6.93

Found, C, 88.17; H, 4.89; S, 6.81

The NMR spectrum, 4.40τ(2H singlet, methine protons), 2.40τ to 3.19τ(20H bands, protons on the aromatic rings; the 5,10-protons were a (2H) singlet at 2.40τ). The mass spectrum, M^+/e 462 (parent peak), 341(M^+-PhCS), 121($PhCS^+$)

Sulfurization of diacetyldibenzocyclooctadiene to form the thiophene 239

This was prepared by refluxing the diacetyl adduct (0.3 g) 252 and phosphorus pentasulfide (1 g) in toluene (50 ml) for 2½ days. The unreacted phosphorus pentasulfide was filtered off and the filtrate was washed twice with water and once with dilute sodium carbonate solution.

After drying with anhydrous sodium sulfate, the filtrate was evaporated off to give an oil which was purified by t.l.c. using 20% benzene in petroleum ether solution as developing solvent, and crystallized from petroleum ether. Colourless platelets, m.p. = 282°C; yield = 22%, were obtained.

Anal. calculated for $C_{20}H_{16}S$; C, 83.33; H, 5.56; S, 11.11

Found, C, 83.21; H, 5.51; S, 11.05

The NMR spectrum, 7.72 τ (6H singlet, two methyl groups) 4.95 τ (2H singlet, methine protons), 2.73 τ to 3.22 τ (8H bands, A_2B_2 pattern for the aromatic protons). The mass spectrum, M^+/e 288 (parent peak), 229 (M^+ - CH_3CS), 59 (CH_3CS^+)

Sulfurization of diacetyldibenzomethylcyclooctadiene to form the thiophene 263

This was prepared by refluxing the diacetyl adduct (0.25 g) 257 and phosphorus pentasulfide (0.60 g) in toluene (50 ml) for 3 days. Working up as described above gave colourless platelets;

m.p. = 247°C; yield = 38%.

Anal. calculated for $C_{21}H_{18}S$; C, 83.44; H, 5.96; S, 10.60

Found, C, 83.67; H, 5.87; S, 10.34

The NMR spectrum, 7.72 τ (3H singlet, 4-methyl), 7.68 τ (6H singlet, the 1,3-dimethyls), 4.96 τ (1H singlet, methine proton), 2.71 τ to 3.22 τ (8H bands, A_2B_2 pattern for the aromatic protons)

The mass spectrum, M^+/e 302 (parent peak), 287 (M^+-CH_3), 243 (M^+-CH_3CS), 59 (CH_3CS^+)

Sulfurisation of dibenzoyldibenzocyclooctatriene 99

The acetylene adduct 99 (0.3 g) and phosphorus pentasulfide (1 g) were refluxed in 50 ml of pyridine for 6½ days. Working up as described above gave a yellow oil which was purified by t.l.c. and crystallized from petroleum ether. The product, which was a single purple fluorescent band on the t.l.c. plate was found to exhibit no sharp melting point, but a range from 216° - 226°C. The mass spectrum indicated two parent peaks with almost equal intensities at M^+/e 412 and M^+/e 396; suggesting that the sulfurization of the acetylene adduct 99 gave a product which was a mixture of the thiophene 241 and the furan 102. These could not be separated by t.l.c.

Anal. calculated for $C_{30}H_{20}S_1$; C, 87.38; H, 4.85; S, 7.77

Found, C, 85.22; H, 5.61; S, 5,17; 0, 4.00

The analysis corresponds to a mixture 42:58 of the thiophene 241 and the corresponding furan 102.

Preparation of 1,3-diphenyl-4,9-dihydro-4,9-o-benzenonaphtho [2,3-c] pyrrole (265)

Dibenzoyldibenzocyclooctadiene (o.5 g) and ammonium acetate (5 g) in acetic acid (50 ml) were refluxed for 2½ hours. After cooling, the mixture was thrown into ice. The resultant precipitate was filtered off and washed three times with water. Crystallization from hot water or petroleum ether gave a white powdery solid; m.p. = 269-271°C; yield = 74%.

Anal. calculated for $C_{30}H_{21}N$; C, 91.14; H, 5.32; N, 3.54

Found, C, 90.98; H, 5.25; N, 3.49

The IR spectrum, 3450 cm^{-1} (NH str)

The NMR spectrum, 4.52 τ (2H singlet, methine protons), 2.60 τ to 3.33 τ (19H bands, protons on the aromatic rings plus the NH proton)

Reaction of Dibenzoyldibenzocyclooctatriene with hydrazine

The method of Baumgartner (79) was modified in the following way. The octatriene (0.5 g) and hydrazine (5 ml) in methanol (50 ml) were refluxed together for 2½ hours. After cooling, the mixture was poured into ice and extracted with benzene (3 x 20 ml). The benzene extracts, which exhibited blue fluorescence in light, were dried with anhydrous sodium sulfate and evaporated off to yield a white solid. Purification by t.l.c. and crystallization from petroleum ether gave white platelets; m.p. = 268°C, Lit. (79) 270°C; yield = 86%.

Attempted reaction of anthracenes with 2,5-dimethoxy-2,5-dihydrofuran

(1) Equimolar quantities of anthracene and 2,5-dimethoxy-2,5-dihydrofuran were refluxed for 48 hours in the following solvents: (a) xylene (b) toluene (c) dioxane (d) benzene

After purification by t.l.c. the starting materials were recovered unchanged in each case.

(2) Anthracene (2 g) and 2,5-dimethoxy-2,5-dihydrofuran (25 ml) were heated in an oil bath with stirring at 220°C for one hour. Purification by t.l.c. produced anthracene and a polymeric oil.

(3) Equimolar quantities of anthracene and 2,5-dimethoxy-2,5-dihydrofuran plus 1/10 equivalent of aluminum chloride in 100 ml of methylene chloride were stirred at 0°C for 2 hours and at room temperature for 48 hours. Working up gave only decomposed materials.

Reaction of 9-methylanthracene with 1,3-diphenyl-4,9-dihydro-4,9-o-benzenonaphtho [2,3-c] thiophene (241)

1,3-Diphenyl-4,9-dihydro-4,9-o-benzenonaphtho [2,3-c] thiophene (.15 g) and 9-methylanthracene (0.40 g) were heated at 240°C for 15 minutes and at 190°C for 2 hours. The resultant dark brown solid was purified by t.l.c. The two starting materials were recovered unchanged. No 1,3-diphenyl -4-methyl-4,9-dihydro-4,9-o-benzenonaphtho [2,3-c] thiophene was detected.

Attempted reactions of acridine with dibenzoylethylene

(a) Equimolar quantities of acridine and dibenzoylethylene were refluxed together in the following solvents for 48 hours; benzene, ethanol, dioxane, toluene, and xylene. Purification by t.l.c. gave unchanged starting materials each time.

(b) Equimolar ratios of acridine and dibenzoylethylene in dioxane were irradiated for 24 hours with a Hanovia Quartz U.V. Lamp, # 30620. Purification by t.l.c. gave two products; the acridine dimer and tetrabenzoylcyclobutane. No Diels-Alder adduct was detected.

(c) Equimolar ratios of acridine and dibenzoylethylene with 1/10 equivalent of aluminum chloride in methylene chloride solution were stirred for 4 days. Working up produced unidentified coloured materials.

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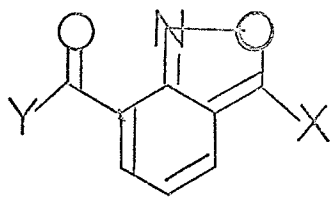


$X = Y = CH_3$

Table I

Temperature (°C).	Solvent	. X(τ) .	Y(τ) .	(X - Y)(τ).
160	C_7D_8	7.68	7.25	0.43
140	"	7.72	7.26	0.46
120	"	7.72	7.22	0.50
100	"	7.75	7.20	0.55
80	"	7.78	7.21	0.57
60	"	7.81	7.19	0.62
40	"	7.84	7.19	0.65
20	"	7.86	7.14	0.72
0°	"	7.90	7.15	0.75
-20	"	7.94	7.14	0.80
160	C_6D_6	7.76	7.20	0.56
140	"	7.77	7.19	0.58
120	"	7.79	7.18	0.61
100	"	7.81	7.17	0.64
80	"	7.84	7.17	0.67
60	"	7.89	7.15	0.74
40	"	7.93	7.16	0.77
20	"	7.95	7.10	0.85
0	"	7.98	7.10	0.88
100	$CDCl_3$	7.19	7.16	0.03
80	"	7.18	7.16	0.02
60	"	7.17	7.16	0.01
40	"	7.16	7.15	0.01
20	"	7.13	7.13	0.00
0	"	7.12	7.12	0.00
-20	"	7.11	7.09	0.02
-40	"	7.11	7.08	0.03
-60	"	7.12	7.07	0.05

Table II - Diels-Alder Adducts

Anthracenes	Dienophiles	Adducts	M.P. (°C)	Yield %	C=O cm^{-1}
Anthracene	$C_{16}H_{10}O_2$	$C_{30}H_{20}O_2$	208	87	1670
9,10-dimethyl	$C_{16}H_{10}O_2$	$C_{32}H_{24}O_2$	264	96	1675
9-dimethyl	$C_{16}H_{10}O_2$	$C_{31}H_{22}O_2$	179	91	1674
2-methyl	$C_{16}H_{10}O_2$	$C_{31}H_{22}O_2$	223	88	1680
Anthracene	$C_{16}H_{12}O_2$	$C_{30}H_{22}O_2$	167	56	1676
9,10-dimethyl	$C_{16}H_{12}O_2$	$C_{32}H_{26}O_2$	195	98	1700
9-methyl	$C_{16}H_{12}O_2$	$C_{31}H_{24}O_2$	92	88	1710
2-methyl	$C_{16}H_{12}O_2$	$C_{31}H_{24}O_2$	112	70	1690
1,2-benz	$C_{16}H_{12}O_2$	$C_{34}H_{24}O_2$	116	19	1685
9-bromo	$C_{16}H_{12}O_2$	$C_{30}H_{21}O_2Br$	98	12	1695
9-methoxy	$C_{16}H_{12}O_2$	$C_{31}H_{24}O_3$	180	43	1680
2,3-benz	$C_{16}H_{12}O_2$	$C_{34}H_{24}O_2$	133	67	1680
Anthracene	$C_6H_8O_2$	$C_{20}H_{18}O_2$	182	41	1725
9-methyl	$C_6H_8O_2$	$C_{21}H_{20}O_2$	188	55	1725

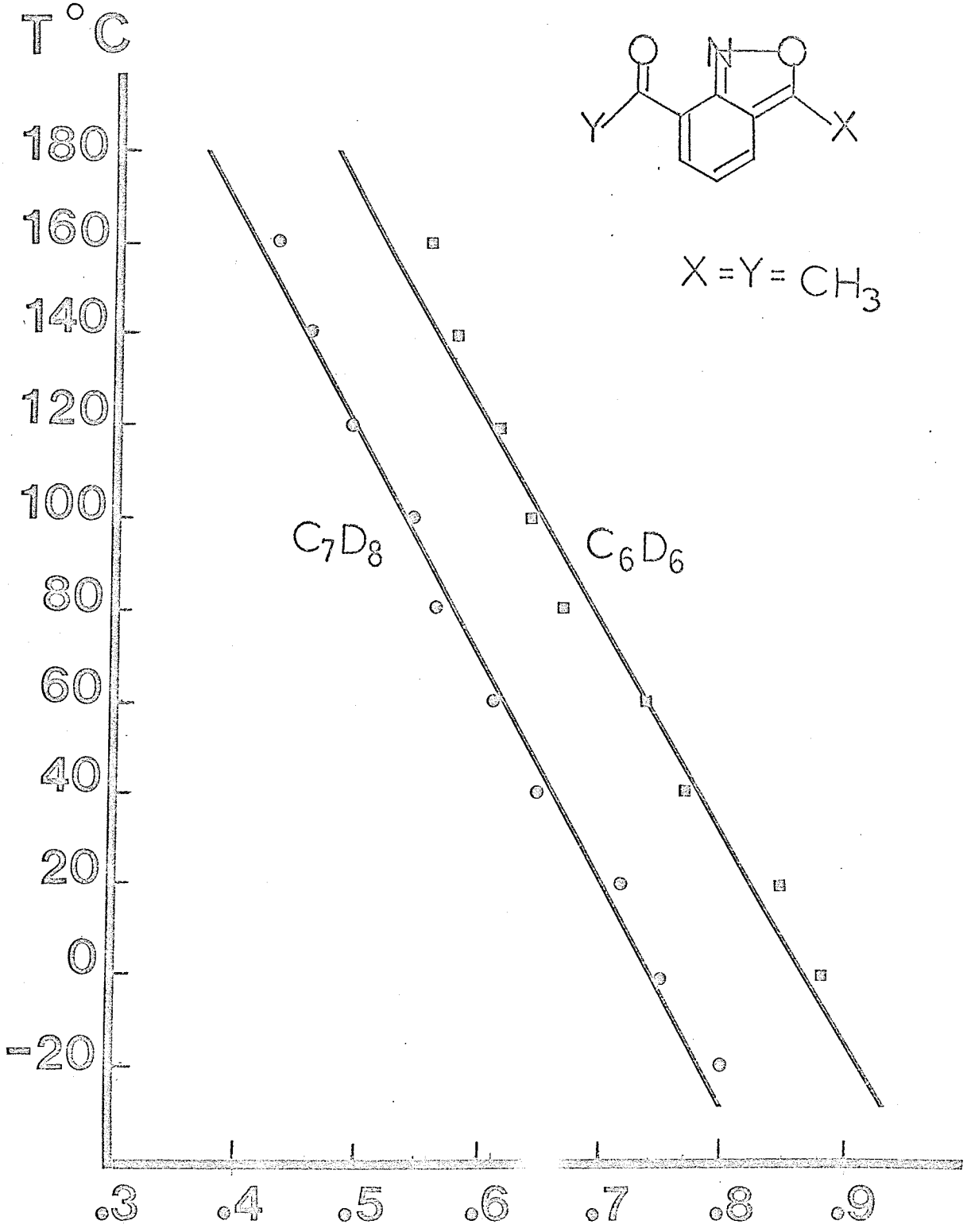
Table III

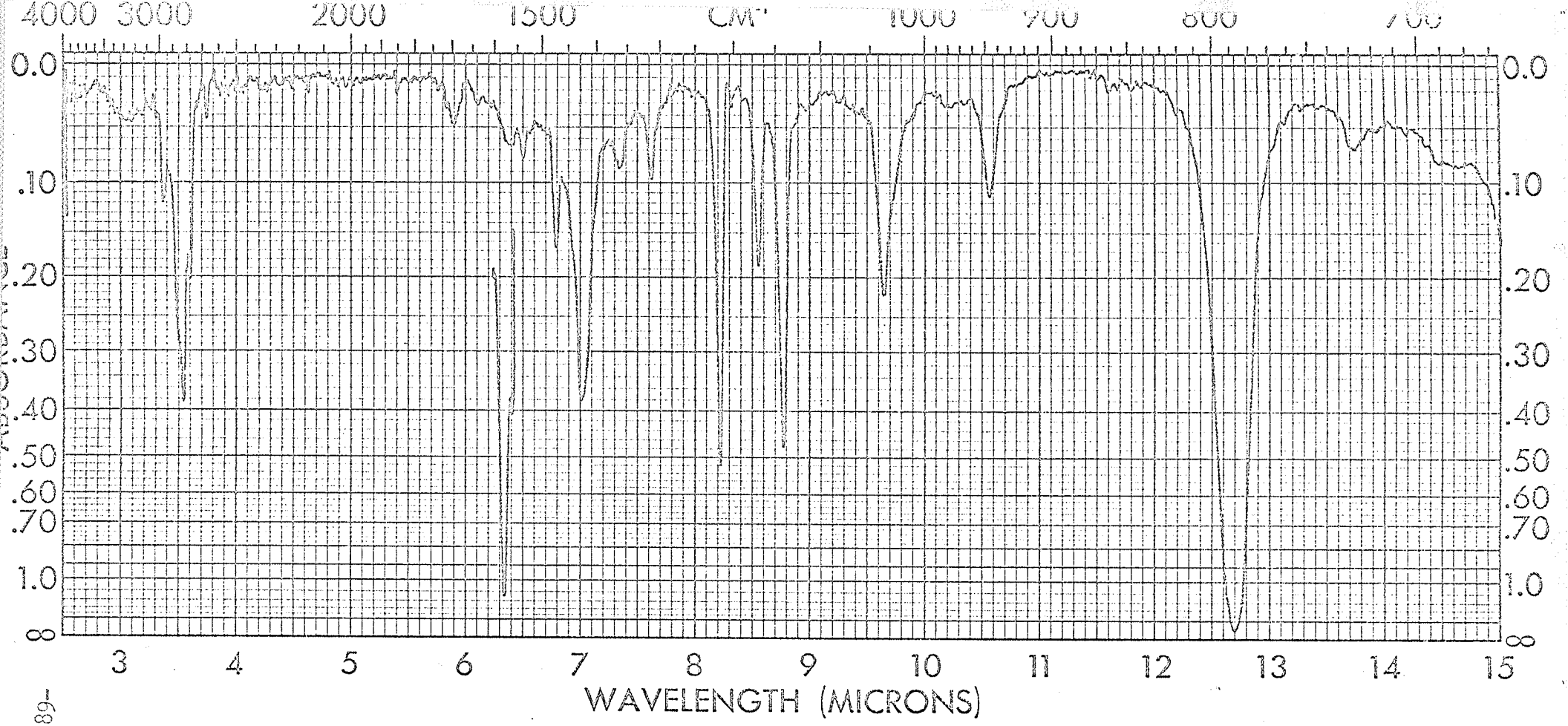
1,3-Diphenylthiophene Analogues of Triptycene

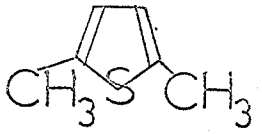
Compound	M.P. (°C)	Yield %	Chemical Shifts (τ) in $CDCl_3$ Methine Protons	Aromatics
$C_{30}H_{20}S$	235	59	4.52	2.51-3.26
$C_{32}H_{24}S$	248	48	-	2.43-3.05
$C_{31}H_{22}S$	147	27	4.45	2.47-3.12
$C_{31}H_{22}S$	209	67	4.47	2.38-3.29
$C_{34}H_{22}S$	161	71	3.74,4.35	1.80-3.21
$C_{30}H_{19}Br$	142	77	4.54	2.22-3.09
$C_{31}H_{22}OS$	137	47	4.45	2.17-3.15
$C_{34}H_{22}S$	177	58	4.40	2.40-3.19

1,3-Dimethylthiophene Analogues of Triptycene

$C_{20}H_{16}S$	280	22	4.95	2.73-3.22
$C_{21}H_{18}S$	247	38	4.96	2.71-3.22

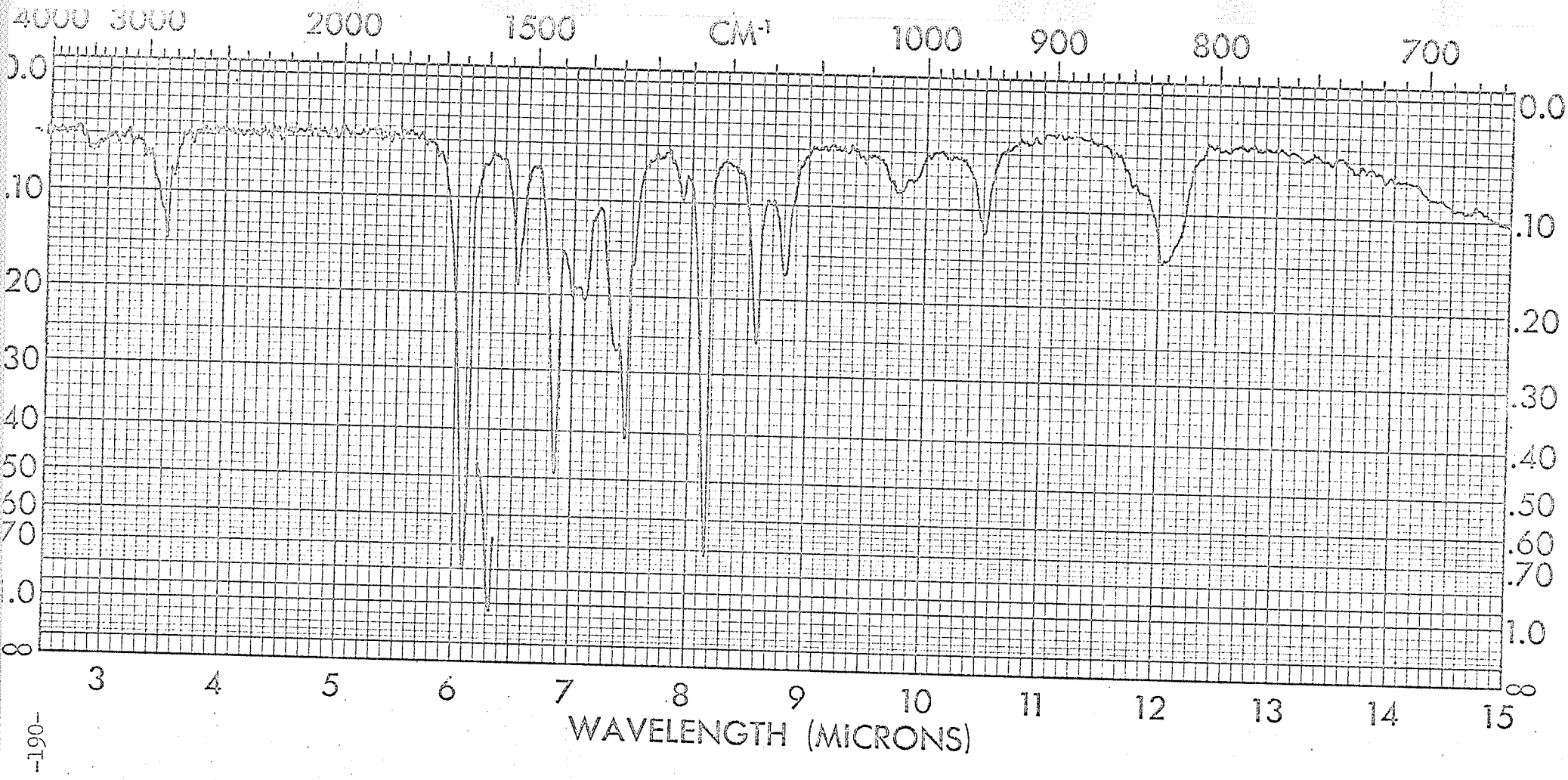

T °C
180
160
140
120
100
80
60
40
20
0
-20
.3
.4
.5
.6
.7
.8
.9
(X-Y) 7
C7D8
C6D6
X = Y = CH3
Y
X

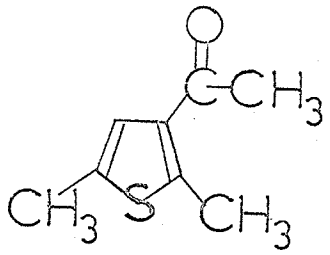




IR spectrum No. 1 :

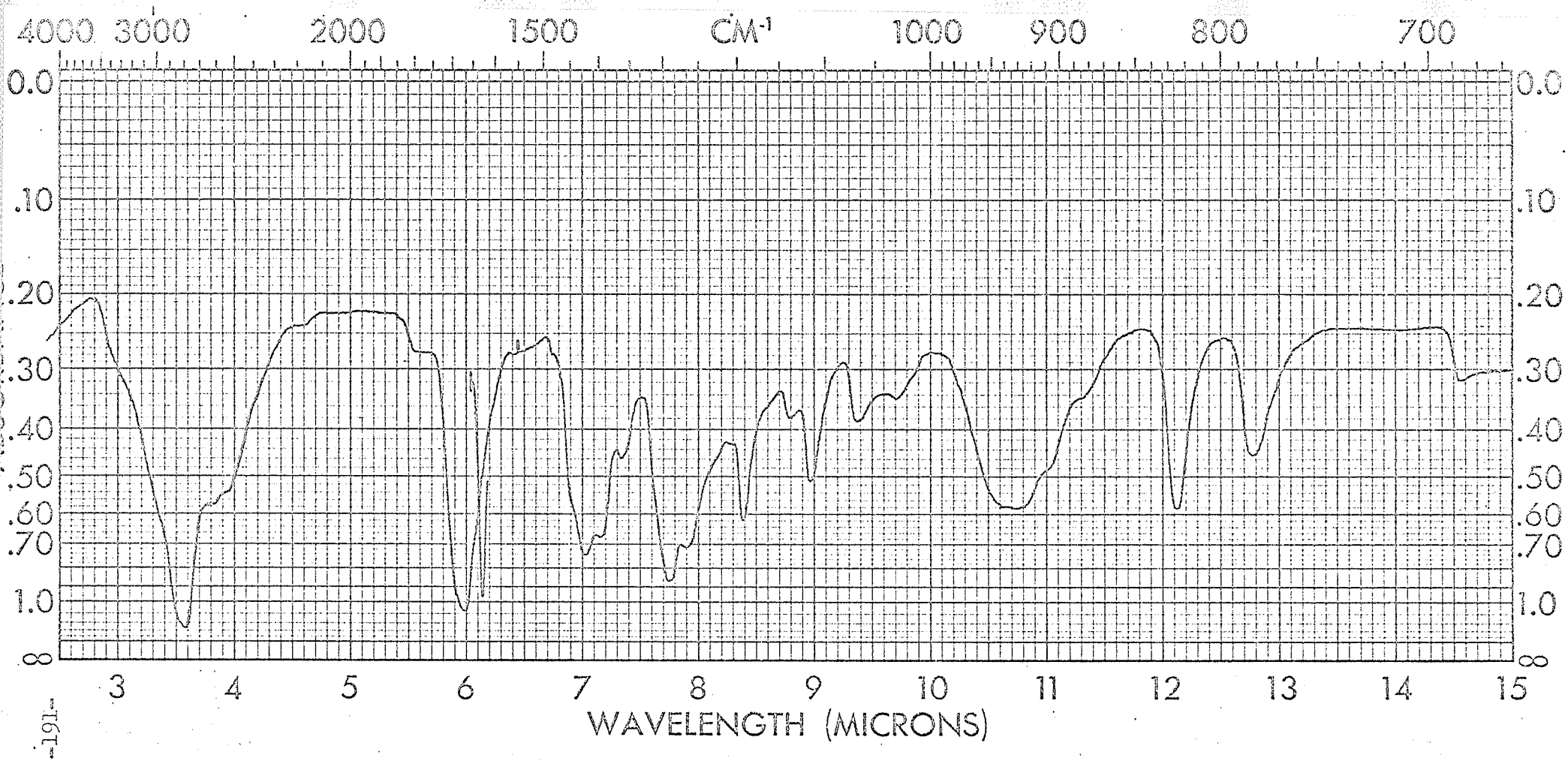
2,5-dimethylthiophene (106).

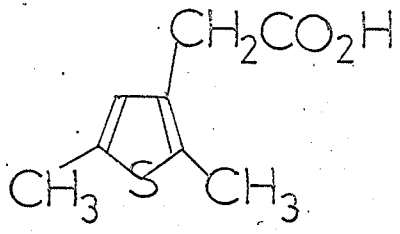




IR spectrum no. 2:

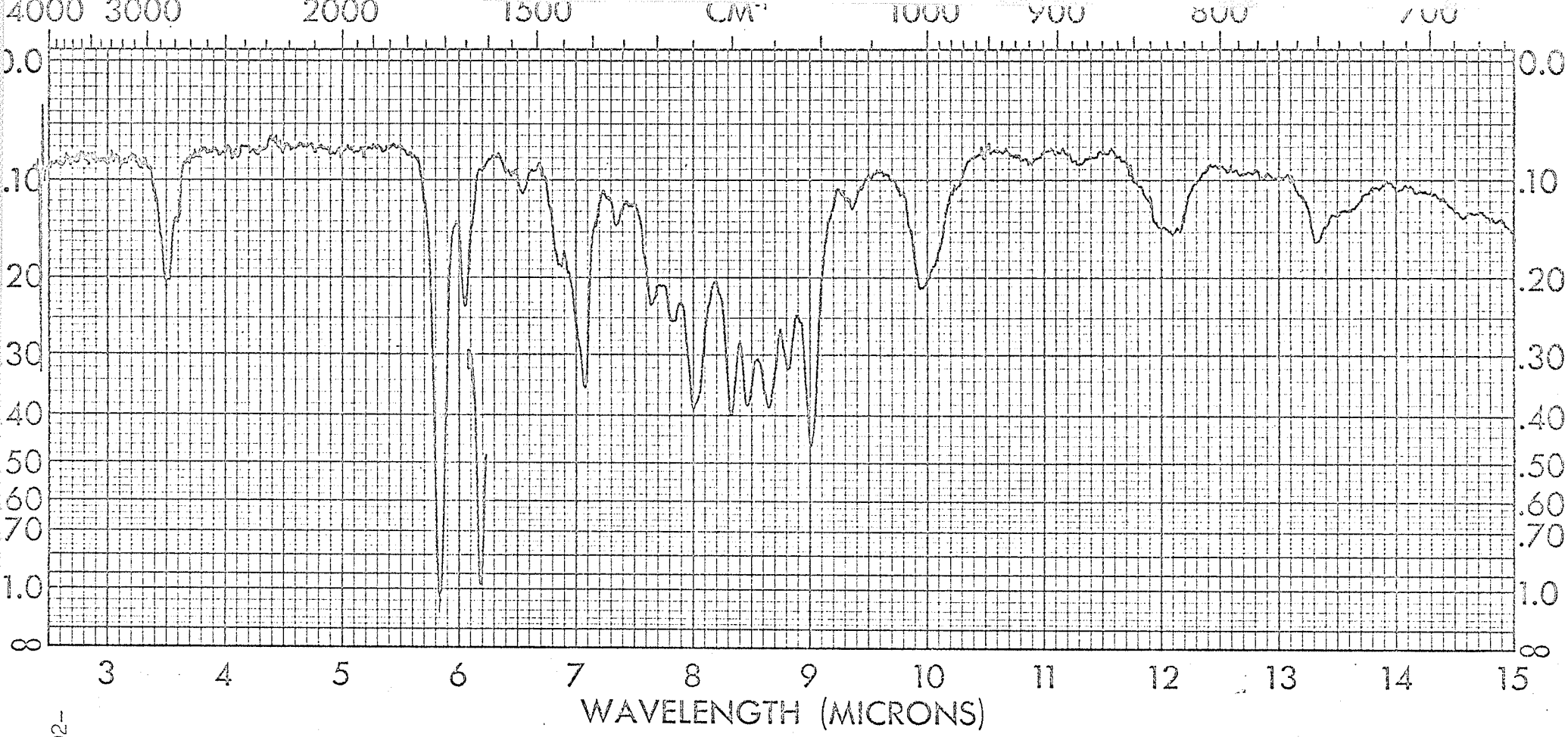
3-acetyl-2,5-dimethylthiophene (107).

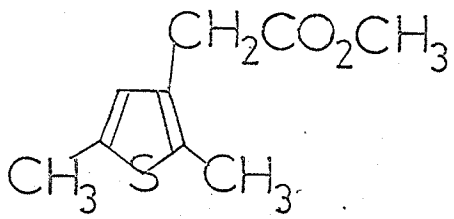




IR spectrum no. 3:

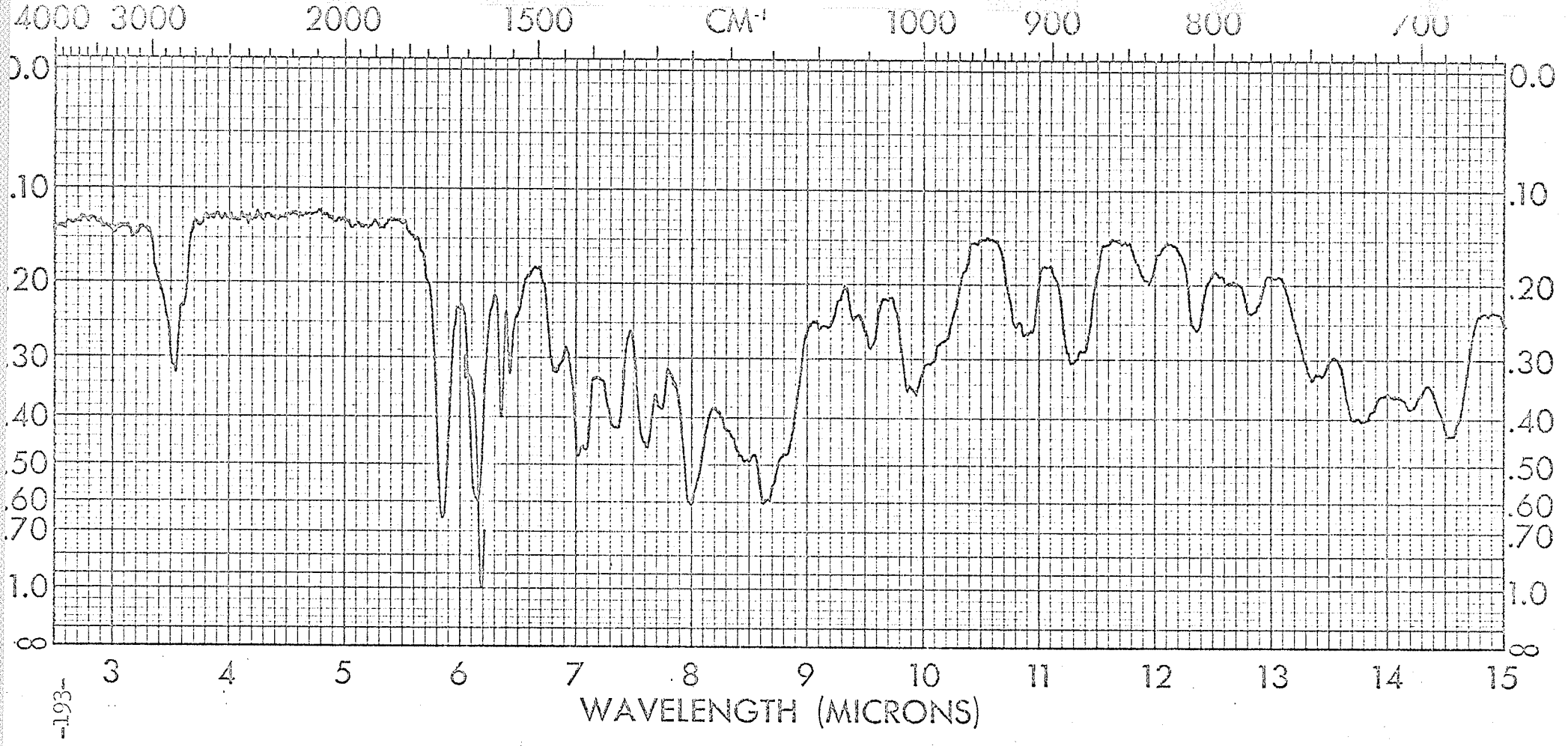
2,5-dimethyl-3-thienylacetic acid (108).

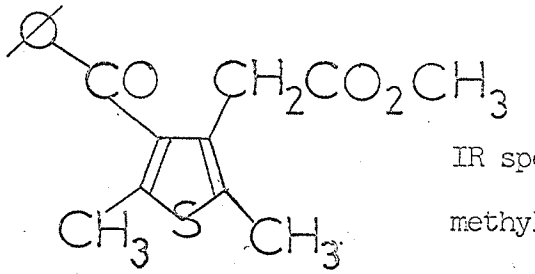




IR spectrum no. 4:

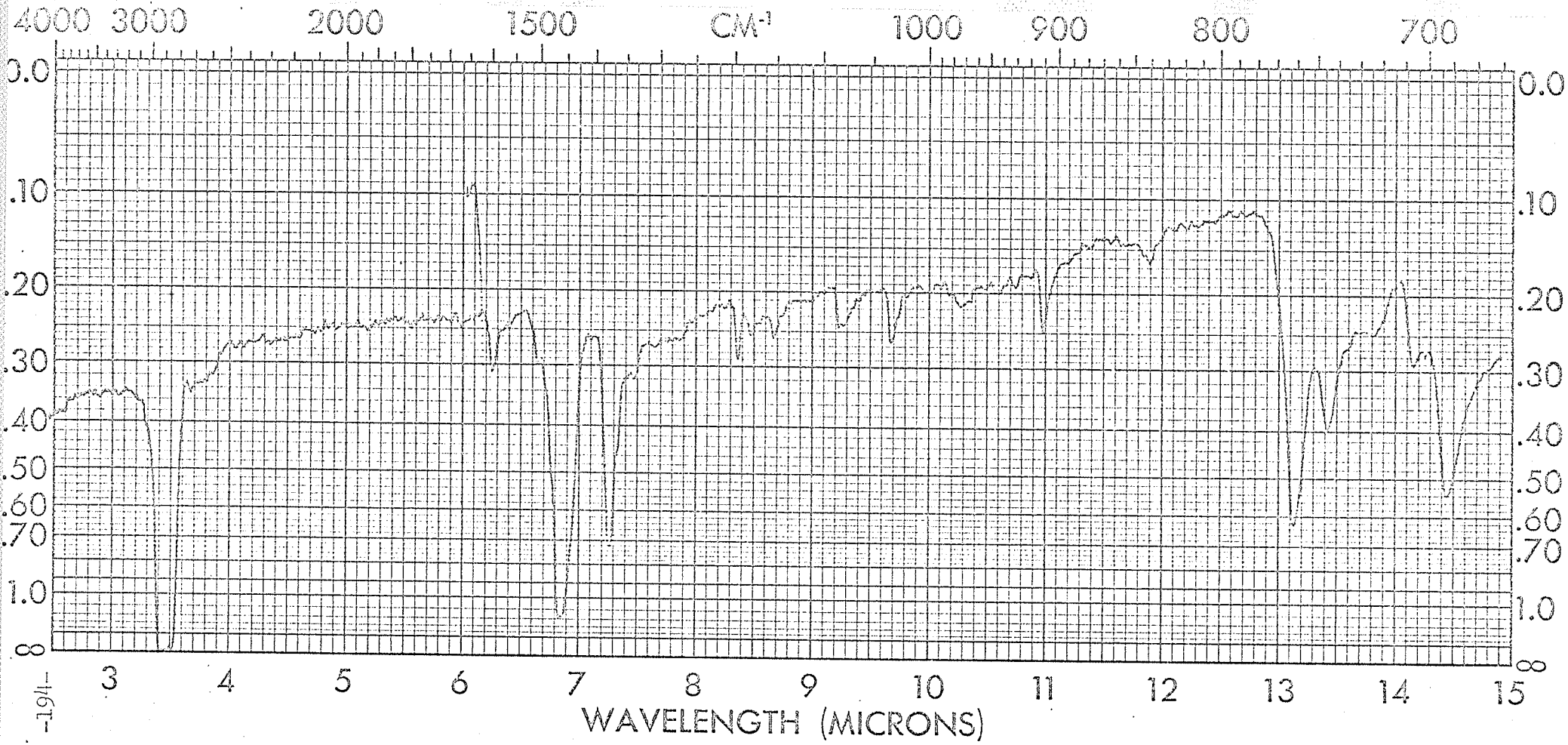
methyl 2,5-dimethyl-3-thienylacetate (109).

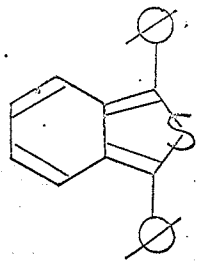




IR spectrum no. 5:

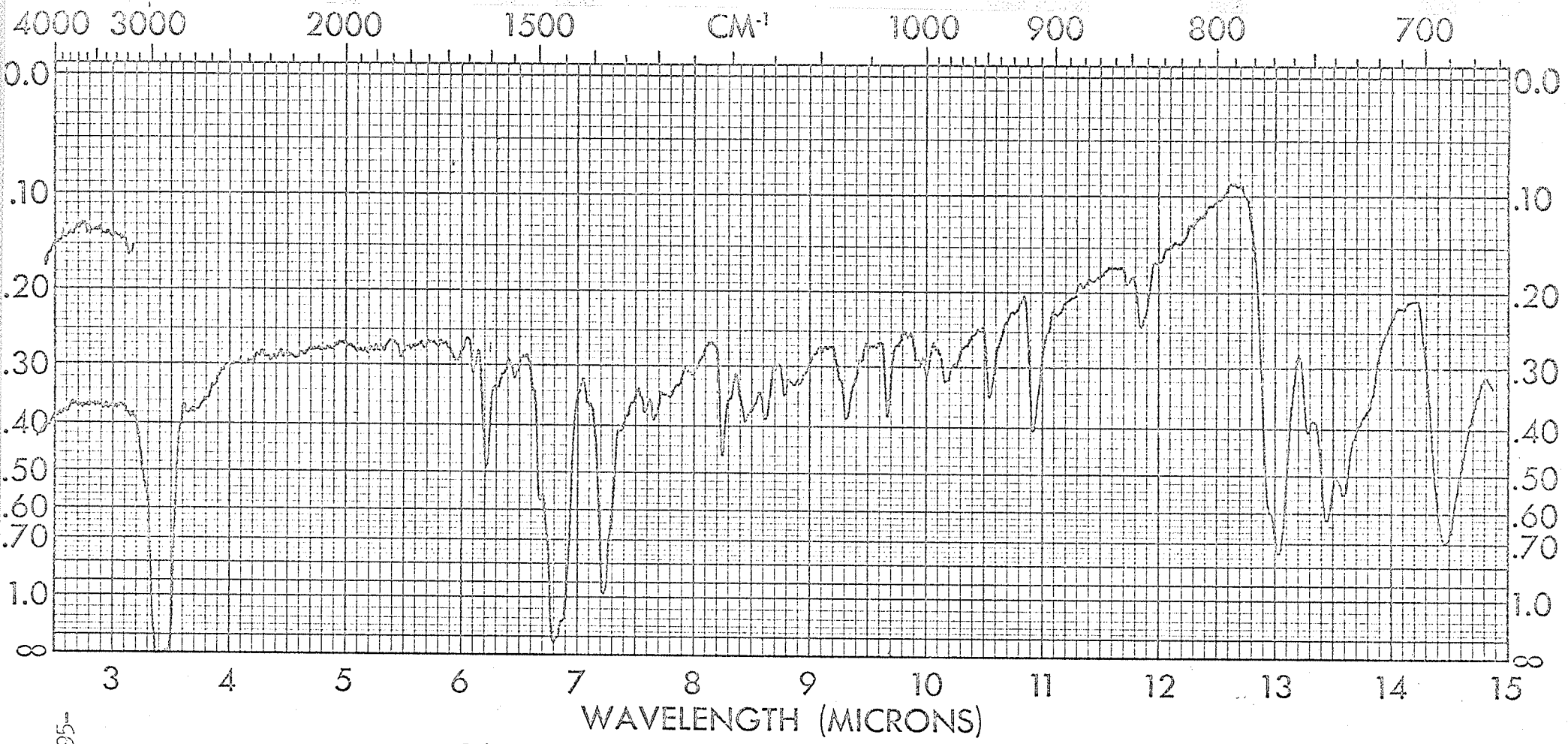
methyl 2,5-dimethyl-4-benzoyl-3-thienylacetate (110).

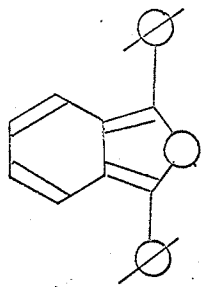




IR spectrum no. 6:

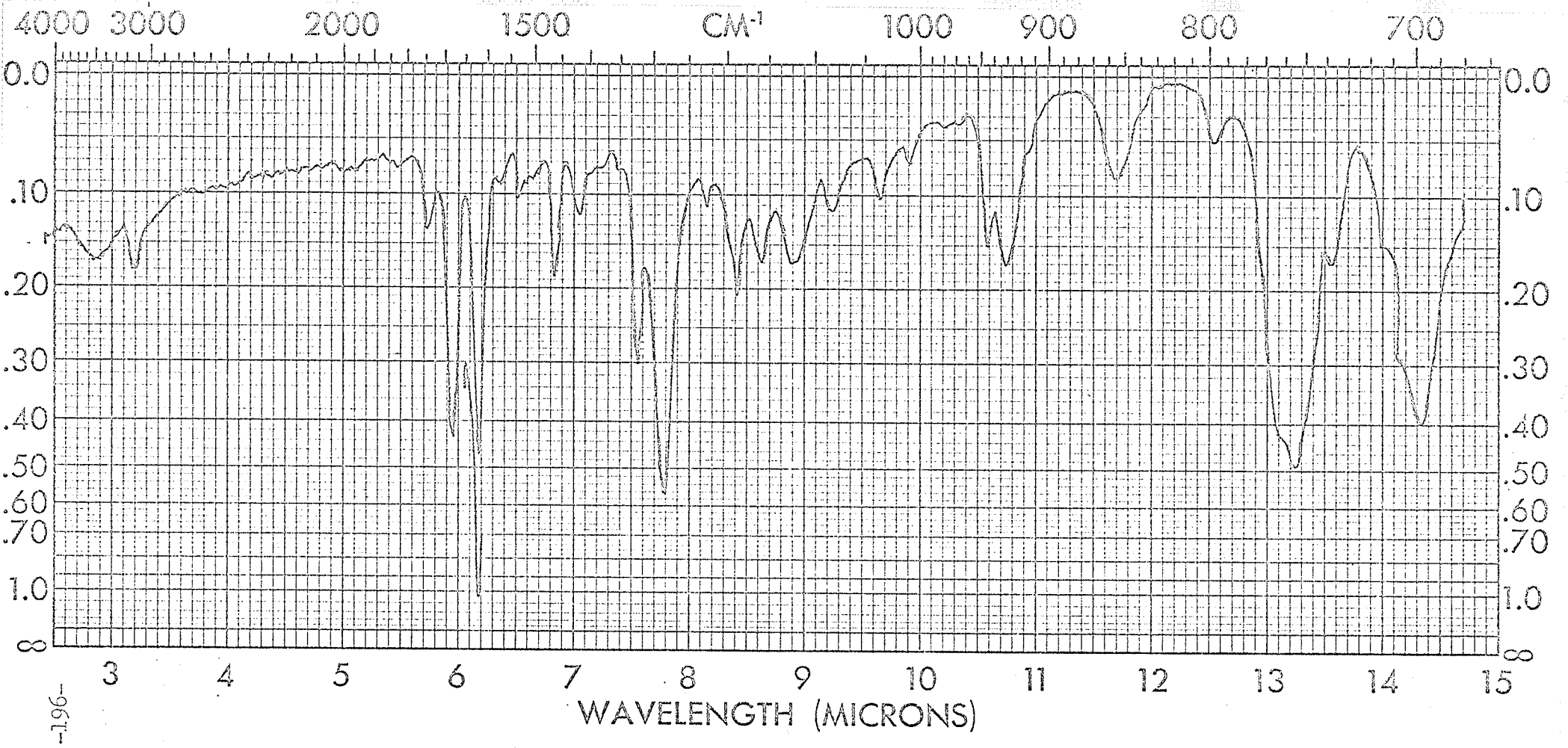
1,3-diphenylbenzo(c)thiophene (42), nujol mull.



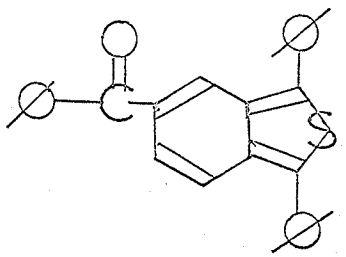


IR spectrum no. 7:

1,3-diphenylbenzo(c)furan (44), nujol mull.

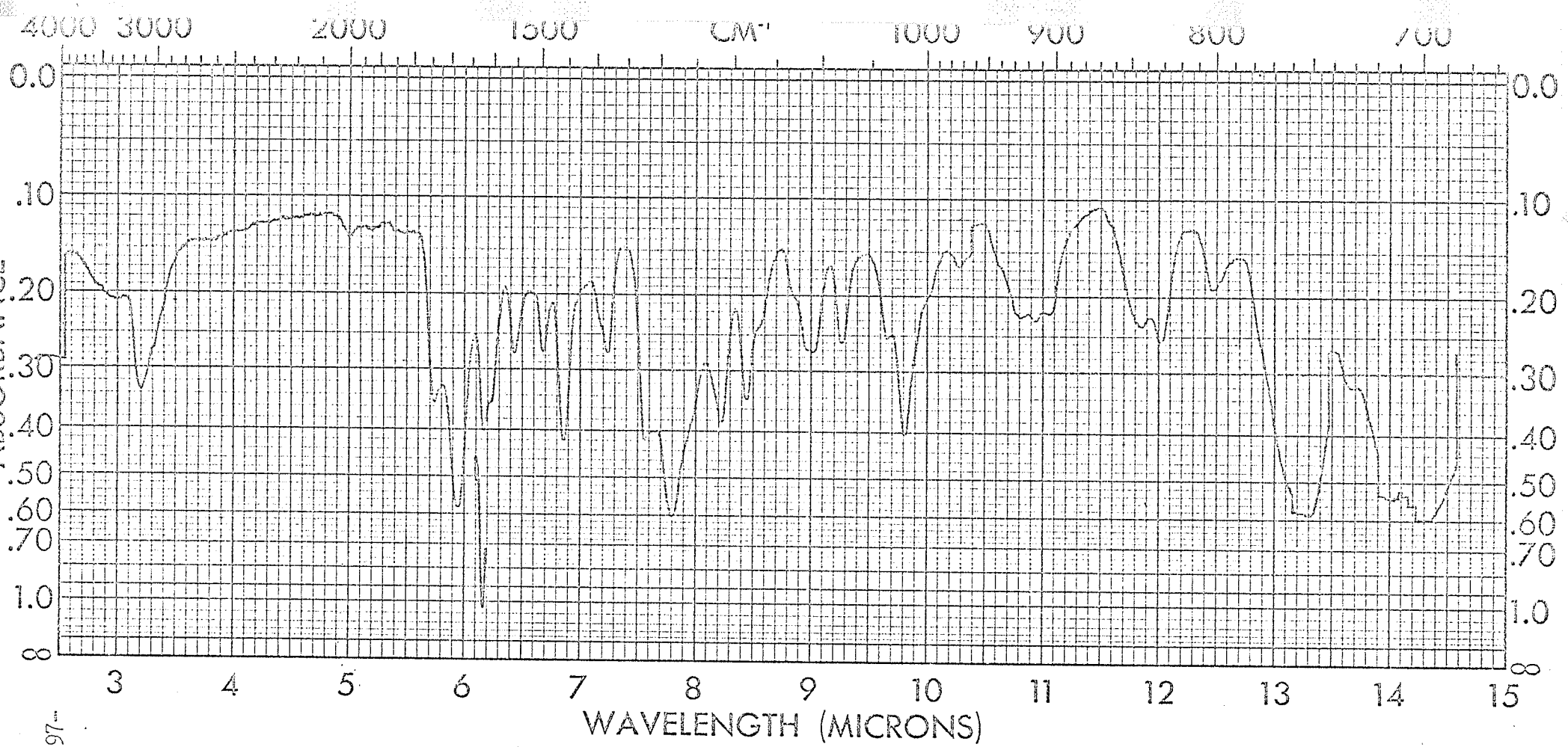


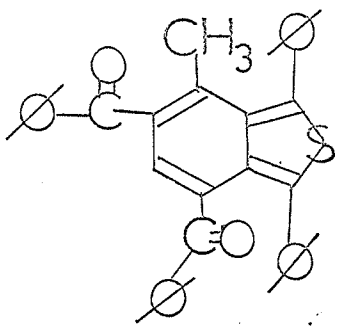
-196-



IR spectrum no. 8:

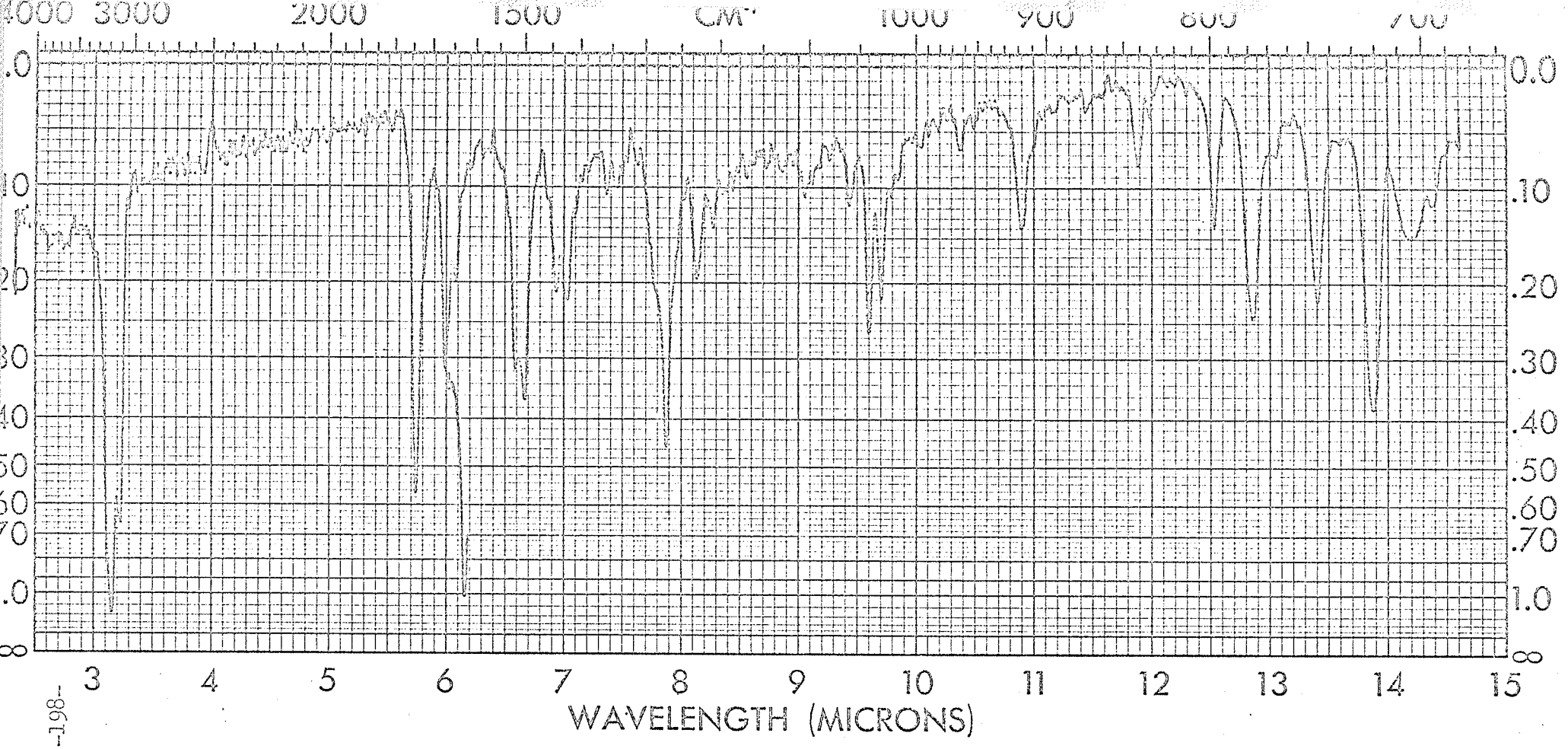
1,3-diphenyl-5-benzoylbenzo(c)thiophene (113)

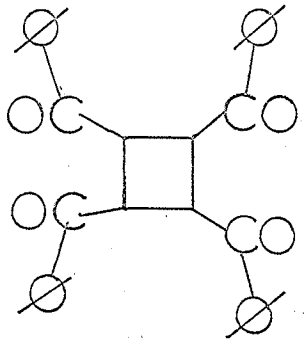




IR spectrum no. 9:

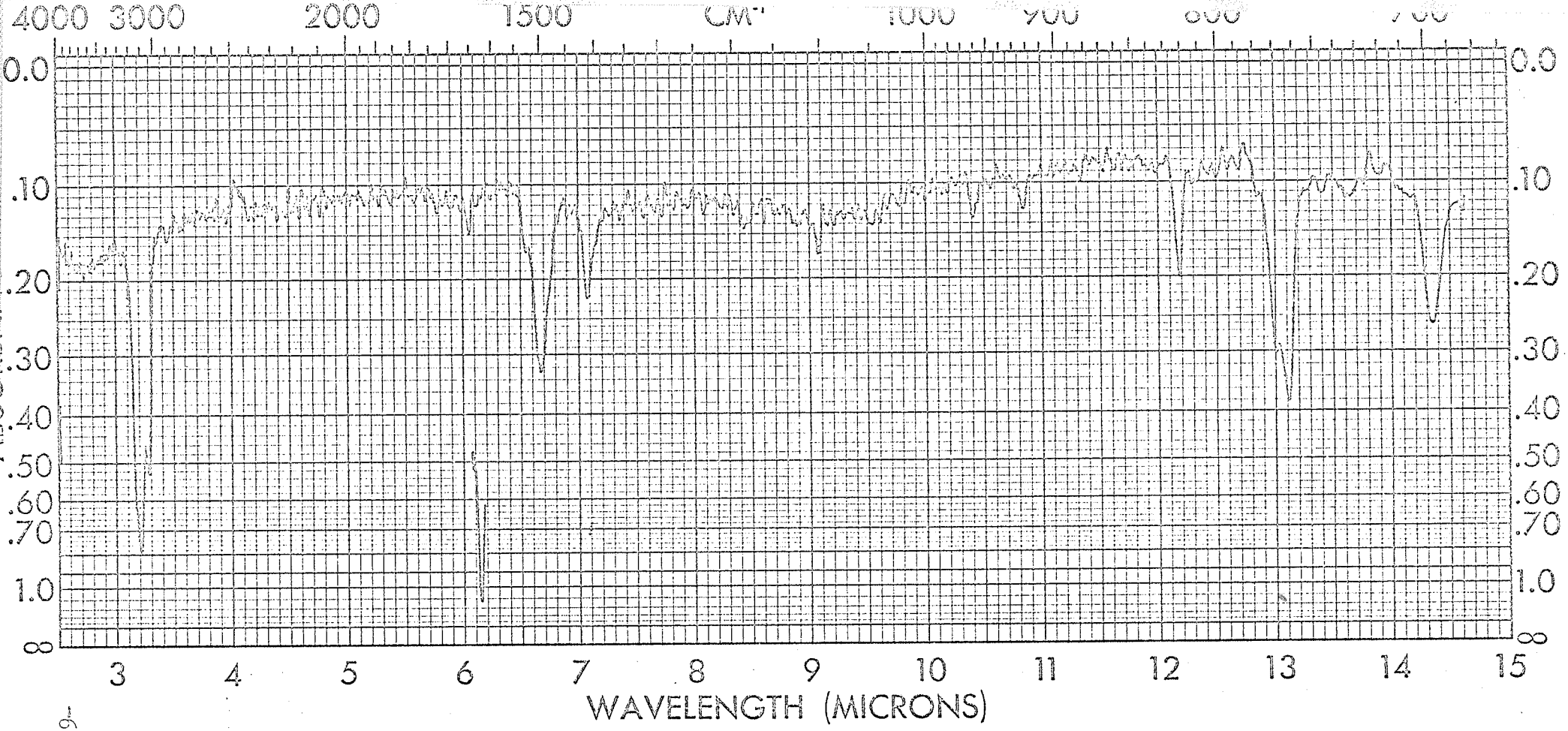
1,3-diphenyl-4-methyl-5,7-dibenzoylbenzo(c)thiophene.

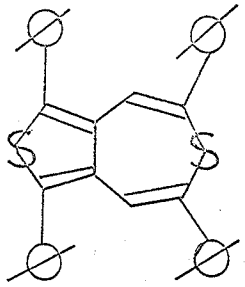




IR spectrum no. 10:

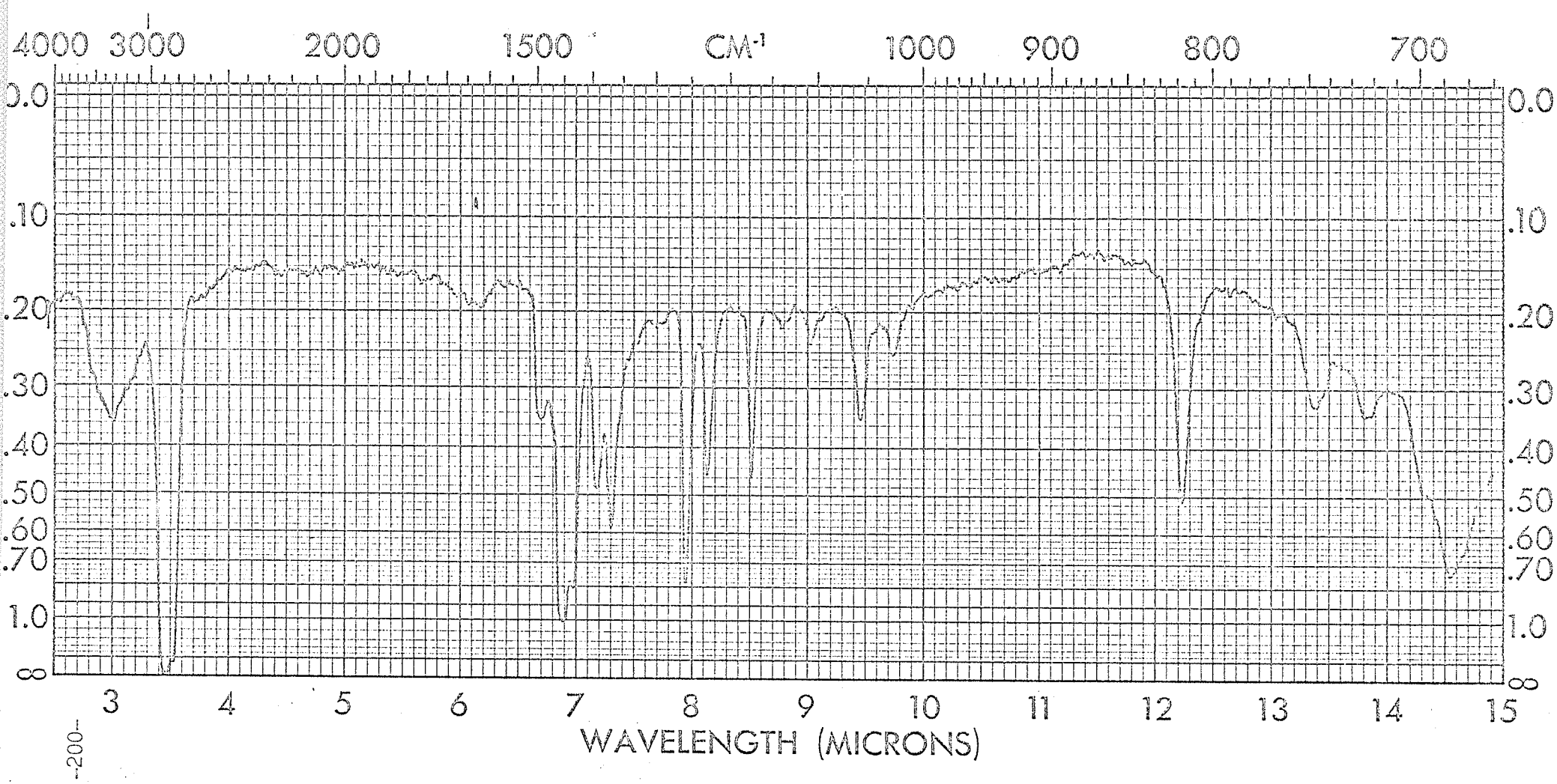
tetrabenzoylcyclobutane (119), nujol mull.

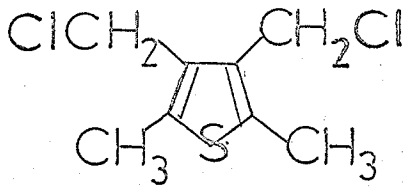




IR spectrum no. 11:

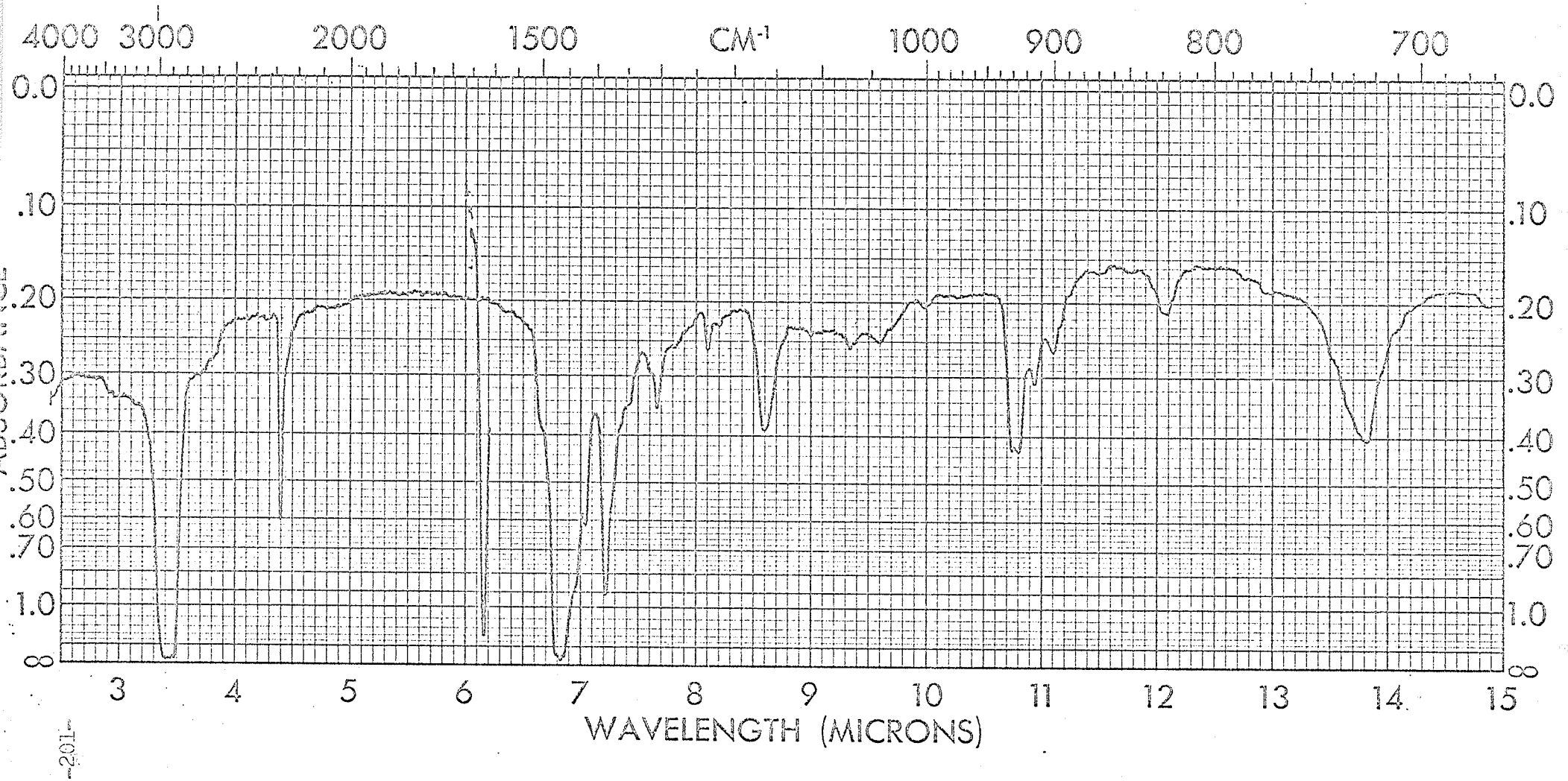
tetraphenylthieno(c)thiepine (120), nujol mull.

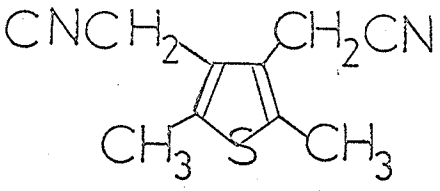




IR spectrum no. 12:

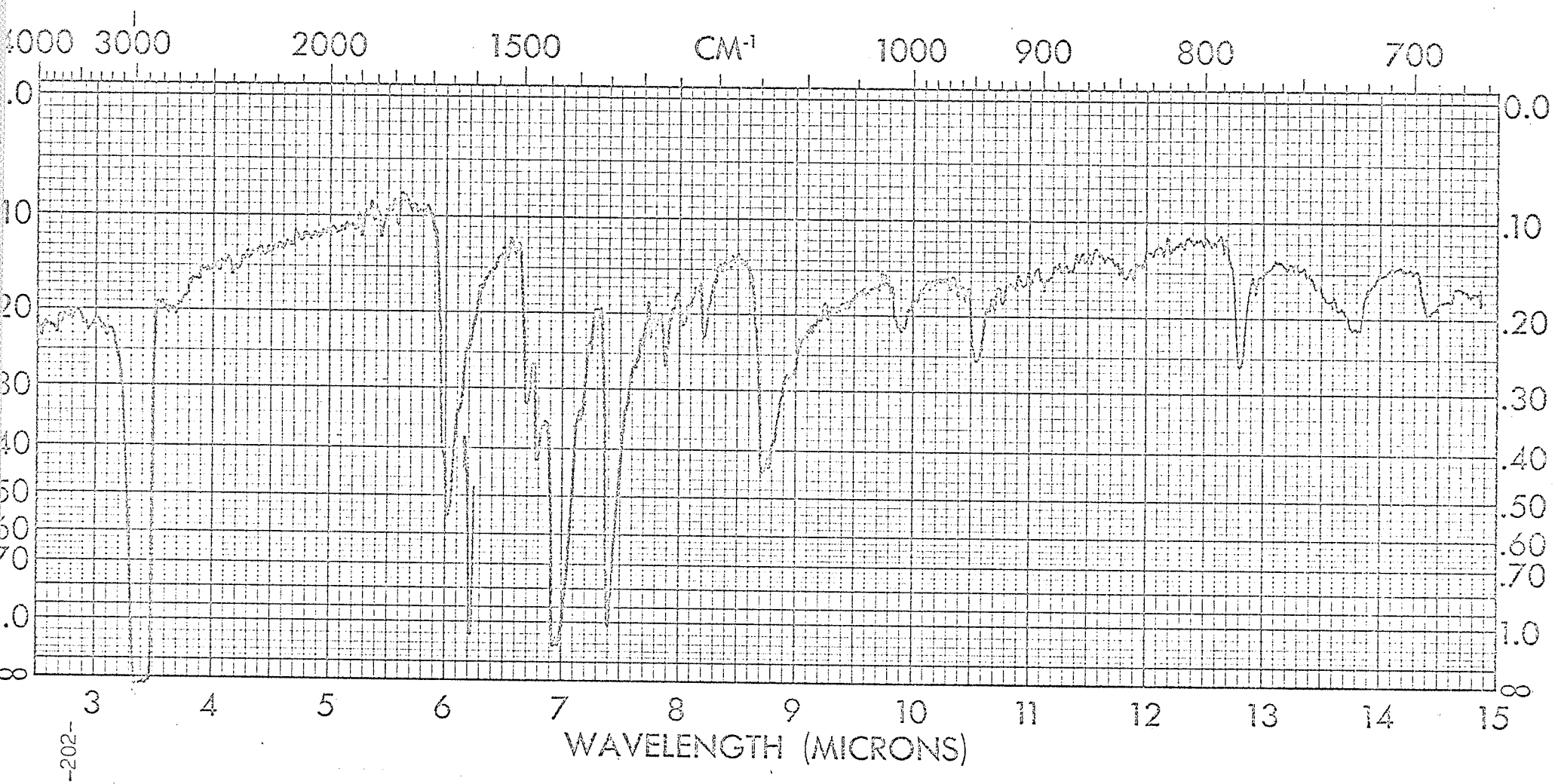
2,5-dimethyl-3,4-dichloromethylthiophene (121), nujol mull

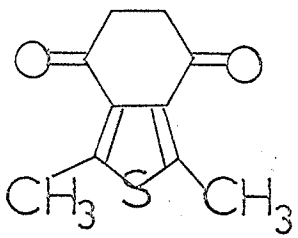




IR spectrum no. 13:

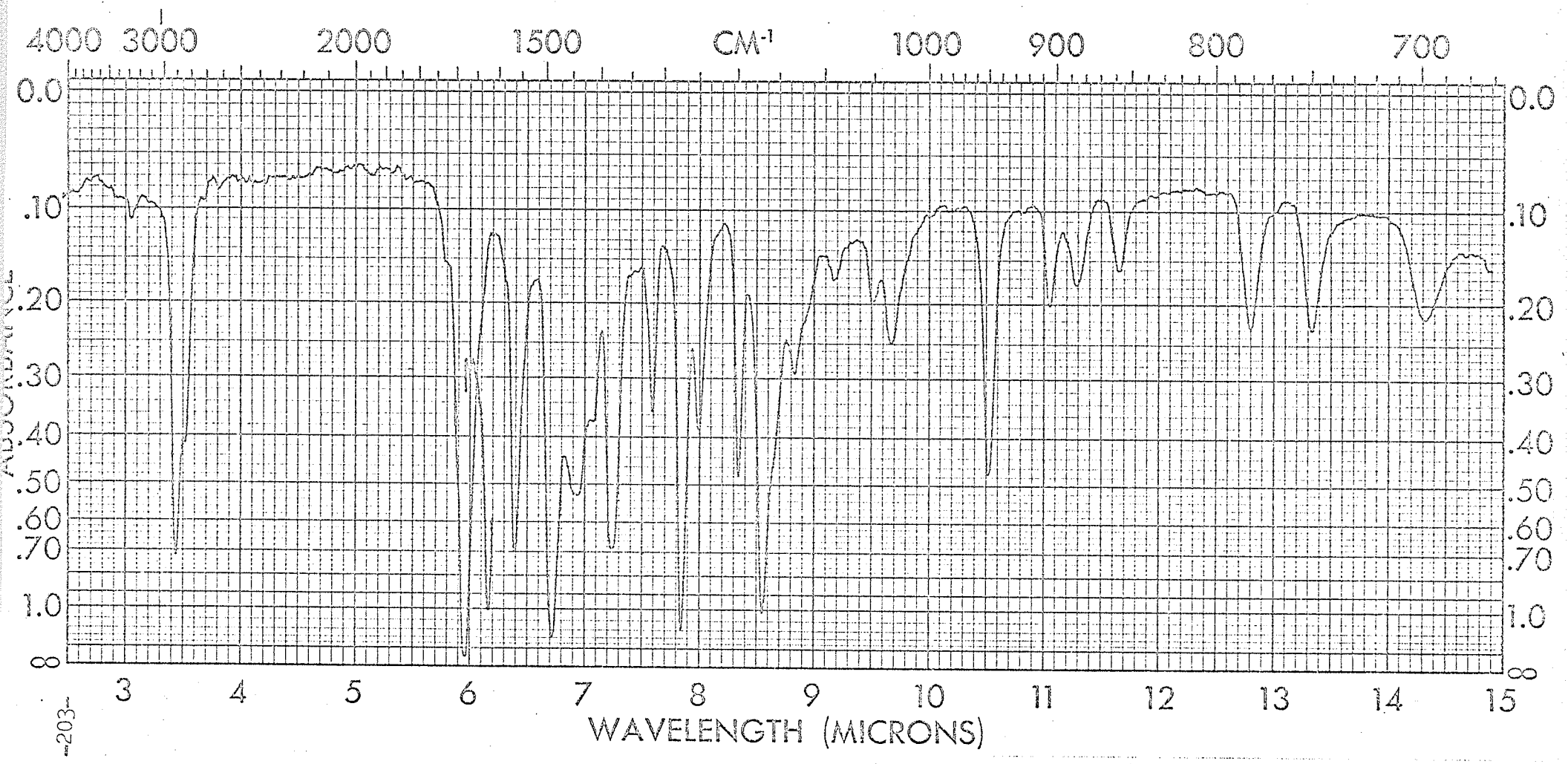
2,5-dimethyl-3,4-dicyanomethylthiophene (122), nujol mull

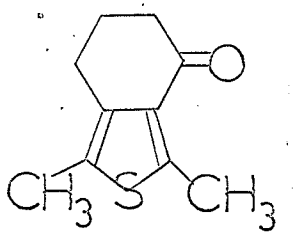




IR spectrum no. 14:

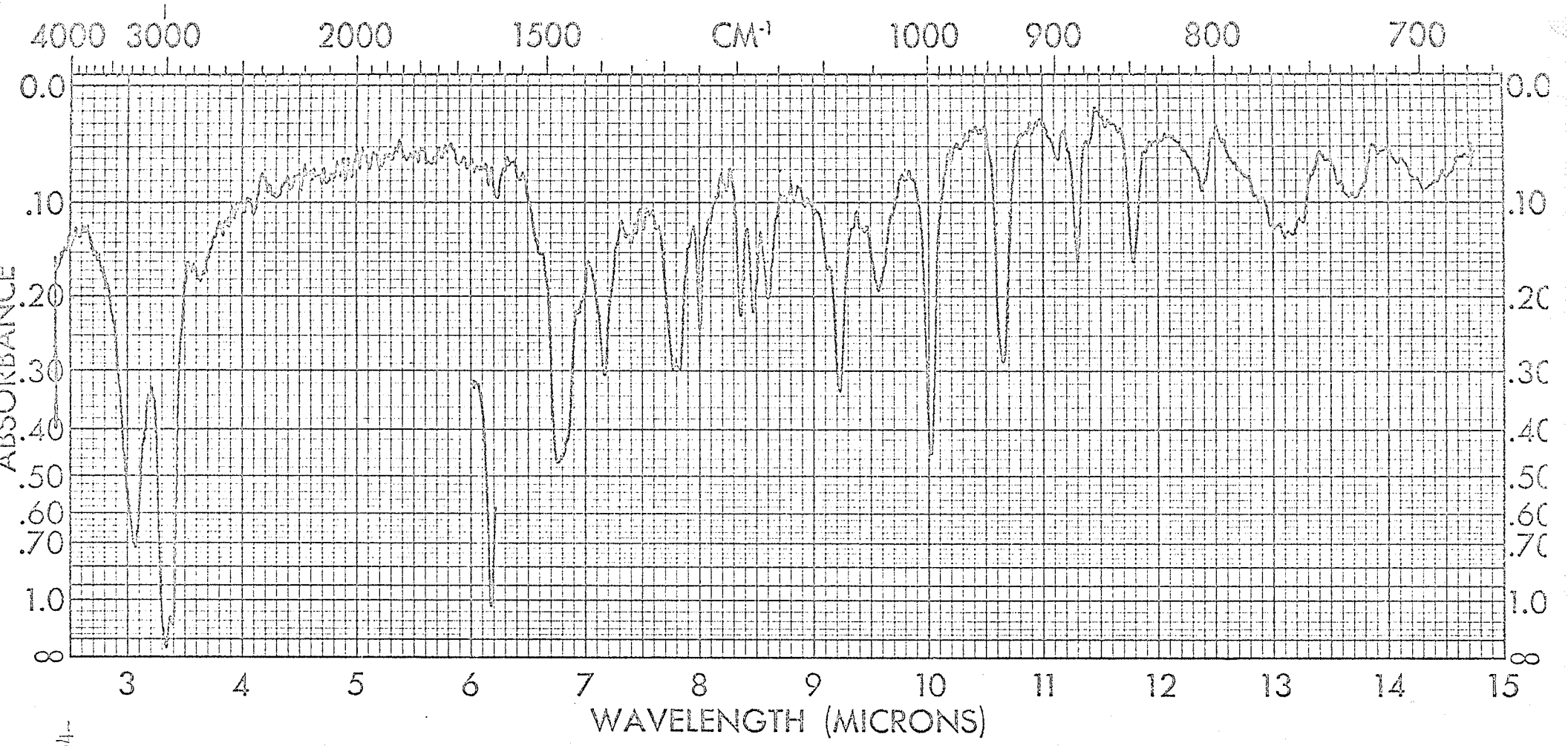
1,3-dimethyl-4,7-diketo-5,6-dihydrobenzo-(c)thiophene (137), nujol mull.

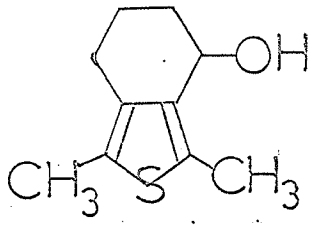




IR spectrum no. 15:

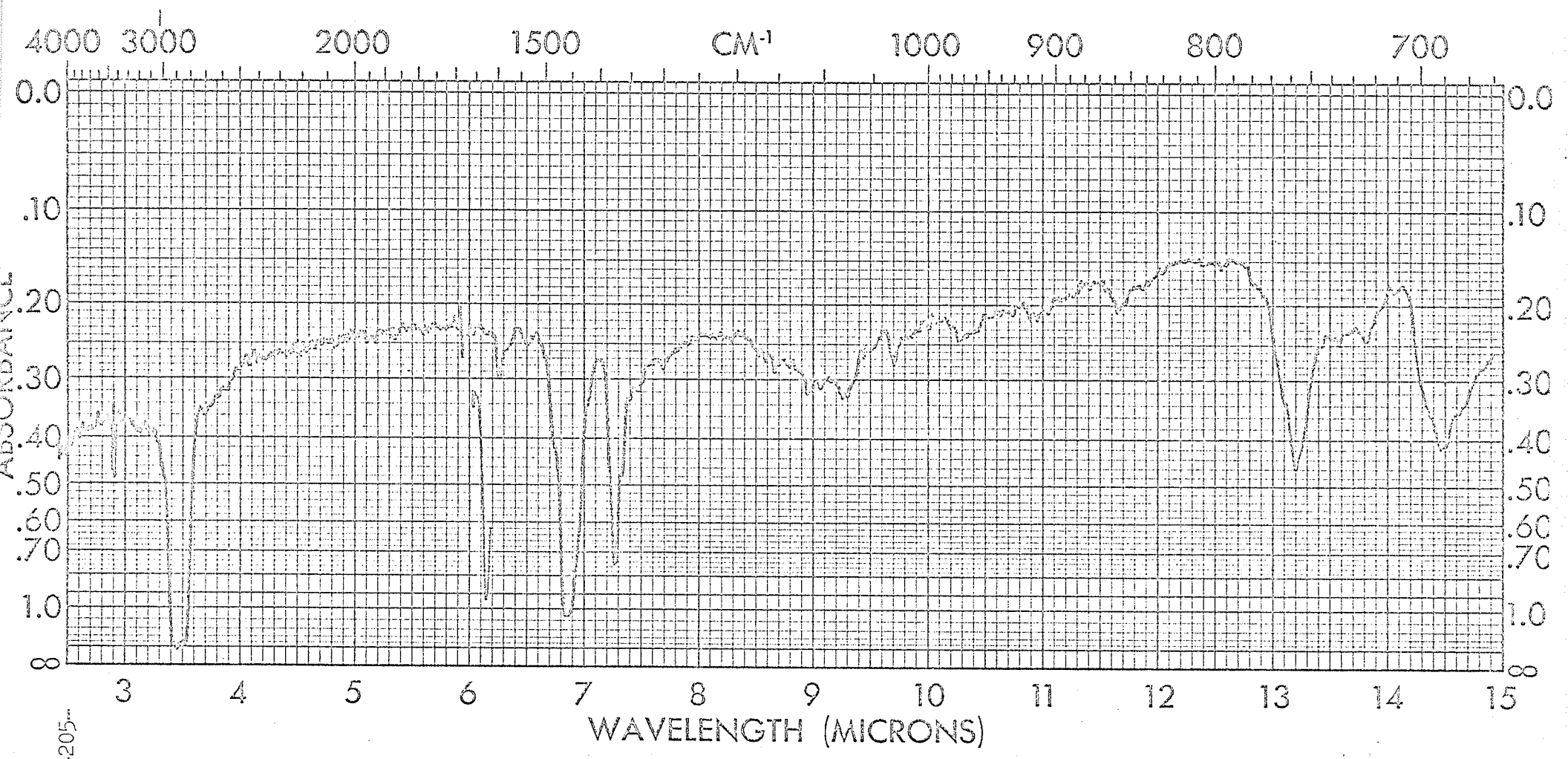
1,3-dimethyl-4-keto-5,6,7-trihydrobenzo(c)-thiophene (37), nujol mull.

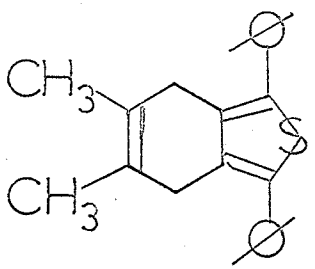




IR spectrum no. 16:

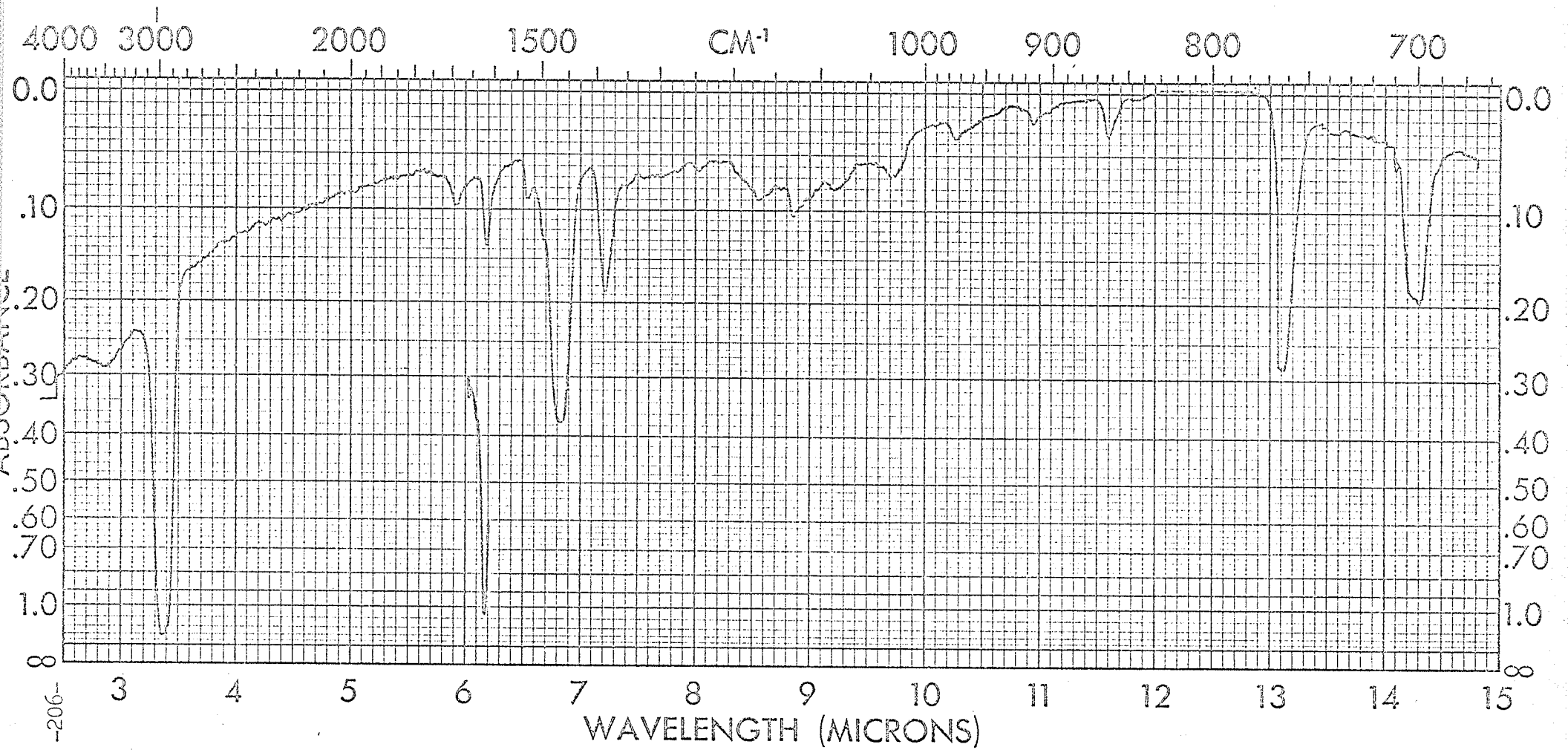
1,3-dimethyl-4-hydroxy-4,5,6,7-tetrahydro-benzo(c)thiophene (132), nujol mull.

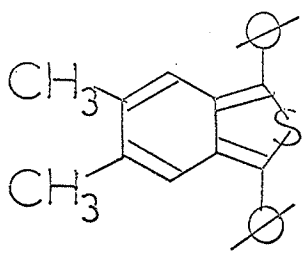




IR spectrum no. 17:

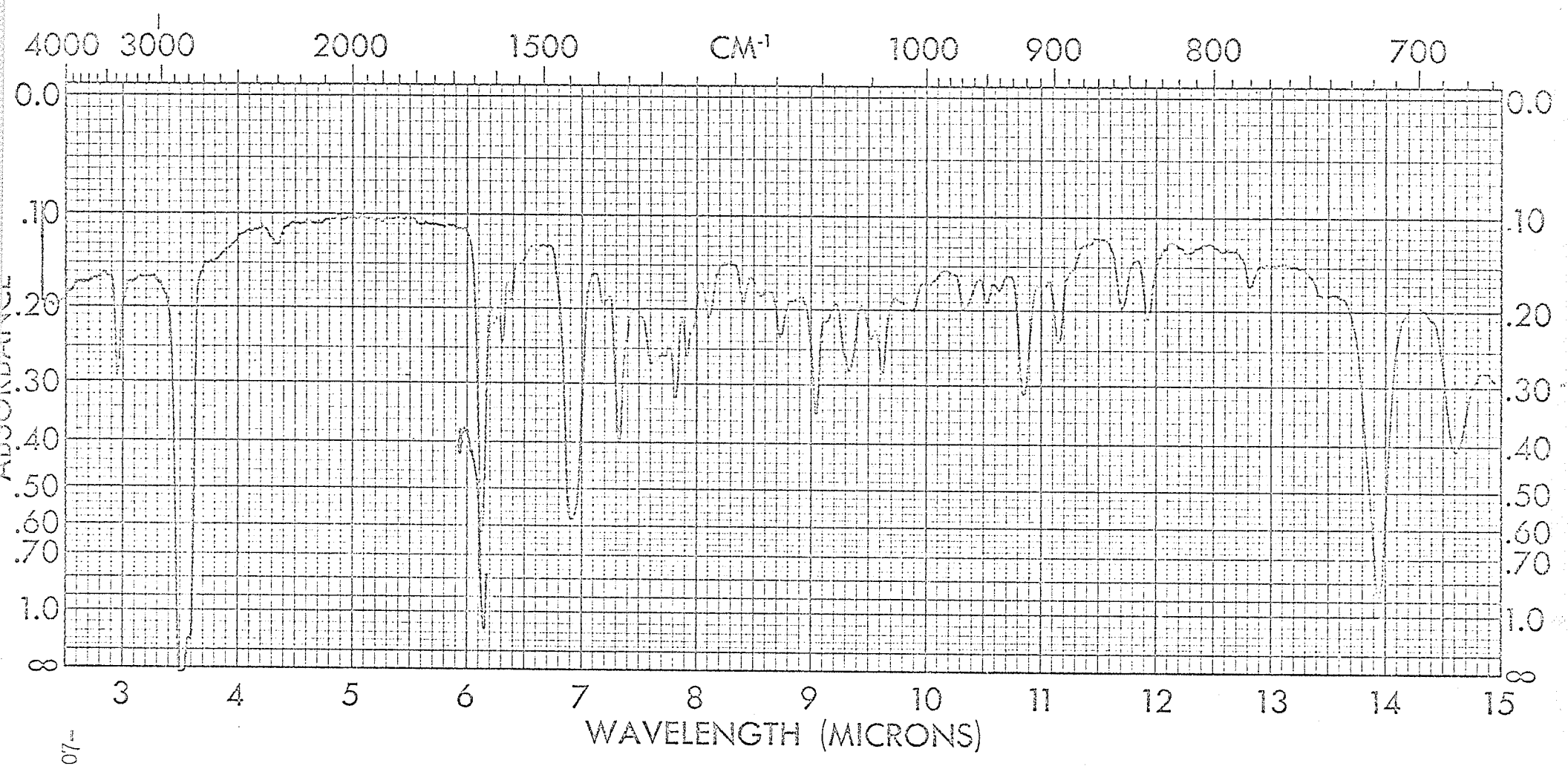
1,3-diphenyl-4,7-dihydro-5,6-dimethylbenzo-(c)thiophene (142), nujol mull.

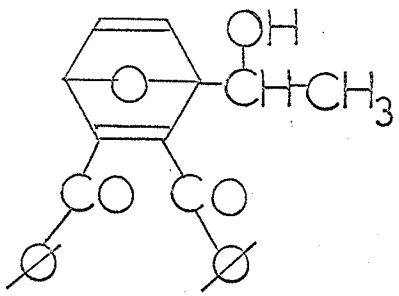




IR spectrum no. 18:

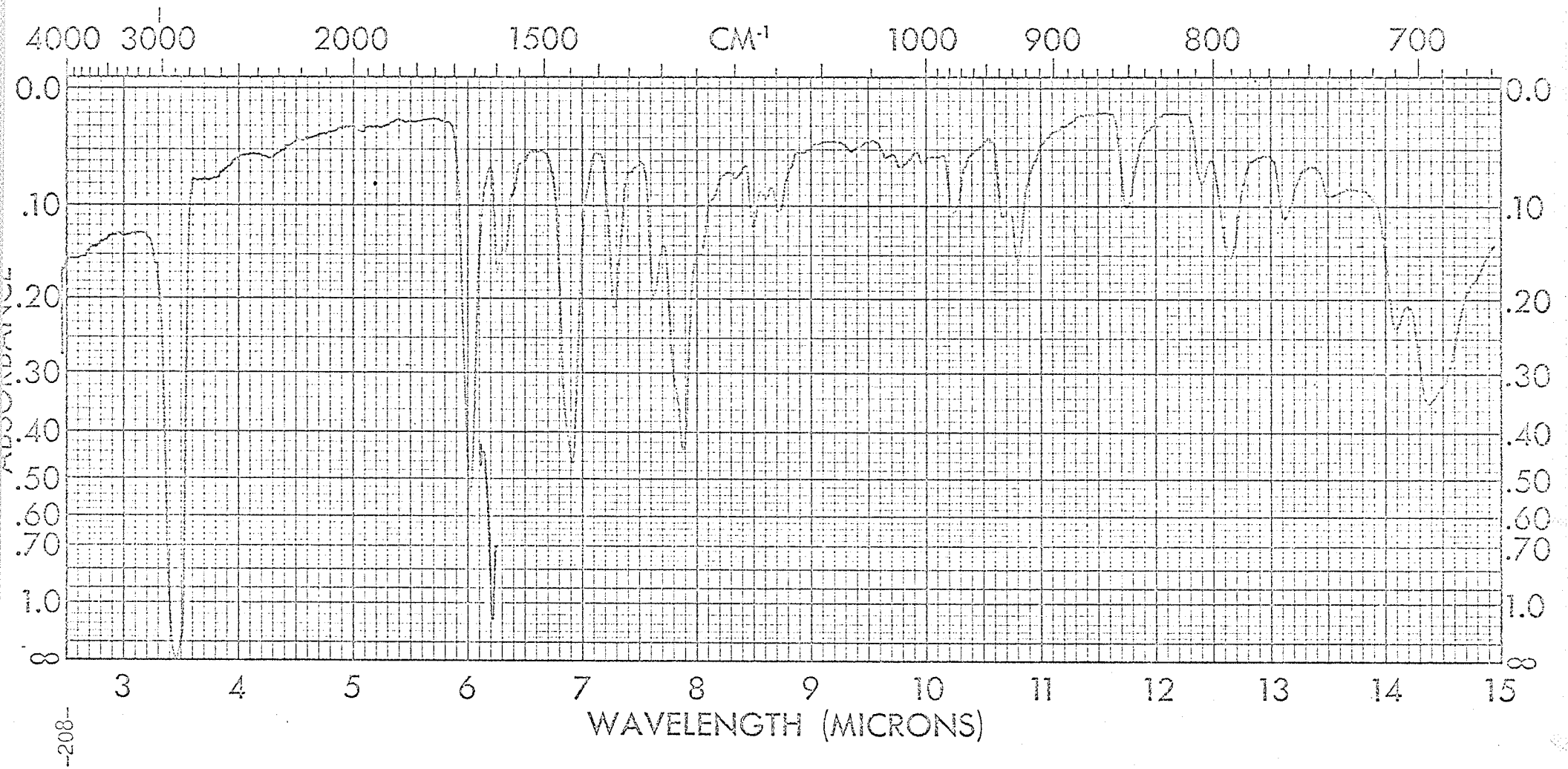
1,3-diphenyl-5,6-dimethylbenzo(c)thiophene (49), nujol mull.

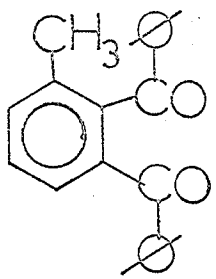




IR spectrum no. 19:

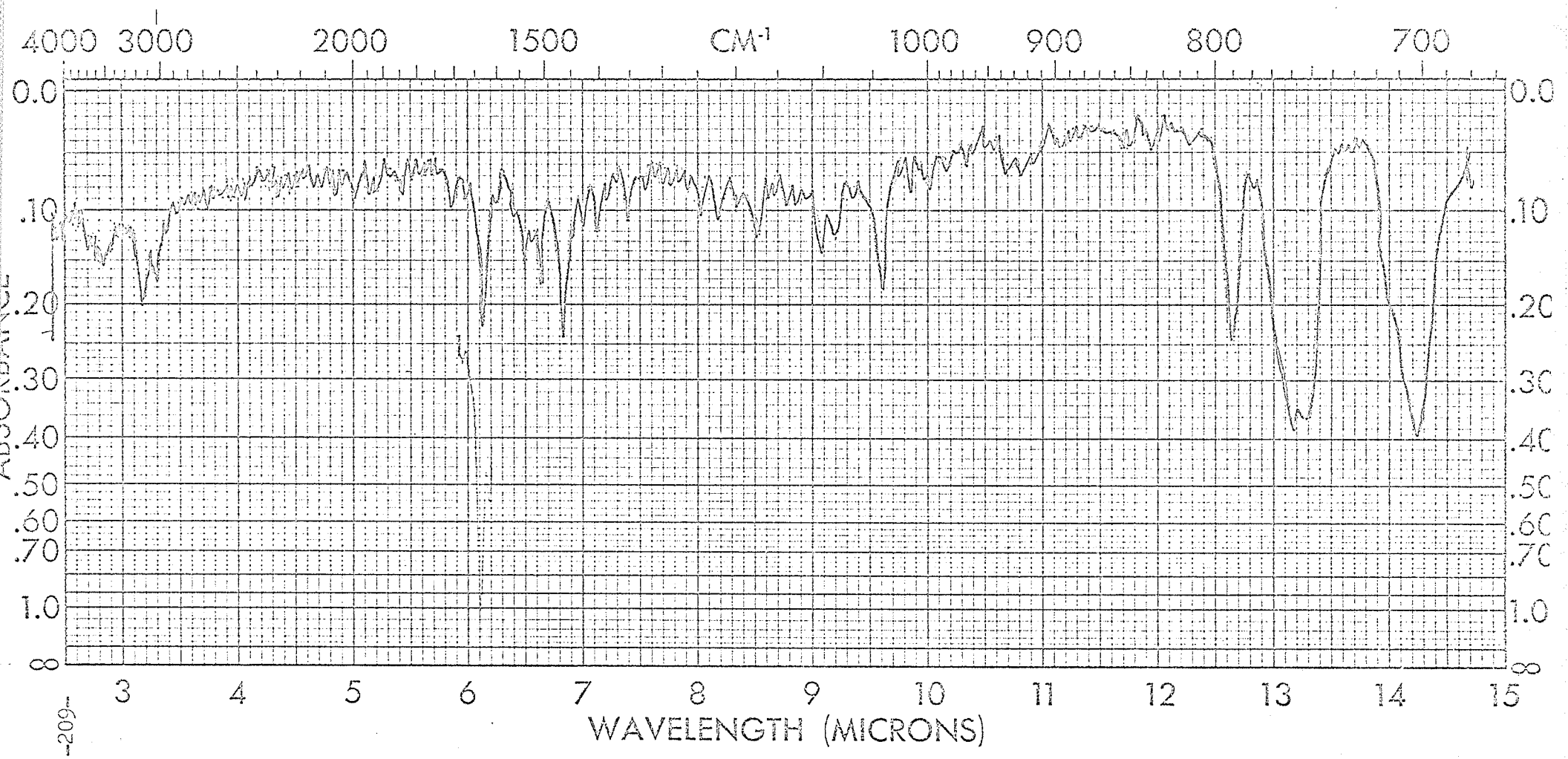
Diels-Alder adduct 152, nujol mull.

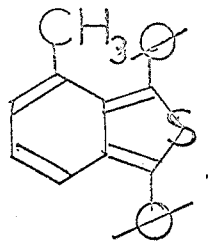




IR spectrum no. 20:

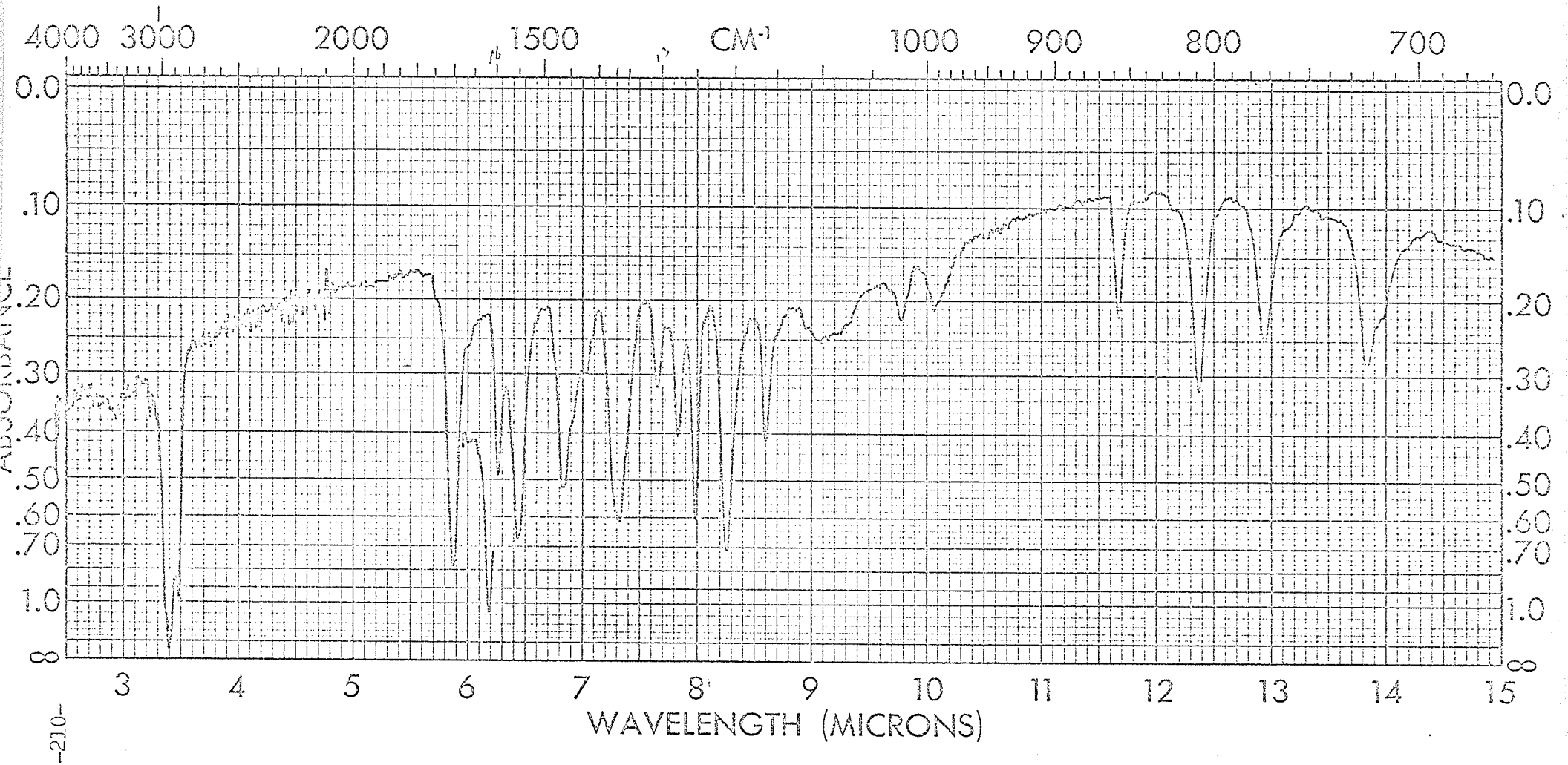
2,3-dibenzoyltoluene (159), nujol mull.

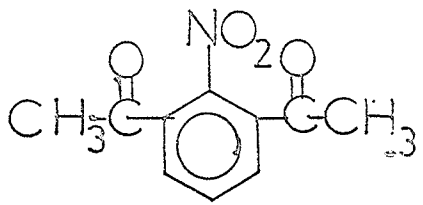




IR spectrum no. 21:

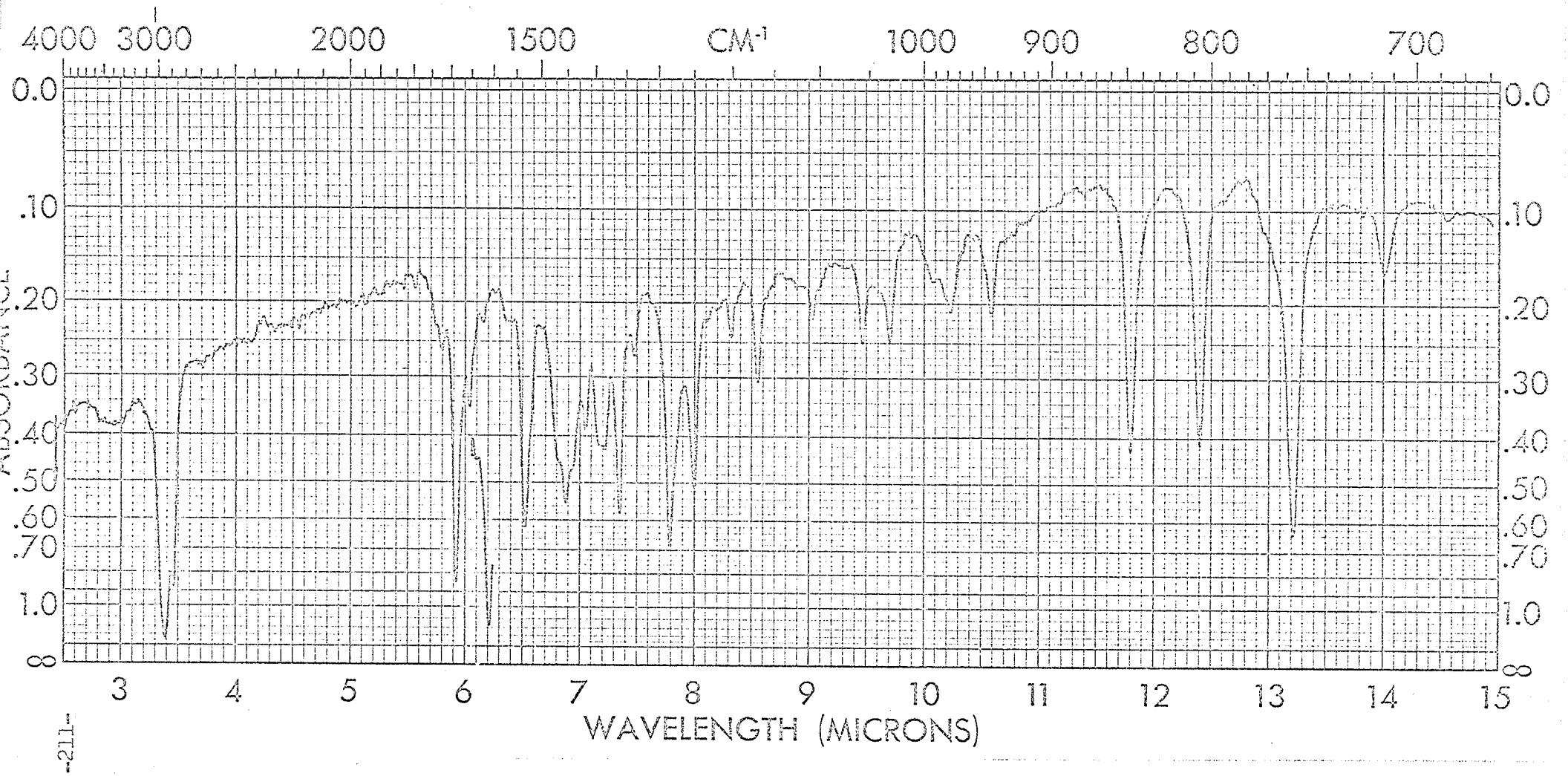
1,3-diphenyl-4-methylbenzo(c)thiophene(160),

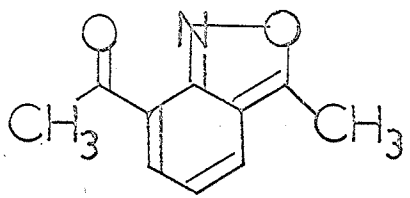




IR spectrum no. 22:

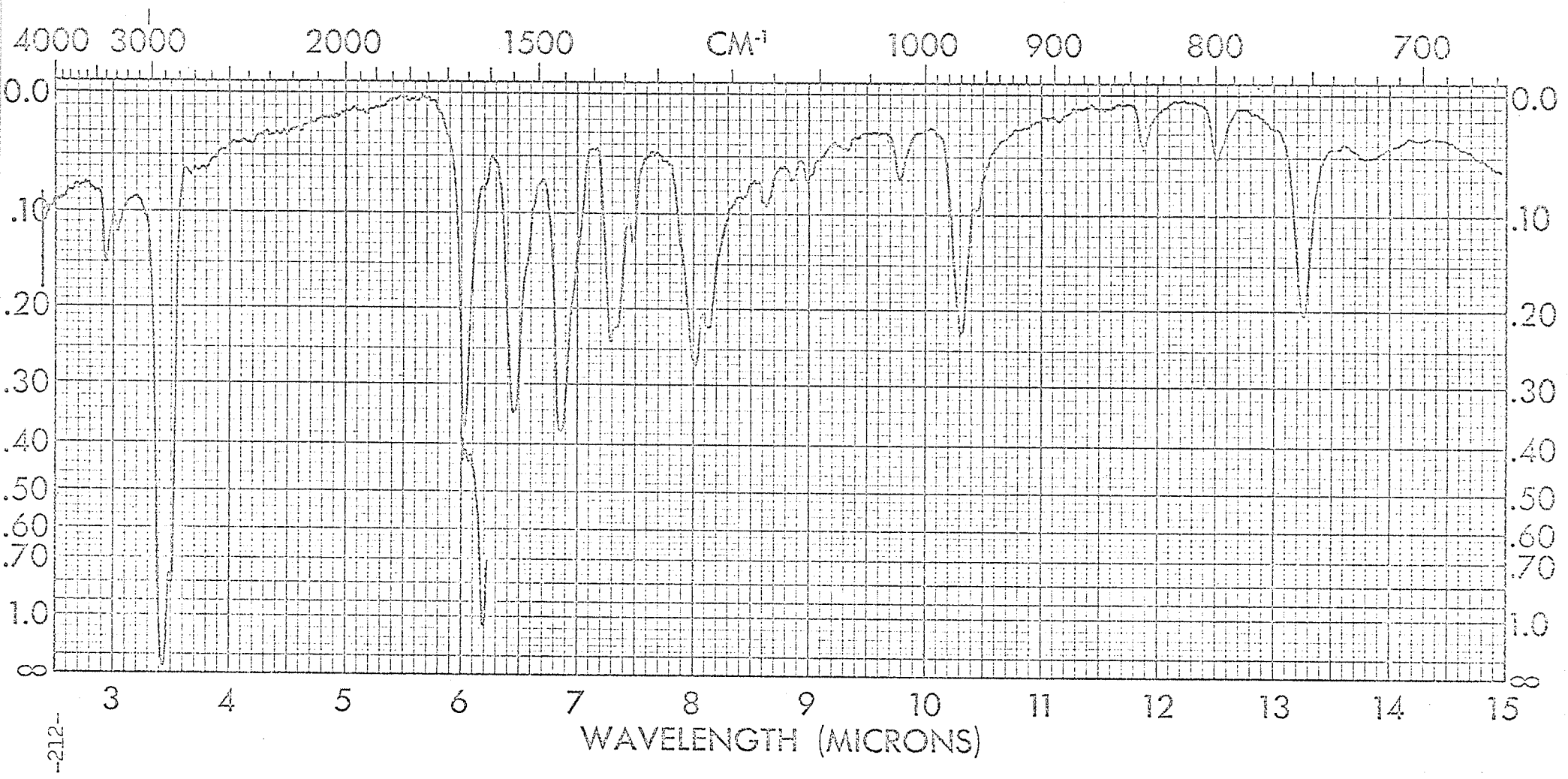
2,6-diacetylnitrobenzene (182), nujol mull.

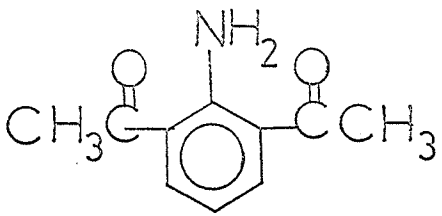




IR spectrum no. 23:

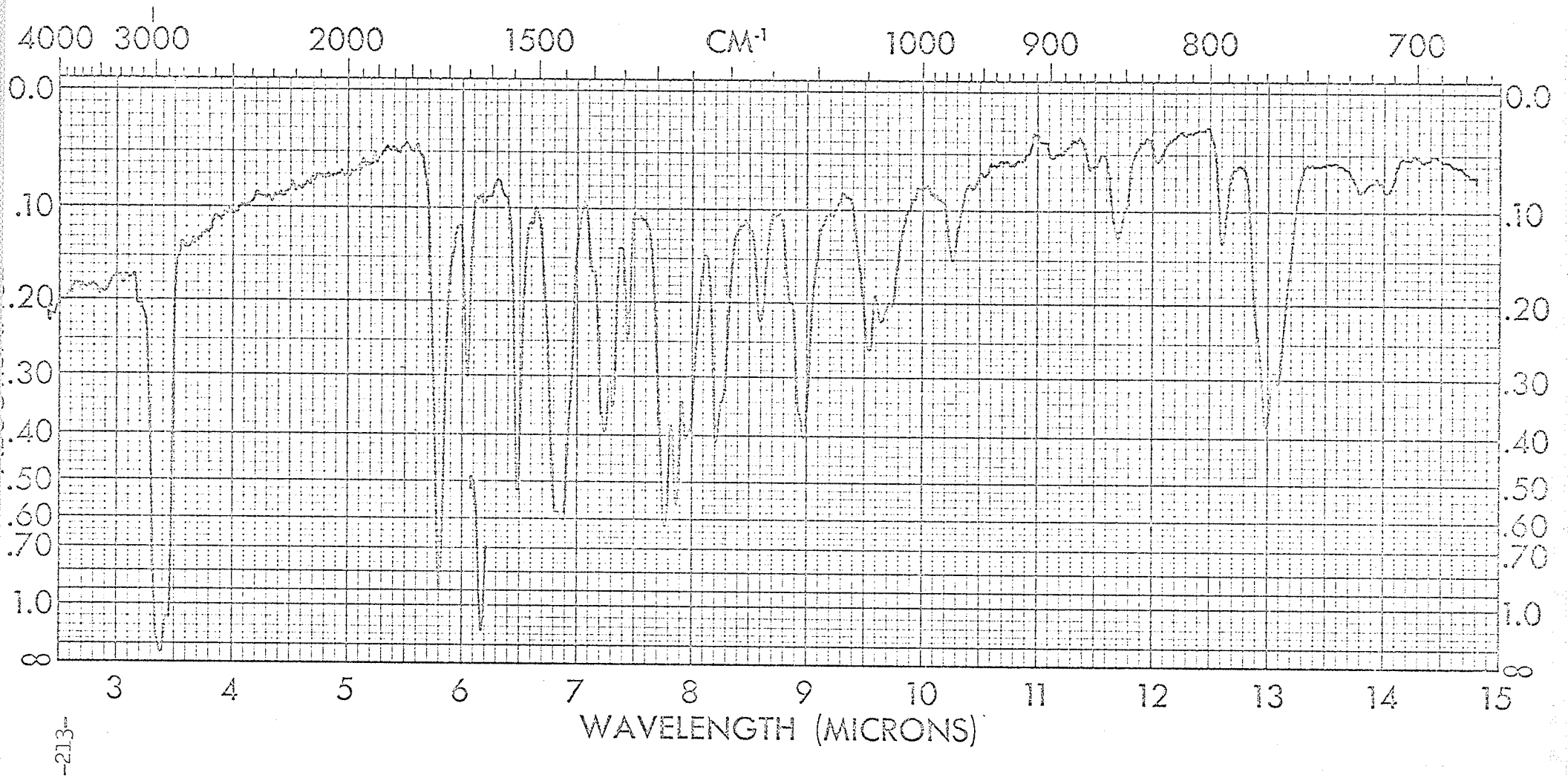
7-acetyl-3-methylanthranil (199), nujol mull.

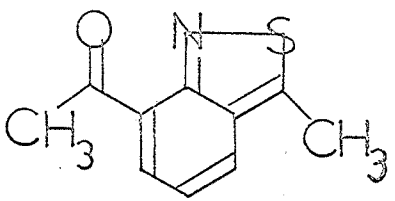




IR spectrum no. 24:

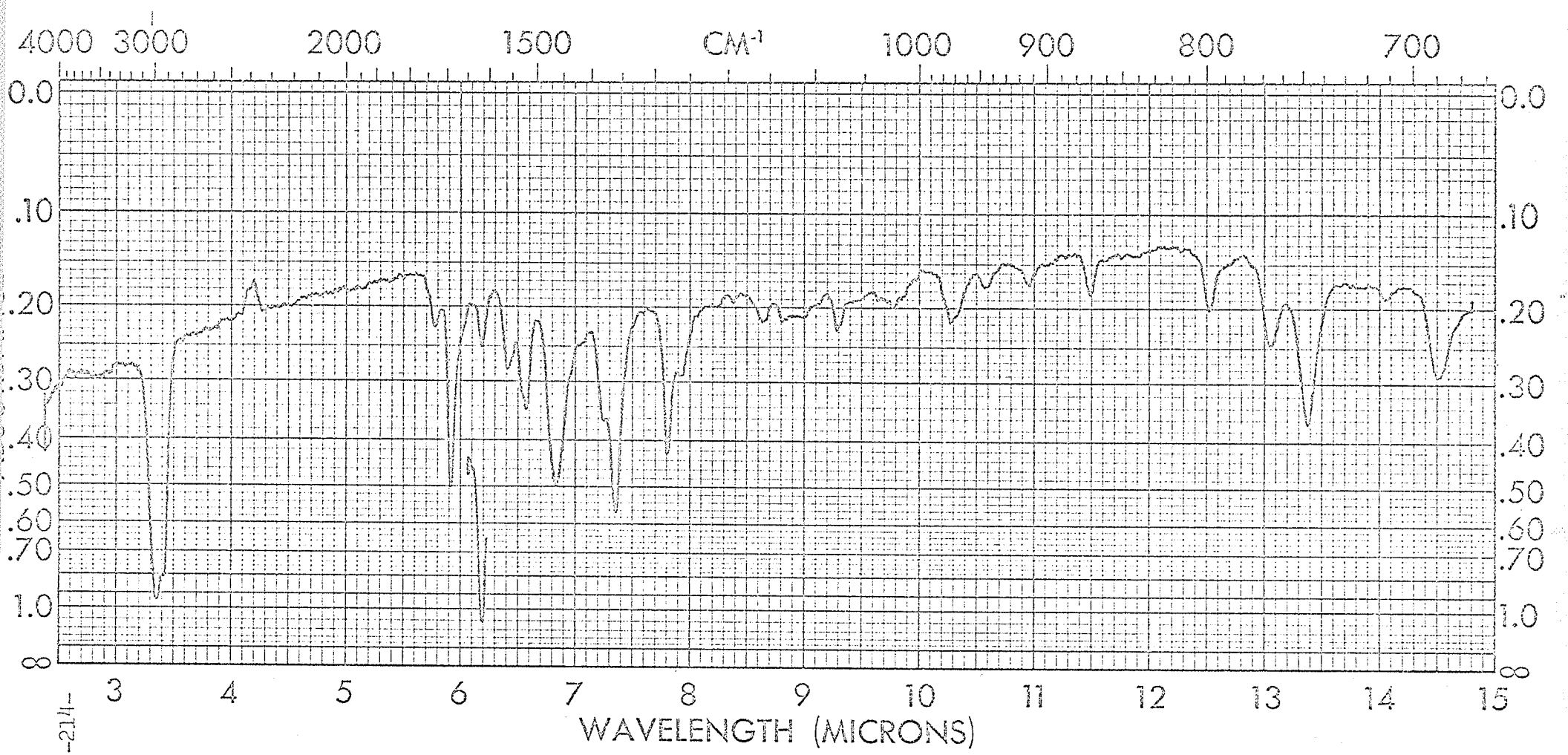
2,6-diacetylaniline (183), nujol mull.

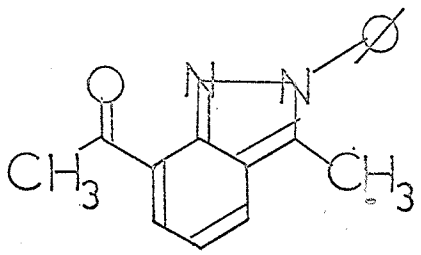




IR spectrum no. 25:

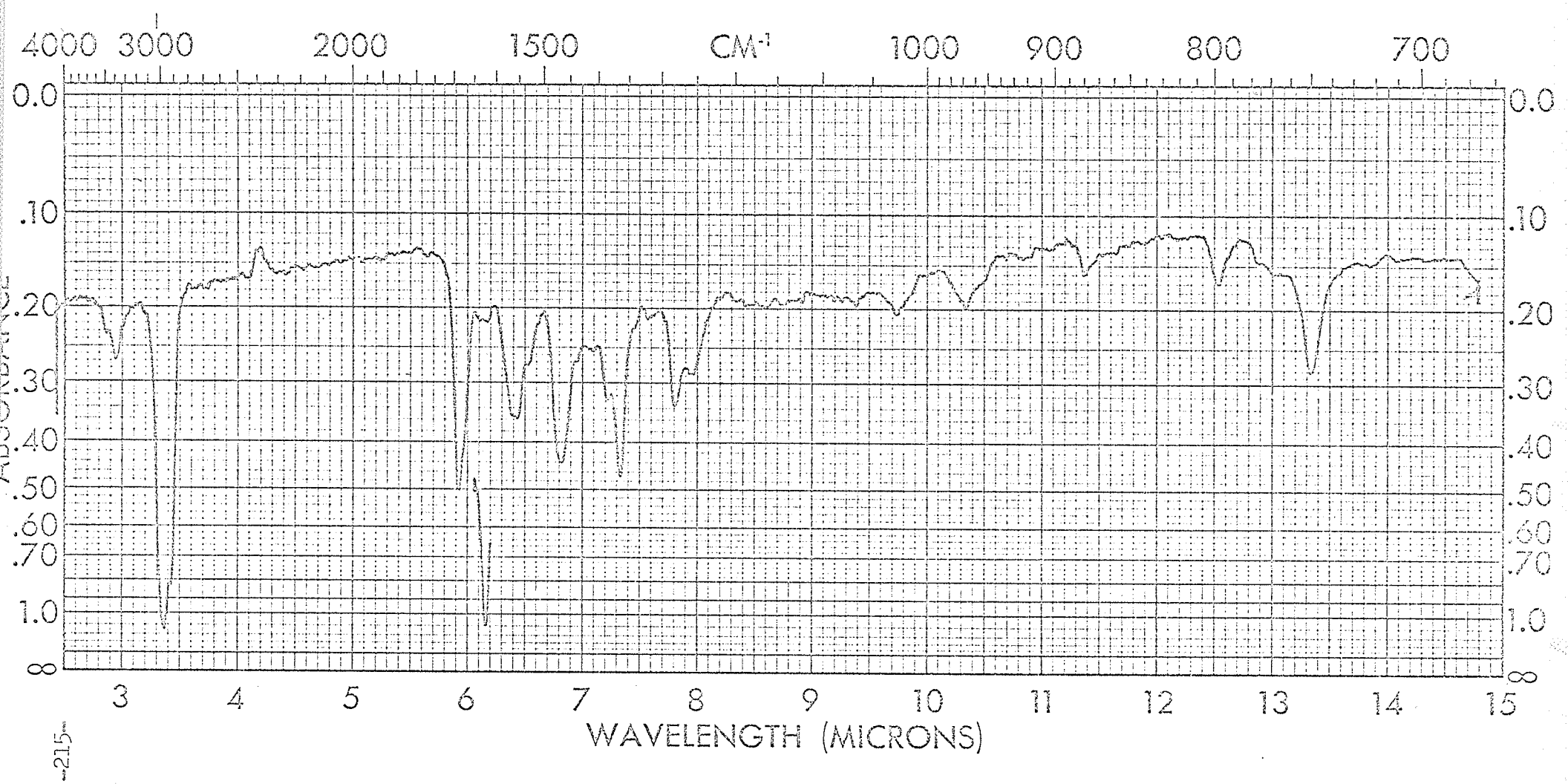
7-acetyl-3-methylthioanthranil (209), nujol mull.



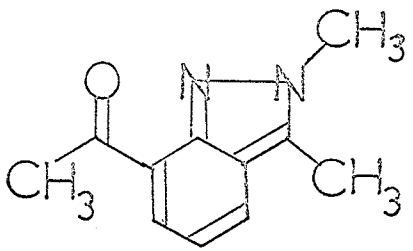


IR spectrum no. 26:

7-acetyl-3-methyl-2-phenylbenzo(c)pyrazole (222b), nujol mull

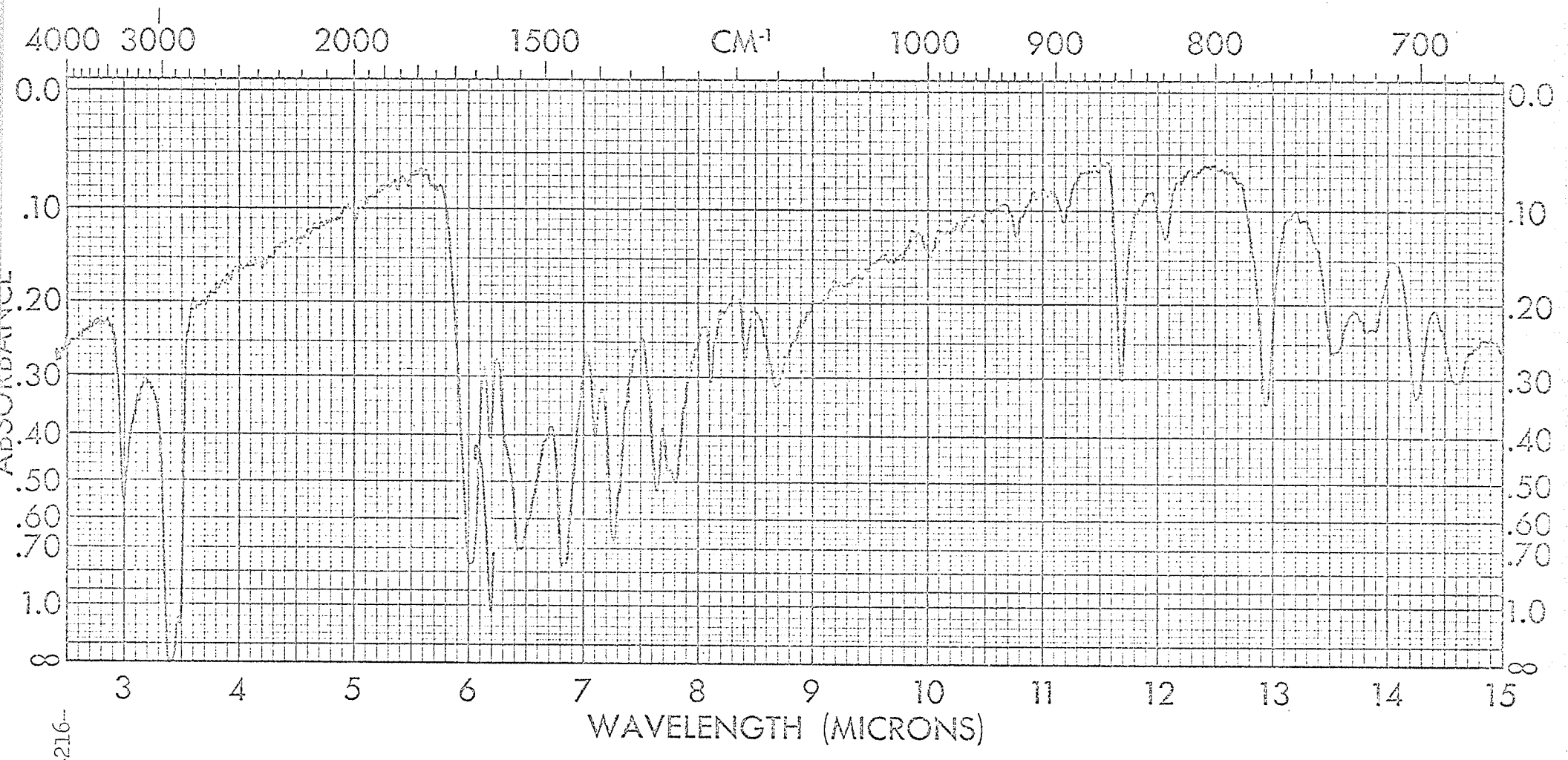


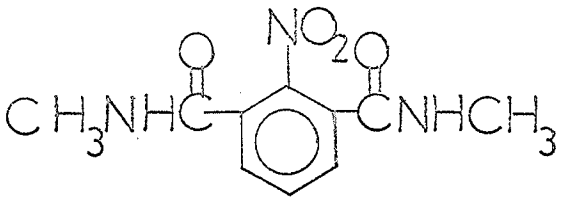
-215-



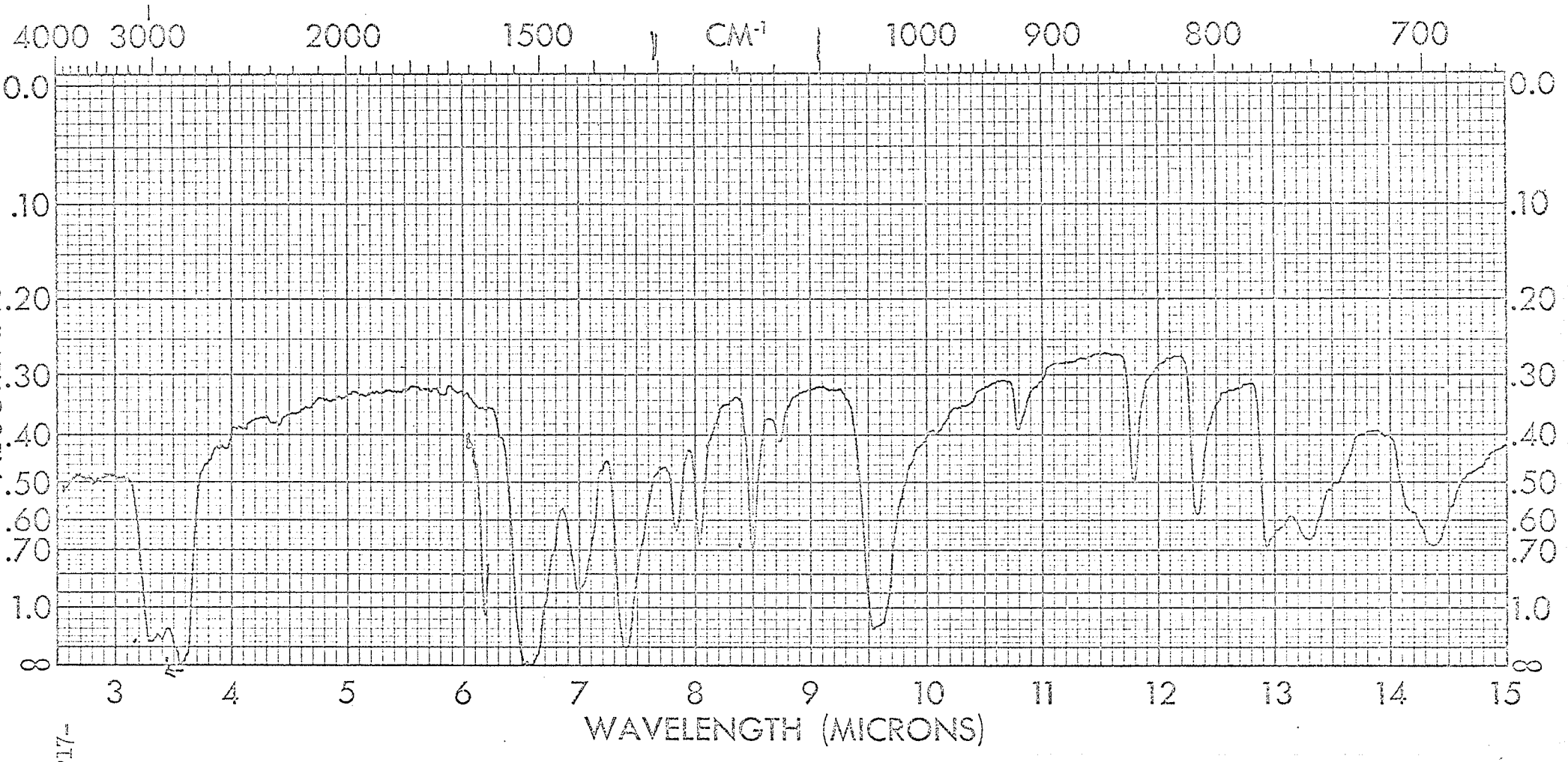
IR spectrum no. 27:

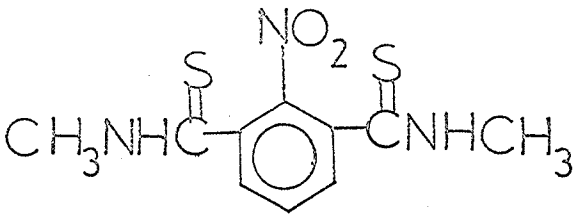
7-acetyl-2,3-dimethylbenzo(c)pyrazole (222a), nujol mull.





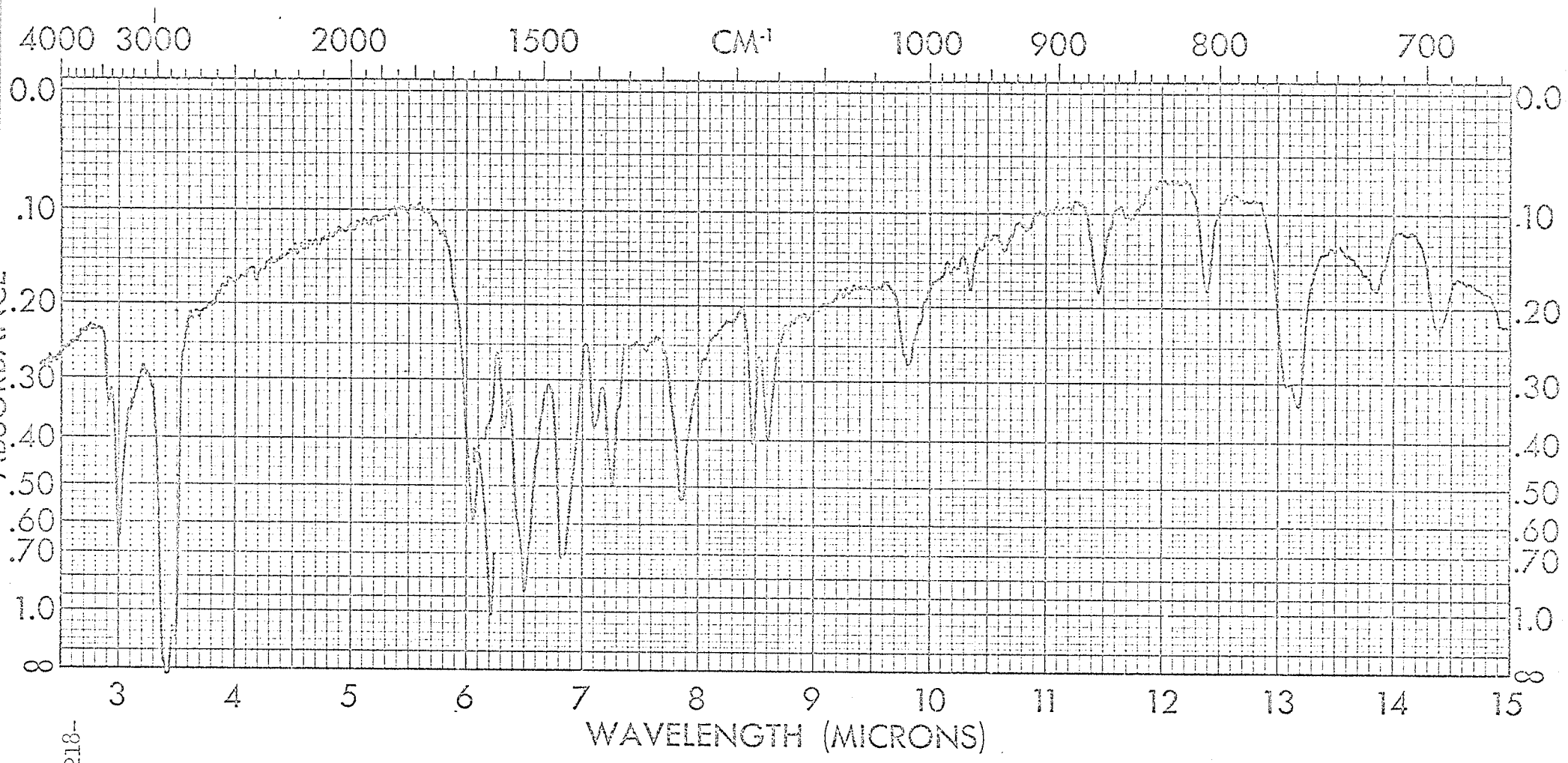
IR spectrum no. 28:
N,N'-dimethyl-2-nitroisophthalamide (224), nujol mull.

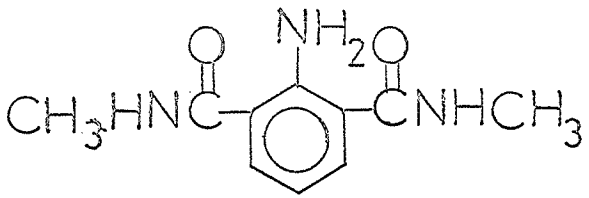




IR spectrum no. 29:

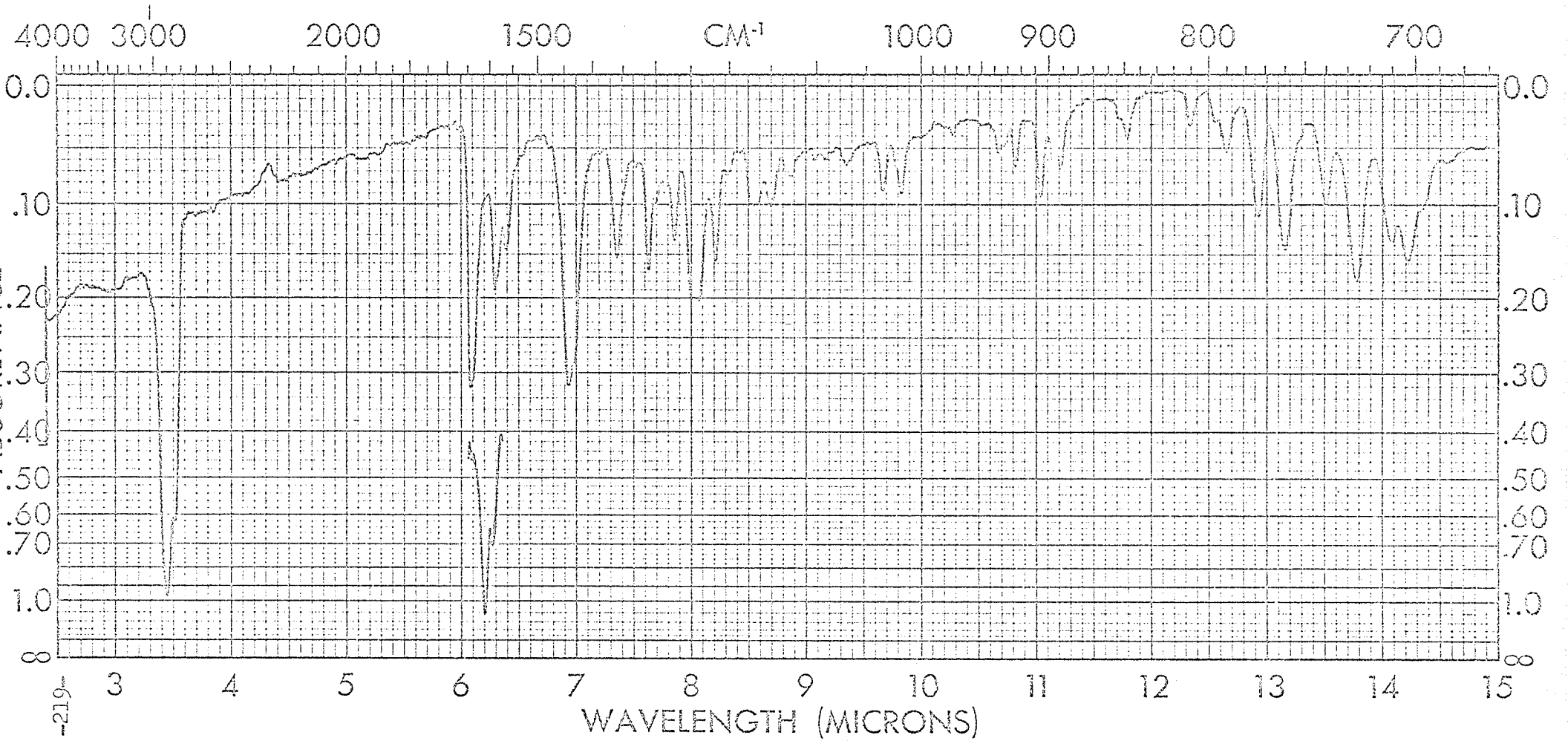
N,N'-dimethyl-2-nitroisothiophthalamide (225), nujol mull.

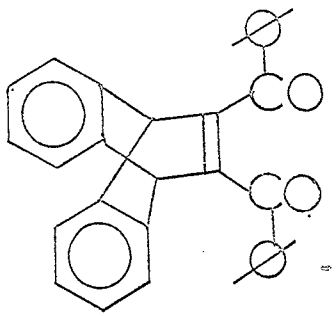




IR spectrum no. 30:

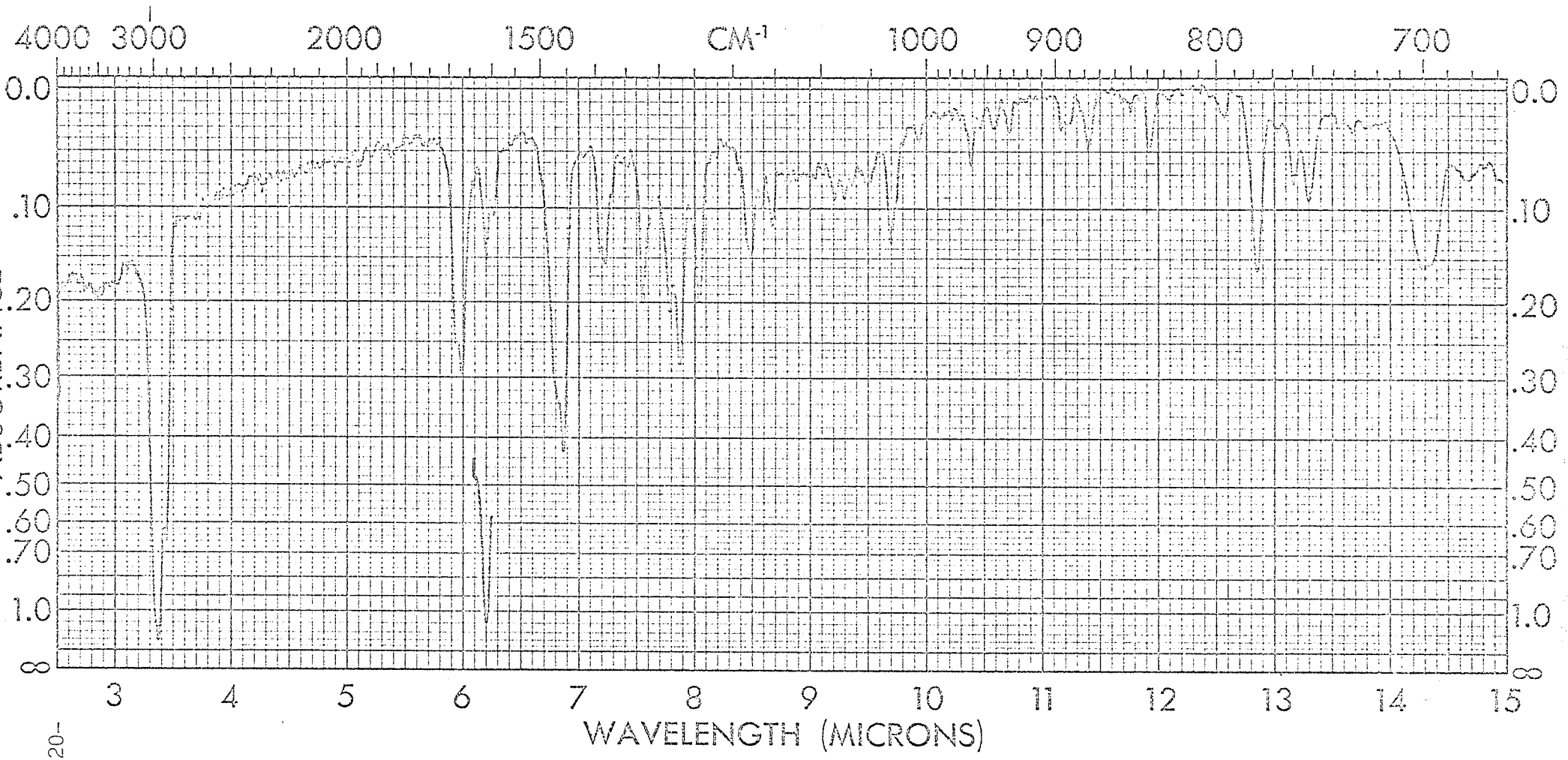
N,N'-dimethyl-2-aminoisophthalamide (crude),
nujol mull.

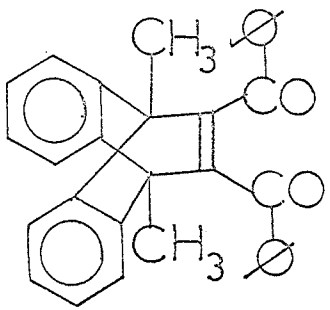




IR spectrum no. 31:

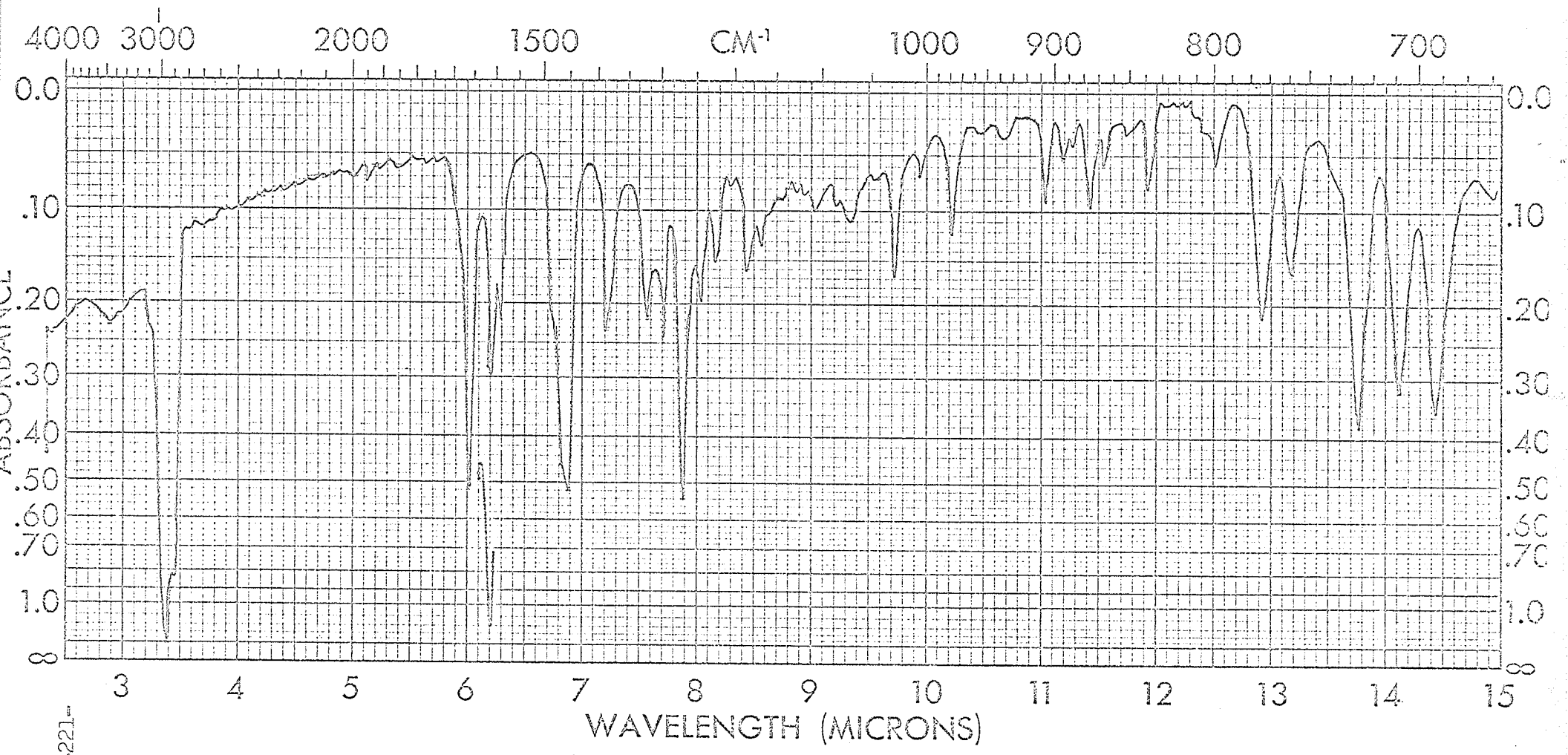
anthracene-9,10-endo-dibenzoylacetylene (99), nujol mull.

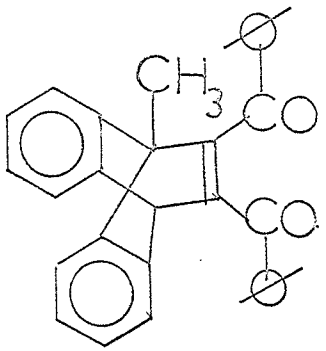




IR spectrum no. 32:

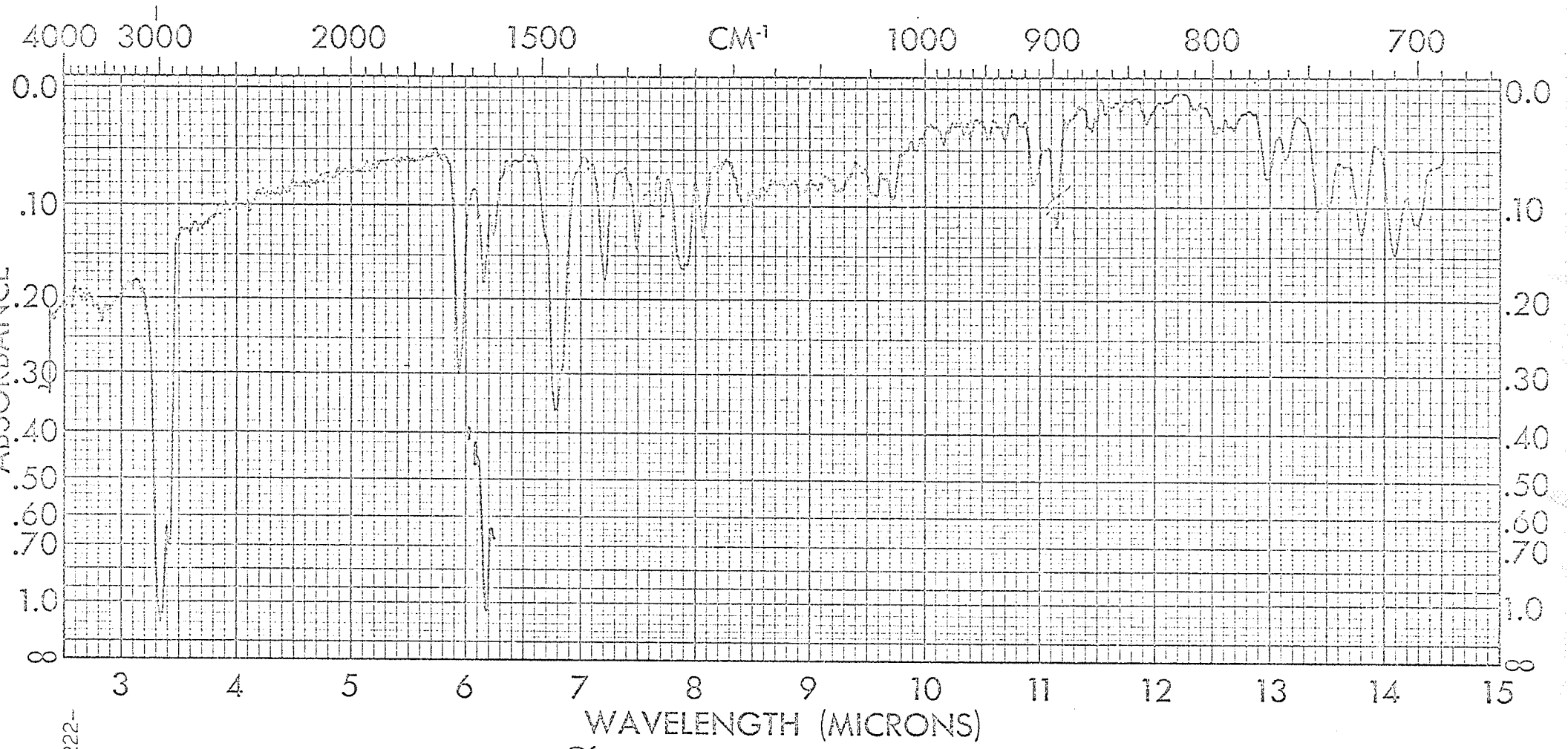
9,10-dimethylanthracene-9,10-endo-dibenzoylacetylene,
nujol mull.

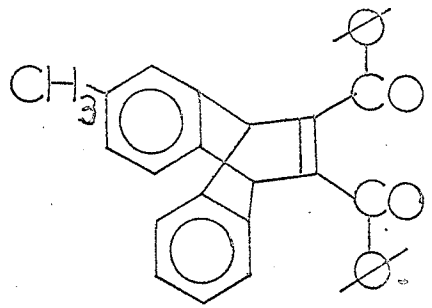




IR spectrum no. 33:

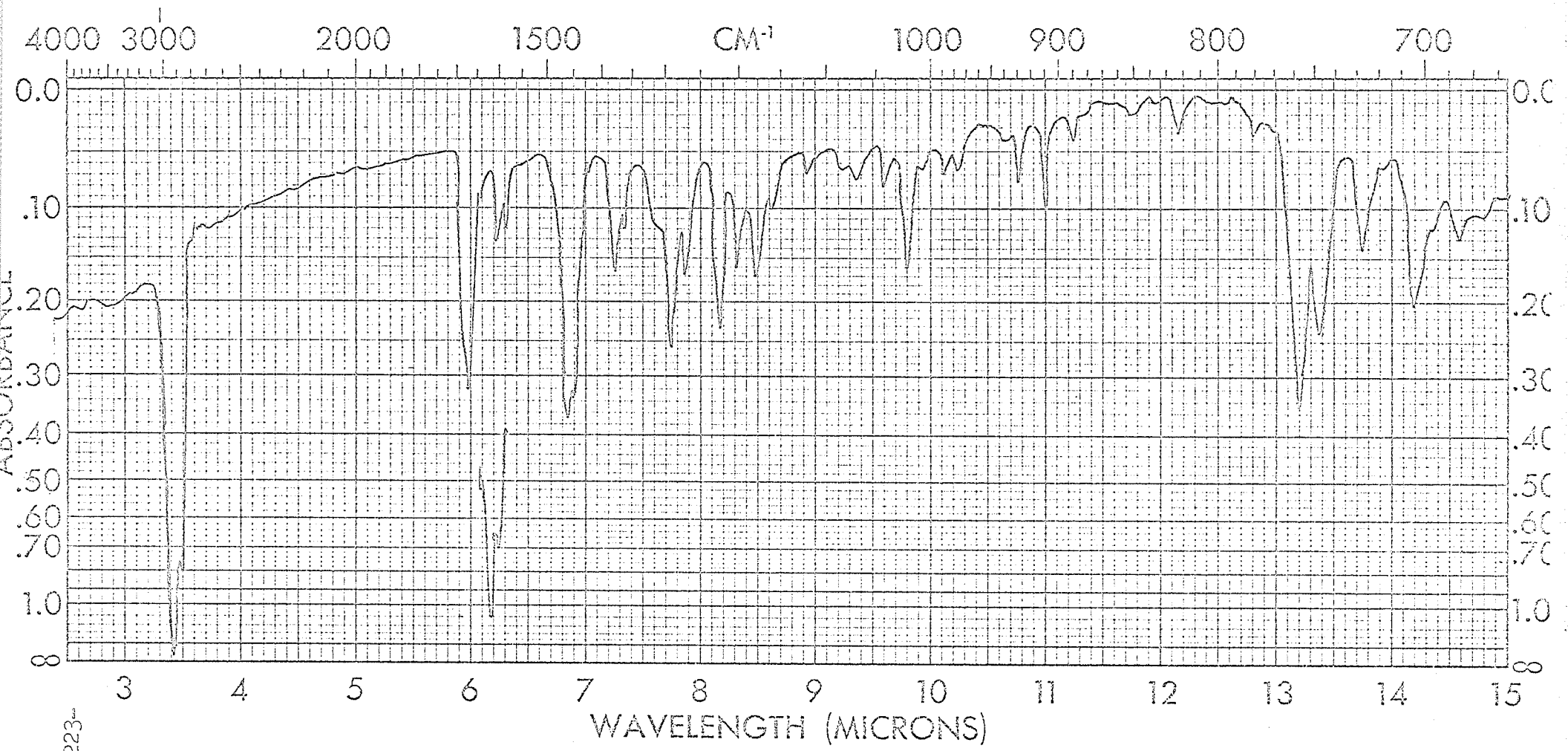
9-methylanthracene-9,10-endo-dibenzoylacetylene, nujol mull.



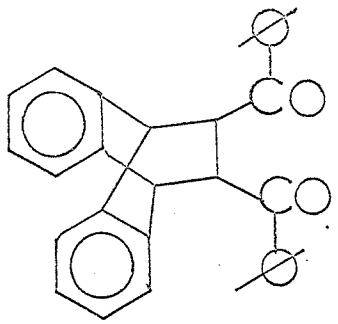


IR spectrum no. 34:

2-methylanthracene-9,10-endo-dibenzoylacetylene,
nujol mull

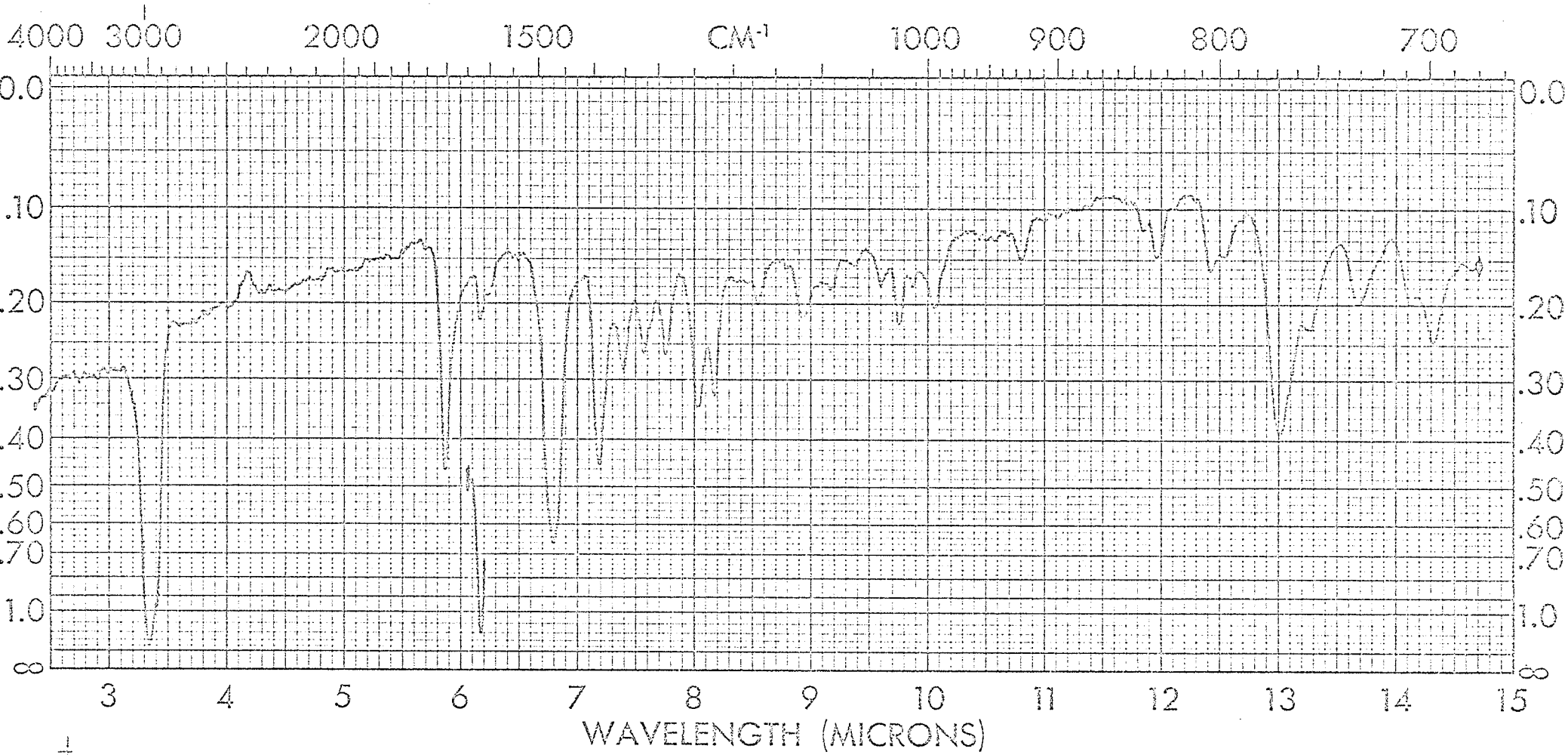


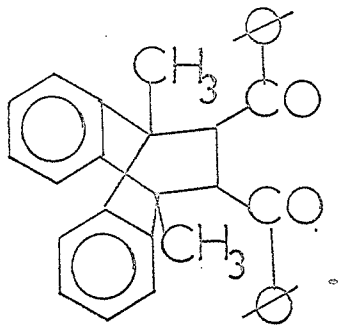
-223-



IR spectrum no. 35:

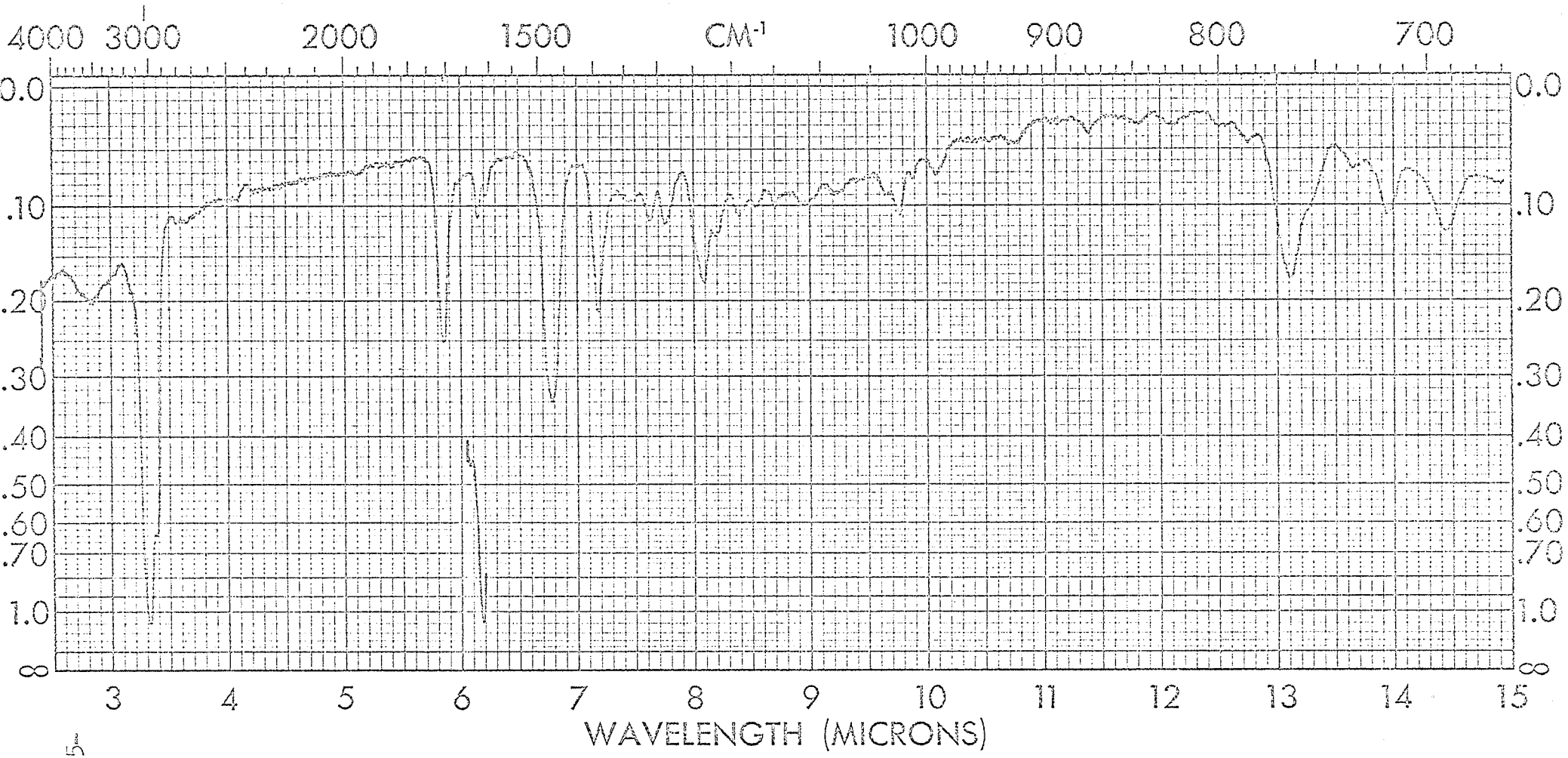
anthracene-9,10-endo-dibenzoylethylene (100), nujol mull.

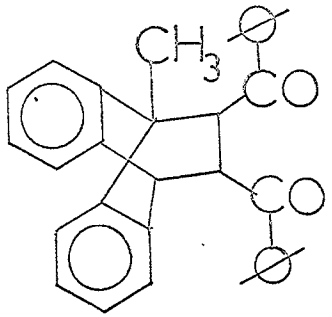




IR spectrum no. 36:

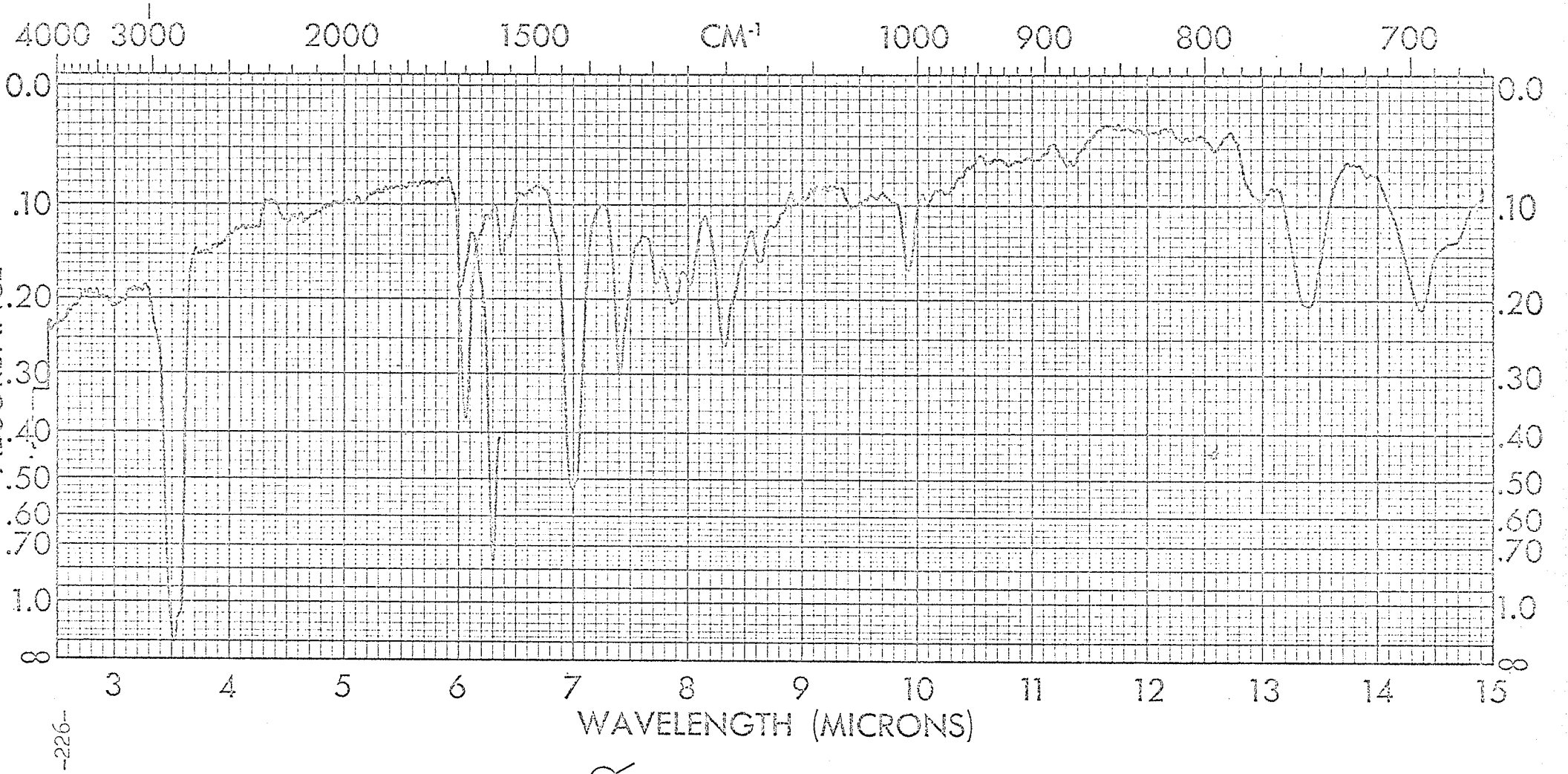
9,10-dimethylanthracene-9,10-endo-dibenzoylethylene (253), nujol mull.

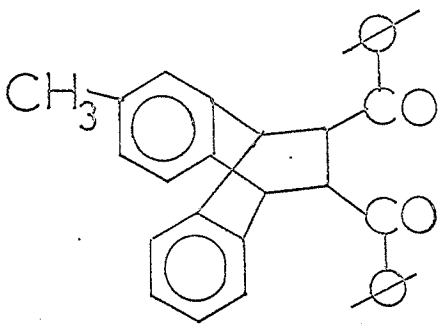




IR spectrum no. 37:

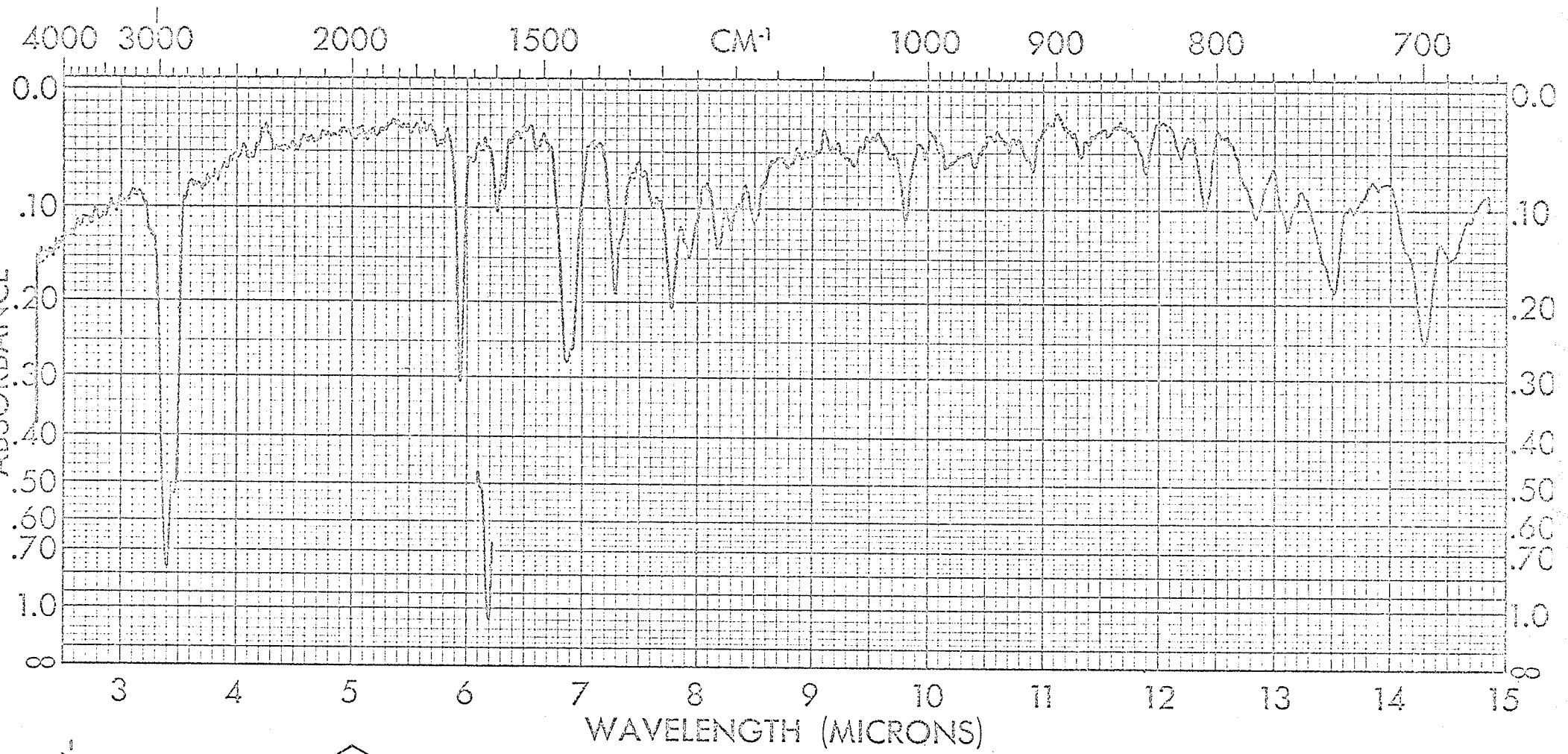
9-methylanthracene-9,10-endo-dibenzoylethylene (289),
nujol mull.

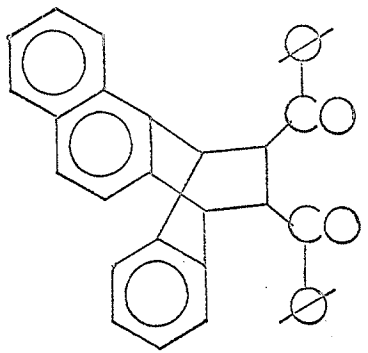




IR spectrum no. 38:

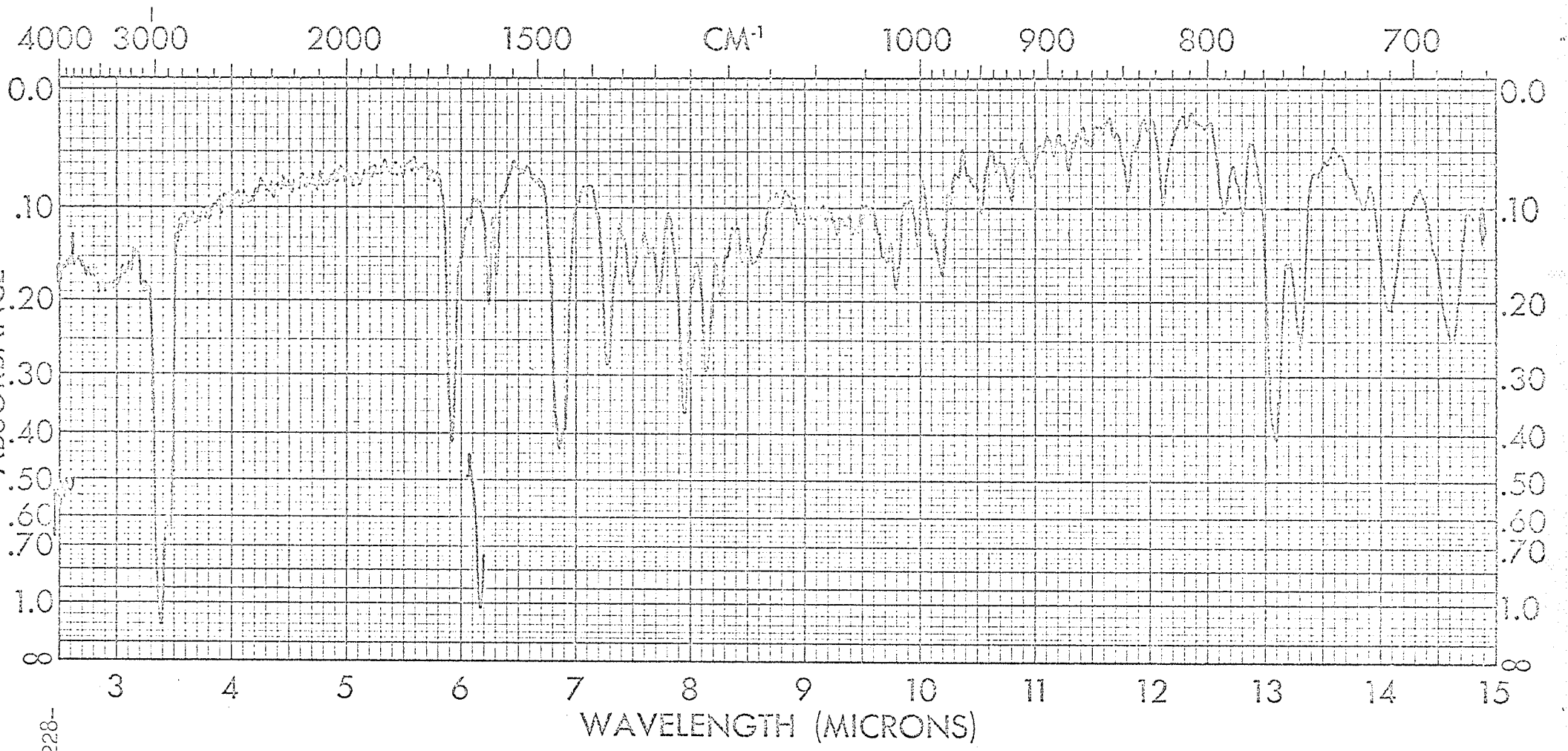
2-methylanthracene-9,10-endo-dibenzoylethylene (290),
nujol mull.

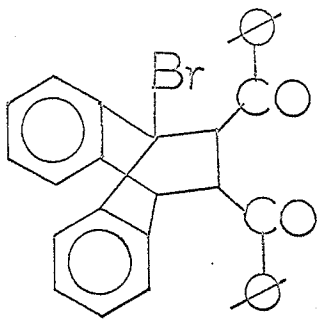




IR spectrum no. 39:

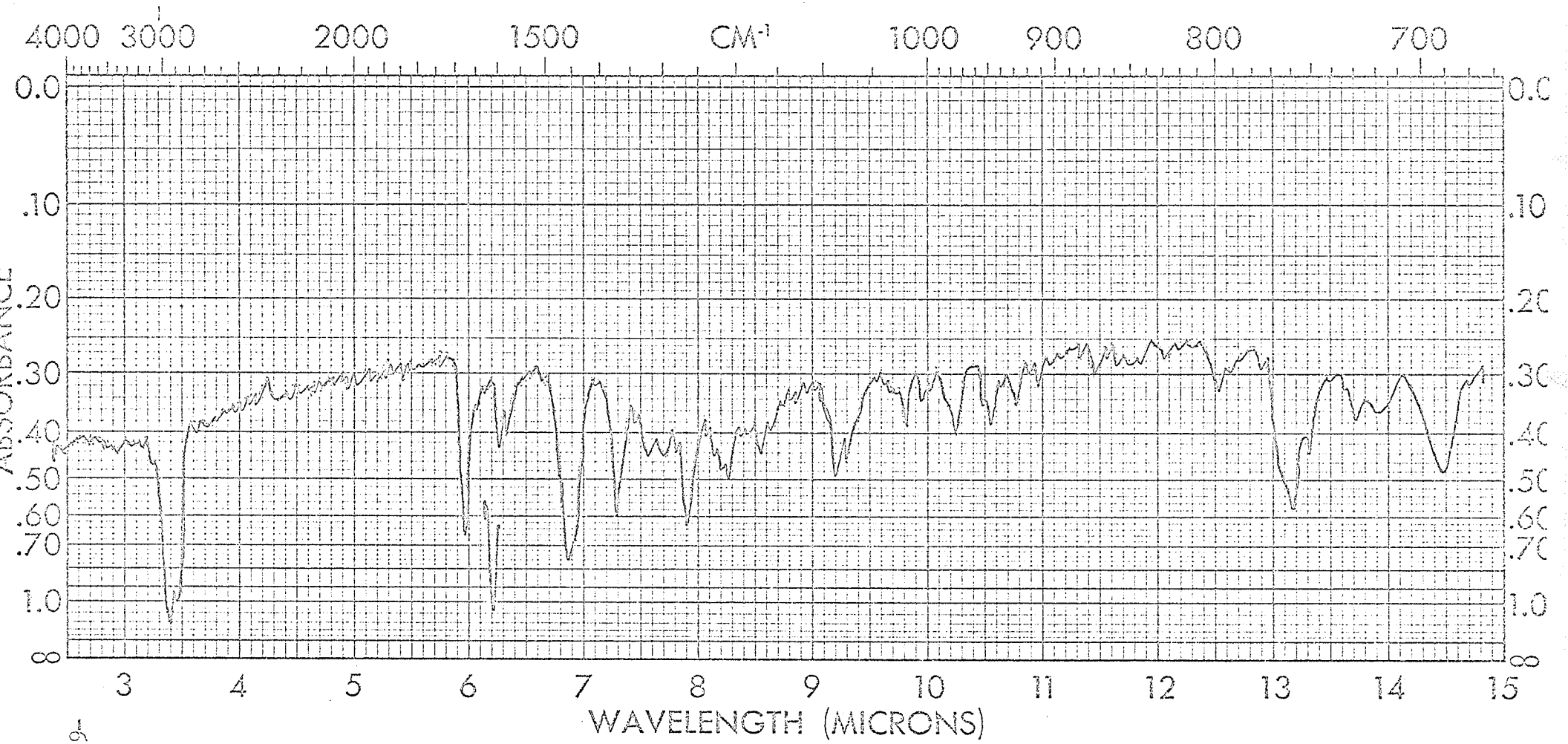
1,2-benzanthracene-9,10-endo-dibenzoylethylene (255),
nujol mull.



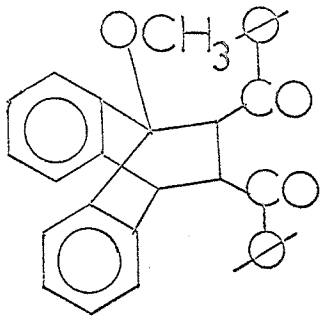


IR spectrum no. 40:

9-bromoanthracene-9,10-endo-dibenzoylethylene (254),
nujol mull.

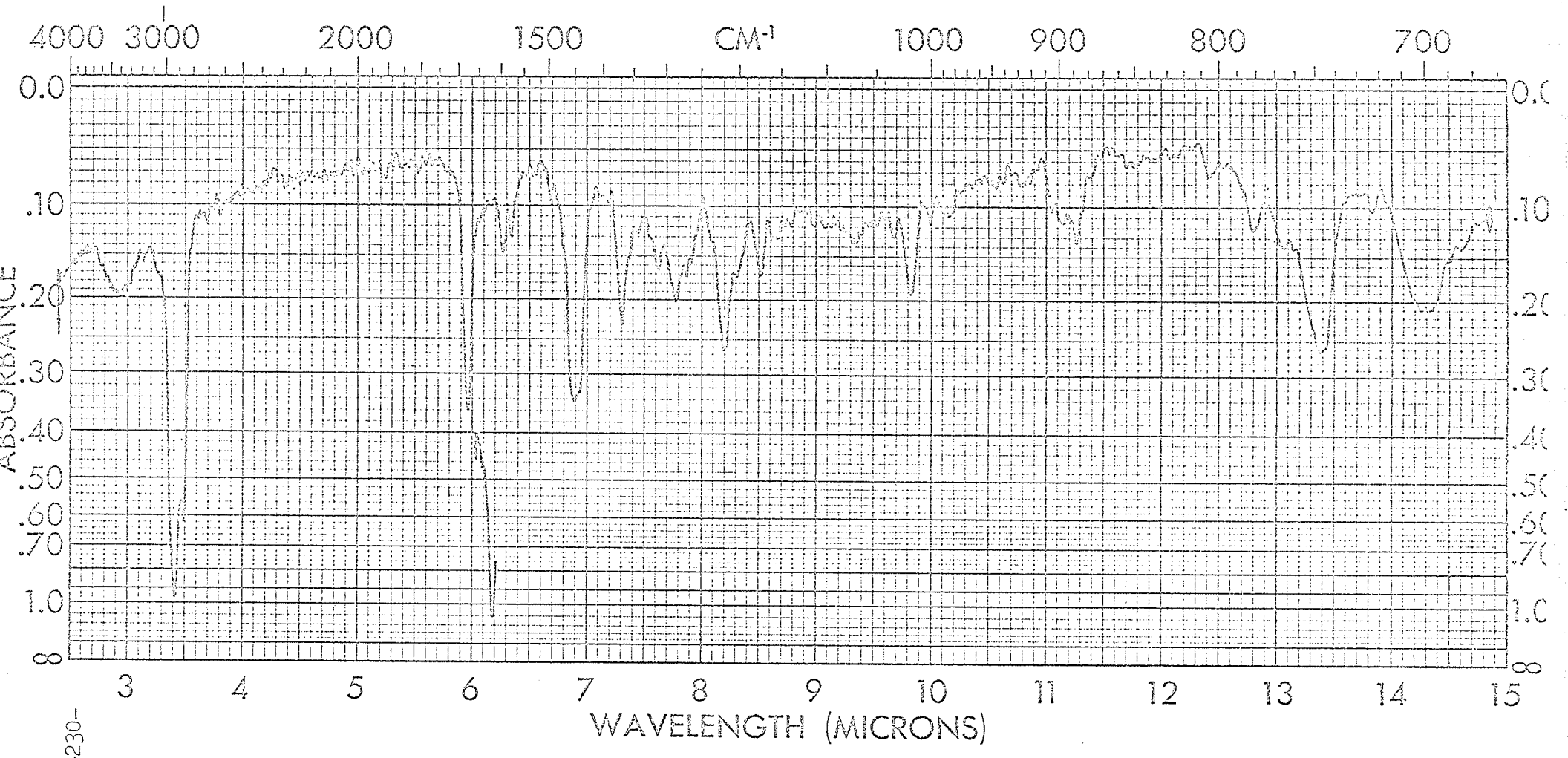


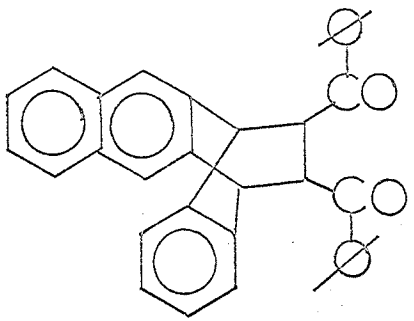
-229-



IR spectrum no. 41:

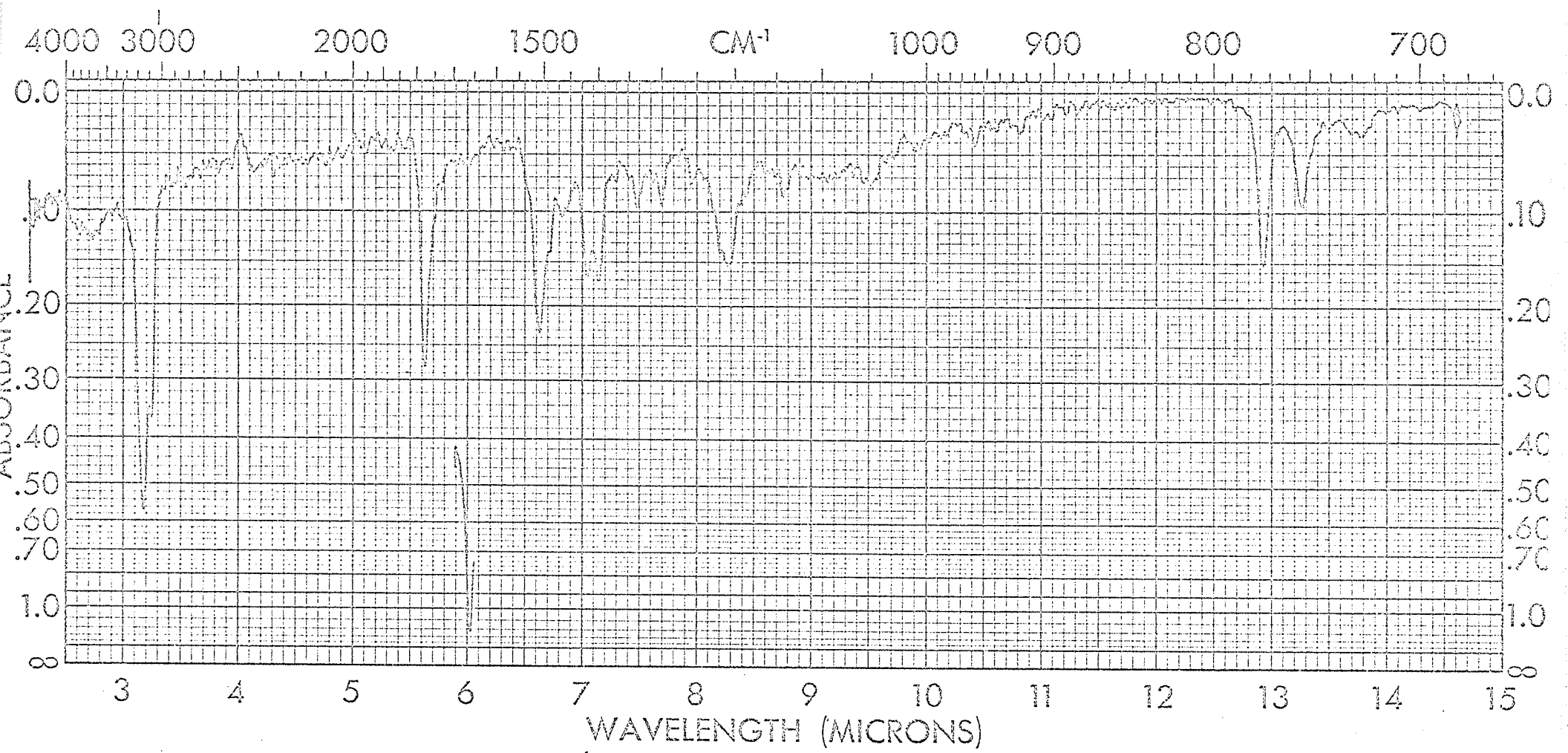
9-methoxyanthracene-9,10-endo-dibenzoylethylene (291),
nujol mull.

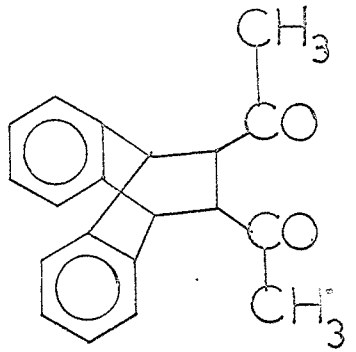




IR spectrum no. 42:

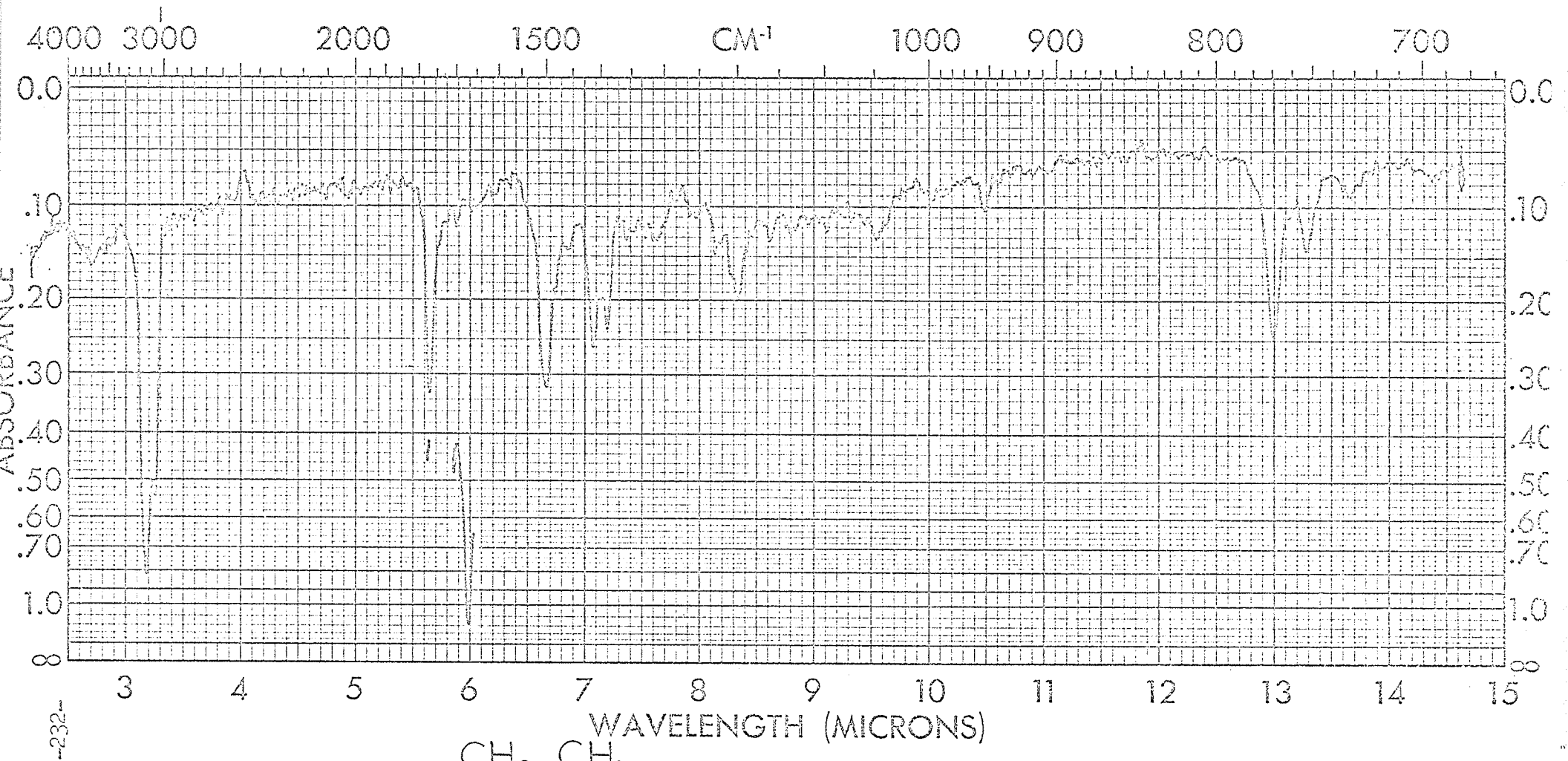
2,3-benzanthracene-9,10-endo-dibenzoylethylene (292) ,
nujol mull

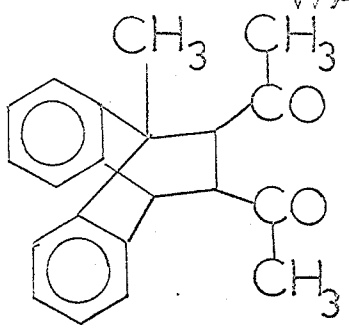




IR spectrum no. 43:

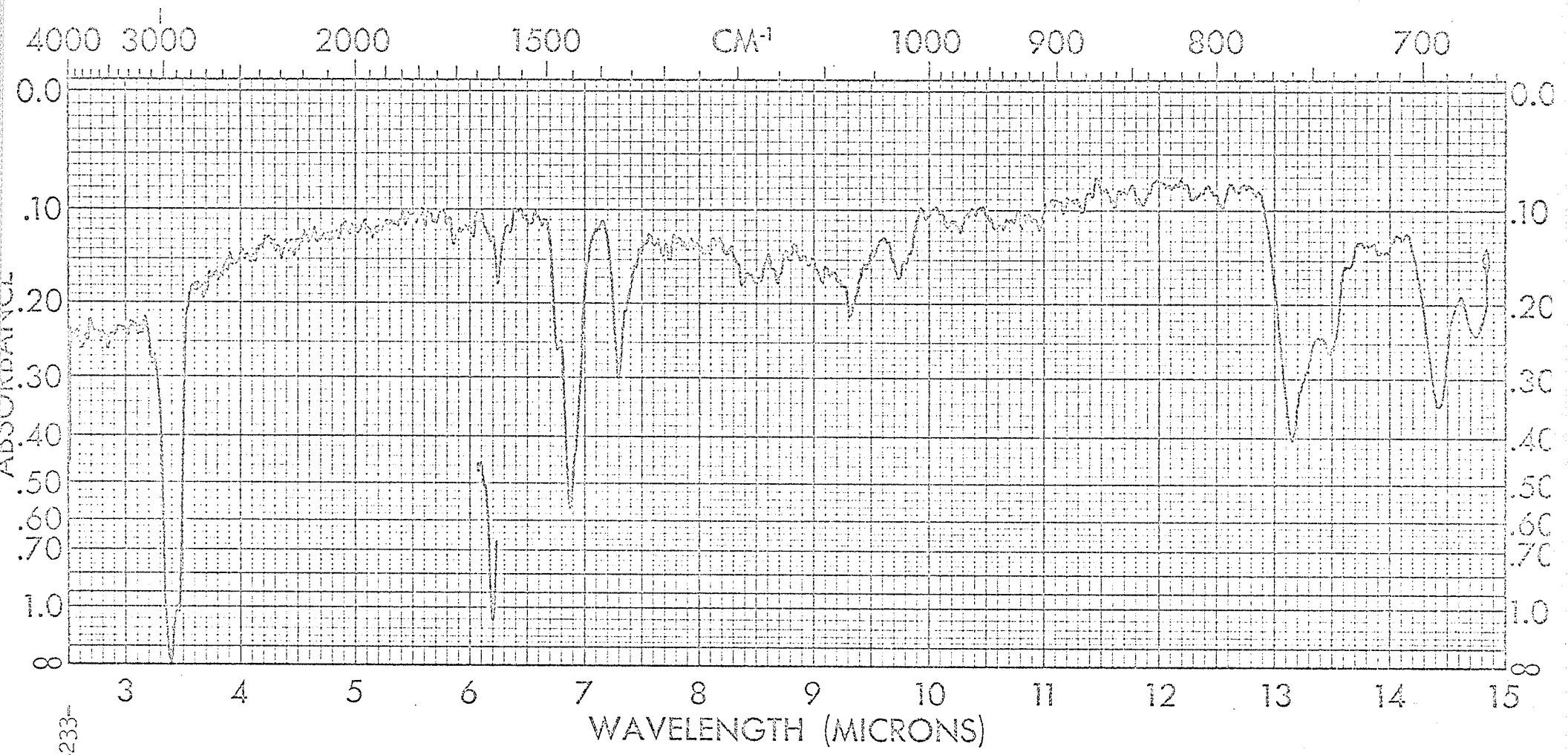
anthracene-9,10-endo-diacetylethylene (252), nujol mull.

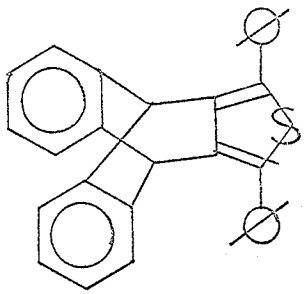




IR spectrum no. 44:

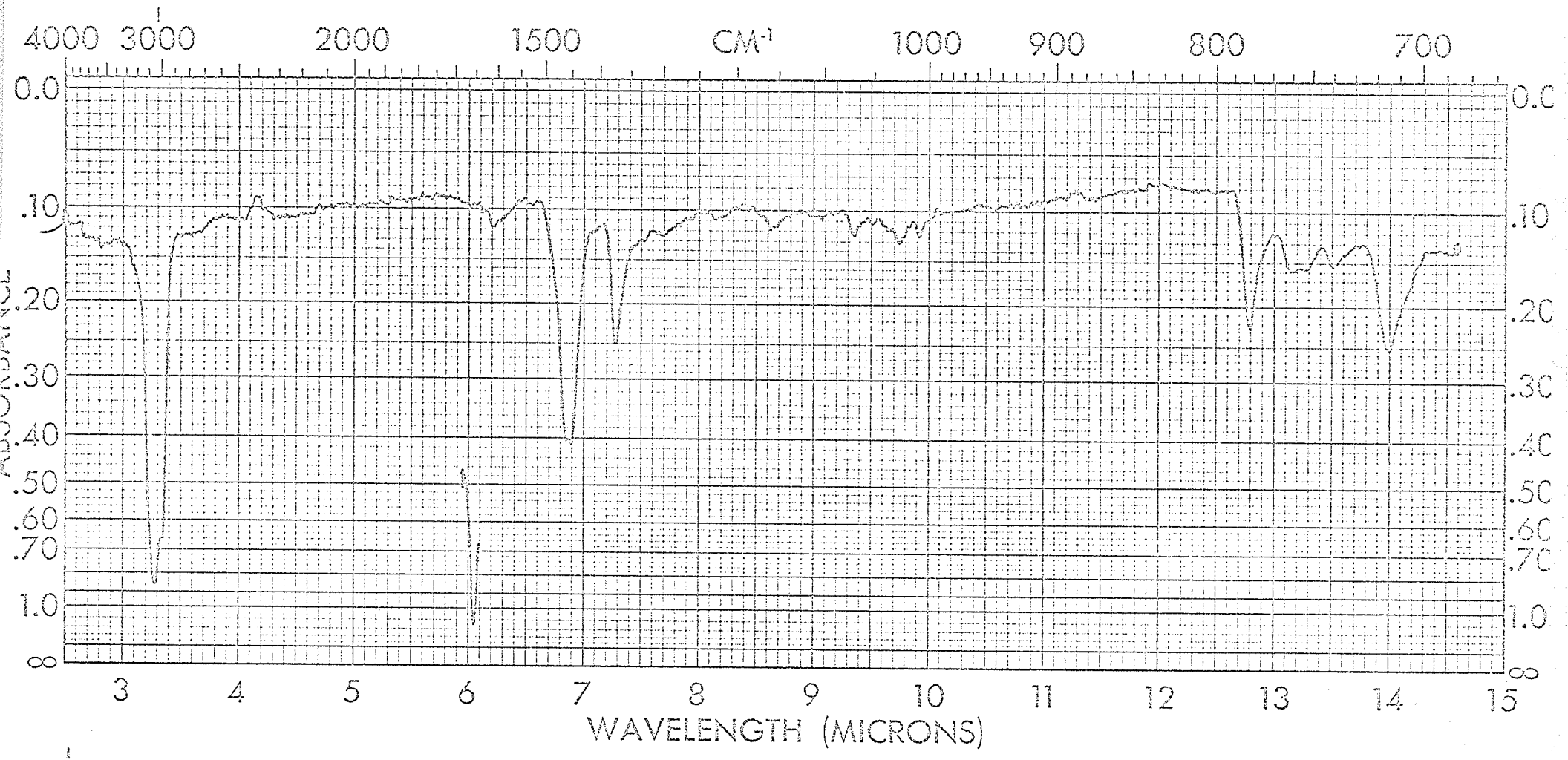
9-methylanthracene-9,10-endo-diacetylethylene (257),
nujol mull.

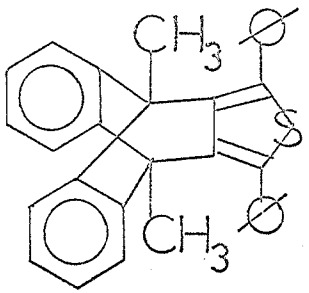




IR spectrum no. 45:

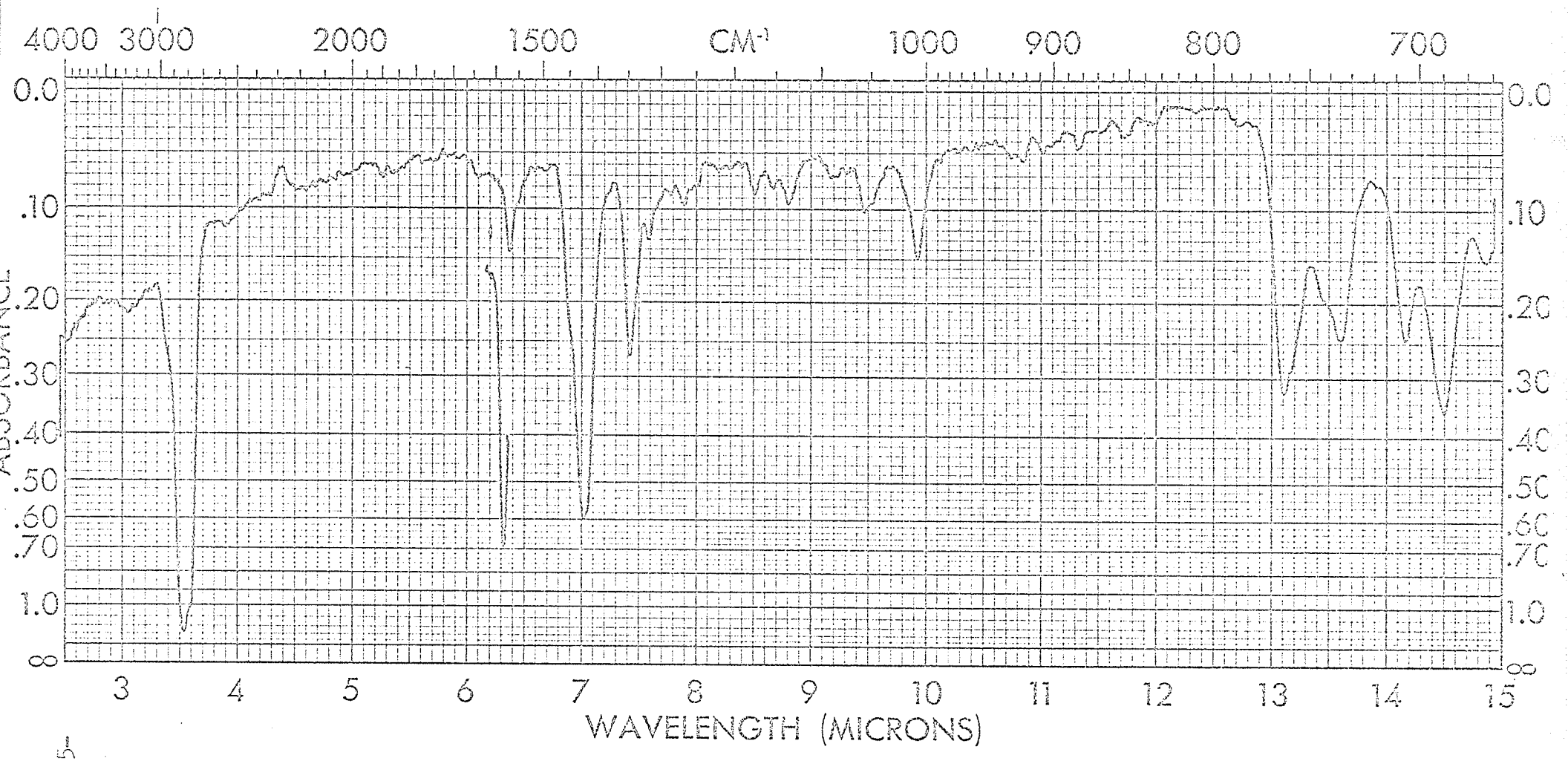
1,3-diphenyl-4,9-dihydro-4,9-o-benzenonaphtho(2,3-c) thiophene (241), nujol mull.

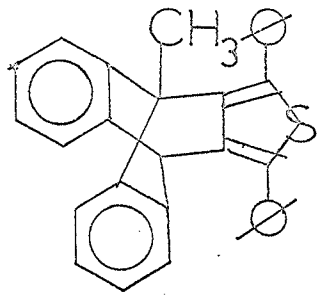




IR spectrum no. 46:

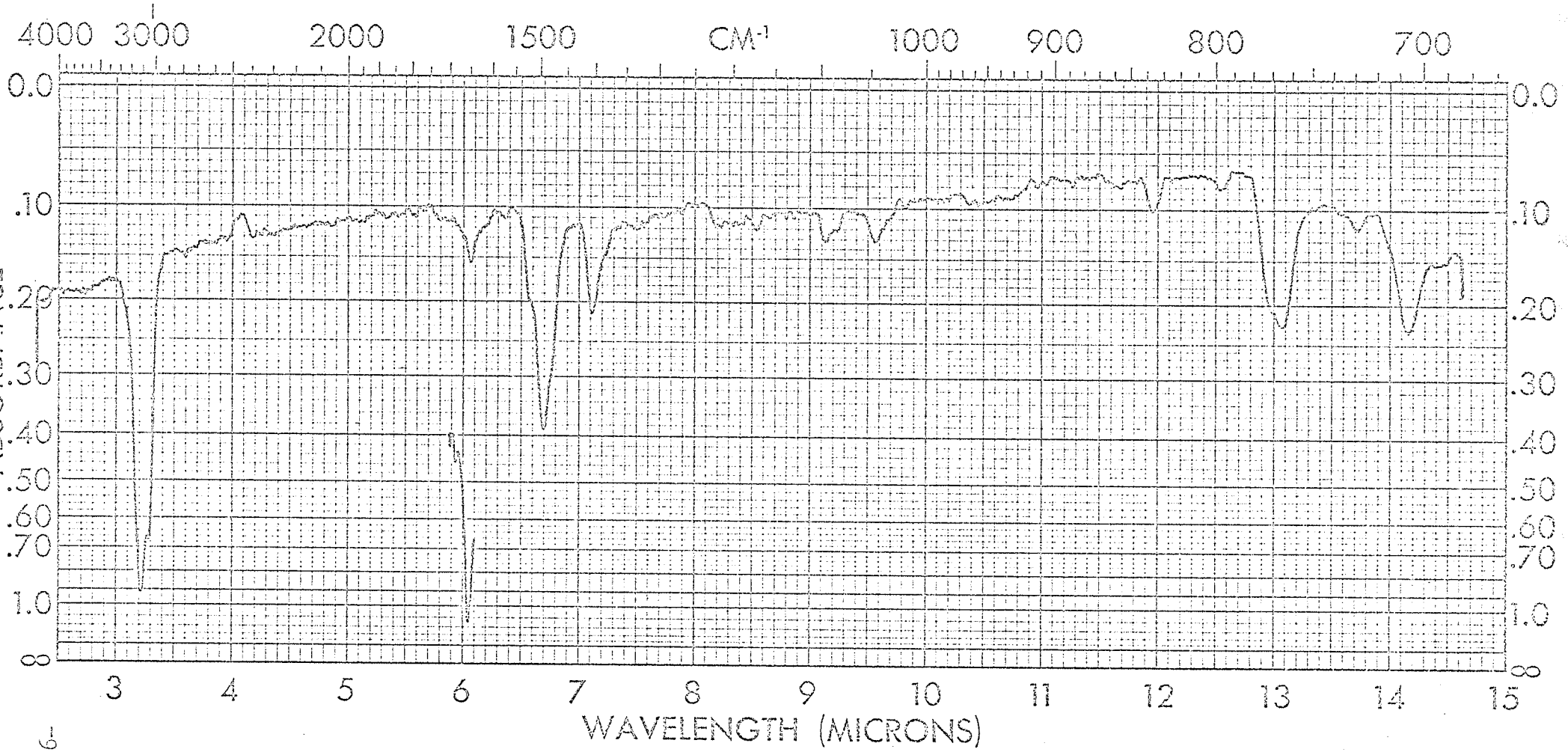
1,3-diphenyl-4,9-dimethyl-4,9-dihydro-4,9-o-benzeno-naphtho(2,3-c)thiophene, nujol mull.

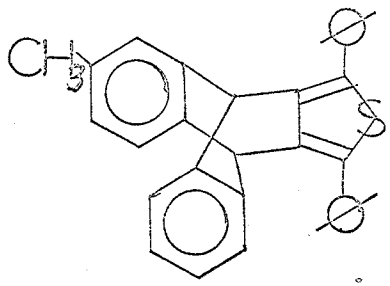




IR spectrum no. 47:

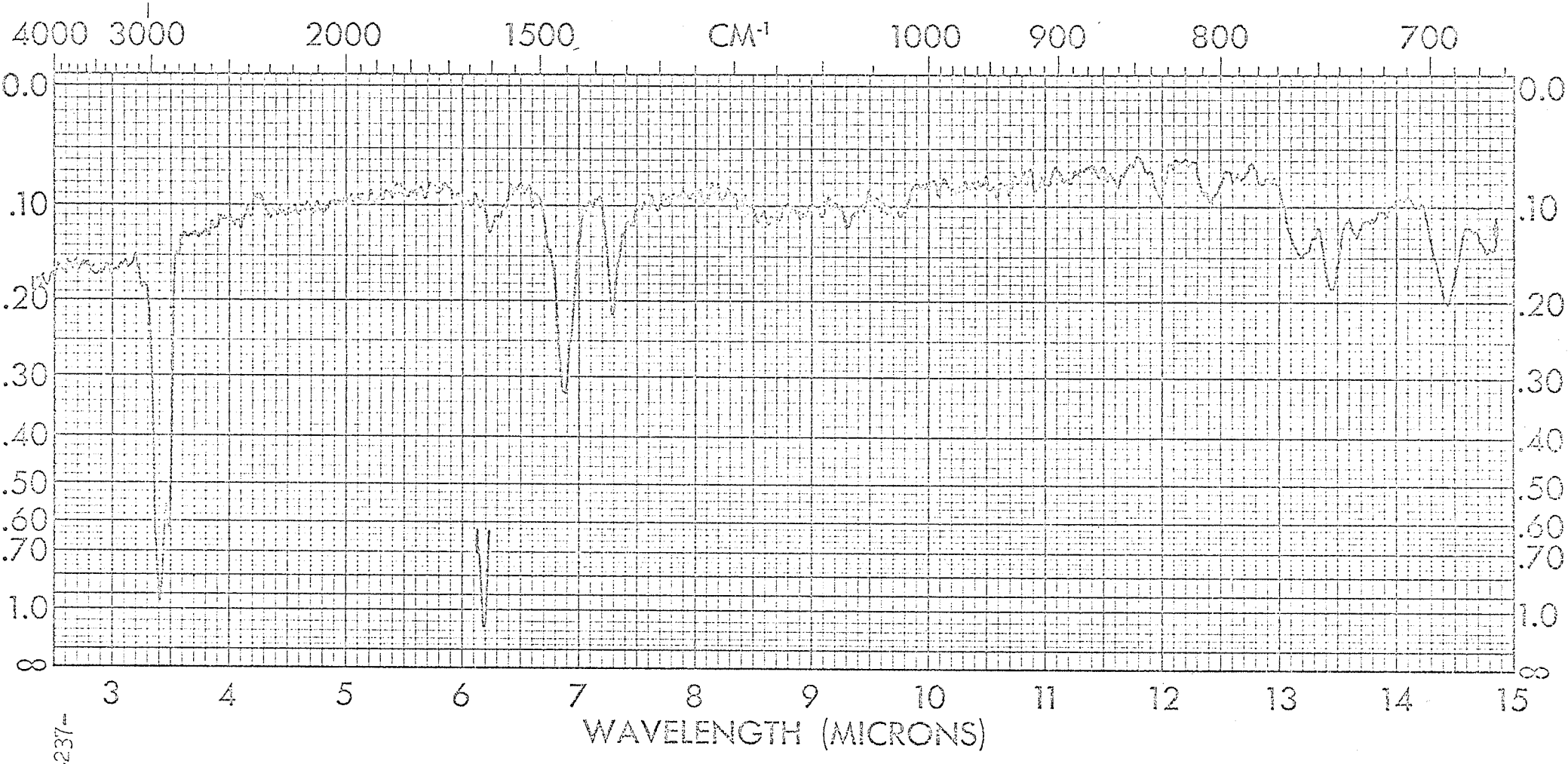
1,3-diphenyl-4-methyl-4,9-dihydro-4,9-o-benzenonaphtho-(2,3-c)thiophene, nujol mull.

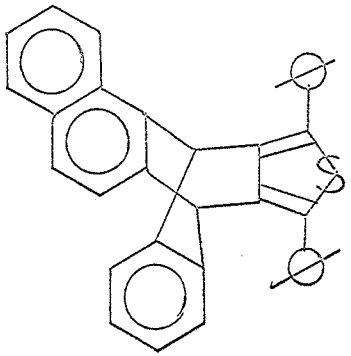




IR spectrum no. 48:

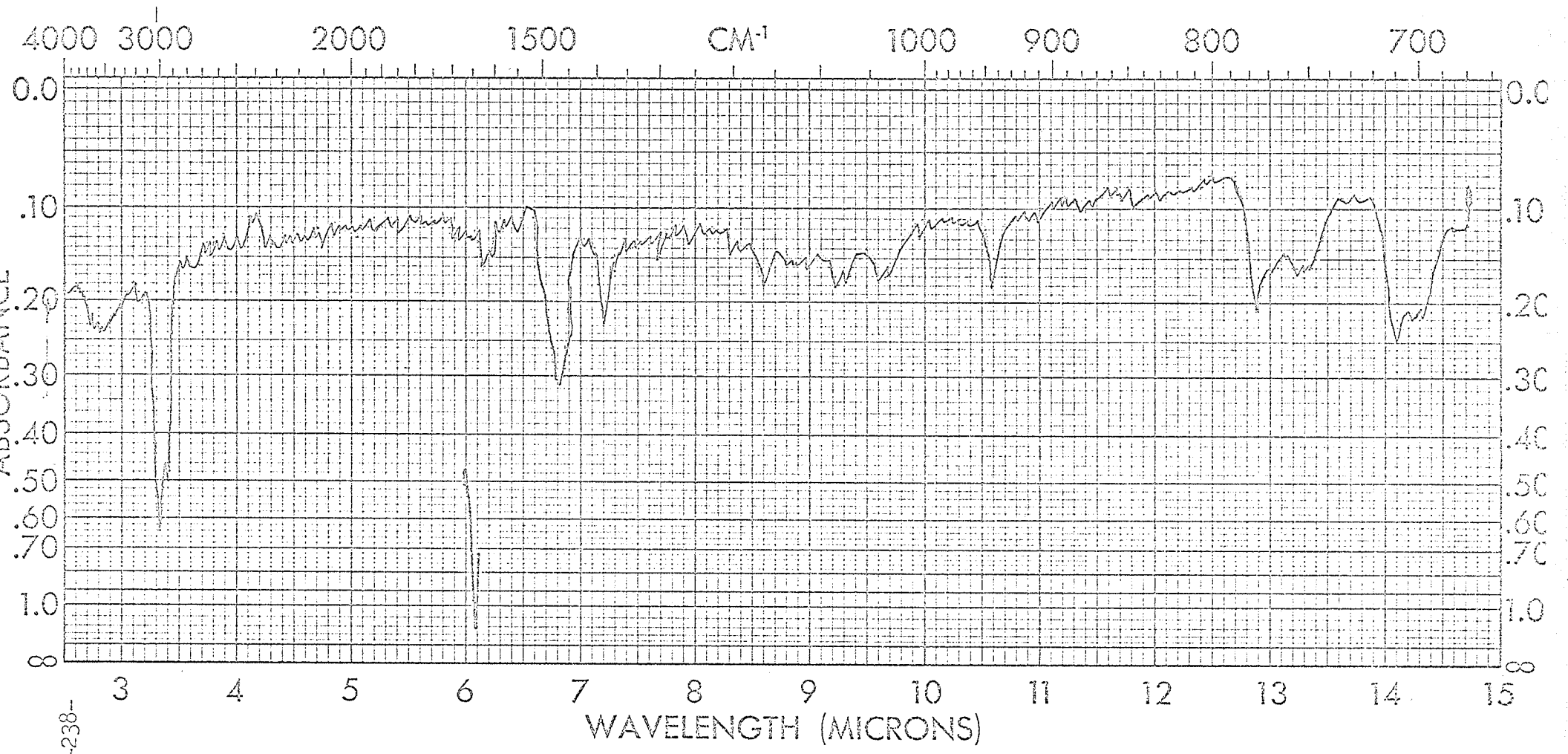
1,3-diphenyl-6-methyl-4,9-dihydro-4,9-o-benzenonaphtho-(2,3-c)thiophene (268), nujol mull.

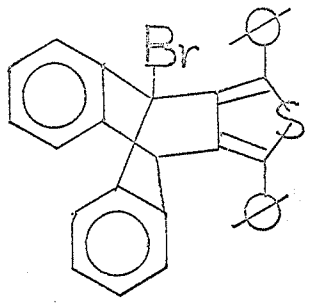




IR spectrum no. 49:

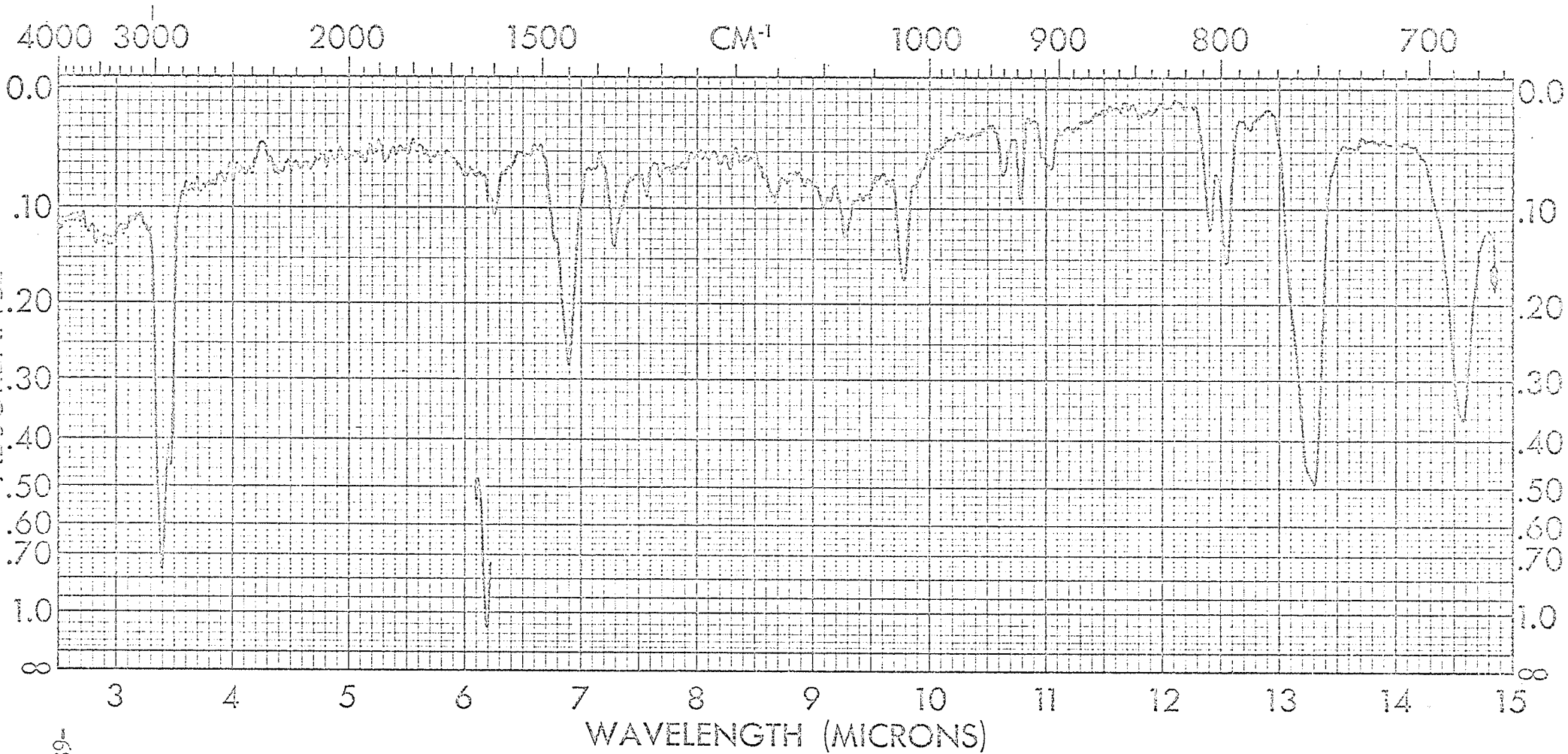
1,3-diphenyl-4,11-dihydro-4,11-o-benzenophenanthro-(2,3-c)thiophene (266), nujol mull.

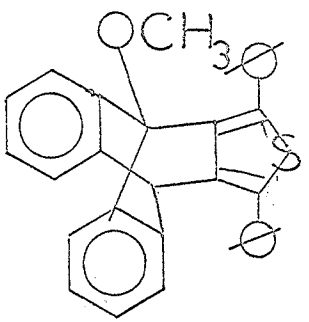




IR spectrum no. 50:

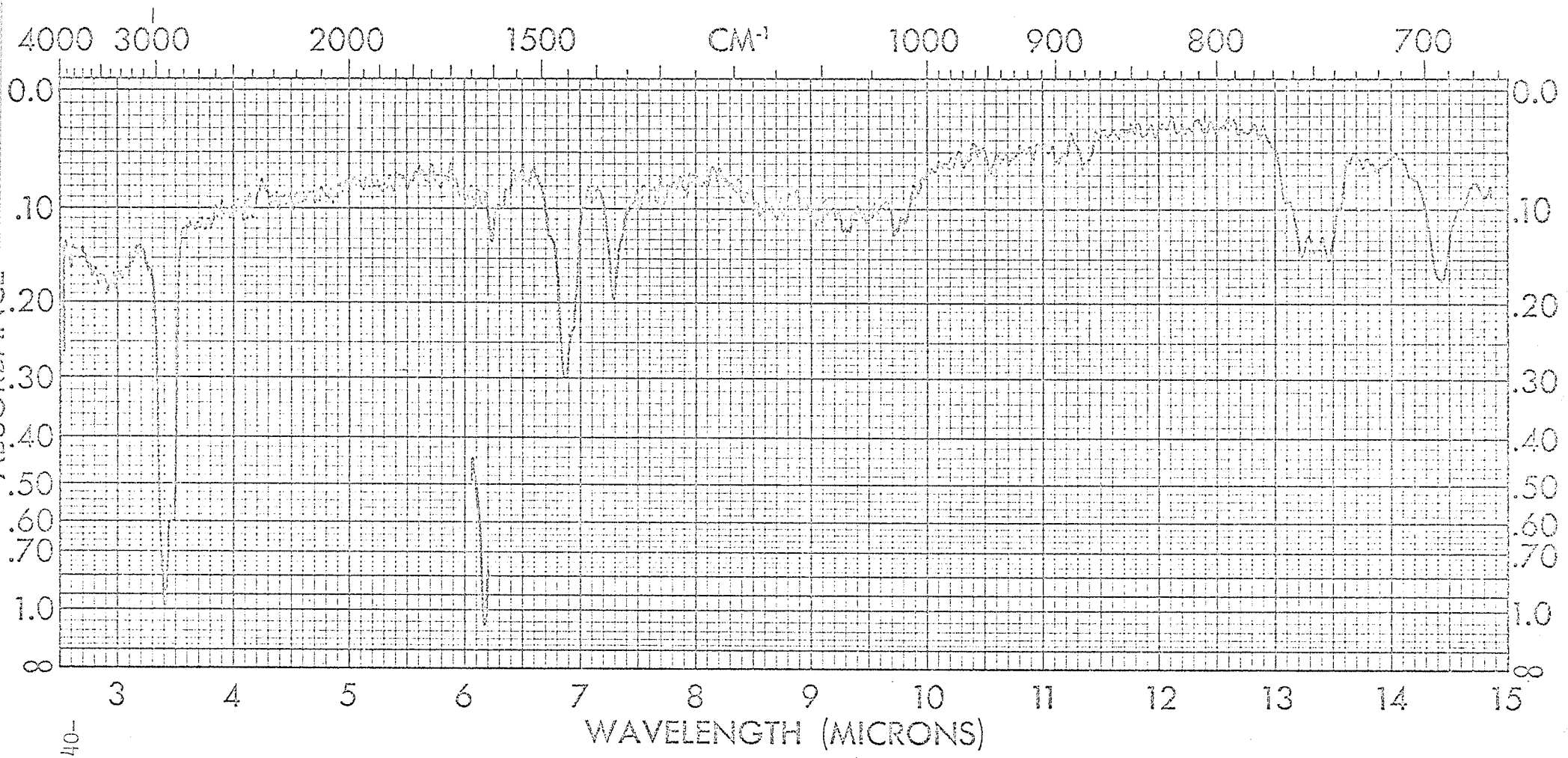
1,3-diphenyl-4-bromo-4,9-dihydro-4,9-0-benzenonaphtho-(2,3-c)thiophene, nujol mull.

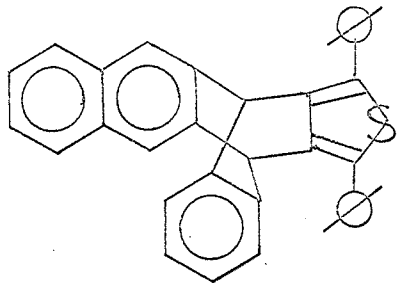




IR spectrum no. 51:

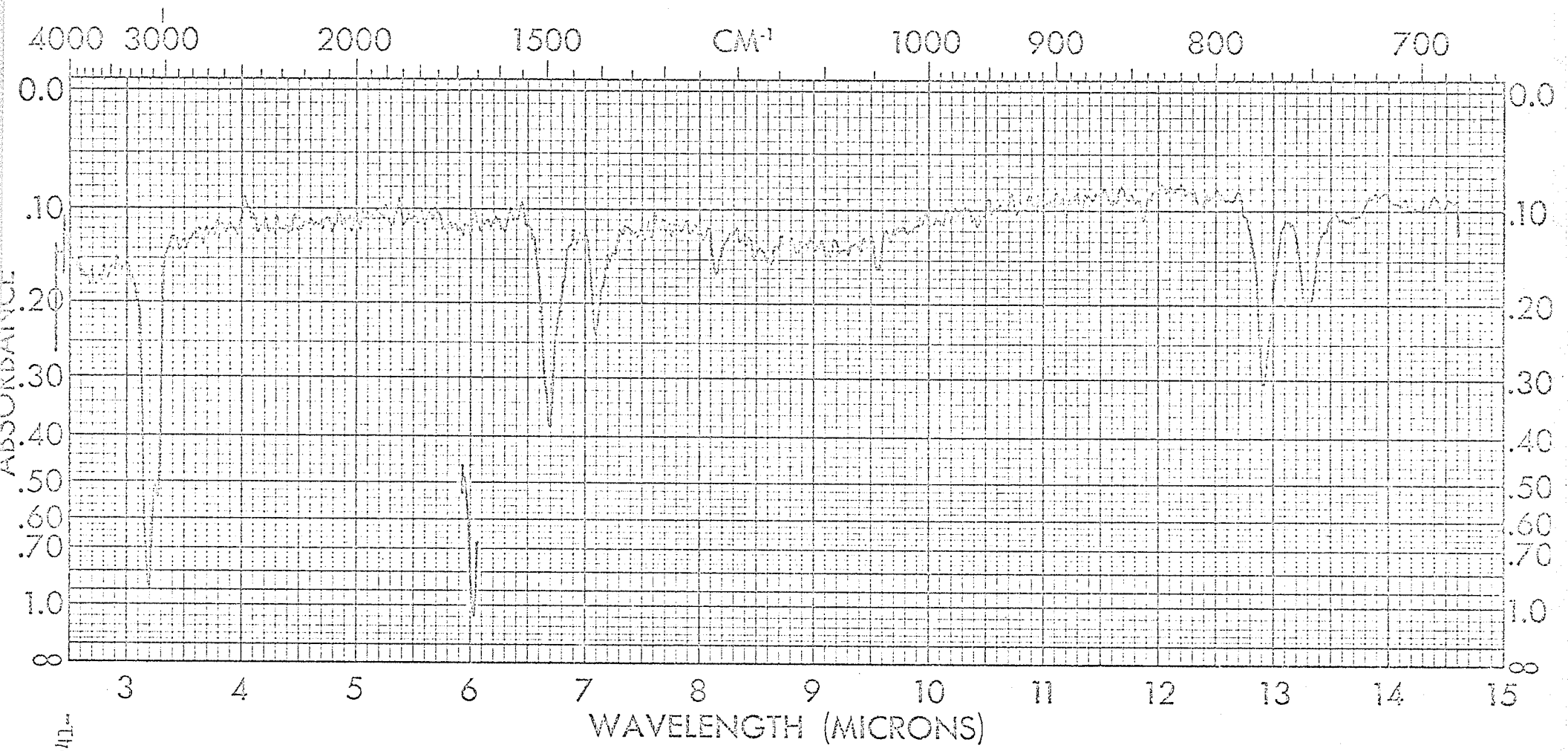
1,3-diphenyl-4-methoxy-4,9-dihydro-4,9-o-benzenonaphtho-(2,3-c)thiophene, nujol mull.



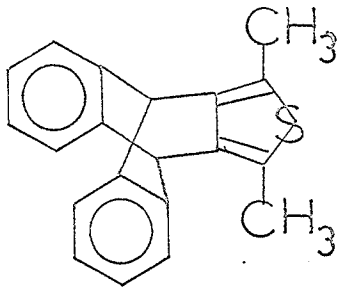


IR spectrum no. 52:

1,3-diphenyl-4,11-dihydro-4,11-o-benzenoanthra(2,3-c)-thiophene (267), nujol mull.

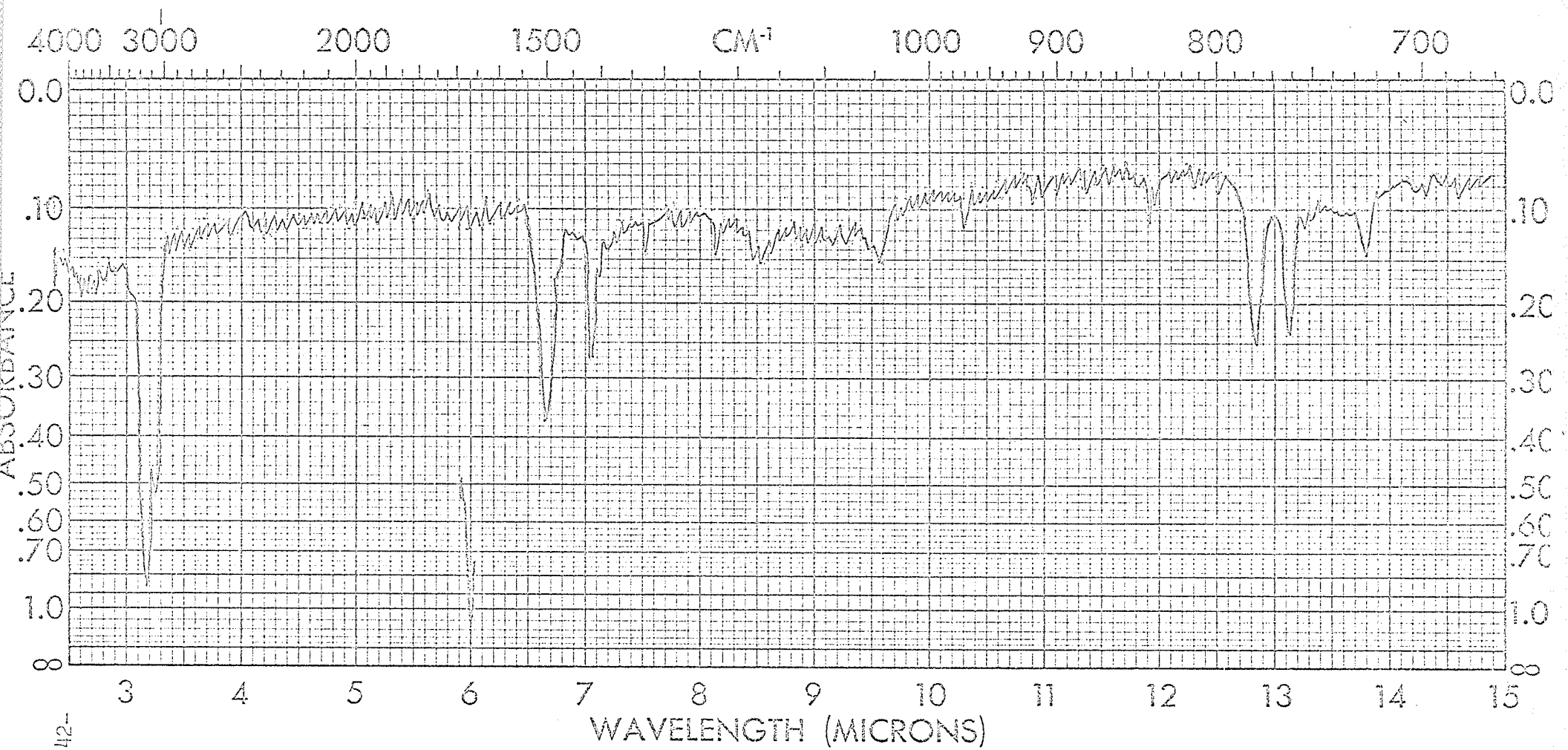


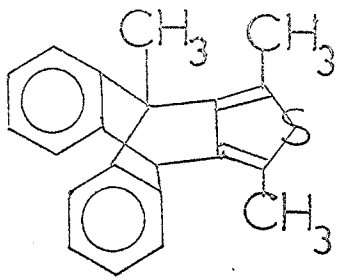
-241-



IR spectrum no. 53:

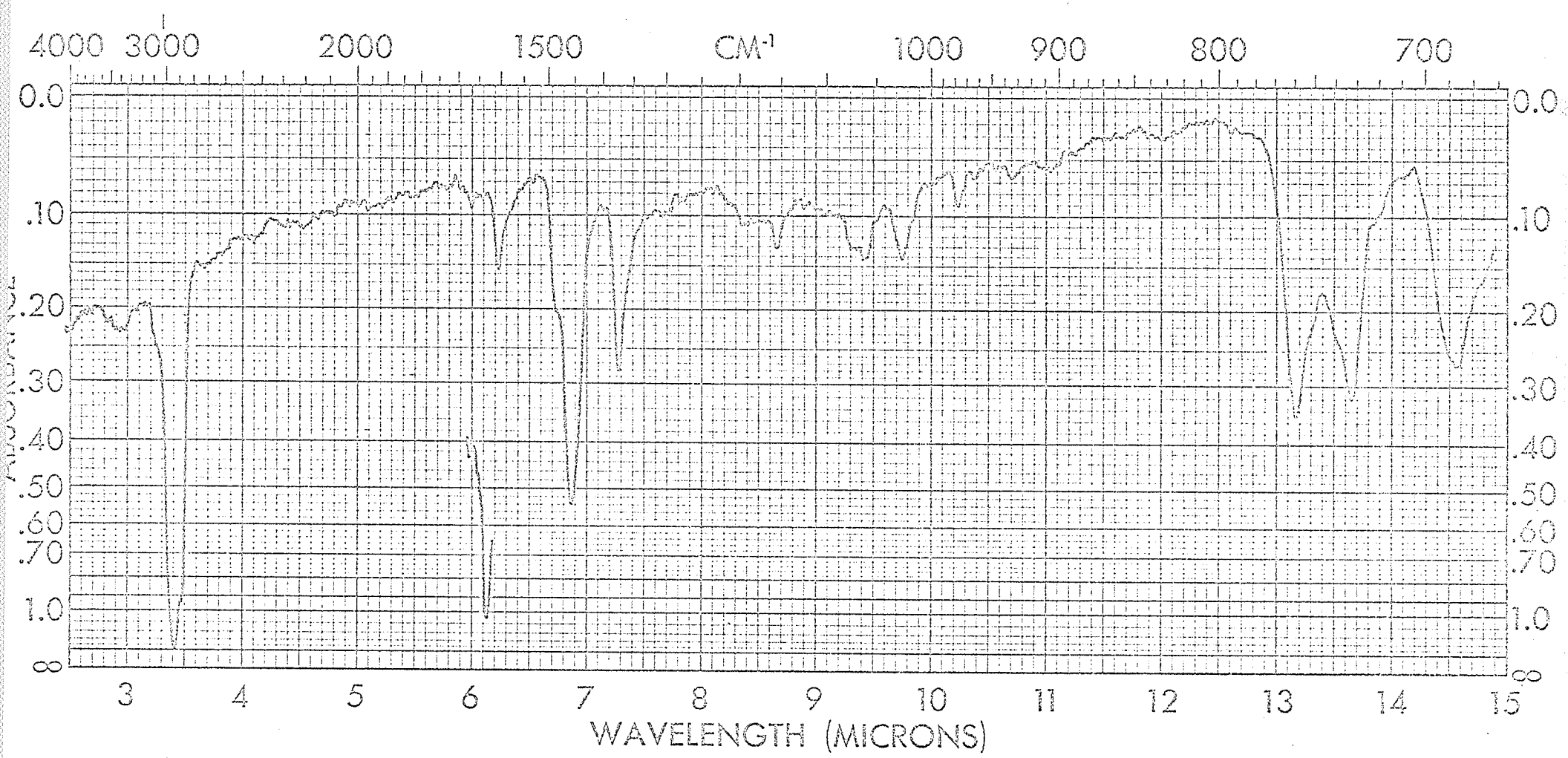
1,3-dimethyl-4,9-dihydro-4,9-o-benzenonaphtho(2,3-c)-thiophene (239), nujol mull.

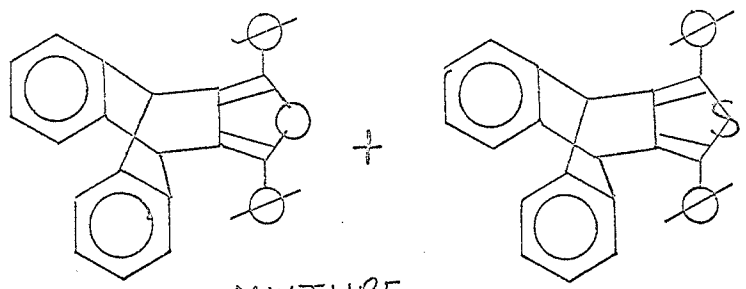




IR spectrum no. 54:

1,3-dimethyl-4-methyl-4,9-dihydro-4,9-o-benzenonaphtho-(2,3-c)thiophene (263), nujol mull.

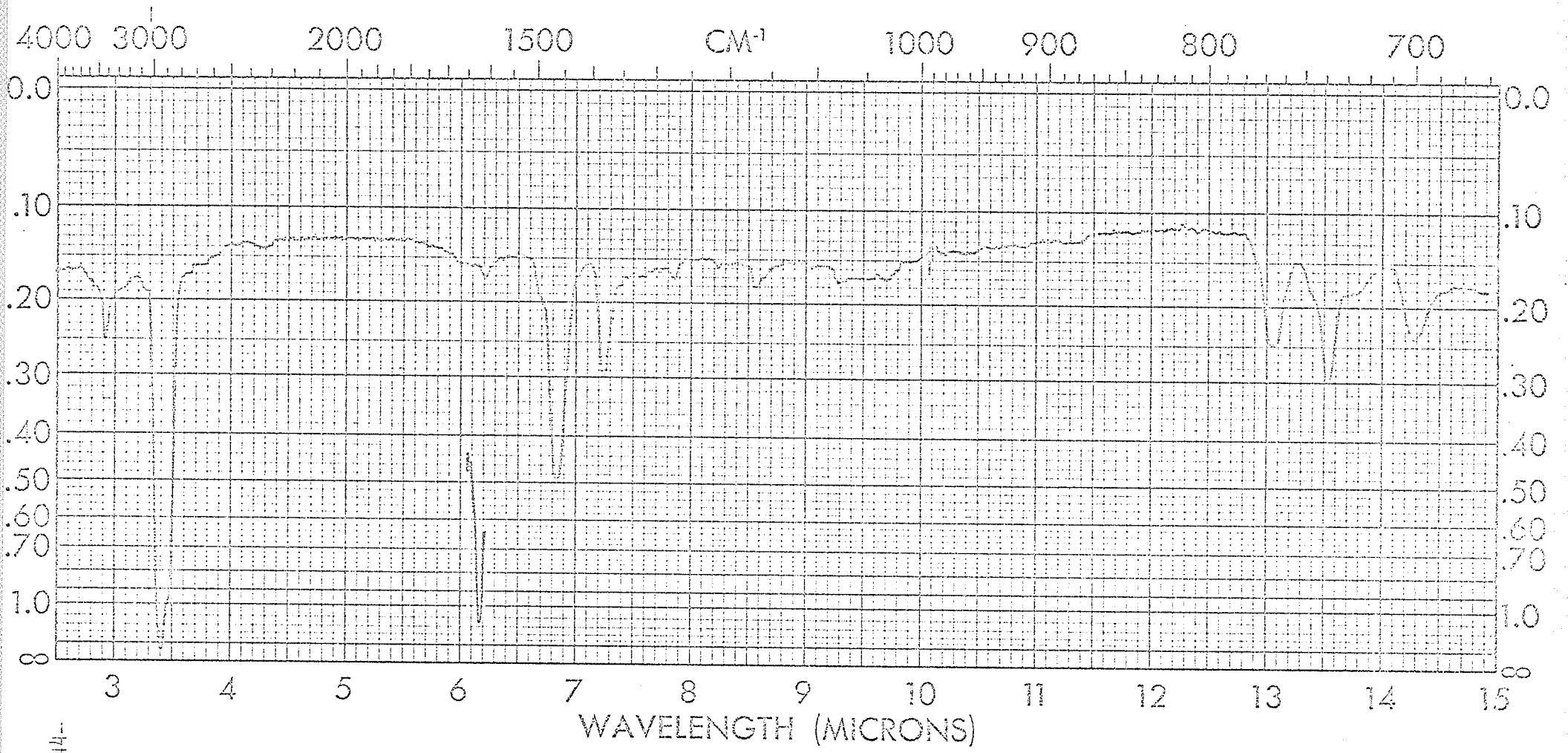


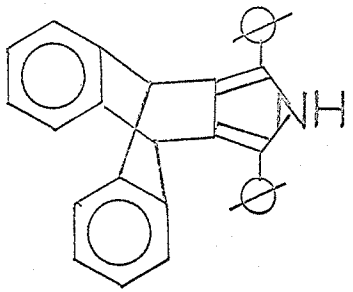


MIXTURE

IR spectrum no. 55:

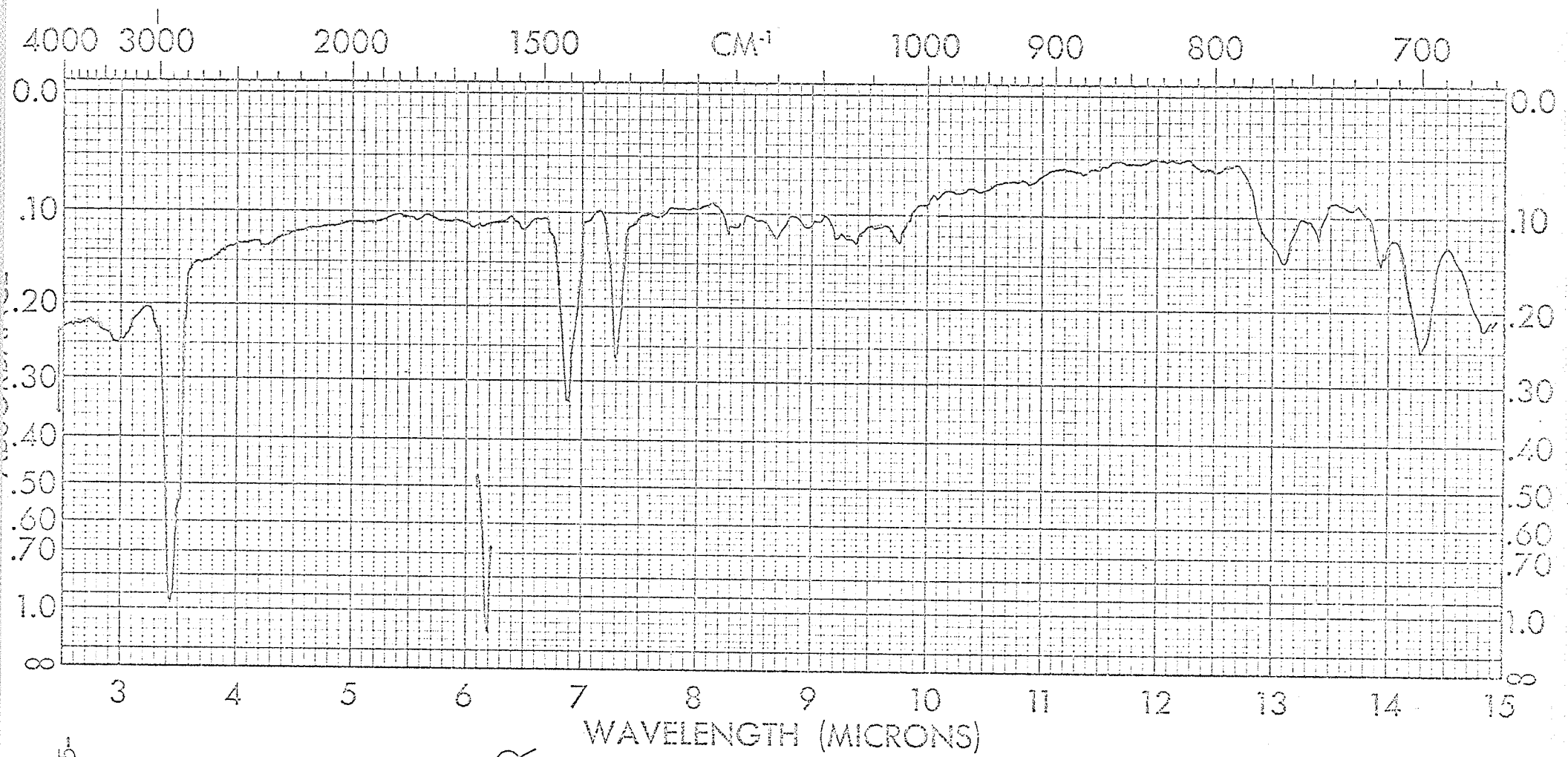
1,3-diphenyl-4,9-dihydro-4,9-o-benzeno-naphtho(2,3-c)thiophene (241) and -furan(102) mixture, nujol mull.

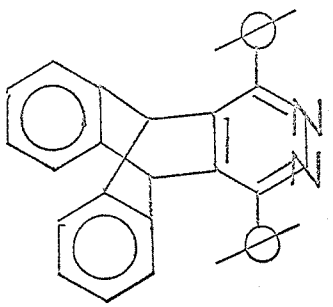




IR spectrum no. 56:

1,3-diphenyl-4,9-dihydro-4,9-o-benzenonaphtho(2,3-c)-pyrrole (265), nujol mull.

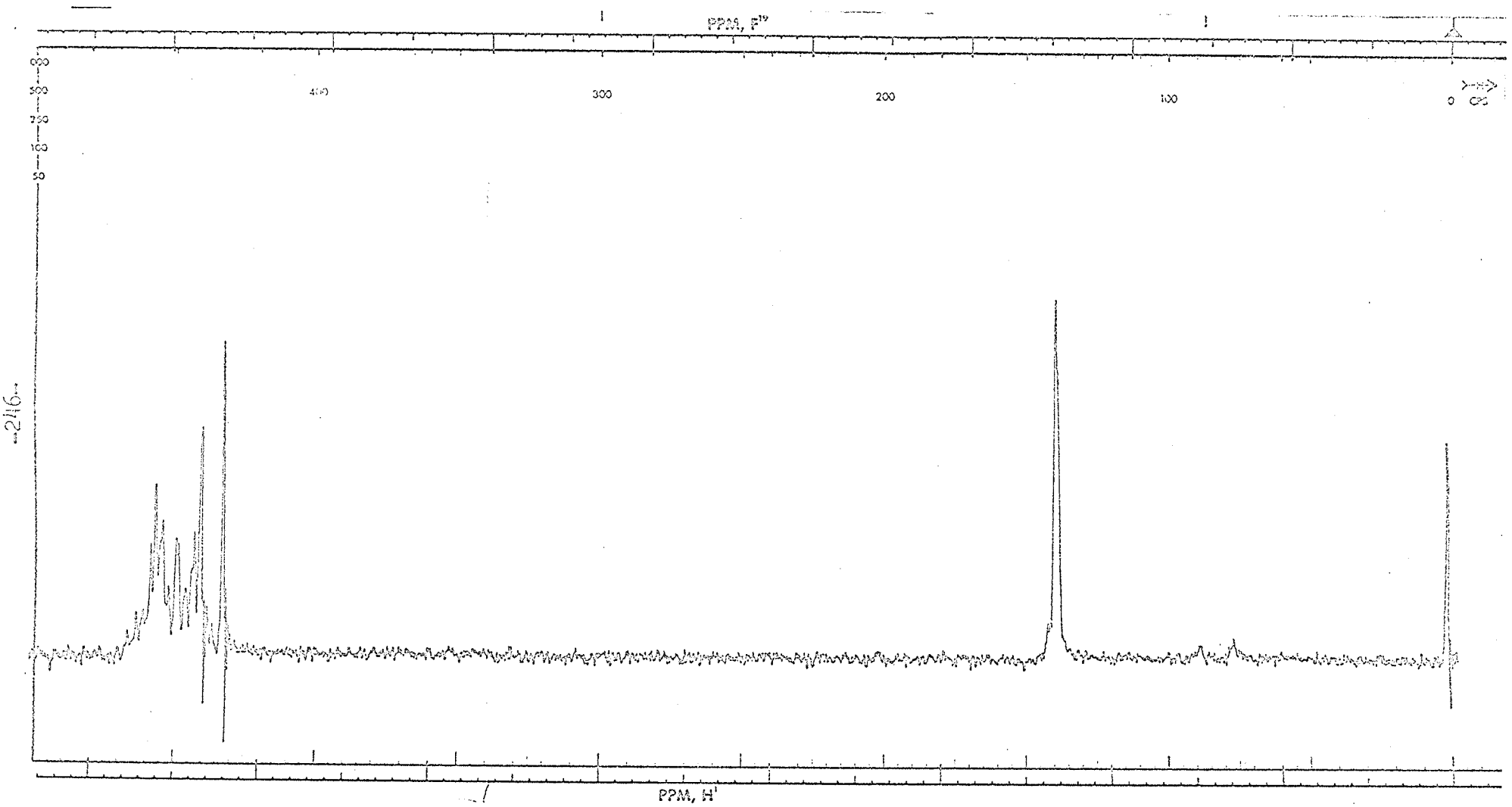


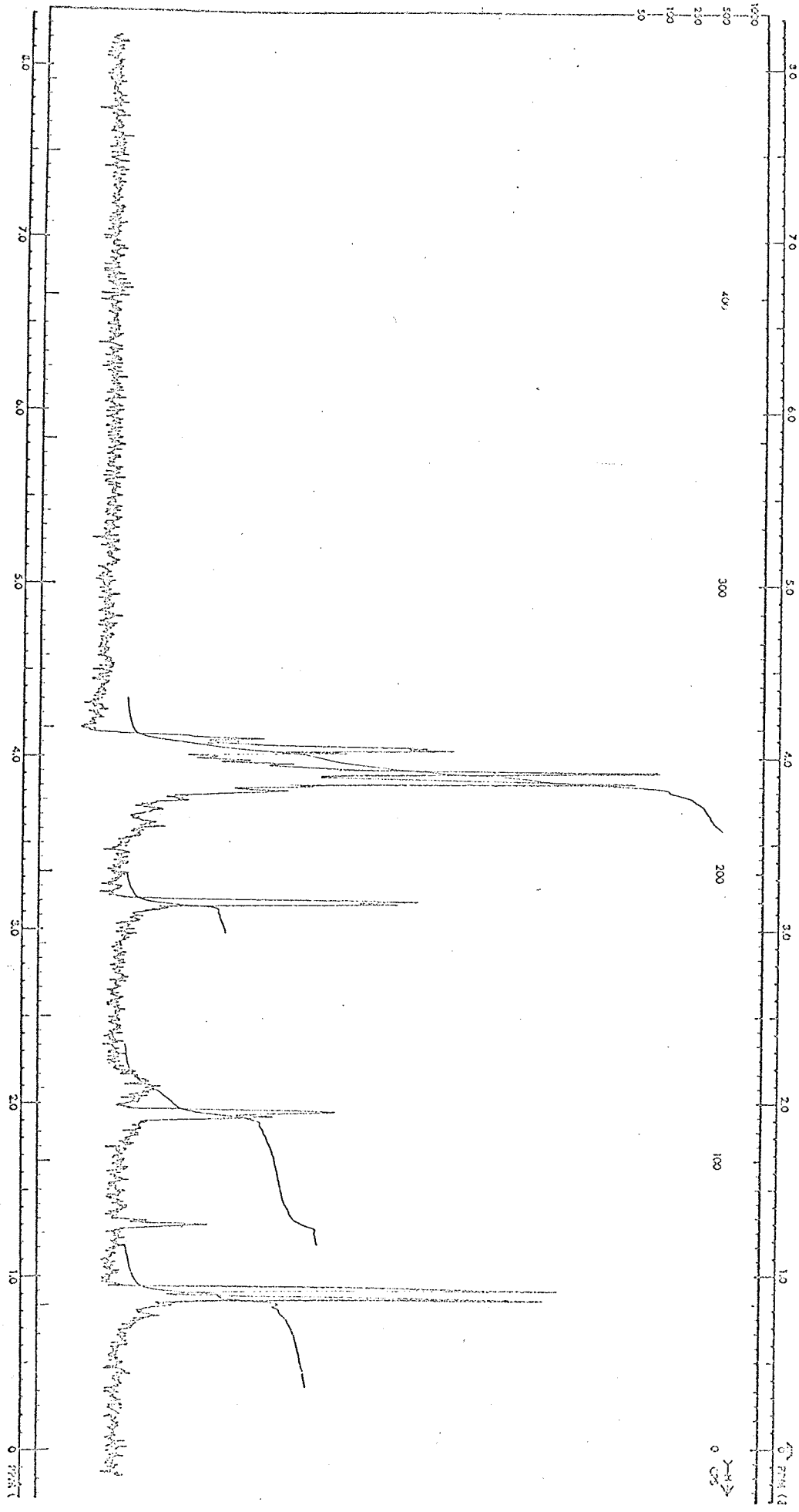


IR spectrum no. 57:

pyridazino analogue of triptycene 104, nujol mull.

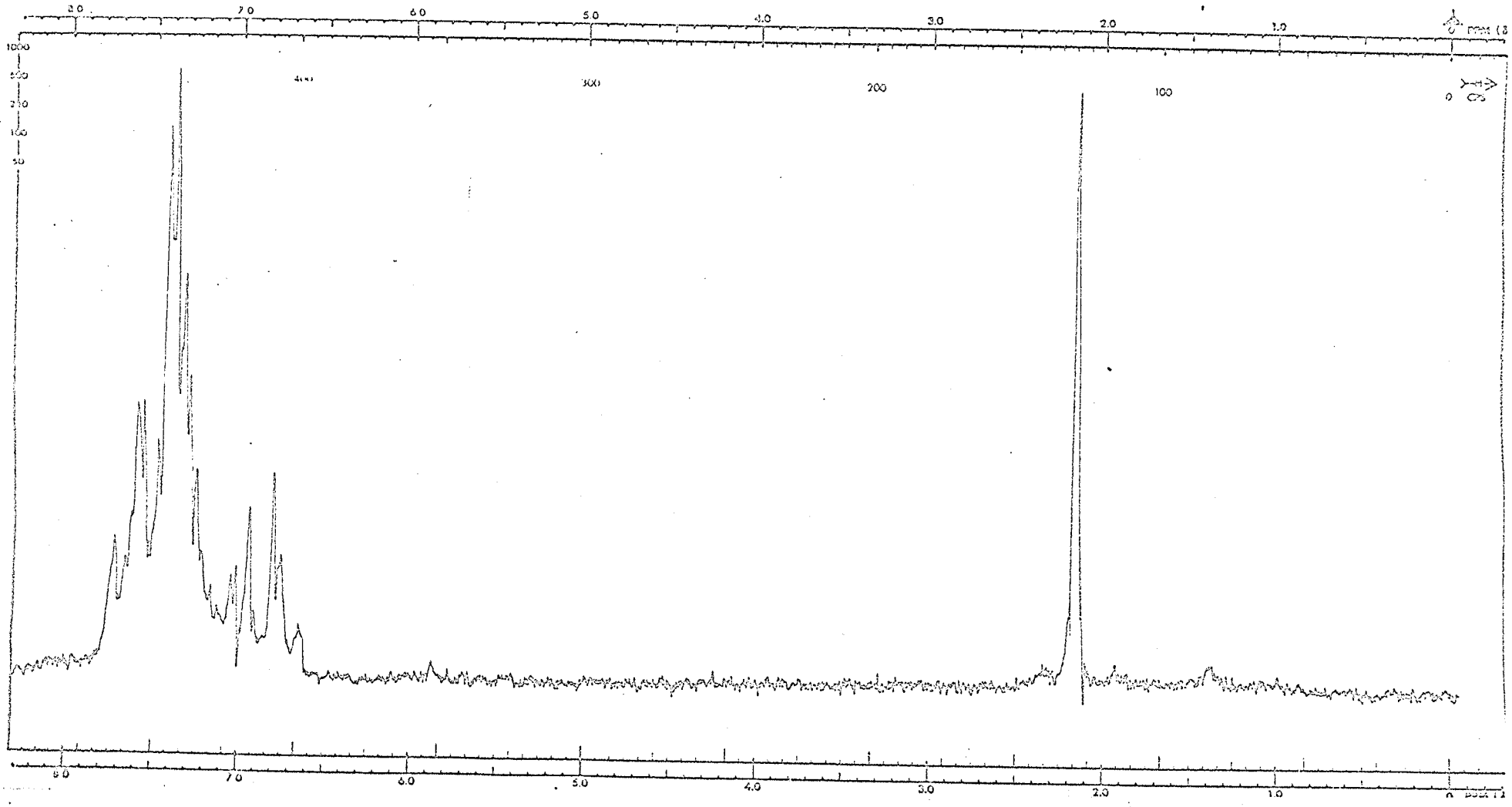
NMR spectrum no. 1 : 1,3-diphenyl-5,6-dimethylbenzo(c)thiophene (49), in $CDCl_3$. Sweep width= 500 Hz.



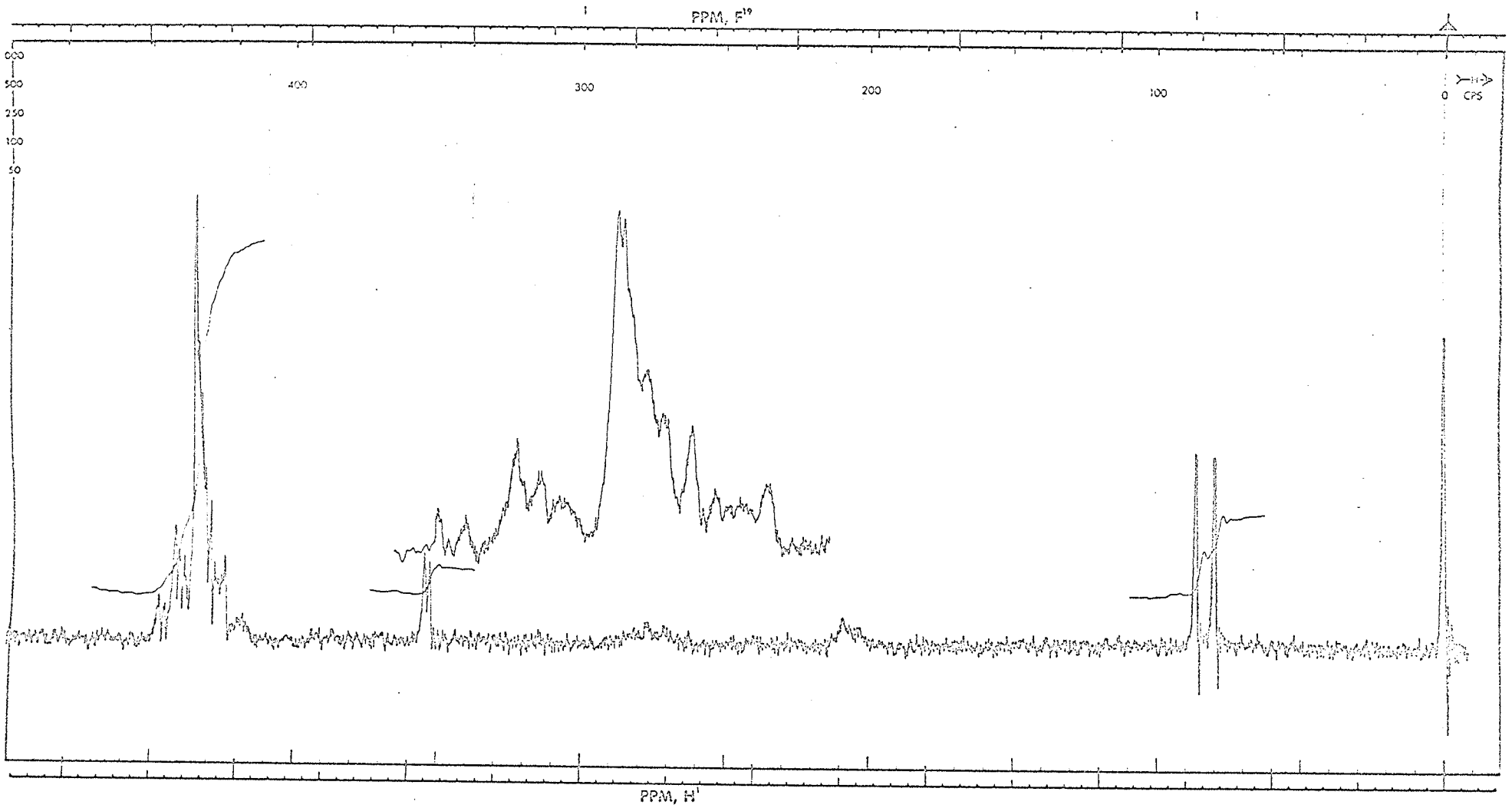


NMR spectrum no. 2: 1,3-diphenyl-4-methyl-4,7-dihydrobenzo(c)thiophene in $CDCl_3$. Sweep width = 1000 Hz.

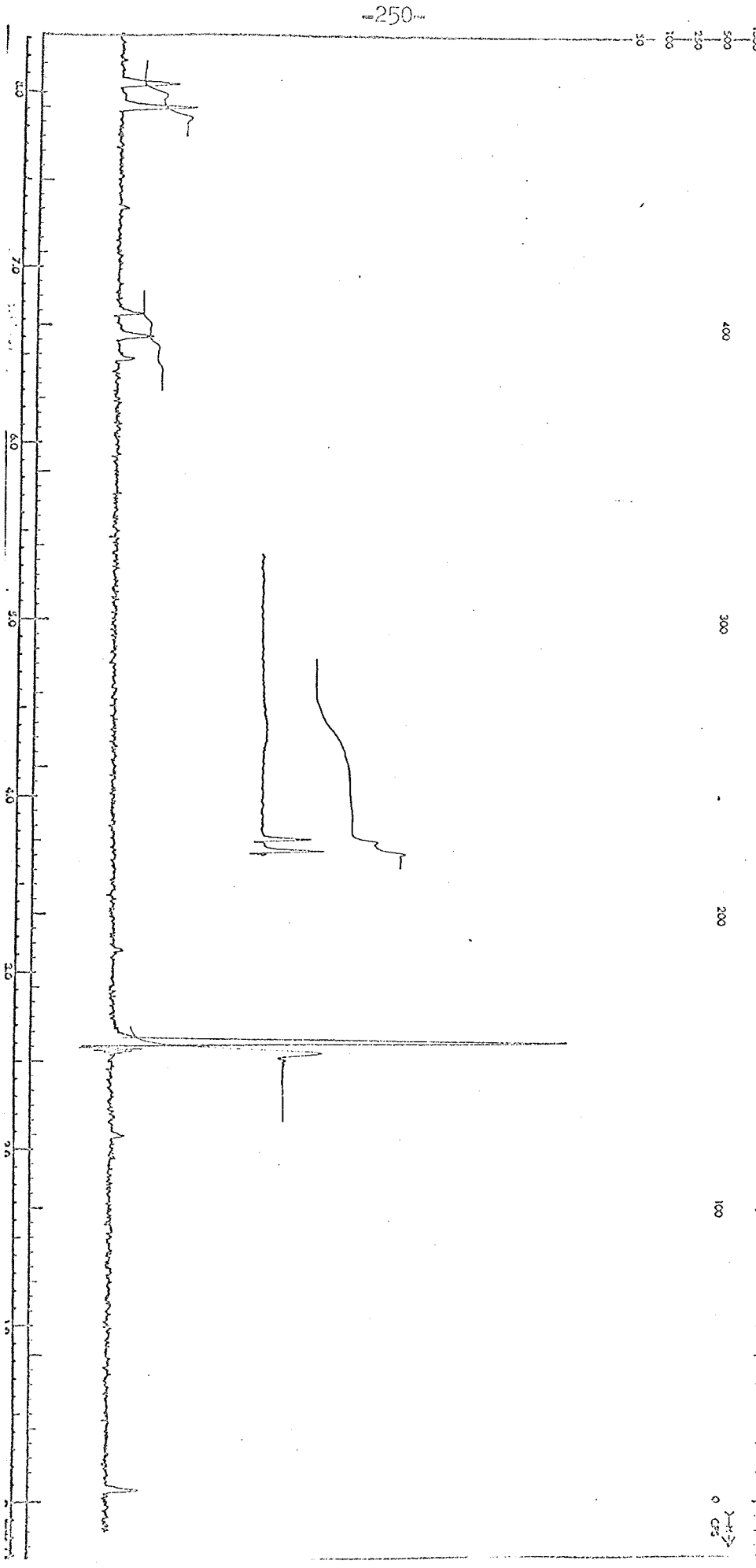
NMR spectrum no. 3 : 1,3-diphenyl-4-methylbenzo(c)thiophene (160) in $CDCl_3$. Sweep width = 500 Hz.



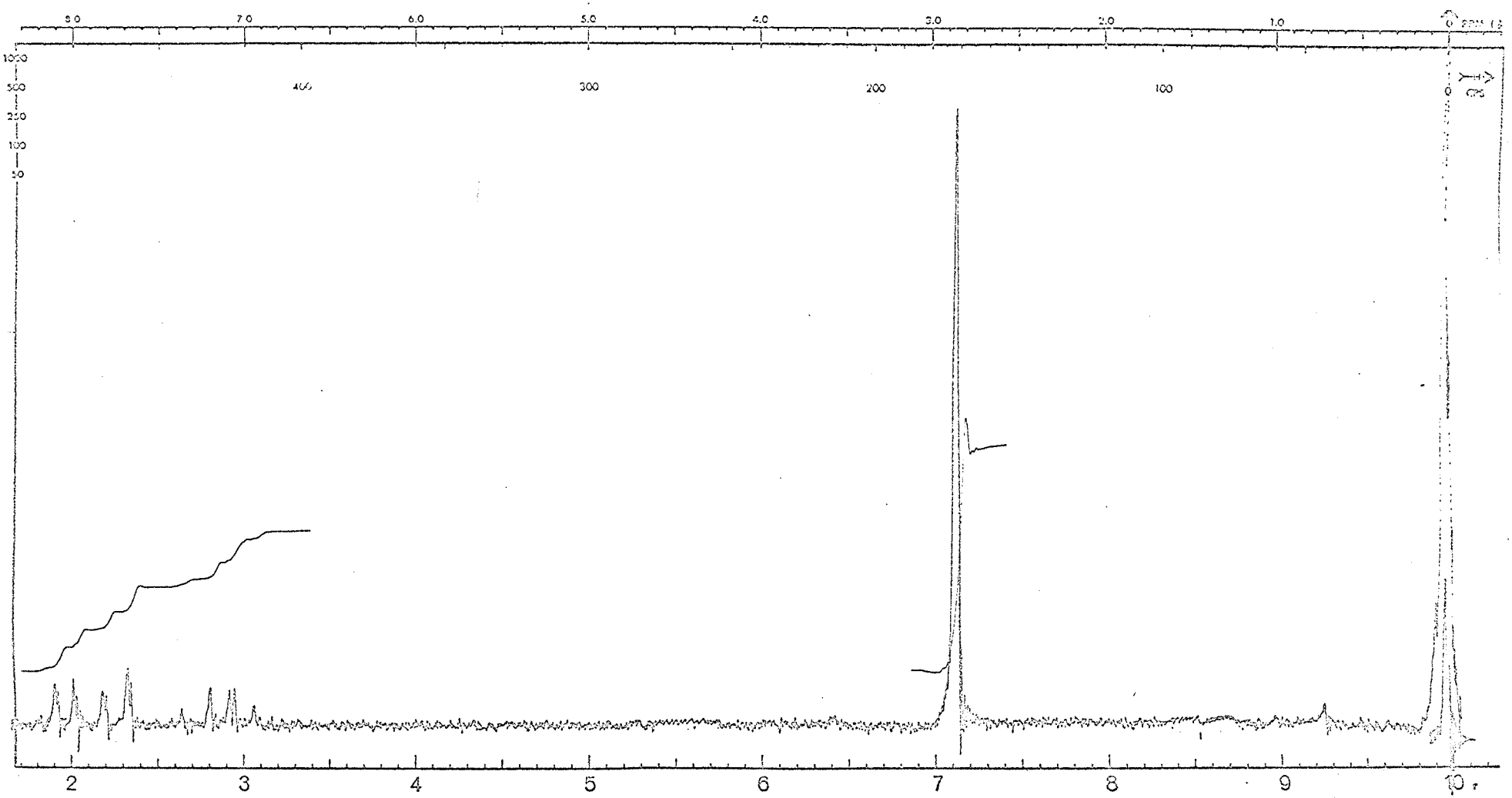
NMR spectrum no. 4 : Diels-Alder adduct 152 in $CDCl_3$. Sweep width = 500 Hz., upper scan is offset 350 Hz., 100 Hz. sweep width.

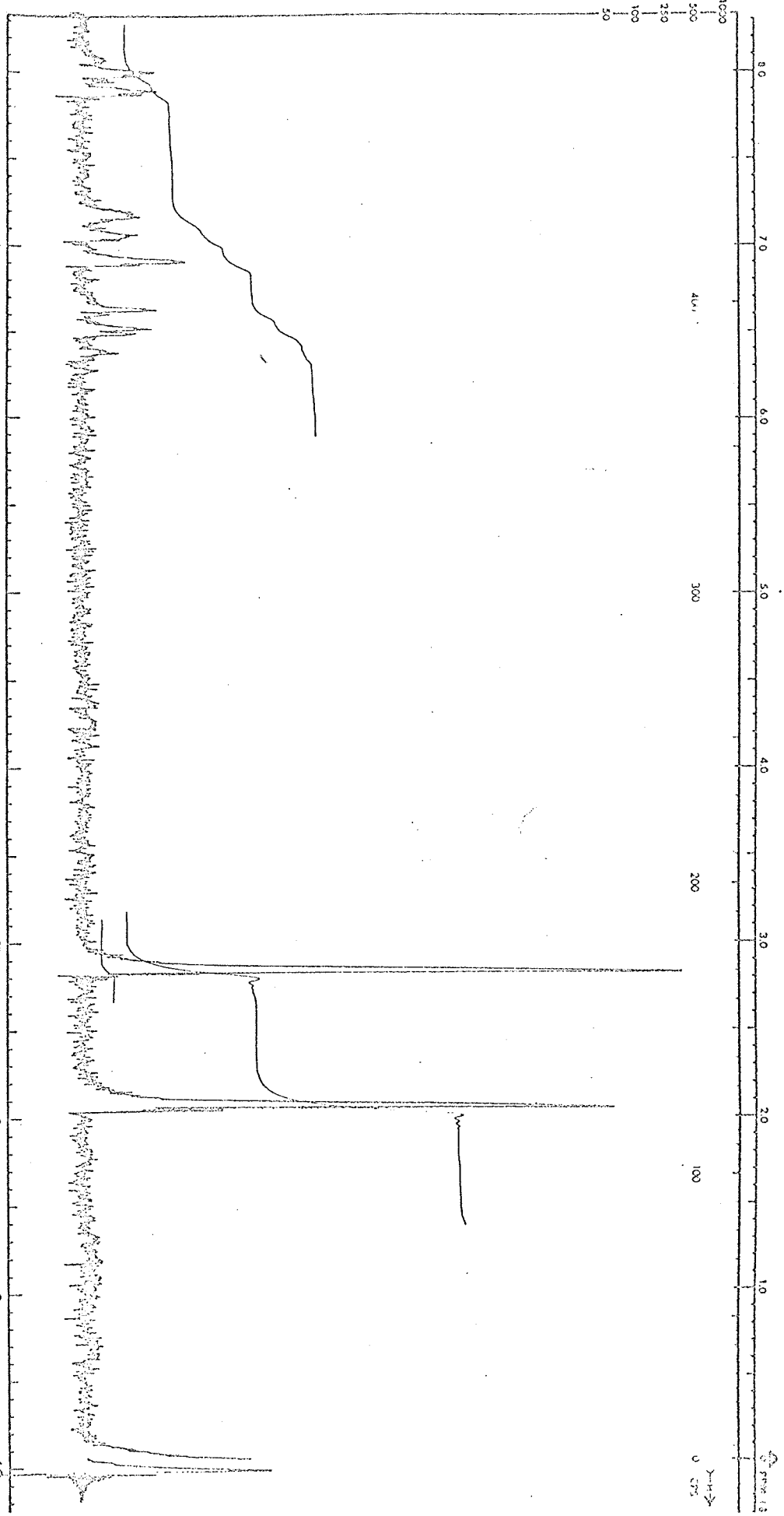


NMR spectrum no. 5 : 2,6-diacetylaniline (183) , in $CDCl_3$. Sweep width = 500 Hz., upper scan is offset 400 Hz.



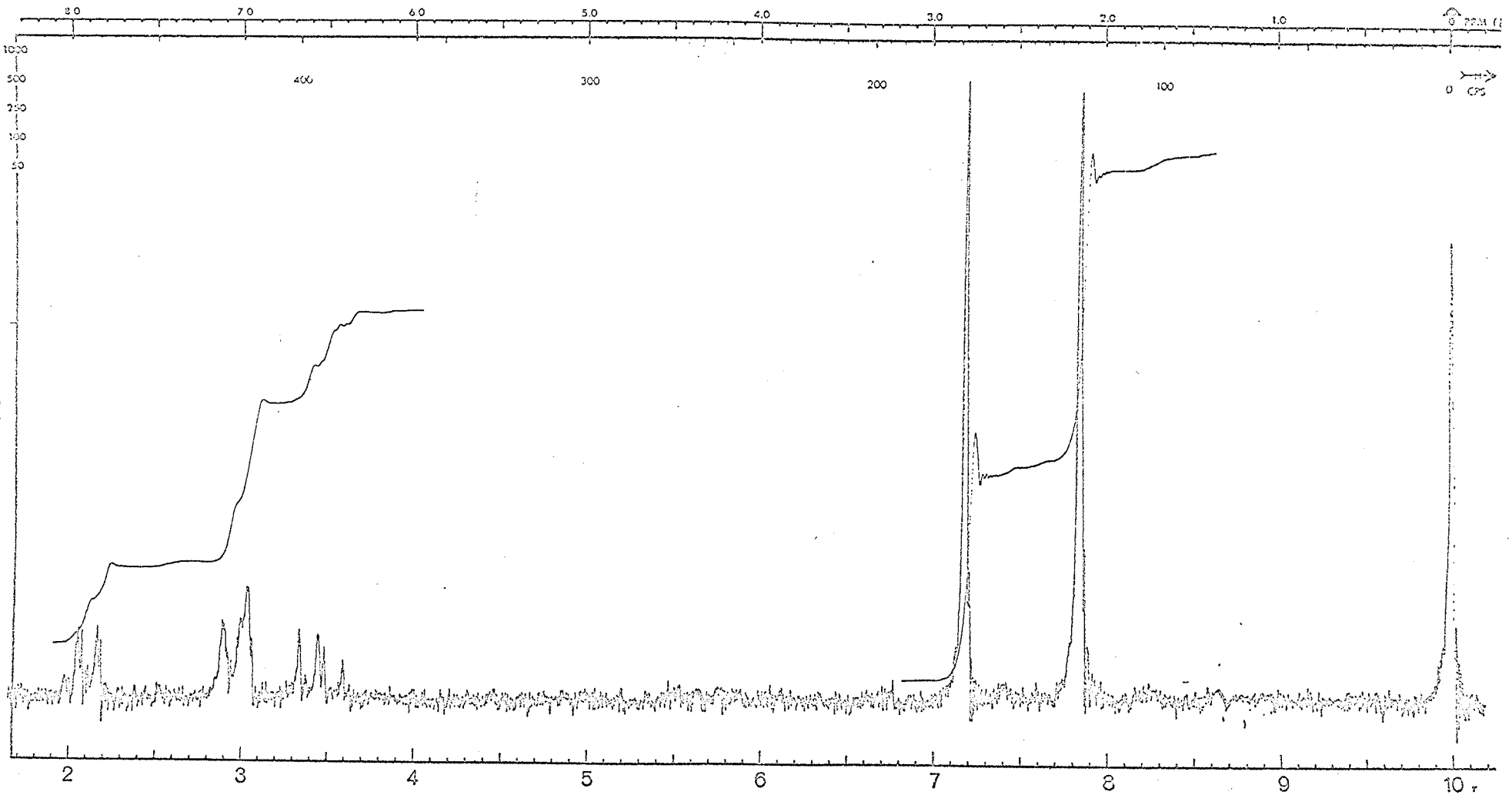
NMR spectrum no. 6 : 7-acetyl-3-methylanthranil (199) in $CDCl_3$. Sweep width = 500 Hz., Temp. = 40 °C.

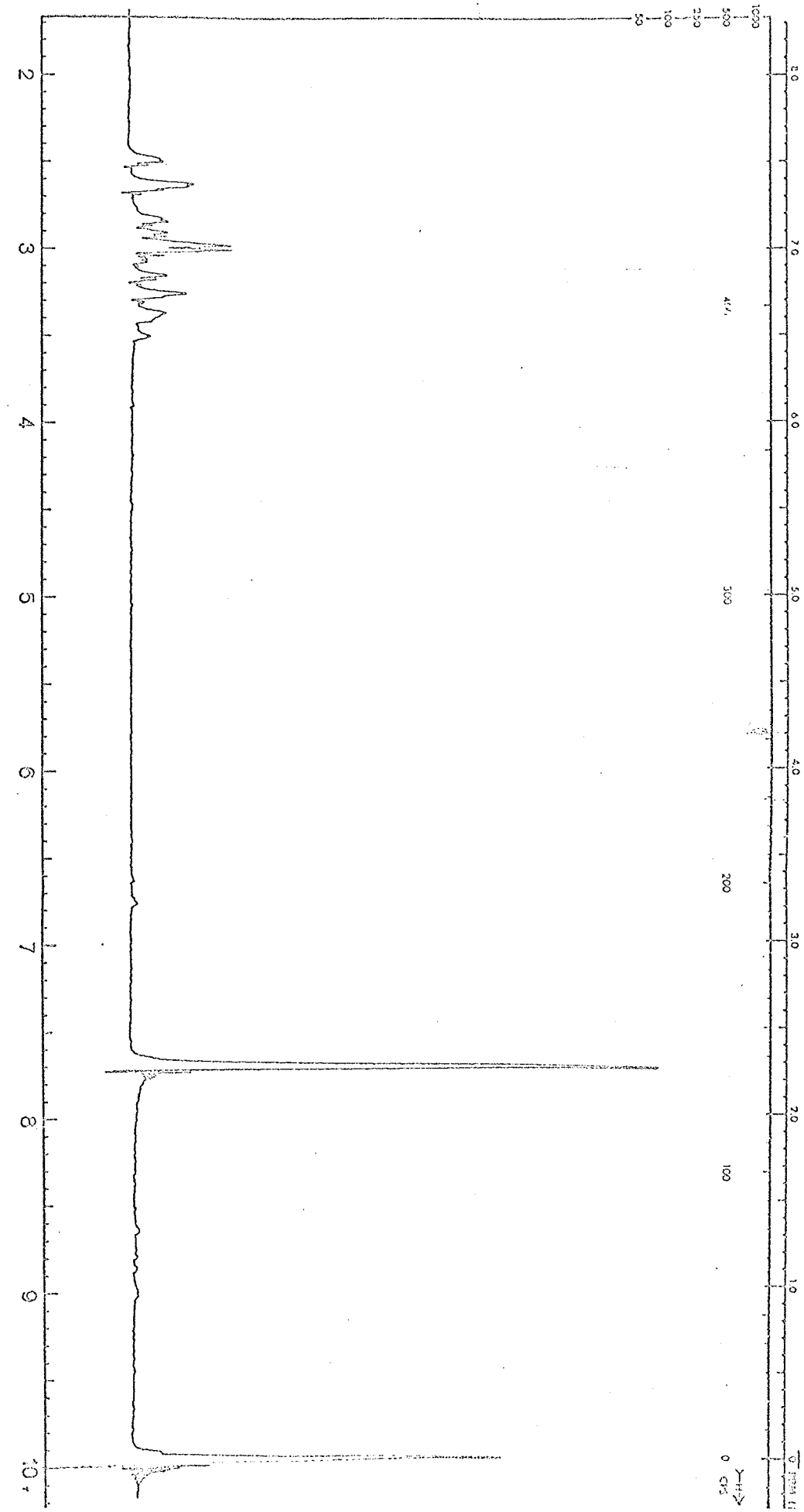




NMR spectrum no. 7 : 7-acetyl-3-methylanthranil (199) in C_6D_6 . Sweep width = 500 Hz., Temp. = 40 °C.

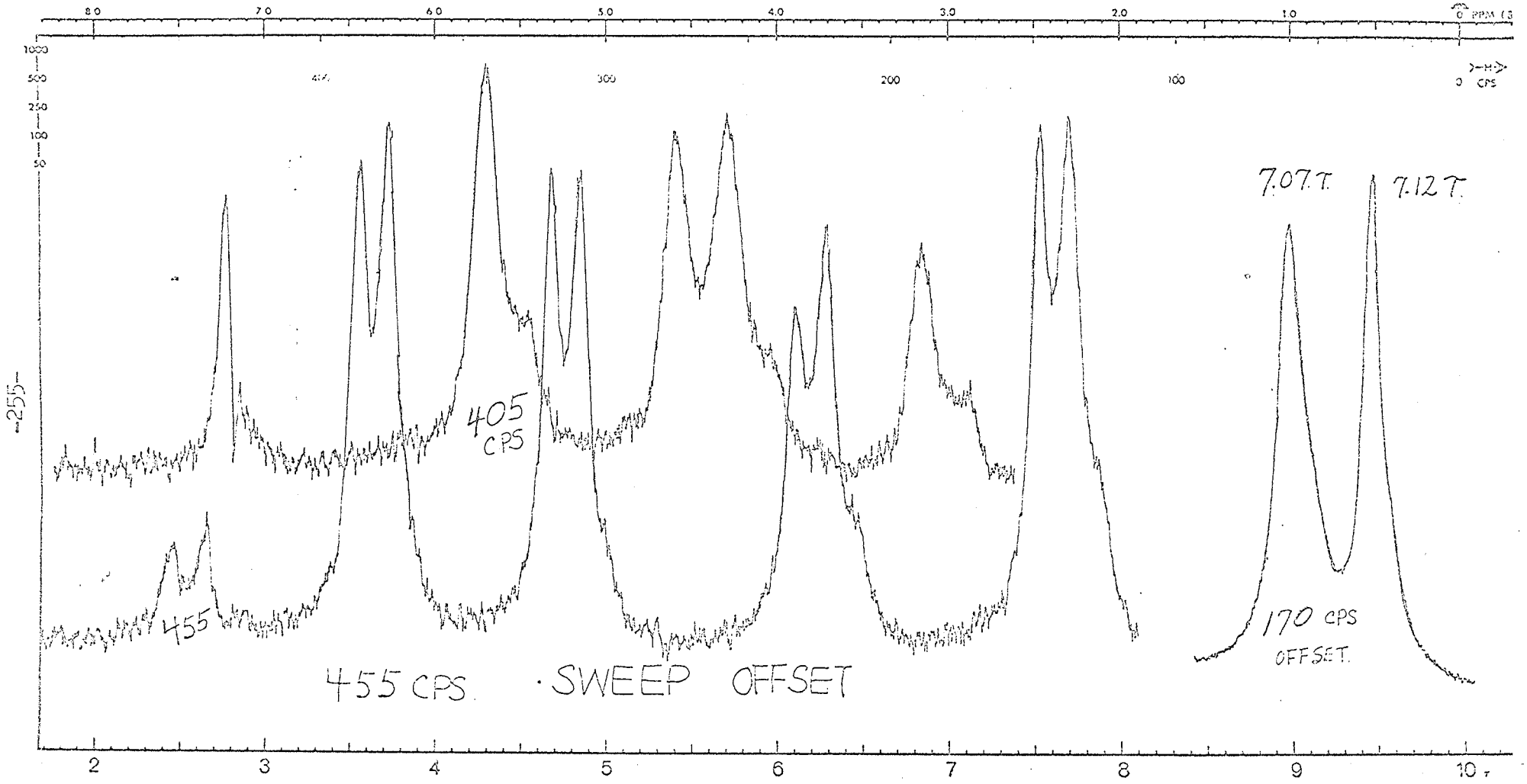
NMR spectrum no. 8 : 7-acetyl-3-methylanthranil (199) in C_7D_8 . Sweep width = 500 Hz., Temp. = 40 °C.



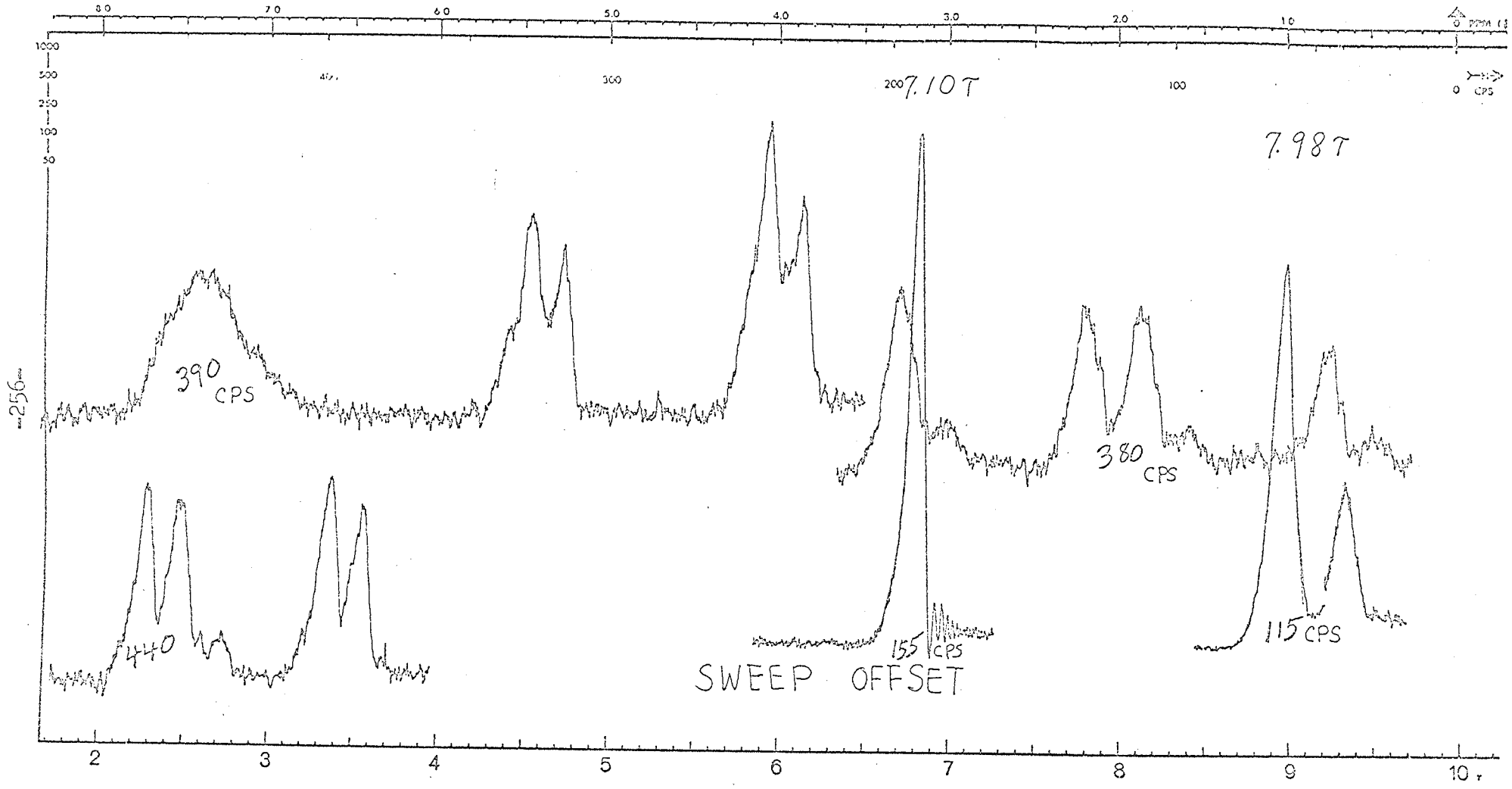


NMR spectrum no. 9 : 3-methylanthranil (66) in C_6D_6. Sweep width = 500 Hz. Temp. = 40 °C.

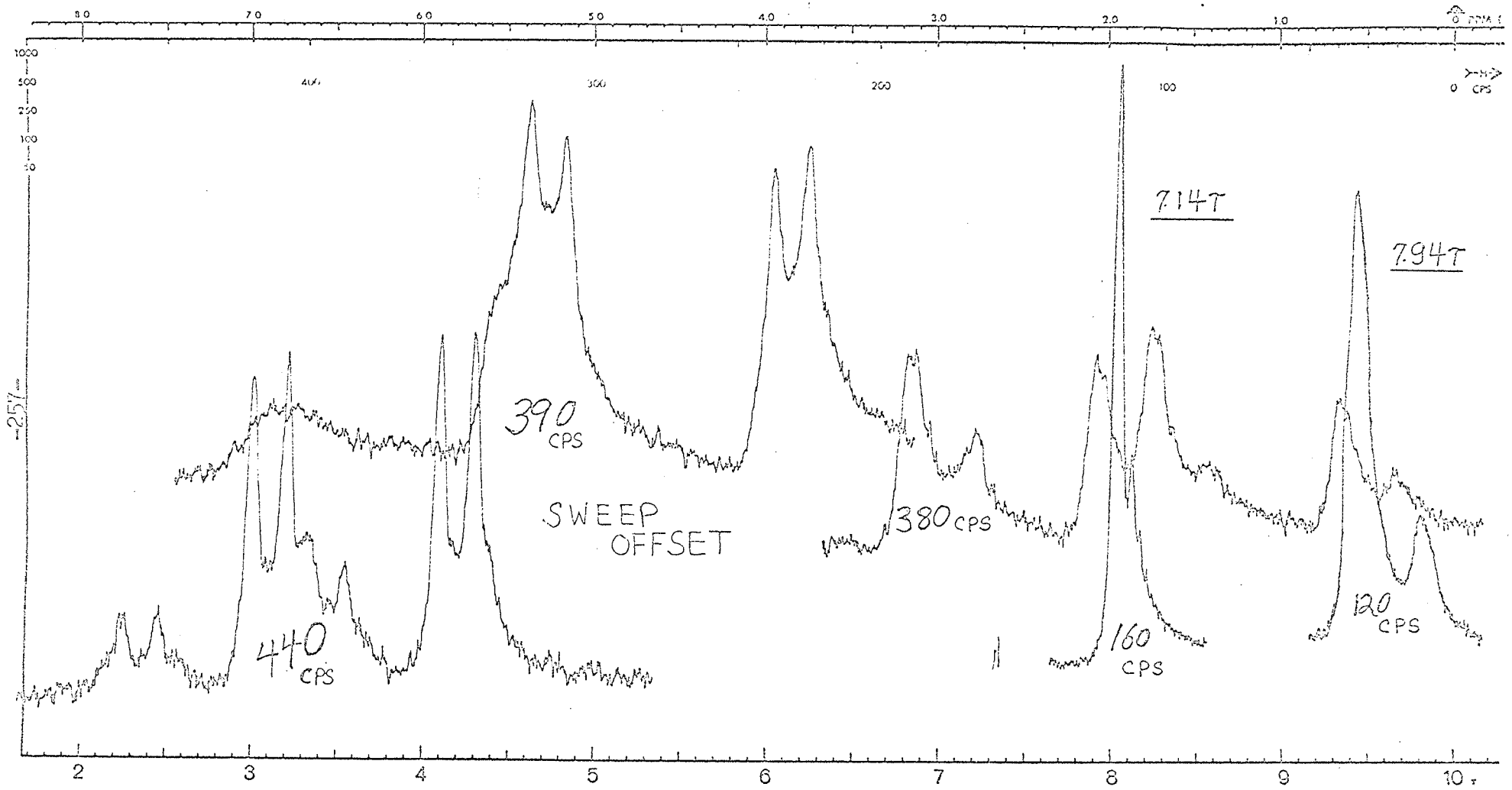
NMR spectrum no. 10 : 7-acetyl-3-methylanthranil (199) in $CDCl_3$. Sweep width = 50 Hz., Temp. = -60 °C.

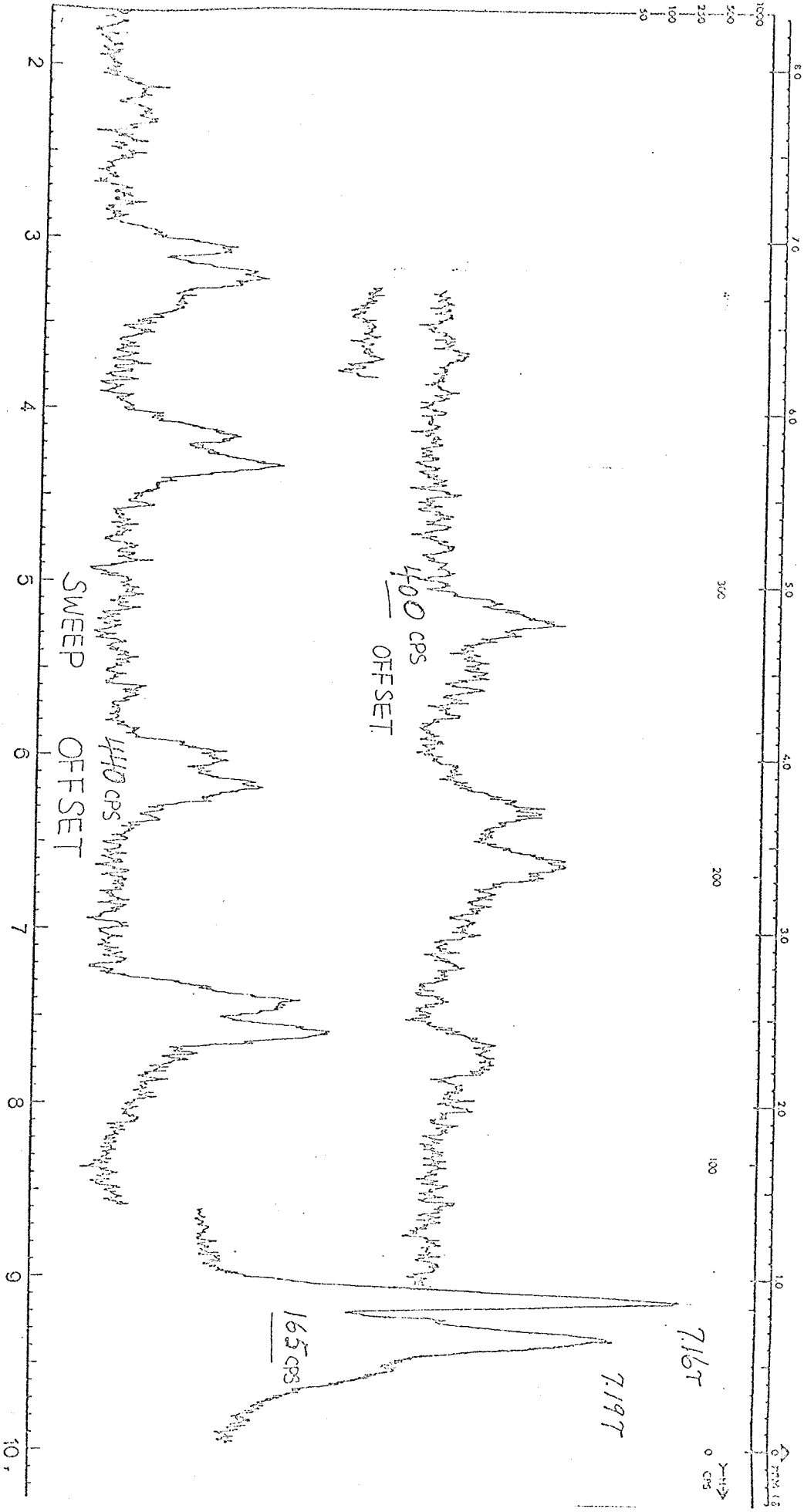


NMR spectrum no. 11 : 7-acetyl-3-methylanthranil (199) in C_6D_6 . Sweep width = 50 Hz, Temp. = 0 °C.



NMR spectrum no. 12 : 7-acetyl-3-methylanthranil (199) in C_7D_8 . Sweep width = 50 Hz., Temp. = -20 °C.

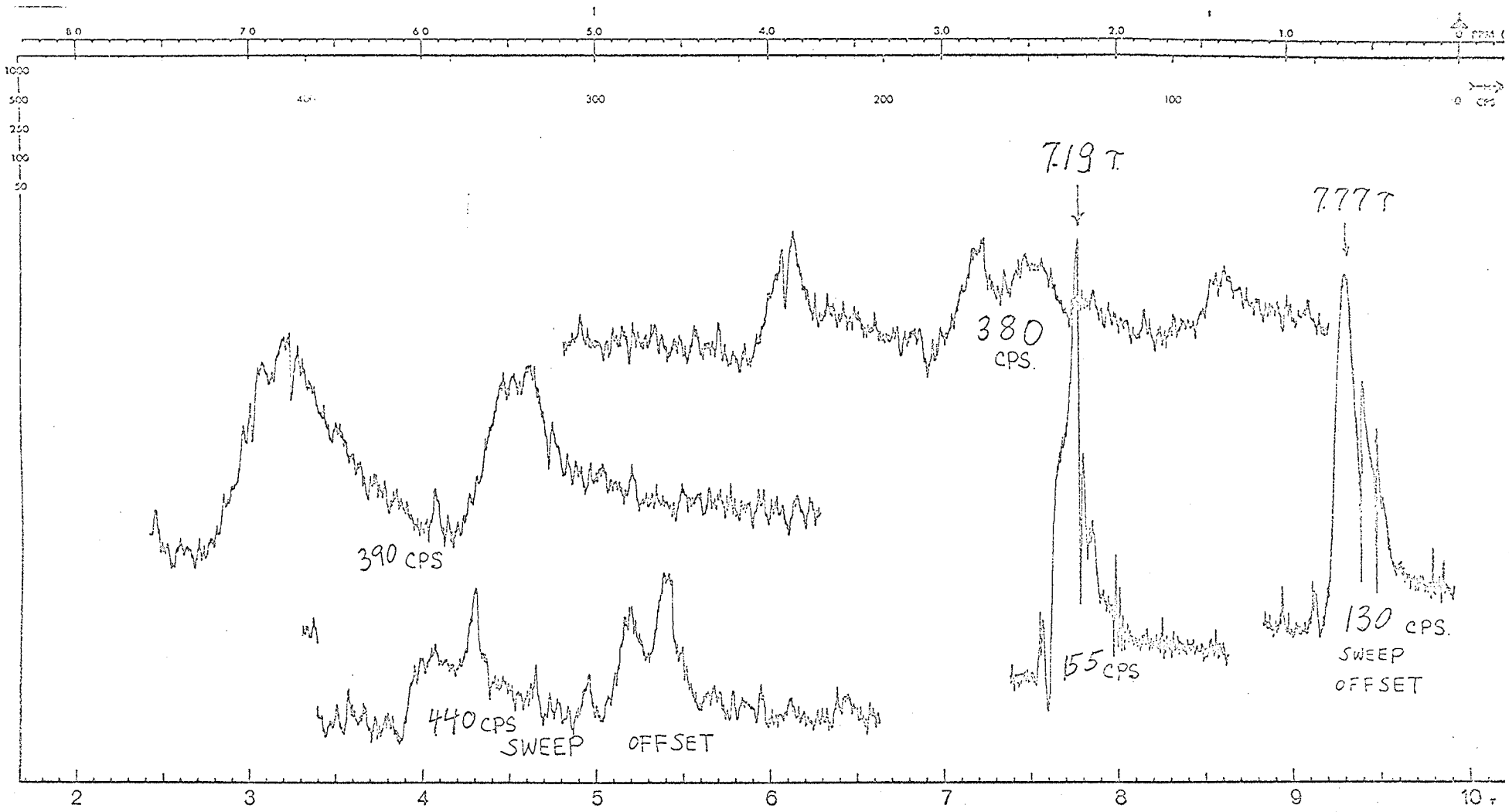




NMR spectrum no. 13 : 7-acetyl-3-methylanthranil (199) in $CDCl_3$. Sweep width = 50 Hz.
Temp. = 100 °C.

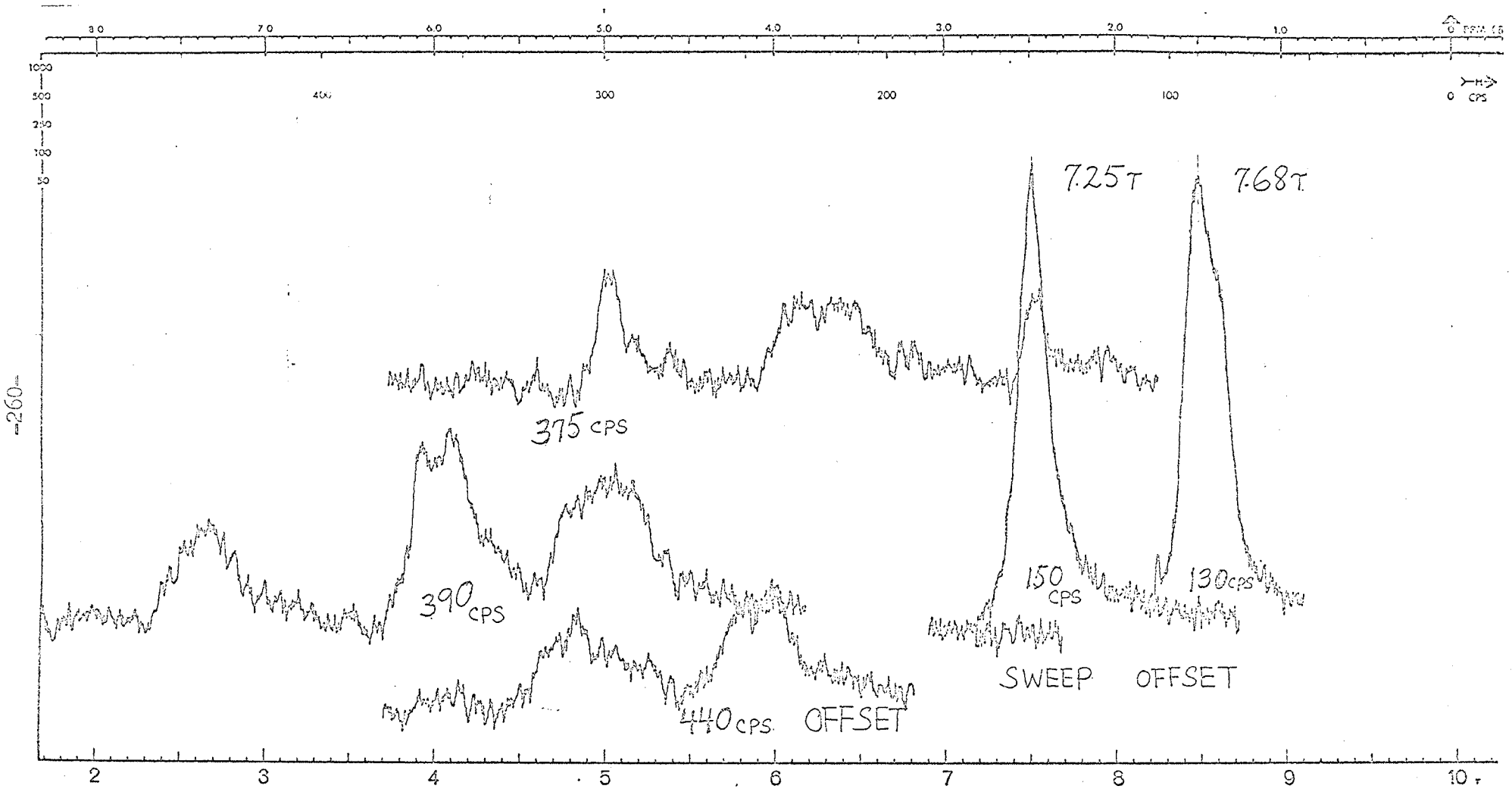
NMR spectrum no. 14 : 7-acetyl-3-methylanthranil (199) in C_6D_6 . Sweep width = 50 Hz.

Temp. = 140 °C.



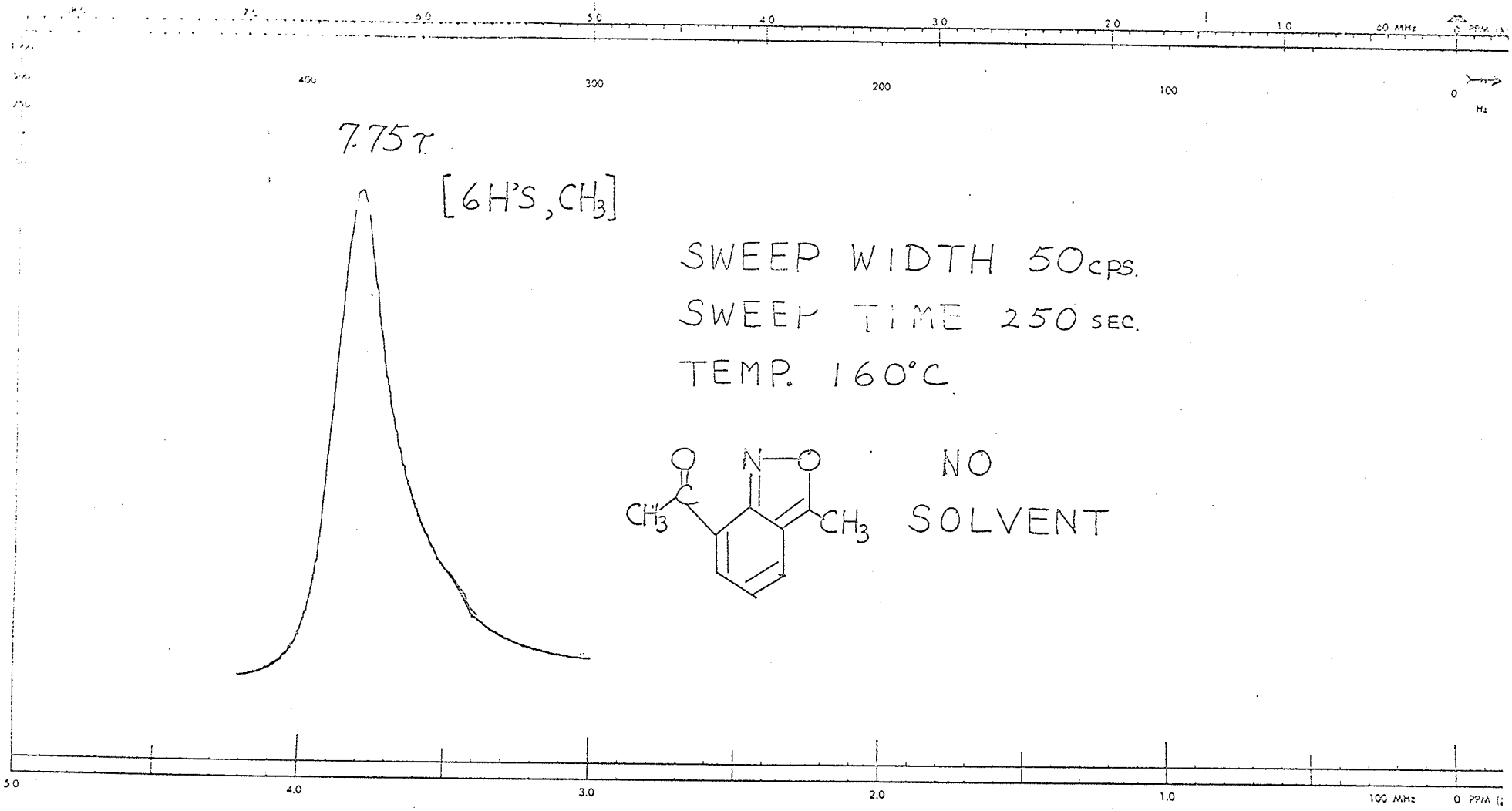
NMR spectrum no. 15 : 7-acetyl-3-methylanthranil (199) in C_7D_8 . Sweep width = 50 Hz.

Temp. = 160 °C.



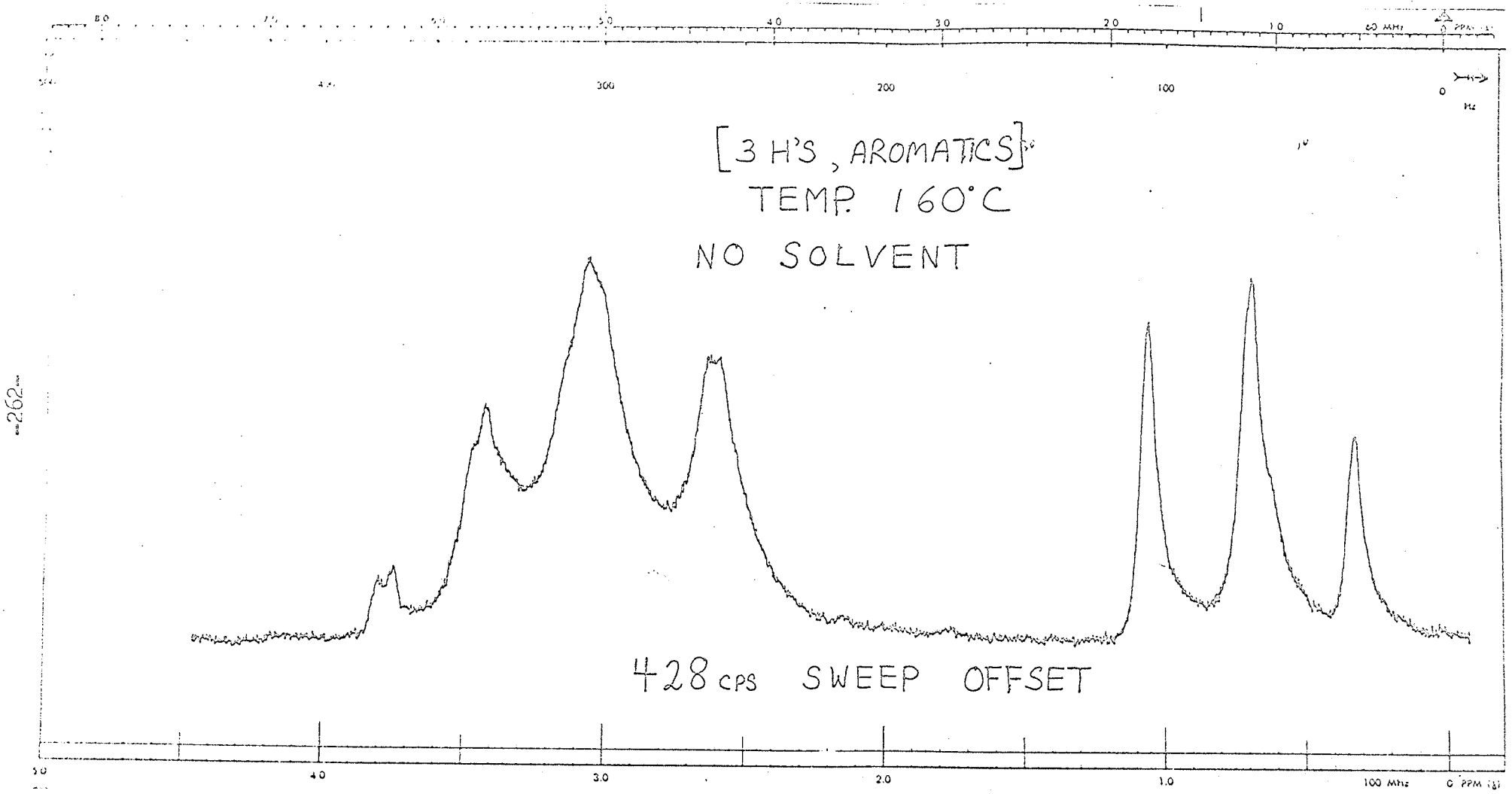
NMR spectrum no. 16 : 7-acetyl-3-methylanthranil (199) (no solvent).

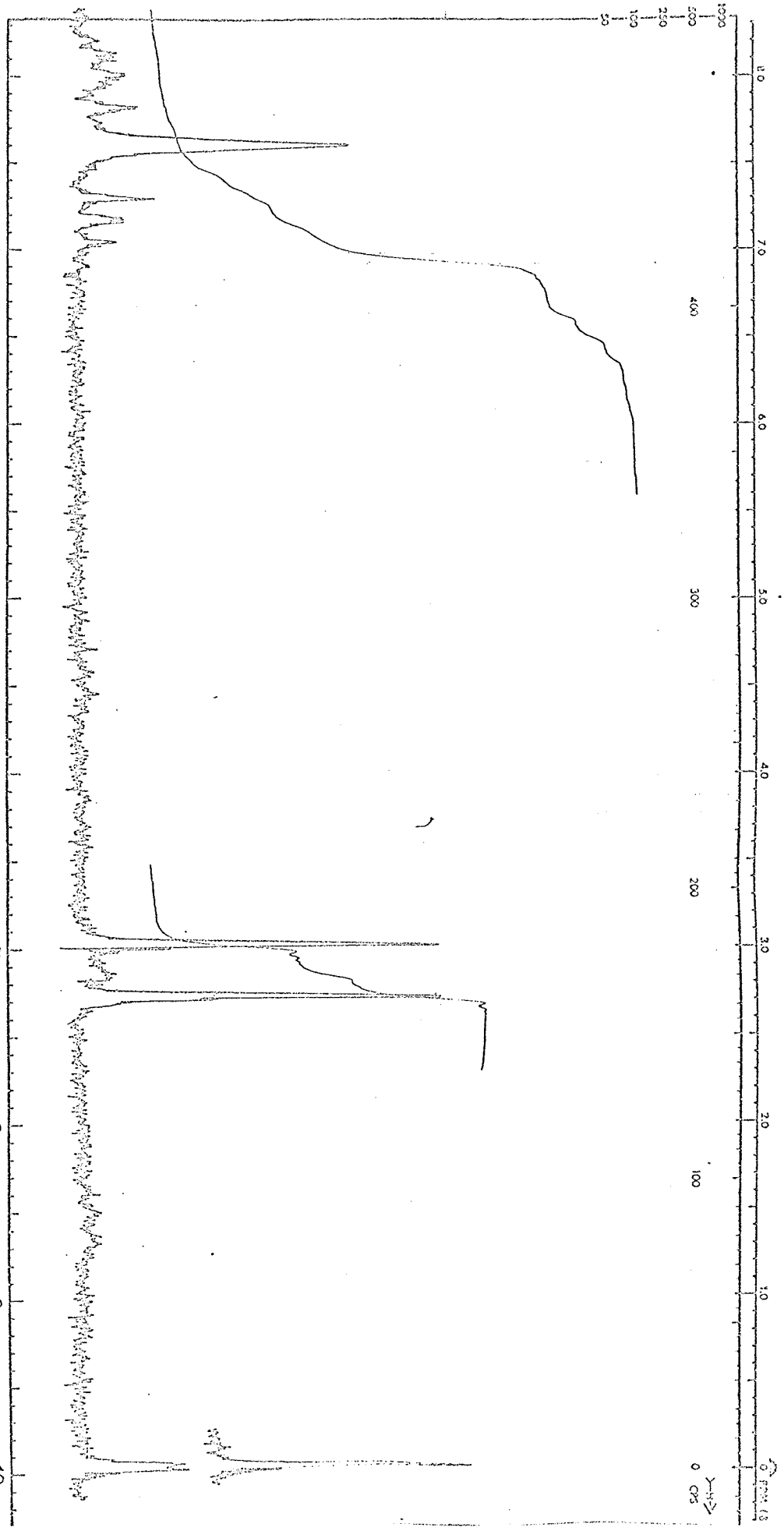
Sweep width = 50 Hz., temp. = 160 °C.



NMR spectrum no. 17 : 7-acetyl-3-methylanthranil (199) (no solvent).

Sweep width = 50 Hz., temp. = 160 °C.



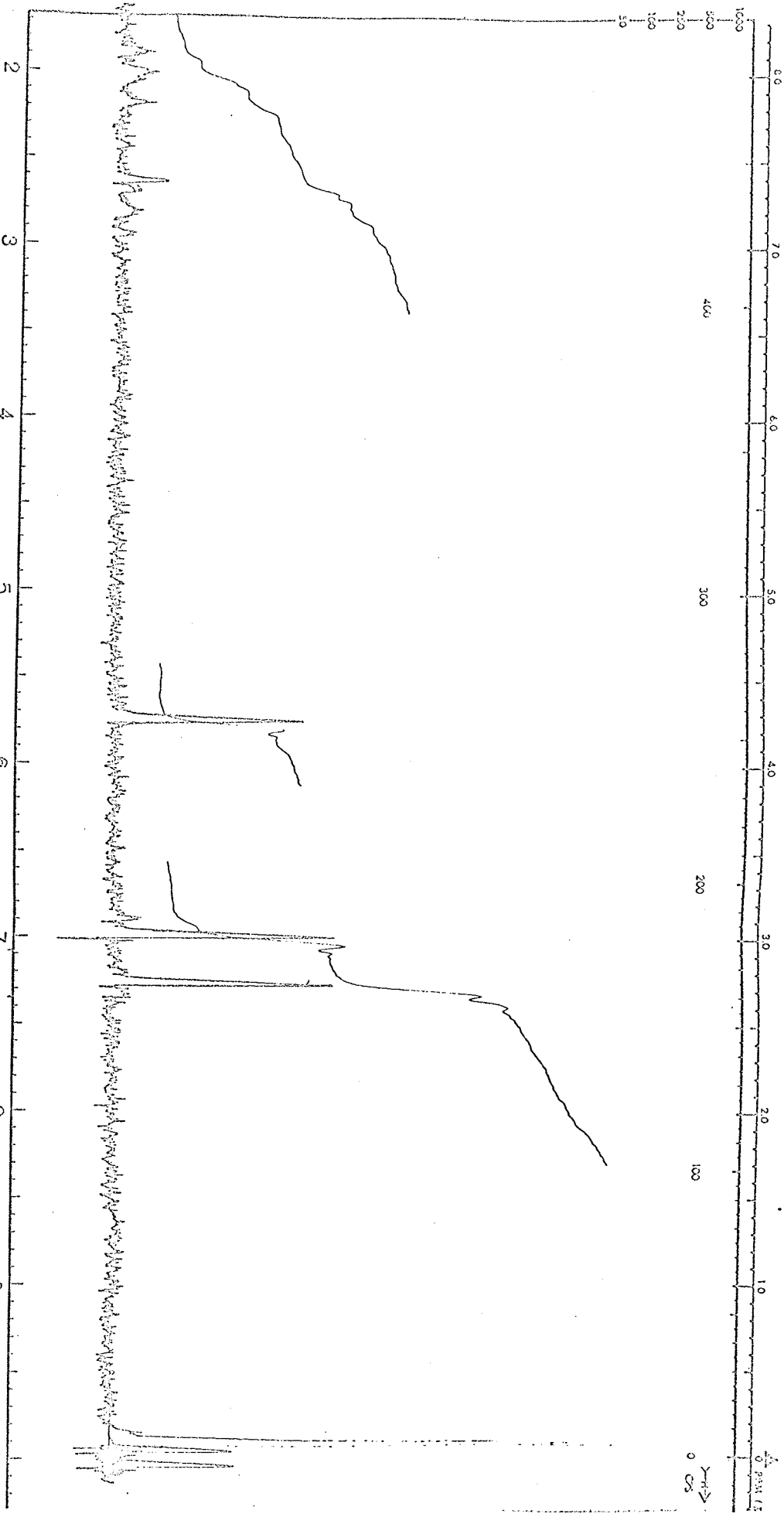


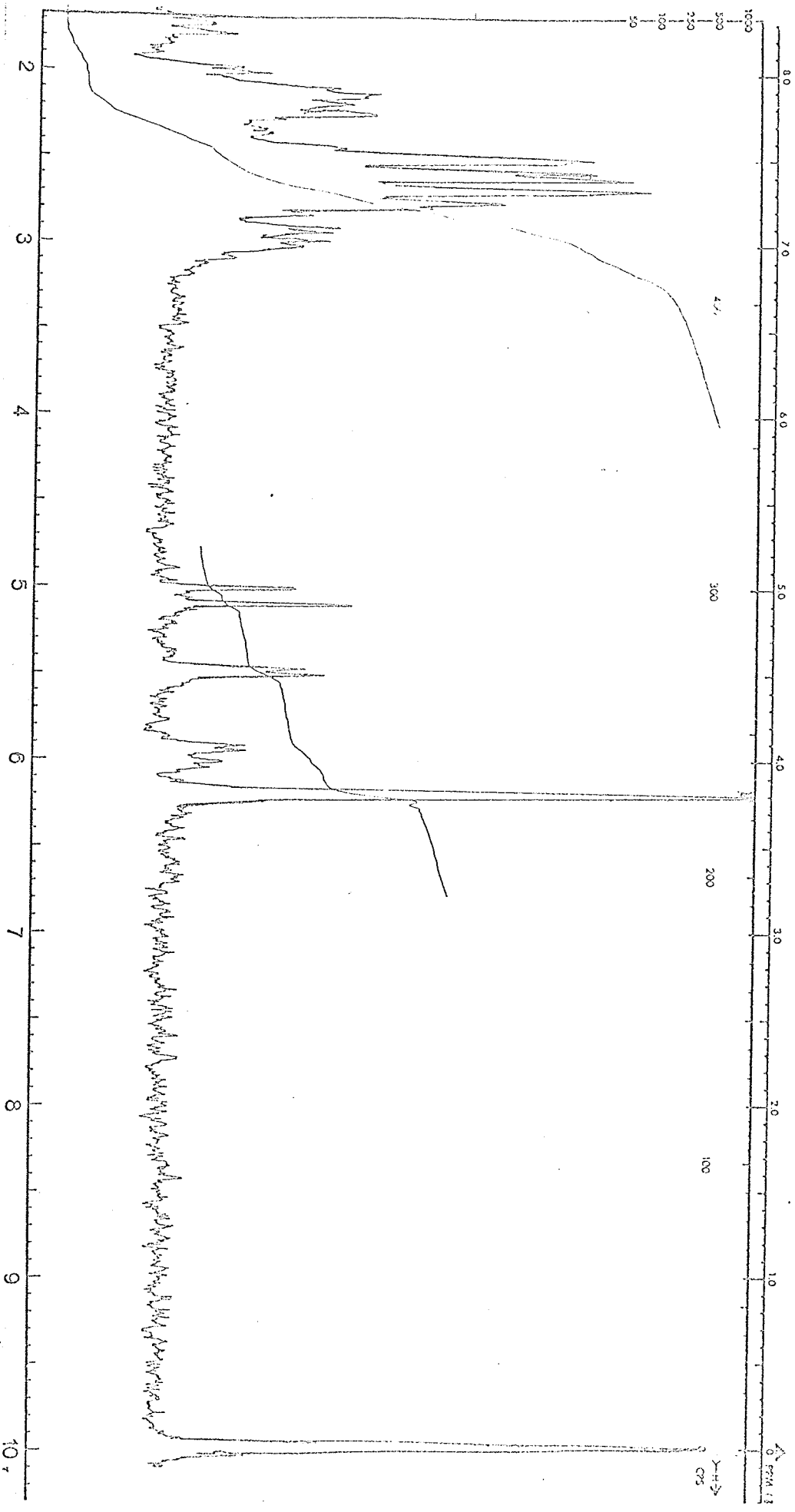
NMR spectrum no. 18 : 7-acetyl-3-methyl-2-phenylbenzo(c)pyrazole (222b) in $CDCl_3$.

Sweep width = 500 Hz.

NMR spectrum no. 19 : 7-acetyl-2,3-dimethylbenzo(c)pyrazole (222a) in $CDCl_3$.

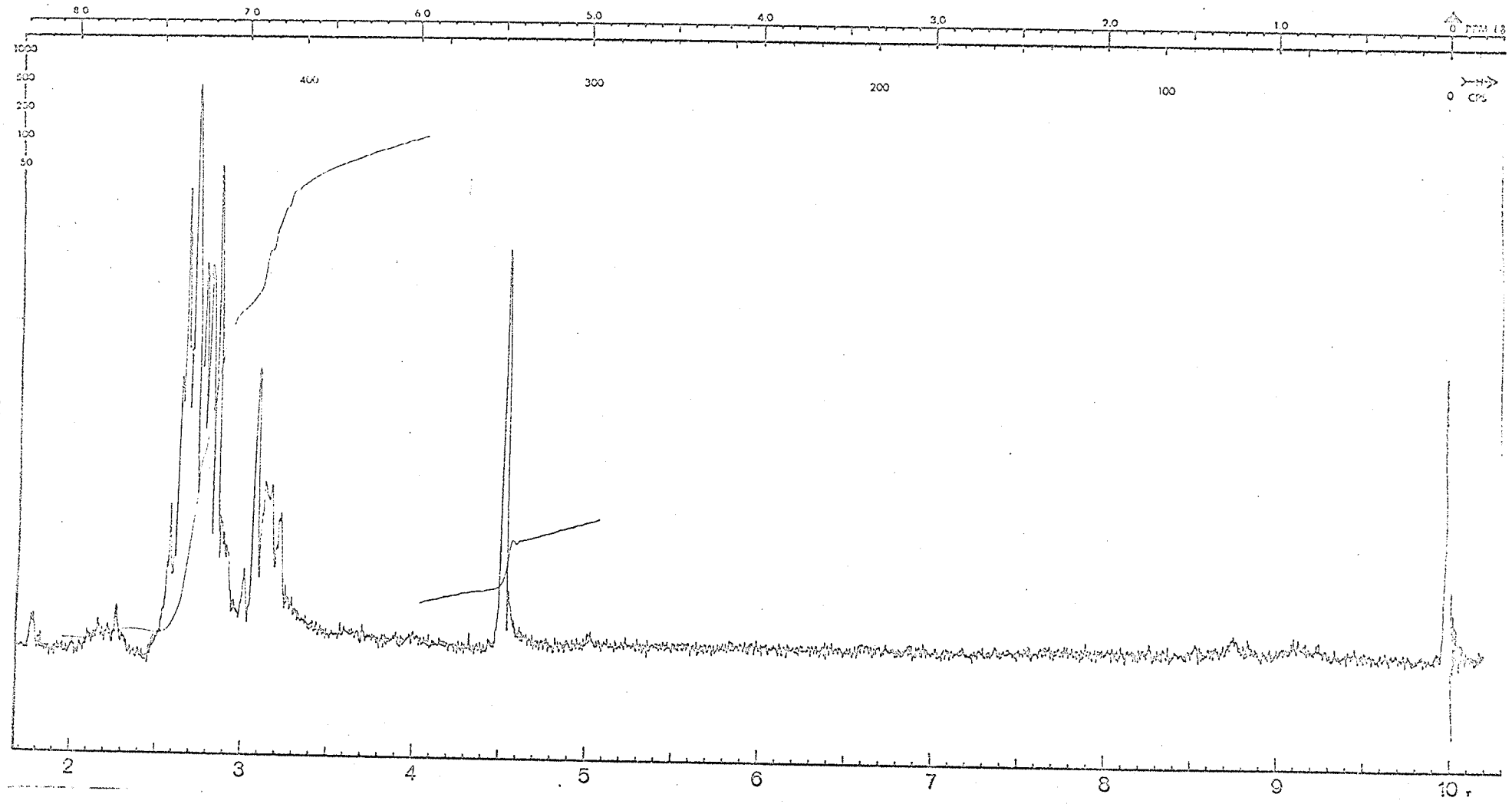
Sweep width = 500 Hz.



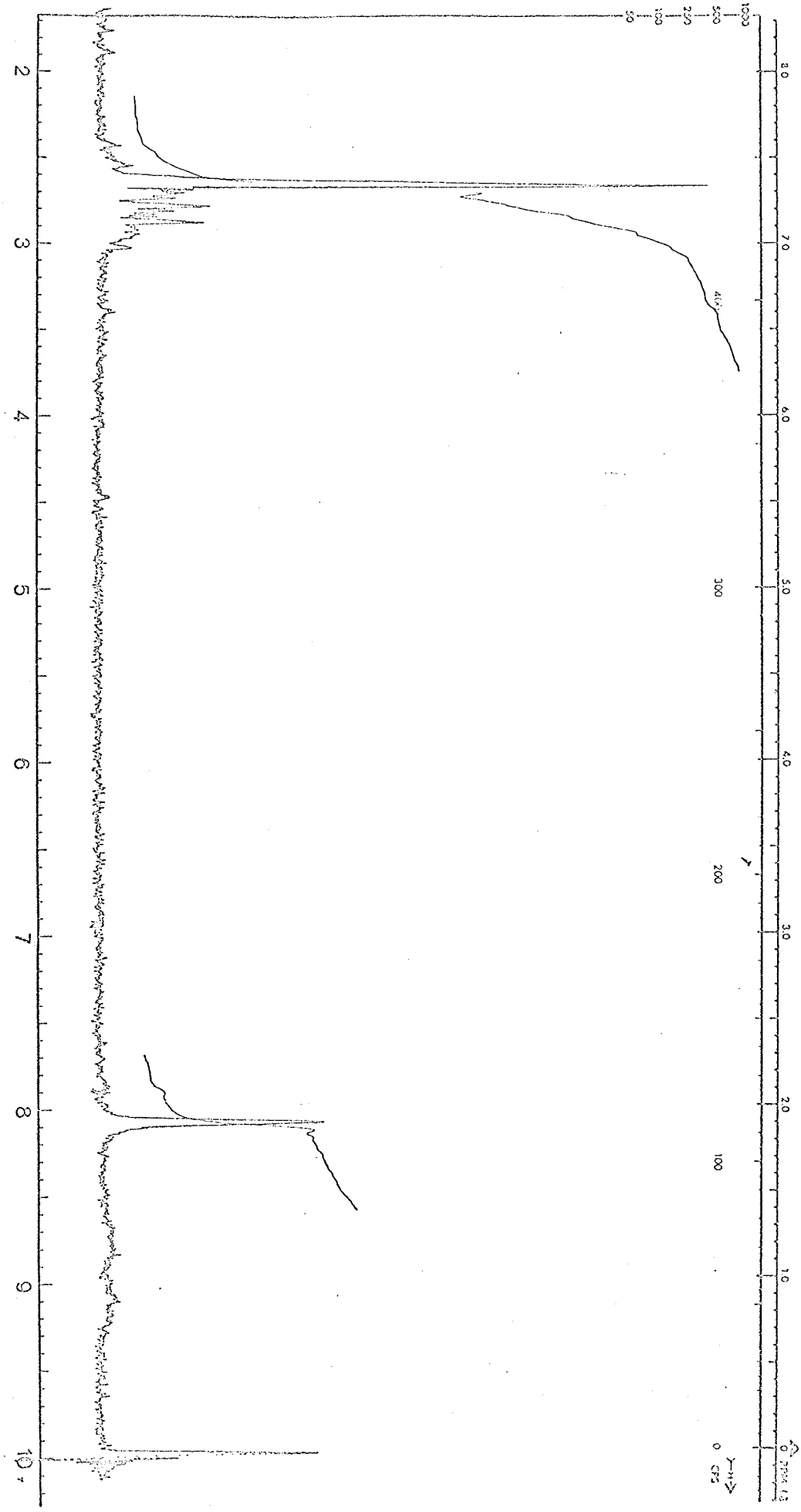


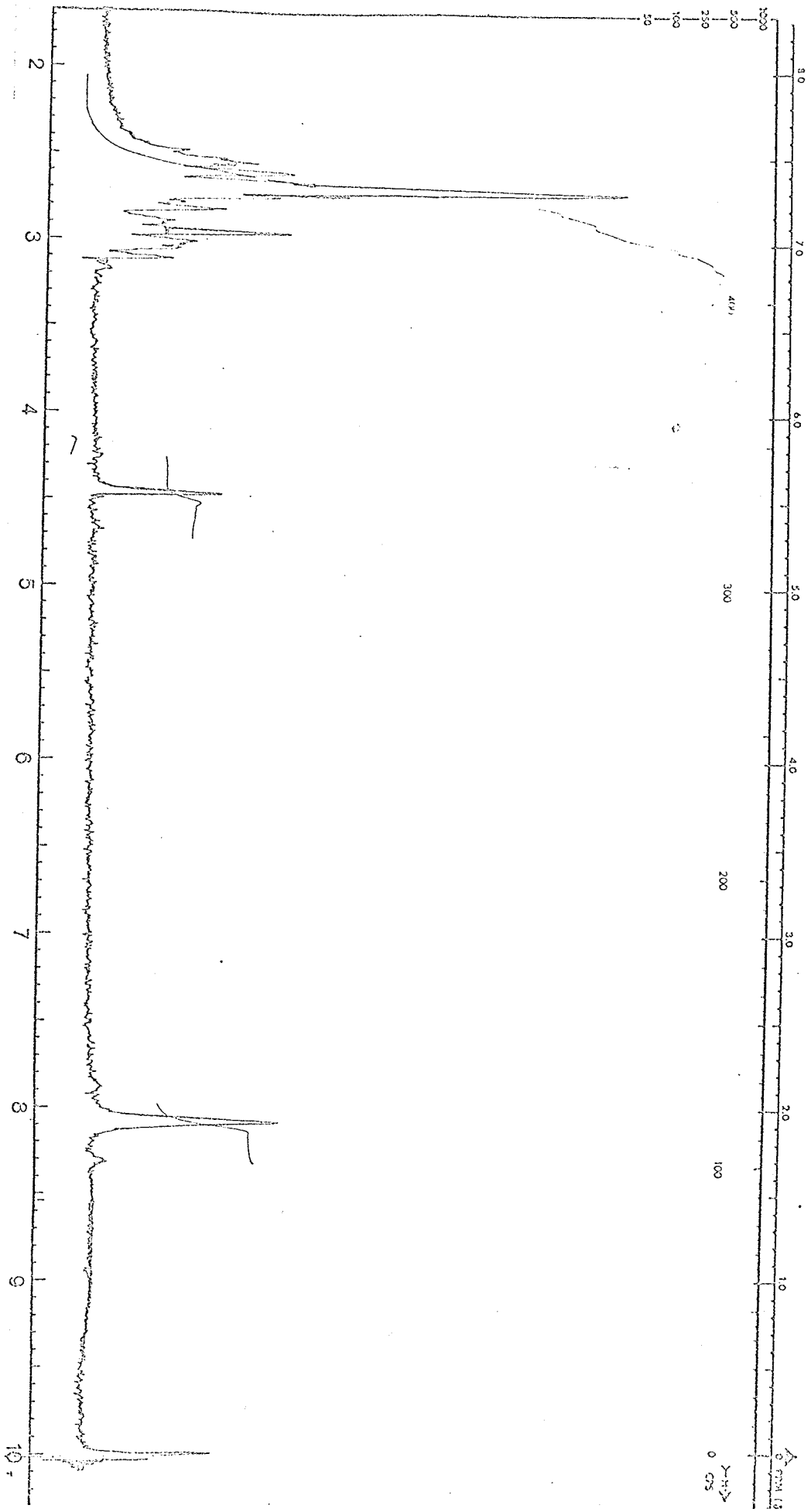
NMR spectrum no. 20 : 9-methoxyanthracene-9,10-endo-dibenzoylethylene (291) in $CDCl_3$. Sweep width = 500 Hz.

NMR spectrum no. 21 : 1,3-diphenyl-4,9-dihydro-4,9-o-benzenonaphtho(2,3-c)thiophene (241) in $CDCl_3$. Sweep width = 500 Hz.

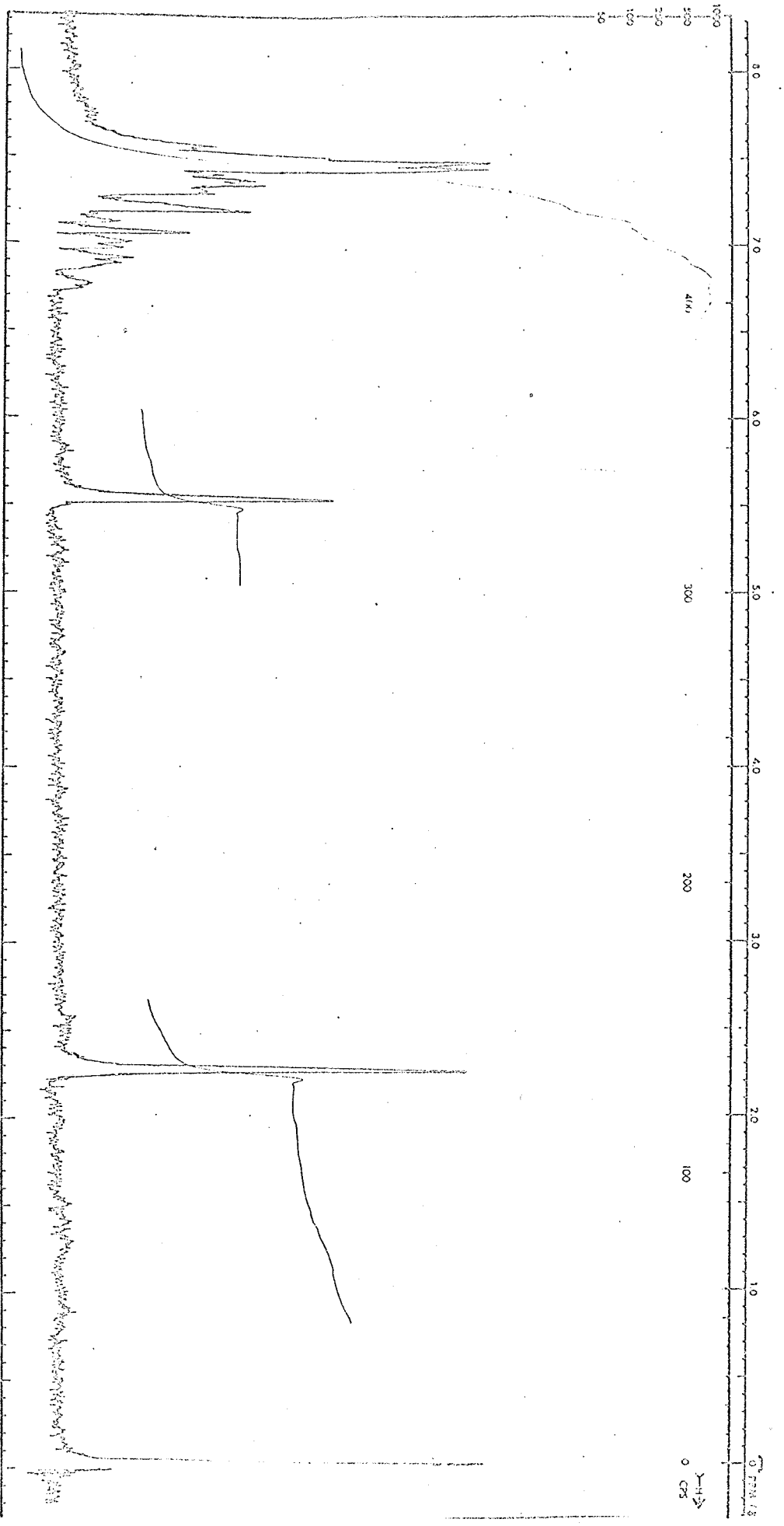


NMR spectrum no. 22 : 1,3-diphenyl-4,9-dimethyl-4,9-dihydro-4,9-o-benzeno-naphtho(2,3-c)thiophene in $CDCl_3$. Sweep width = 500 Hz.

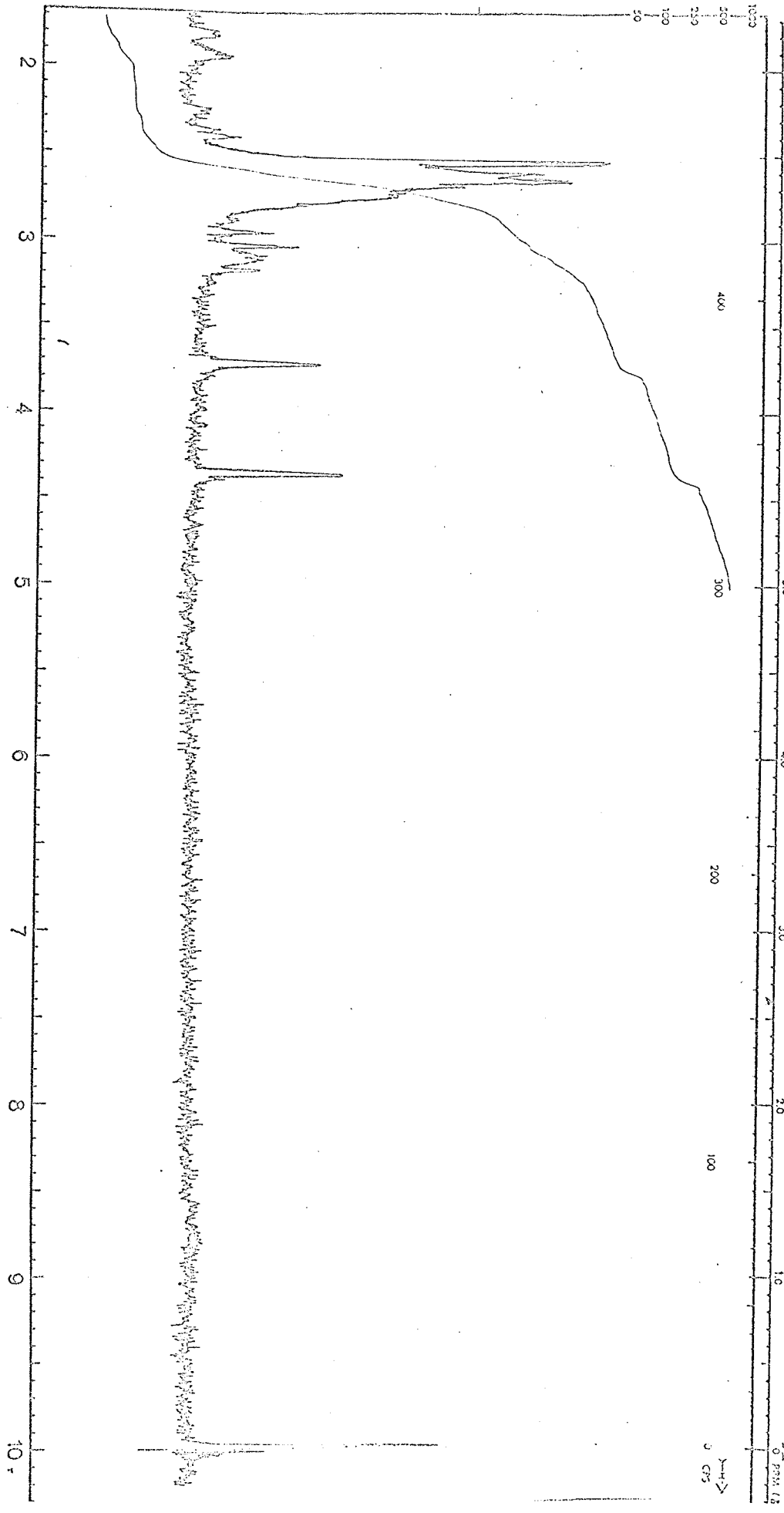




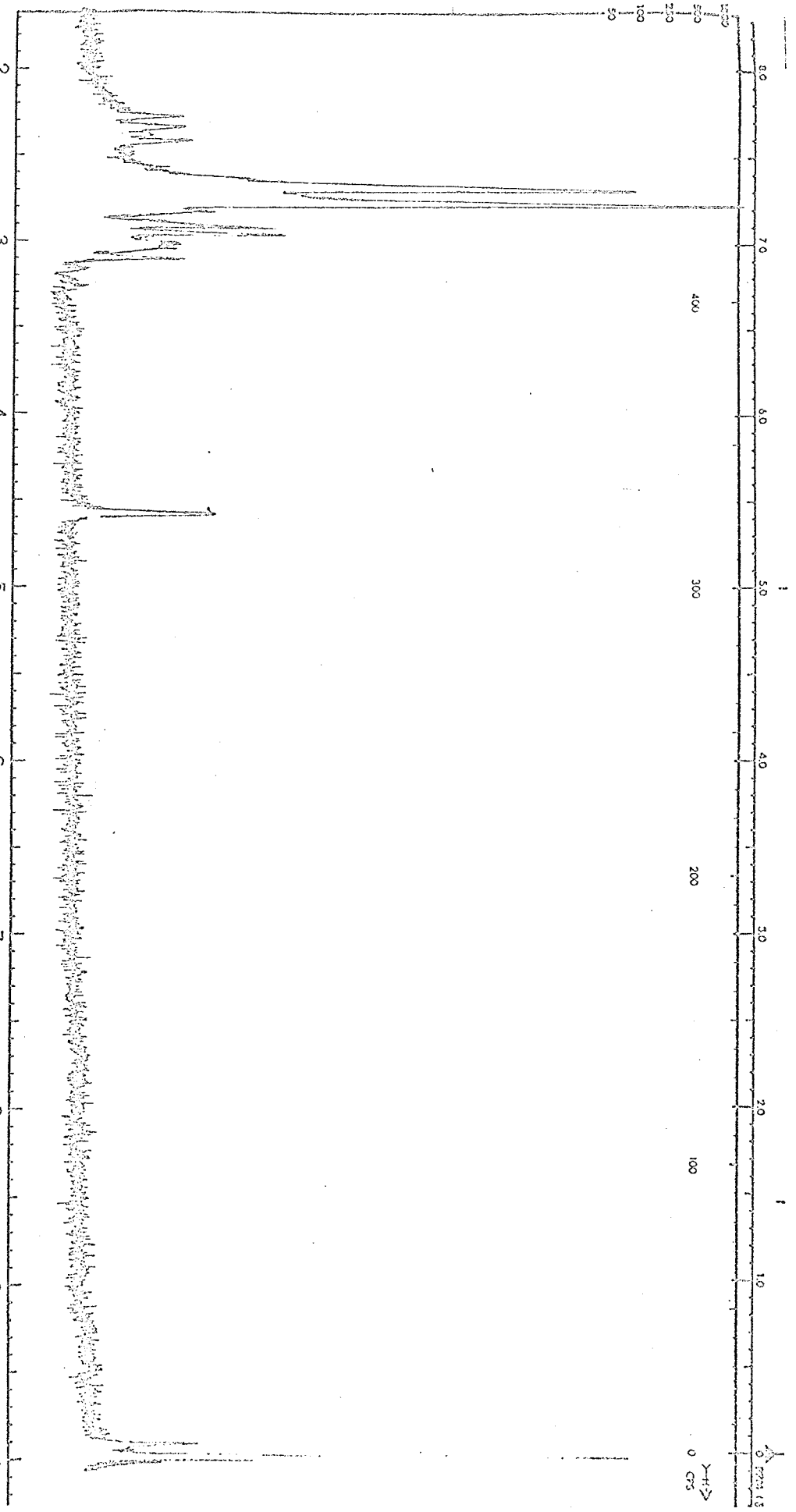
NMR spectrum no. 23 : 1,3-diphenyl-4-methyl-4,9-dihydro-4,9-o-benzeno-naphtino(2,3-c)thiophene in $CDCl_3$. Sweep width = 500 Hz.



NMR spectrum no. 24 : 1,3-diphenyl-6-methyl-4,9-dihydro-4,9-o-benzeno-naphtho(2,3-c)thiophene (268) in $CDCl_3$. Sweep width = 500 Hz.

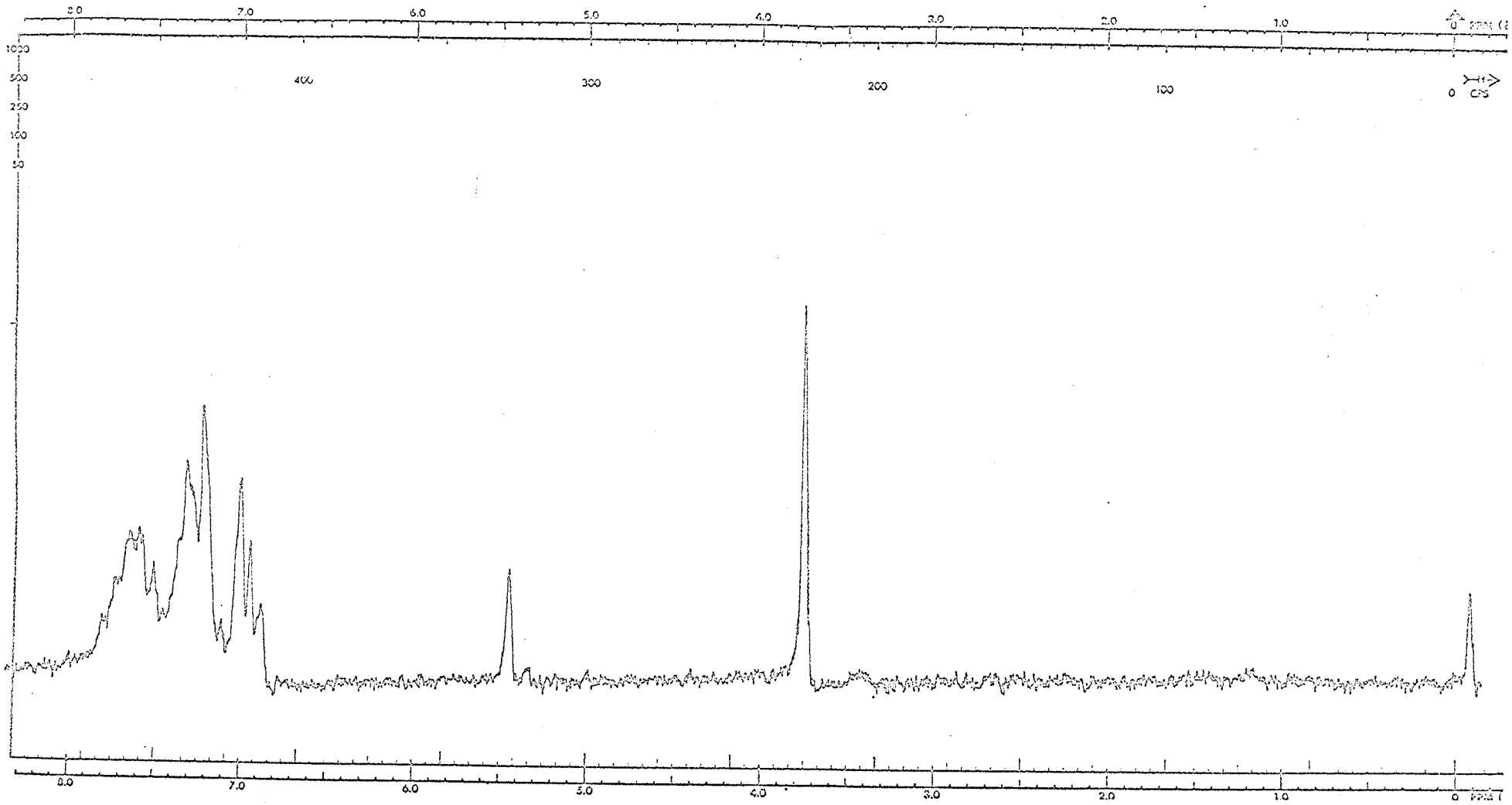


NMR spectrum no. 25 : 1,3-diphenyl-4,11-dihydro-4,11-o-benzenophenanthro-(2,3-c)thiophene (266) in $CDCl_3$. Sweep width = 500 Hz.

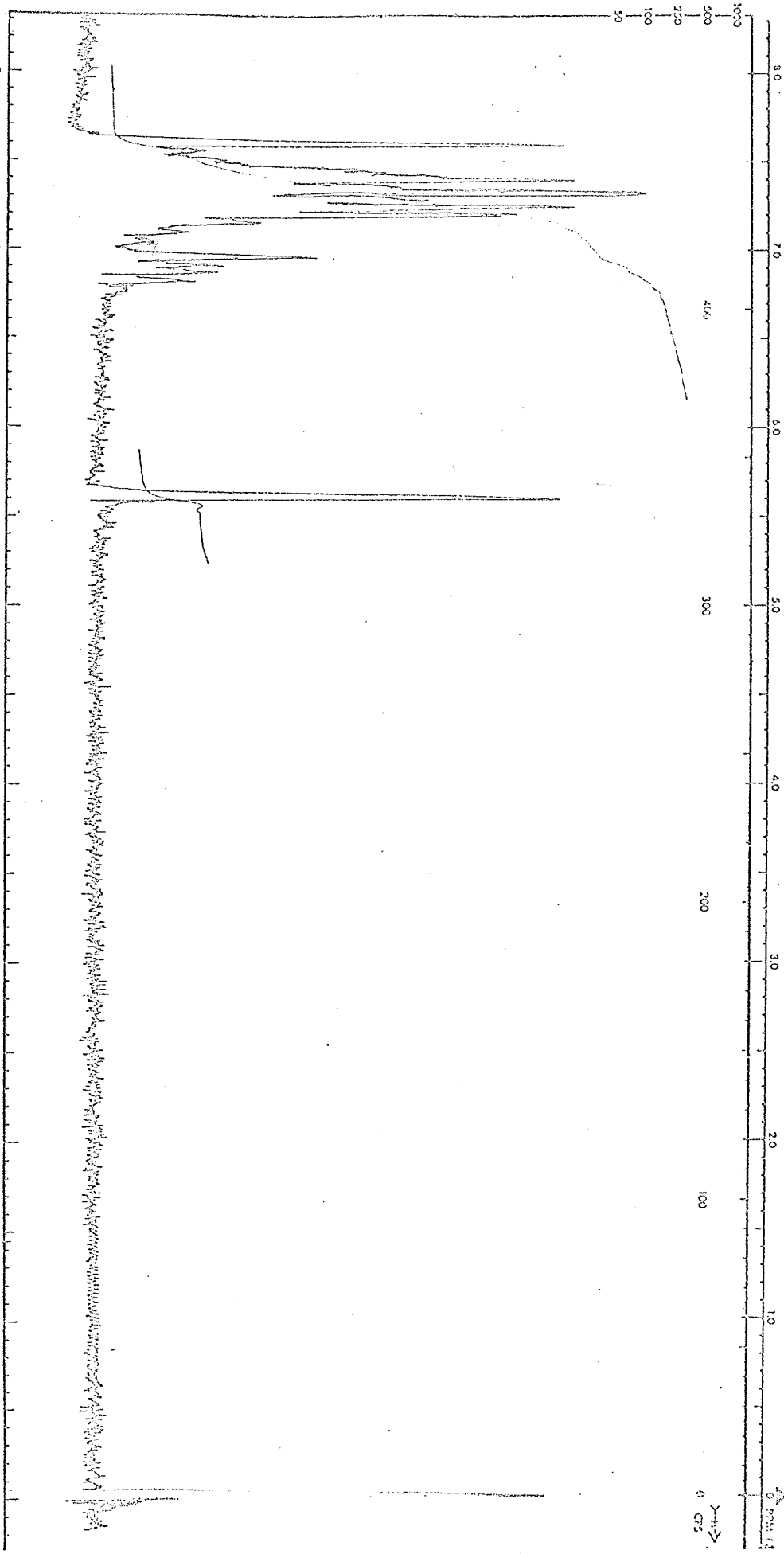


NMR spectrum no. 26 : 1,3-diphenyl-4-bromo-4,9-dihydro-4,9-o-benzeno-naphtho(2,3-c)thiophene in $CDCl_3$. Sweep width = 500 Hz.

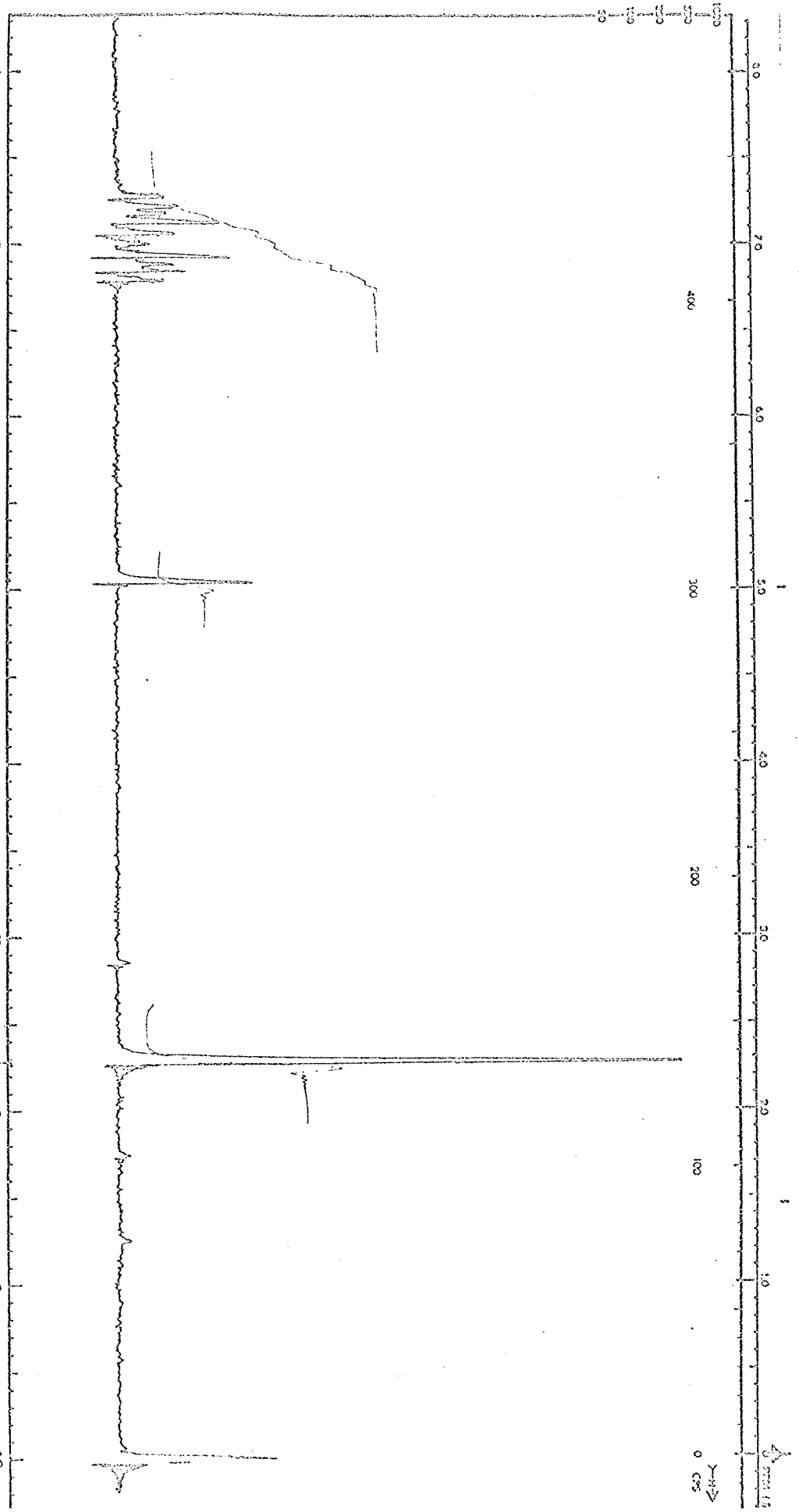
NMR spectrum no. 27 : 1,3-diphenyl-4-methoxy-4,9-dihydro-4,9-o-benzeno-naphtho(2,3-c)thiophene in $CDCl_3$. Sweep width = 500 Hz.



-272-

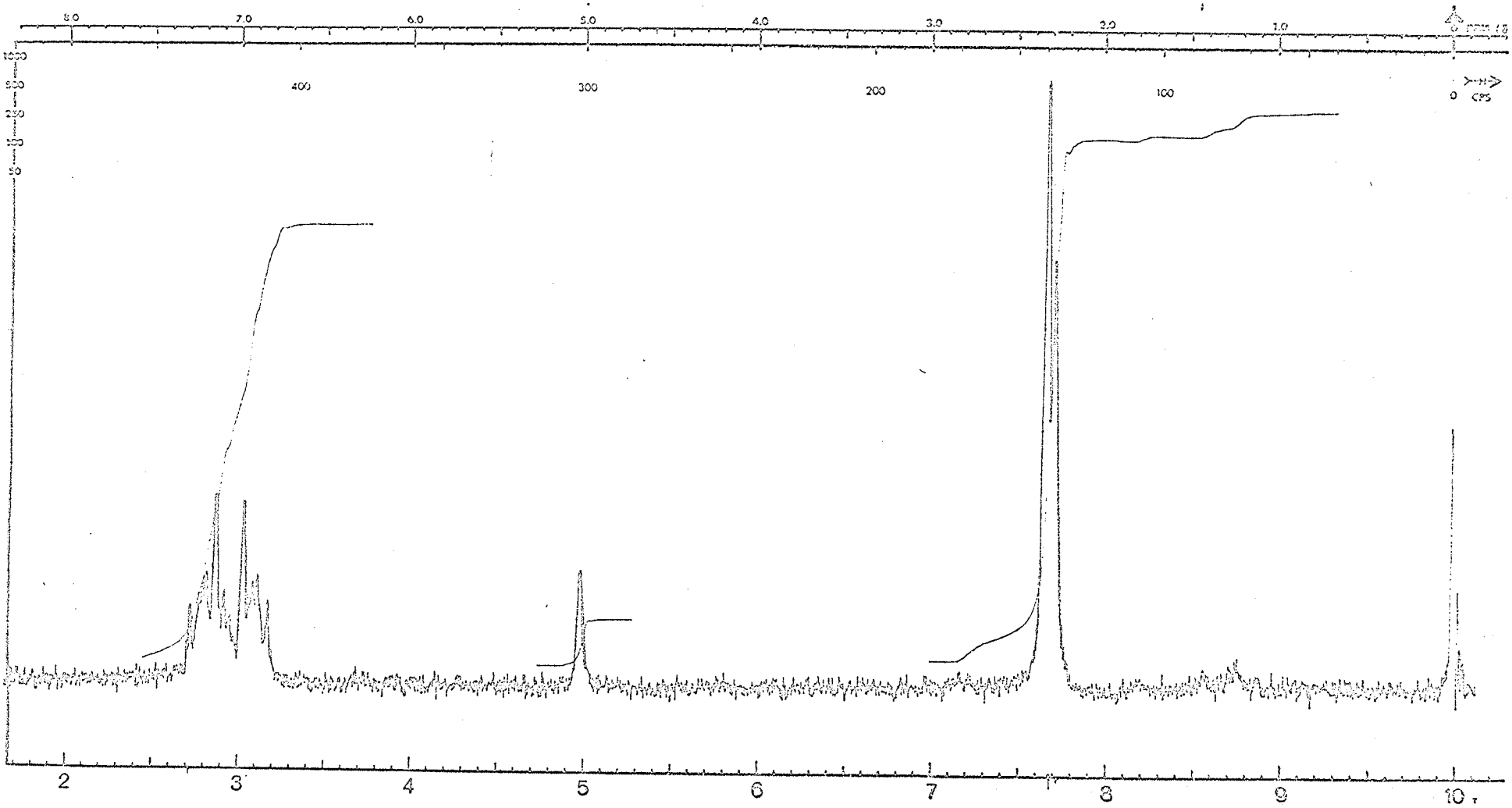


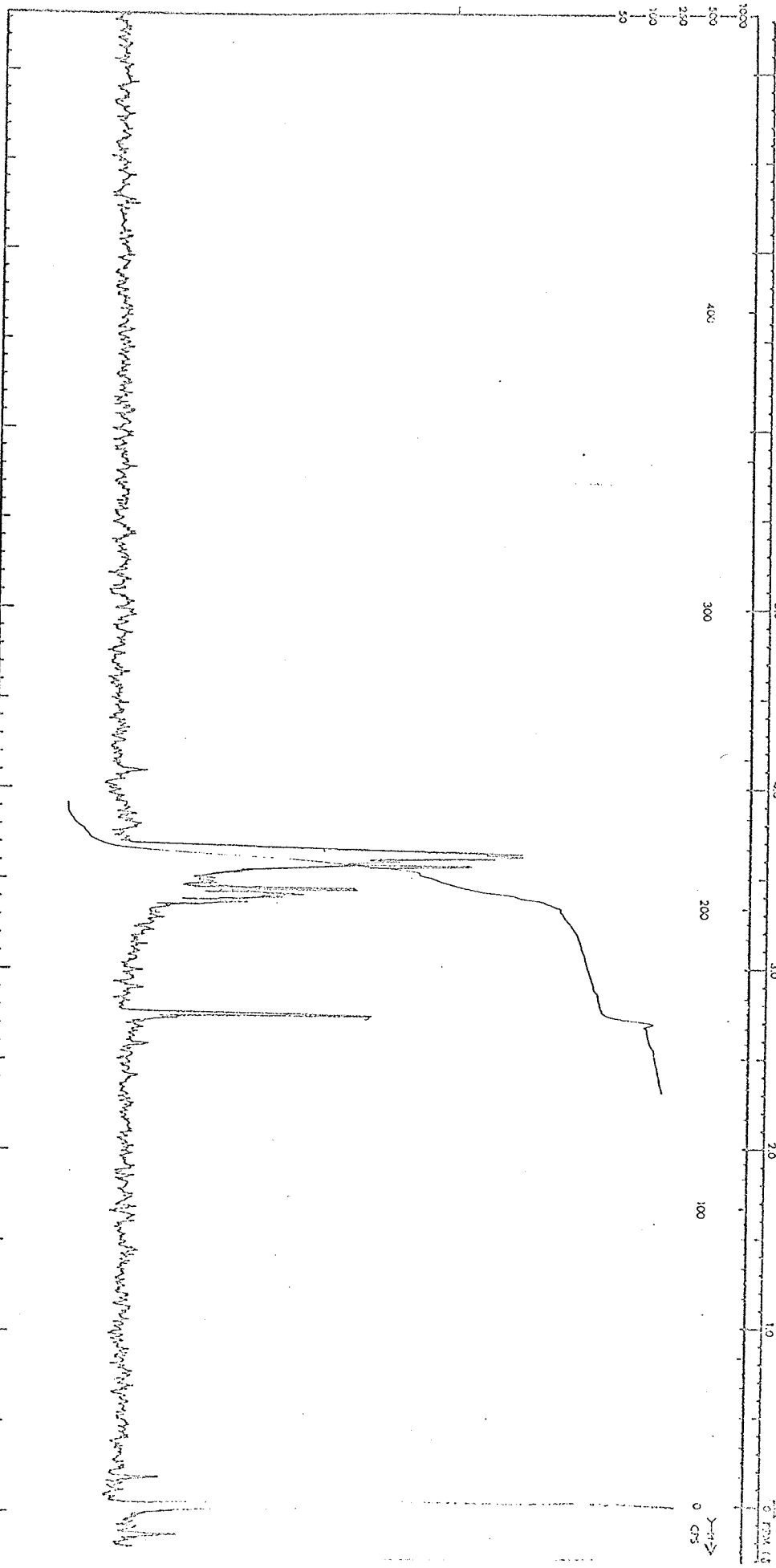
NMR spectrum no. 28 : 1,3-diphenyl-4,11-dihydro-4,11-o-benzenoanthra-(2,3-c)thiophene (267) in $CDCl_3$. Sweep width = 500 Hz.



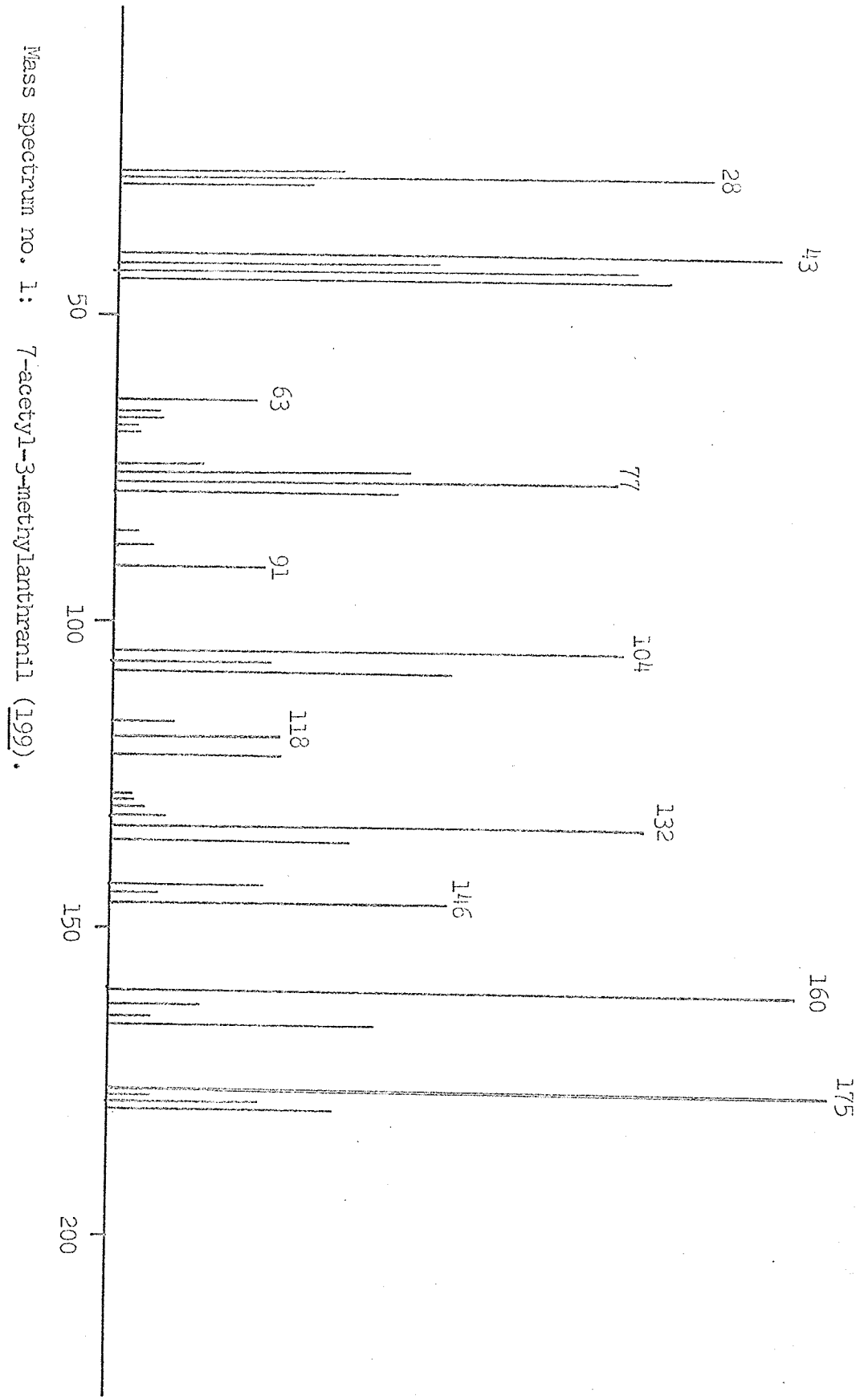
NMR spectrum no. 29 : 1,3-dimethyl-4,9-dihydro-4,9-o-benzenonaphtho(2,3-c)-thiophene (239) in $CDCl_3$. Sweep width = 500 Hz.

NMR spectrum no. 30 : 1,3-dimethyl-4-methyl-4,9-dihydro-4,9-o-benzeno-naphtho(2,3-c) thiophene (263) in $CDCl_3$. Sweep width = 500 Hz.

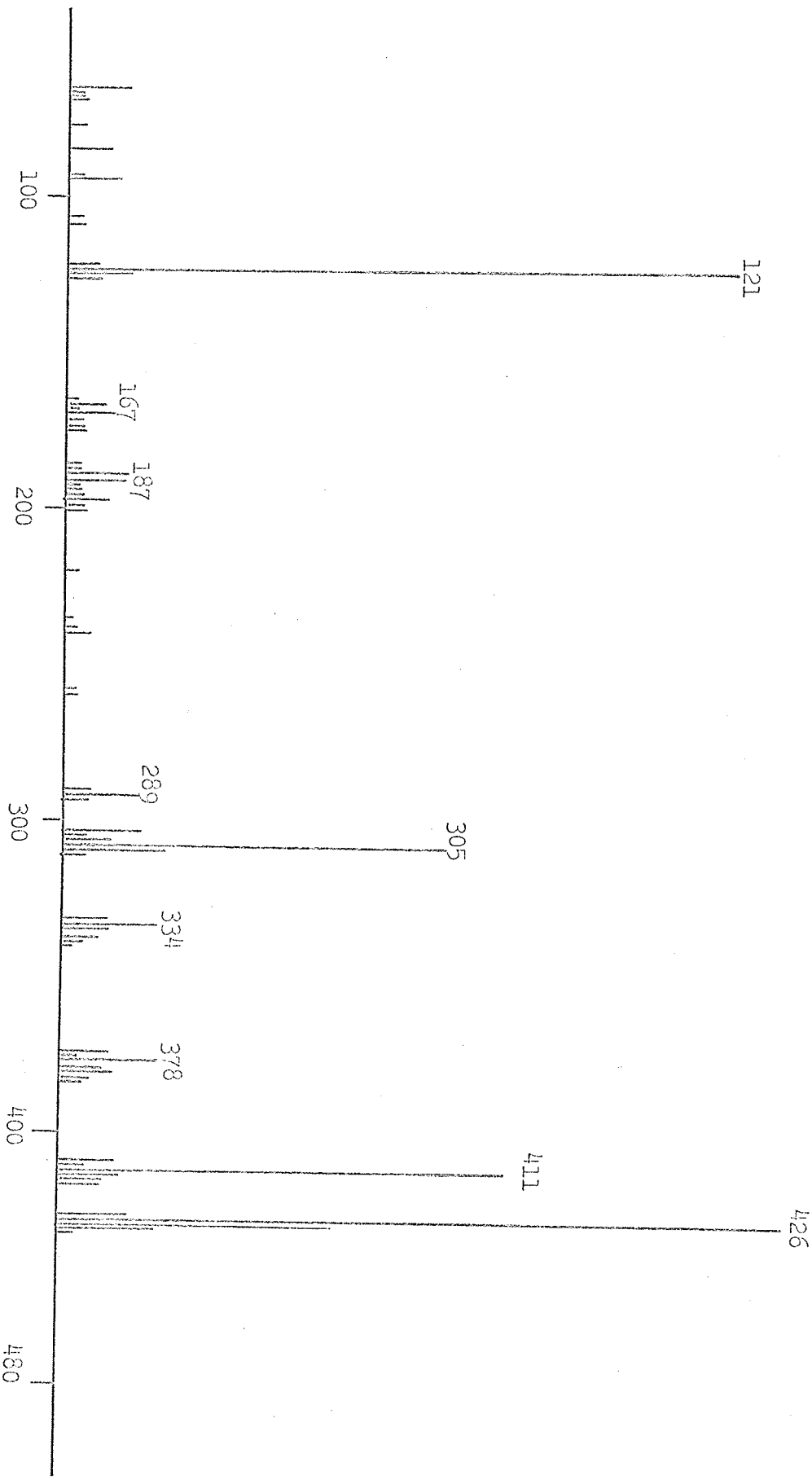




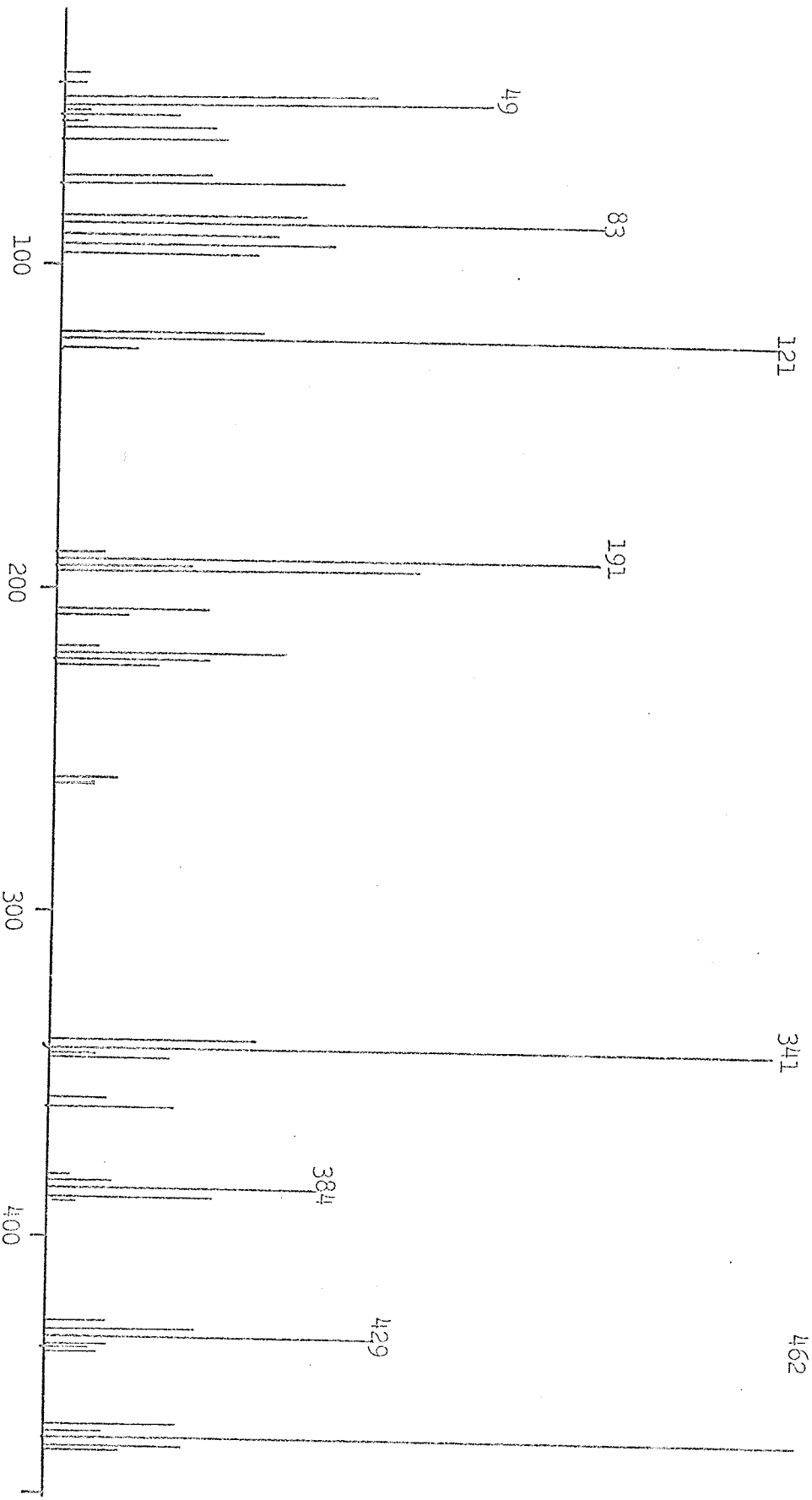
NMR spectrum no. 31 : 1,3-diphenyl-4,9-dihydro-4,9-o-benzenonaphtho-(2,3-c)pyrrole (265) in $CDCl_3$. Sweep width = 1000 Hz.



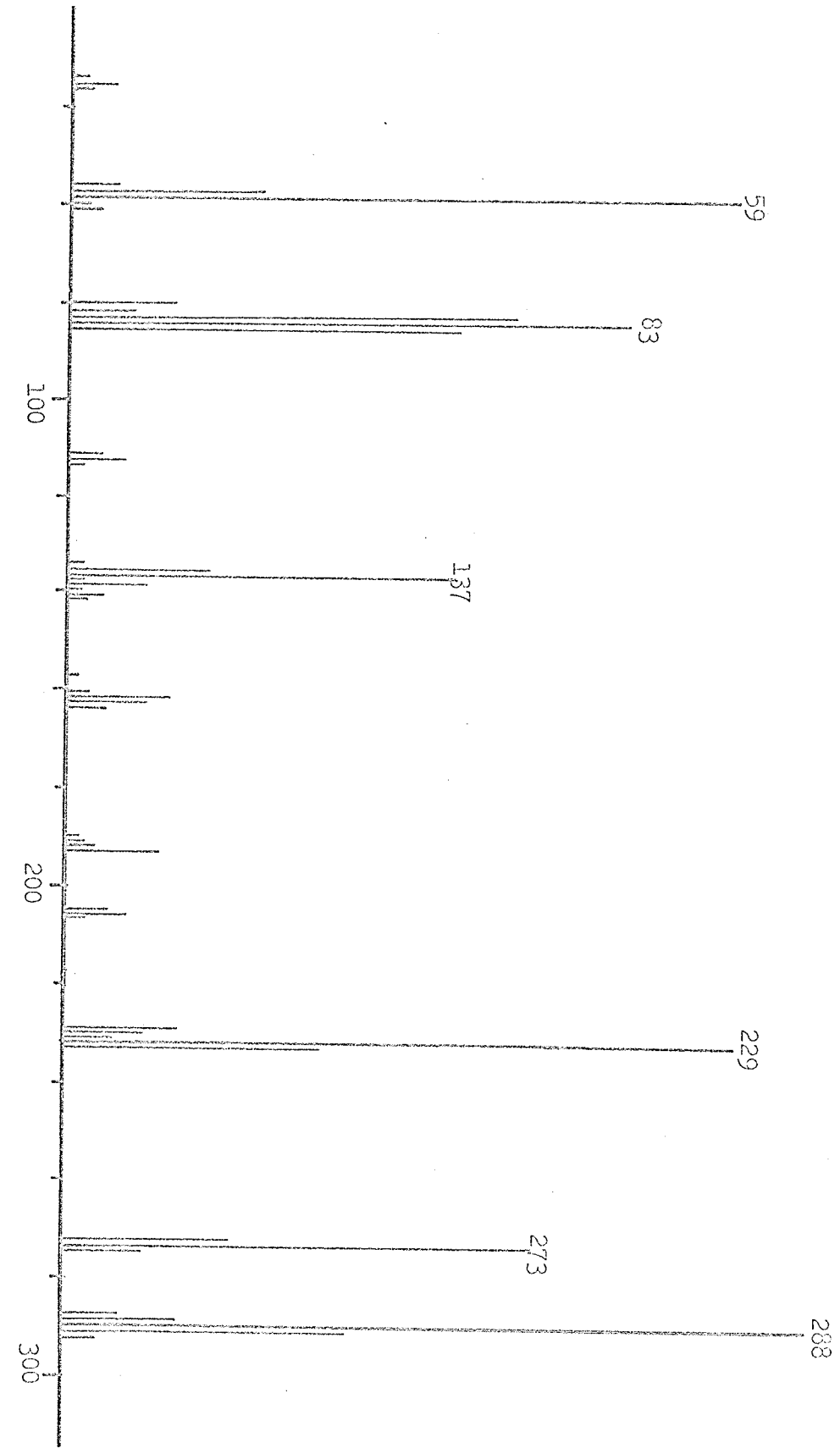
Mass spectrum no. 1: 7-acetyl-3-methylanthranil (199).



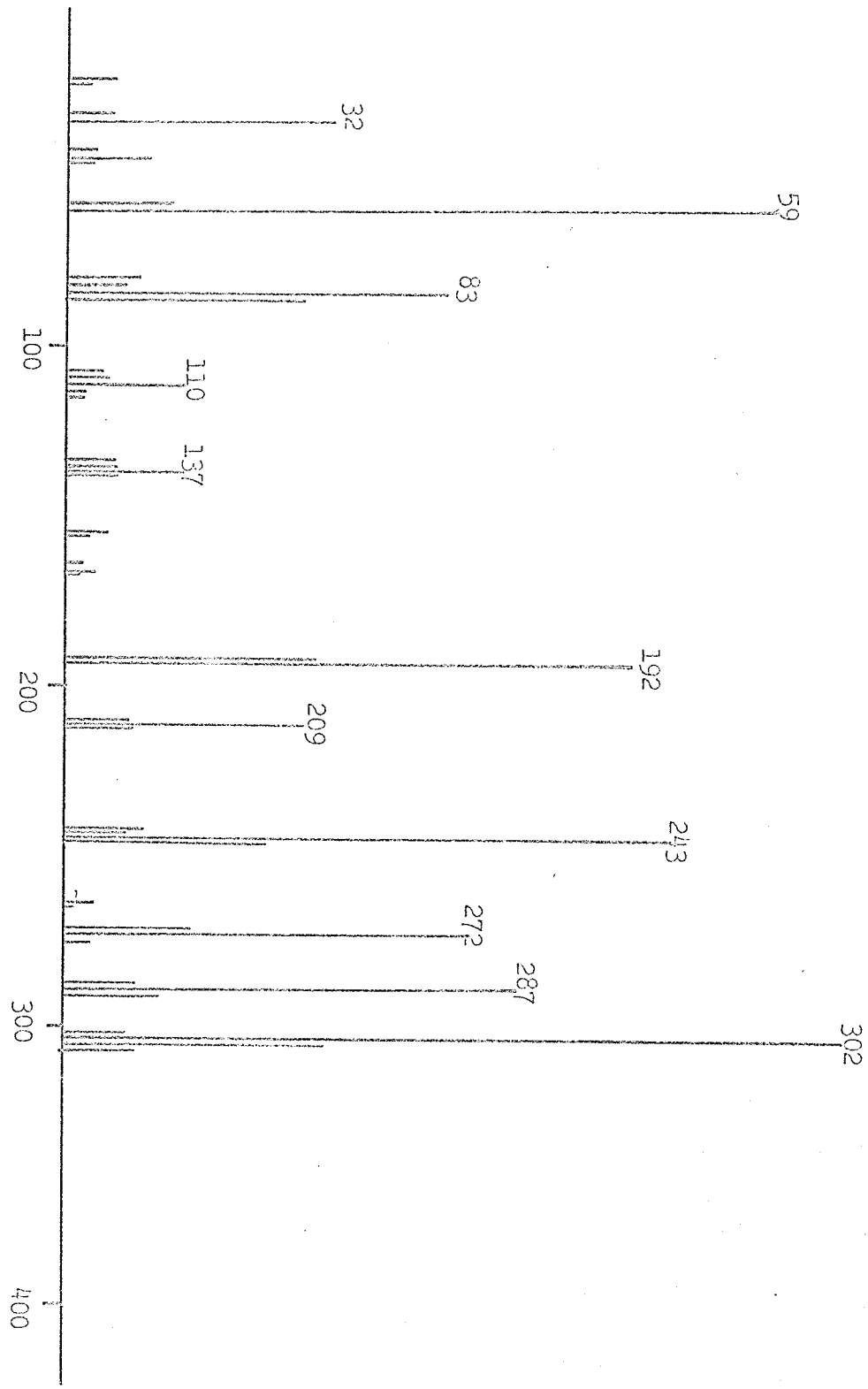
Mass spectrum no. 2: 1,3-diphenyl-4-methyl-4,9-dihydro-4,9-o-benzenonaphtho(2,3-c)thiophene.



Mass spectrum no. 3: 1,3-diphenyl-4,11-dihydro-4,11-o-benzenoanthra(2,3-c)thiophene (267).



Mass spectrum no. 4: 1,3-dimethyl-4,9-dihydro-4,9-o-benzenonaphtho(2,3-c)thiophene (239).



Mass spectrum no. 5: 1,3-dimethyl-4-methyl-4,9-dihydro-4,9-o-benzenonaphtho(2,3-c)thiophene (263)