STUDIES IN SYNTHETIC ORGANOSULFUR CHEMISTRY

by

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ABSTRACT

Desulfurization of β-Ketosulfides and Thiocyanates with Tris(dialkylamino)phosphines

Tris(dimethylamino)phosphine desulfurizes β-ketosulfides to afford a variety of products, including ketones and enol ethers; the mechanism probably involves a phosphonium salt. Benzyl thiocyanate was readily desulfurized by this reagent in a complex reaction to afford benzyl cyanide and dibenzyl sulfide as the main products.

Synthesis of Chiral Sulfur Compounds

The customary route to optically pure sulfoxides involves treatment of a diastereomeric sulfinate ester with a Grignard reagent. Product analysis suggests that the variable yields encountered, even under carefully controlled conditions, are due to the reduction of the sulfoxides. It has been shown that the more convenient lithium organocuprate reagents undergo highly stereospecific reactions with the sulfinate esters. Less reduction occurs, since the organometallic reagents react more sluggishly with the sulfoxides.

The organocuprate reagents react more rapidly with sulfinimides to give still higher yields of sulfoxide. Diastereomeric sulfinimides have been chosen as key intermediates in the synthesis of a variety of sulfinyl derivatives. A synthesis which gives good yields of the chiral imide precursors has been developed. Examples of the diastereomeric sulfinimides have been prepared, paving the way for resolution.

In response to a need demonstrated during this study, a new synthesis of thioimides *via* organosilicon reagents has been uncovered.

ETUDE DE LA CHIMIE DU SOUFRE

RESUME

Les sulfures β-cétoniques sont désulfurés par le tris-(dimethylamino)phosphine et donnent une variété de produits, incluant des cétones et des éthers vinyliques. Un sel de phosphonium est probablement impliqué dans le mécanisme. Le thiocyanate fut désulfuré par ce reactif, et les principaux produits de cette réaction complexe furent le cyanure et le sulfure de benzyle.

Les sulfures optiquement purs sont généralement obtenus par l'action d'un reactif de Grignard sur un diastéréoisomère d'un ester sulfinique. Cependant les rendements sont variables même sous des conditions de réaction rigoureusement contrôlées, et la cause en est la réduction des sulfoxydes comme démontré par l'analyse des produits. Les complexes organiques de lithium et de cuivre se sont avérés hautement stéréospécifiques dans leur réaction avec les esters sulfiniques; comme ils réagissent difficilement avec les sulfoxydes, le niveau de réduction fut beaucoup moindre.

Des rendements encore plus élevés de sulfoxydes ont été obtenus par la réaction d'organocuivreux sur les sulfinimides avec lesquels il réagissent plus rapidement.

Des sulfinimides diastéréoisomeriques ont été identifiés comme étant des intermédiaires importants dans la synthèse d'une variété de dérivés sulfiniques. Une synthèse donnant de bons rendements d'imides dissymétriques a été développée, permettant la préparation de sulfinimides diastéréoisomériques et pavant la voie vers leur résolution.

En relation avec cette étude, une nouvelle synthèse de thioimides utilisant des silanes a été découverte.

ACKNOWLEDGMENTS

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I thank Dr. L.Q. Bao and Mr. Barry Friedlander for their assistance with the work involving the chiral imides. I would also like to thank the 'Foules and Idyotes', Dr. T. Back, and others for many stimulating discussions on diverse subjects.

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PART I

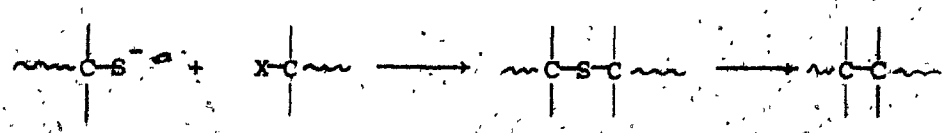
DESULFURIZATION OF β-KETOSULFIDES AND THIOCYANATES WITH TRIS (DIALKYLAMINO) PHOSPHINES

1. INTRODUCTION

Until Wöhler showed in 1828 that urea could be prepared from inorganic materials[1], organic compounds were thought to contain a "spirit" which only living things could transmit. Today we no longer consider organic compounds to have this God-given "spirit" but we do retain the useful classification of organic and inorganic compounds. Since the carbon-carbon bond is especially stable and can form long chains, a vast range of organic compounds is possible.

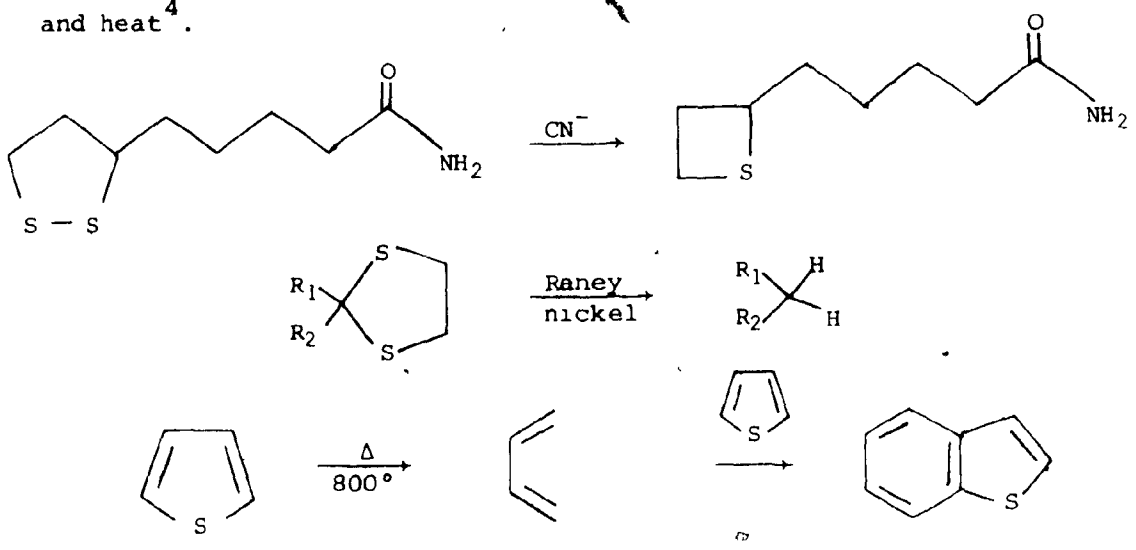
The generation of carbon-carbon bonds is one of the major goals of synthetic organic chemists. Among the innumerable reactions that generate such bonds, examples can be found that involve addition of a carbonium ion or a free radical to an unsaturated system; nucleophilic substitution reactions of organometallic reagents, carbanion condensations; union of two free radicals generated thermally, photochemically or electrochemically; and thermal or photochemical cycloaddition reactions.

Since carbon chains can readily be linked through a sulfur atom, a technique that could selectively remove this sulfur atom would provide a new and potentially valuable synthetic technique for making carbon-carbon bonds.



X = leaving group

A variety of agents have been used to desulfurize compounds containing divalent sulfur. These include cyanide ion[2], Raney nickel[3] and heat[4].

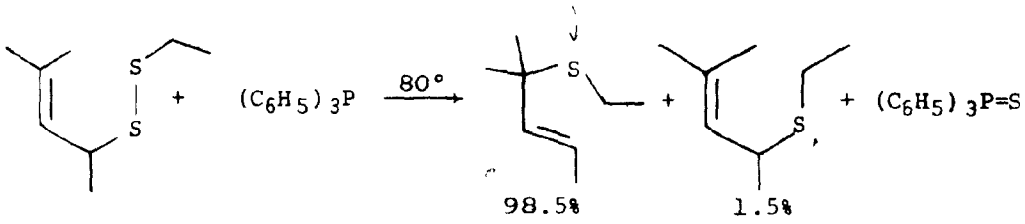


Most of these techniques are not widely applicable or often require drastic conditions; hence more subtle chemical means were sought. Certain sulfur compounds have been desulfurized by treatment with trivalent phosphorus compounds under mild conditions. To determine the viability of the proposed synthetic pathway using such reagents, the scope of these desulfurization reactions was reviewed.

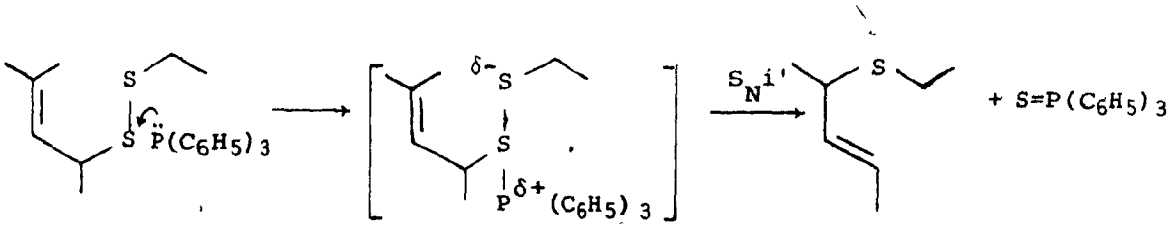
One of the earliest examples of such a reaction was examined by Schönberg[5,6], who showed that simple alkyl disulfides are inert to triphenylphosphine in boiling benzene, but certain reactive disulfides, such as dibenzoyl disulfide, are desulfurized to give the corresponding sulfide. Attempts to extend this procedure to less reactive disulfides were at first unsuccessful[5-7]. Triphenylphosphine does not desulfurize dialkyl or diaryl disulfides in dry benzene at temperatures as high as 140°.

An anomalous report does appear in the literature[8] that several disulfides, including dibenzyl disulfide, are readily desulfurized by triphenylphosphine. These results conflict with the observations of Schönberg[5,6], Moore and Trego[7], and Gleason[9], who report that such disulfides are inert under harsh conditions.

Allylic disulfides are readily desulfurized by triphenylphosphine with accompanying rearrangement[10]. A mechanistic study of this reaction[11] indicates that the reaction rate increases significantly as the solvent



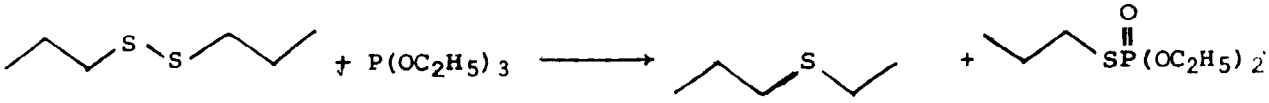
polarity increases. These results led to the suggestion that a charged transition state, such as 1, is involved in the rate-determining step:



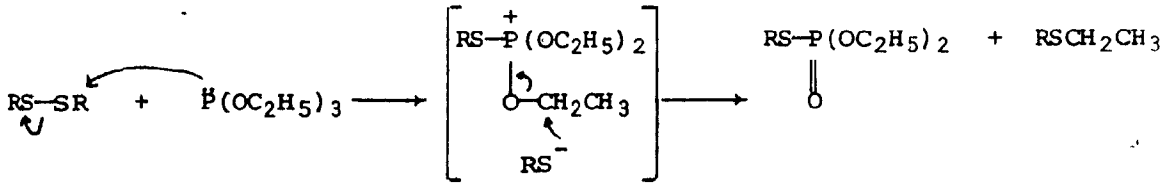
1

In contrast with triaryl- or trialkylphosphines, phosphites readily desulfurize most disulfides[12]. However, Arbusov-type rearrangement occurs[12-14]; for example, the product of the treatment of n-propyl disulfide

with triethyl phosphite is not n-propyl sulfide, but ethyl n-propyl sulfide.

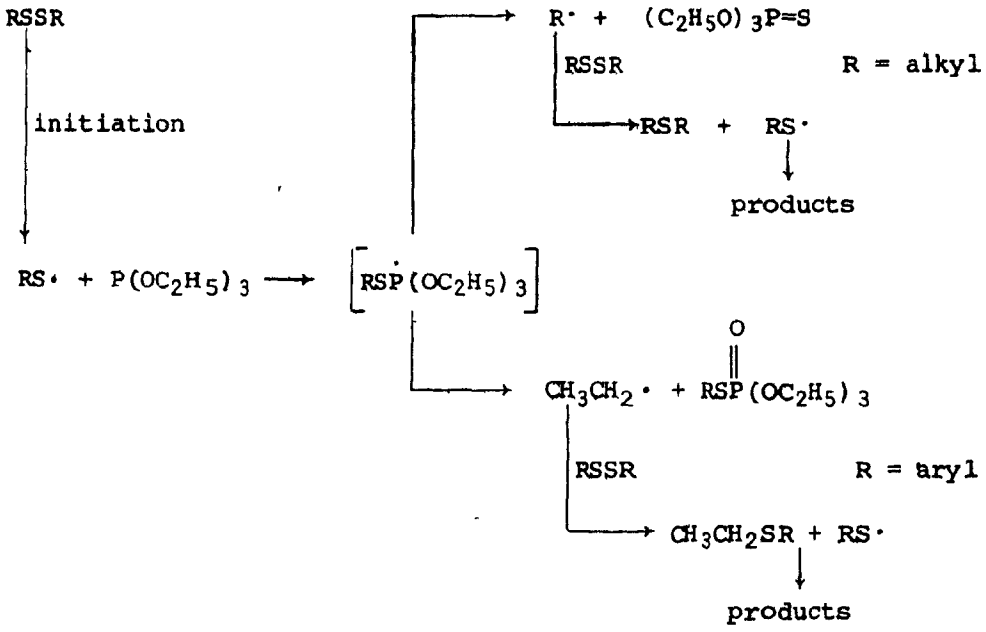


Harvey, Jacobson and Jensen[13] provided evidence for an ionic intermediate in this reaction by showing that unsymmetrical disulfides react much faster than symmetrical disulfides. The enhanced rate can readily be explained since increased polarisation of the S—S bond should result in easier rupture.



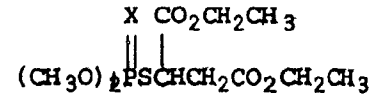
The driving force for such a rearrangement would likely involve the high energy of the P = O bond (140 Kcal $mole^{-1}$)[15].

Walling and Rabinowitz[16,17] treated n-butyl disulfide with triethyl phosphite in the presence of hydroquinone, a radical inhibitor; they obtained n-butyl ethyl sulfide in low yield, showing that the reaction may occur partially through a free-radical pathway.



If the reaction is carried out in the presence of radical initiators or ultraviolet light, the free radical mechanism predominates[17]. Under these conditions, the formation of a complex mixture minimizes the synthetic utility of the reaction. For example, dibenzyl disulfide gives only a small quantity of dibenzyl sulfide (5%); the main products are toluene (19%) and bibenzyl (46%).

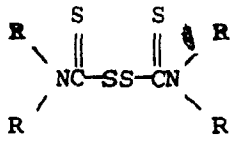
Although the reaction of disulfides with phosphites is of little synthetic utility for the preparation of sulfides, it provides a good route to maloxon (2a)[18], the oxo analogue of the well-known insecticide malathion (2b).



2a X = O 2b X = S

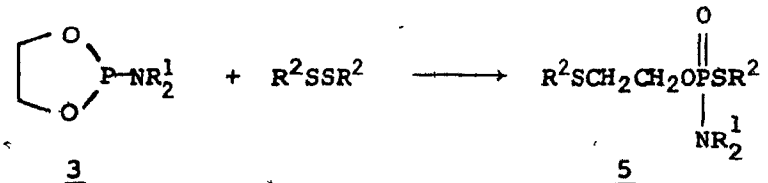
Maloxon is a metabolic product of malathion in both the cockroach and the mouse[19].

Cyclic esters of phosphoramidous acid (3) are known to give poorly-defined products on treatment with alkyl halides, although they react with sulfur to give the corresponding phosphine sulfides[20]. It appeared that those compounds might desulfurize disulfides without the Arbuzov rearrangement[21]. It was found that simple alkyl disulfides gave no reaction even in boiling toluene, while allylic disulfides lose sulfur with accompanying rearrangement in a similar reaction to that observed with phosphines and simple phosphites[12-14]. Aromatic disulfides, tetraalkyl thiuram disulfides 4 and certain heterocyclic disulfides open



4

the ring of the phosphoramidite to form derivatives of phosphoramidous acid (5)[21,22].



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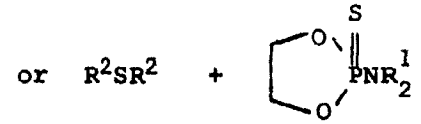


Tris(dialkylamino)phosphines (6) smoothly desulfurize disulfides to give near-quantitative yields of the corresponding sulfides[23,24].

$$(R^1_2N)_3P \quad + \quad R^2SSR^3 \longrightarrow (R^1_2N)_3P{=}S \quad + \quad R^2SR^3$$

6a $R^1 = CH_3$ 7

6b $R^1 = CH_2CH_3$

The reaction is applicable to a wide range of alkyl, aralkyl, alicyclic, and other disulfides. The reaction rate increases markedly with the solvent polarity; second-order kinetics are obeyed[24]. Symmetrical sulfides are side-products in some of these reactions, and inversion of stereochemistry occurs at one of the carbon atoms α to the disulfide group. Diaryldisulfides are not desulfurized. On these grounds the following mechanism was proposed:

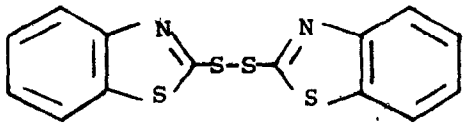
$$R^2{-}S{-}S{-}R^3 \quad + \quad :P\!\!< \xrightarrow[S_N2]{slow} R^2{-}S{-}\overset{+}{P}\!\!< \quad + \quad R^3S^- \xrightarrow[S_N2]{fast} R^2SR^3 \quad + \quad S = P\!\!<$$

The formation of symmetrical sulfide can then be explained as follows:

$$R^2S^- + R^2S{-}SR^3 \longrightarrow R^2S{-}SR^2 \quad + \quad \bar{S}R^3 \xrightarrow{\;\geq P\;} R^2SR^2 \quad + \quad S = P\!\!<$$

Further evidence for an ionic pathway was provided by the detection of a thermally labile phosphonium salt on treatment of

di-2-benzothiazole disulfide (8) with aminophosphine[24].



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Related work has shown that tris(dialkylamino)phosphines (6) are particularly useful for extruding sulfur smoothly from a variety of other molecules. These include thiosulfonates (9a)[25,26], sulfenyl thiosulfonates (9b)[26], thiosulfinate esters (9c)[27,28], trisulfides (9d)[29], sulfenimides (9e)[30], and sulfenate esters (9f)[31,32].

In some cases[24], the desulfurizations are known to be two-step processes, as shown below:

$$R^1SXR^2 + P\!\!\leq \xrightarrow{\text{slow}} R^1S\overset{+}{P}\!\!\leq \xrightarrow{\text{fast}} R^1XR^2 + S=P\!\!\leq$$

$$\bar{X}R^2$$

9a X = $-SO_2-$

b X = $-S-SO_2-$

c X = $-\overset{O}{\overset{\|}{S}}-$

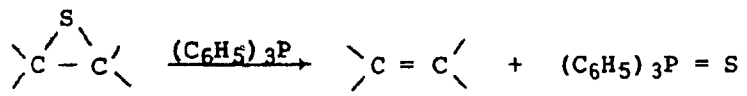
9d X = -SS-

e $XR^2 = -N(-\overset{O}{\overset{\|}{C}}R^3)_2$

f X = -O-

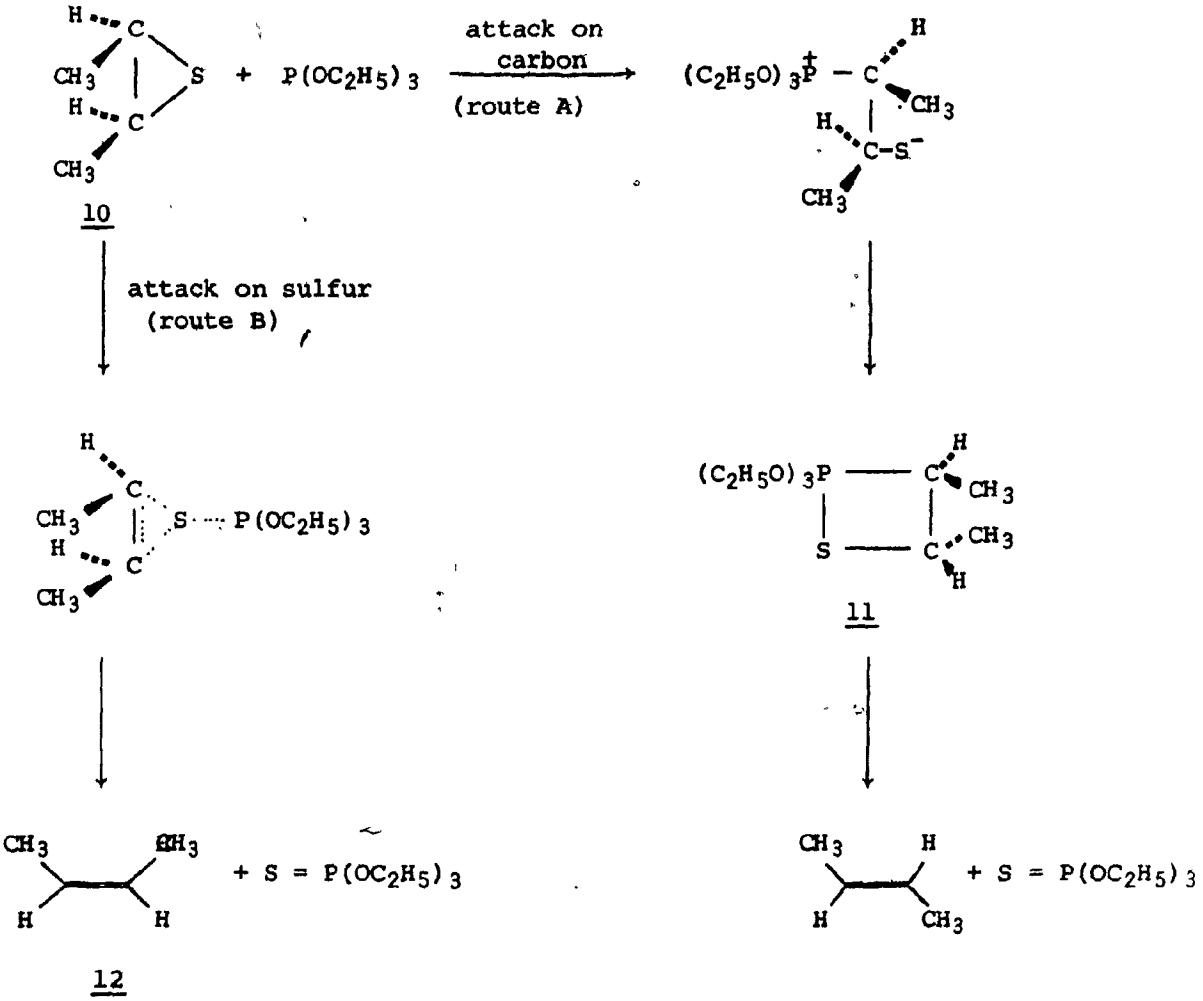
The phosphorus nucleophile attacks the sulfur atom, displacing an $^{-}XR^{1}$ anion in an S_N2-type process; $^{-}XR^{1}$ is then alkylated by the phosphonium salt to give the desulfurized product and phosphine sulfide.

Although simple sulfides do not react with trivalent phosphorus compounds, episulfides are readily desulfurized by phosphines or phosphites. Davis *et al.*[33] showed that, on treatment with a phosphine (or phosphite) for several days at room temperature, episulfides lose sulfur to yield an alkene. It was later shown that the reaction is facilitated by the



use of dry solvents with weak solvating powers, and by low temperatures. If these conditions are satisfied, the proportion of polymeric side-product is greatly reduced[34].

The mechanism of this reaction was studied by Neureiter and Bordwell[35], who showed that triethyl phosphite converts cis-2-butene episulfide (10) to cis-2-butene, and trans-2-butene episulfide to trans-2-butene. The stereochemistry of this reaction rules out the attack of phosphorus on a carbon atom to give an intermediate such as 11 (Route A), since such a mechanism requires that the stereochemistry of the product be opposite to that of the starting material.

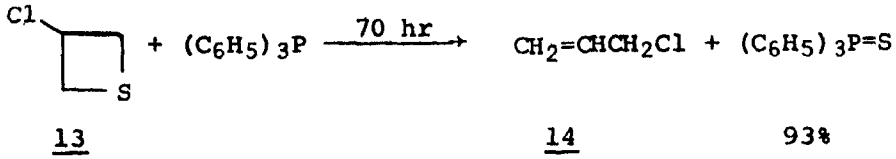


10 11 12

Boskin and Denney provided further evidence for Route B[36] by showing that the kinetics of the reaction are second-order and that its rate is virtually independent of solvent polarity. The mechanism now accepted is one involving direct attack of phosphorus on sulfur.

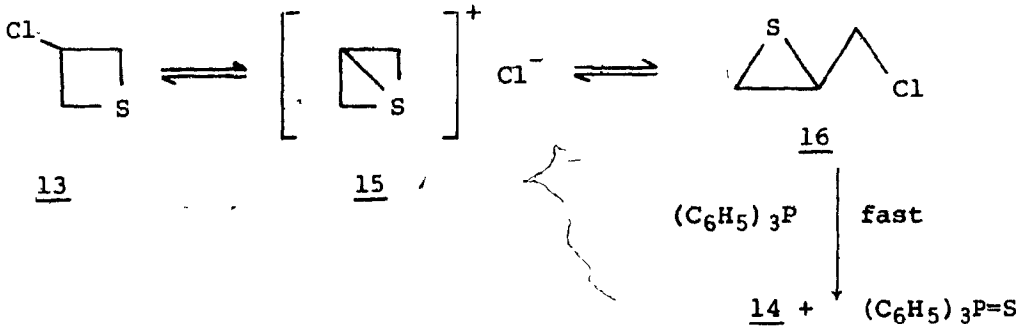
The desulfurization of thietanes on treatment with phosphines or phosphites has also been observed[37]. 3-Chlorothietane (13) loses sulfur to give allyl chloride (14) on treatment with triphenylphosphine or triethyl

phosphite, although the reaction is considerably slower than for episulfides.



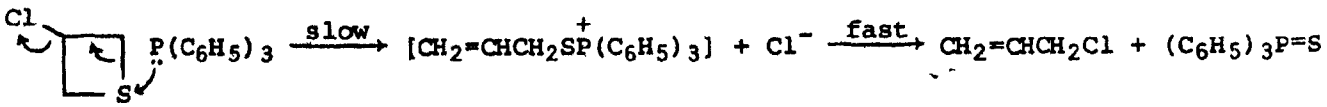
13 14 93%

Two mechanisms were proposed to rationalize the formation of the alkene. One pathway involves the rearrangement of an ionic intermediate 15 to give episulfide 16, which then loses sulfur.



13 15 16 14

The other route involves attack of phosphorus on sulfur to give the alkyl sulfide 17; this undergoes nucleophilic displacement of phosphine sulfide, yielding 14.

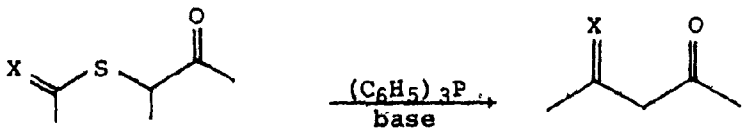


13 17

Rate measurements support the latter process, as the reaction appears to follow second-order kinetics[37].

3-Hydroxythietane and its parent heterocycle, thietane, are also desulfurized, but far less readily. Although triphenylphosphine sulfide is formed, the remaining products of the reaction of these compounds with triphenylphosphine have not been identified[37].

Triphenylphosphine, in the presence of base, has recently been found to desulfurize activated sulfides of the type 18 in good yield[38].

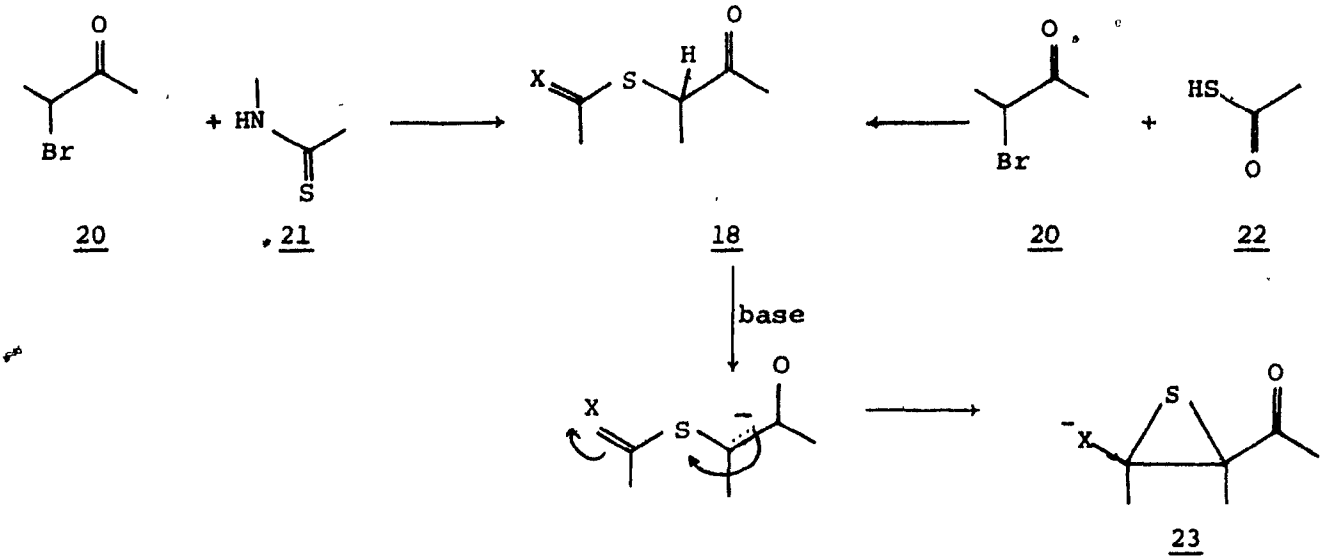


18a X = -N
b X = O

19

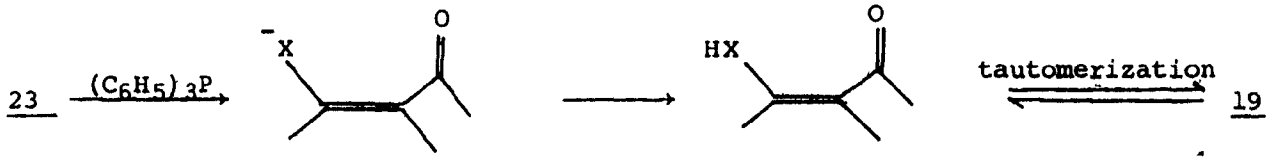
Since the starting sulfides can readily be prepared by coupling an α-halocarbonyl compound of the type 20 with a thiolactam 21 or a thiolcarboxylic acid 22, the reaction is highly useful for the preparation of secondary vinylogous amides or enolizable β-diketones. This reaction provided a key step in a synthesis of corrins that was developed in response to one of the many requirements of Woodward and Eschenmoser's epic synthesis of vitamin B_{12}[38b].

It has been suggested that 18 is first converted by base to an episulfide 23, which is then desulfurized.



20 21 18 20 22

23



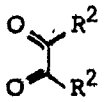
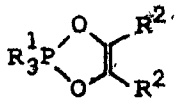
23 19

Although detailed mechanistic evidence is as yet lacking, the ease of desulfurization of such enolizable systems relative to simple sulfides can thus be explained.

All the desulfurizations hitherto described involve valence expansion of phosphorus (P(III) → P(V)), whether the reaction involves a phosphine, phosphite, or aminophosphine. This process has been observed with a great variety of oxidizing agents. A number of these valence expansion reactions are summarized in Table I.

TABLE I

Some Reactions of P(III) Compounds

P(III) Compound	Oxidizing Agent	Product(s)	Ref.
R_3P	O_3	$R_3P{=}O$	39,40
R^1_3P	R^2OOR^2	$R^1_3P{=}O$, R^2OR^2	41,42
R^1_3P			43
R_3P	CCl_4	$R_3P{=}CCl_2$, R_3PCl_2	44,49
R_3P	S_8	$R_3P{=}S$	45
$(R^1O)_3P$	R^2X	$(R^1O)_2\overset{O}{\overset{\|}{P}}R^2$, R^1X	46,47

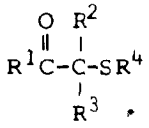
As previously described, most desulfurization reactions seem to occur in two steps, the first step requiring nucleophilic attack of phosphorus on sulfur to give the phosphonium salt intermediate. Triphenylphosphine is a better nucleophile than most phosphites[11,48], and might be expected to attack sulfur compounds more readily. However, the intermediates formed by attack of phosphites are stabilized by electromeric release; the great stability of the P = O bond[15] then provides a powerful driving force for rearrangement.

The intermediate phosphonium salt is similarly stabilized in aminophosphines, which are extremely reactive nucleophiles[49,50] -- more so than phosphites, since nitrogen is less electronegative than oxygen. Electromeric release of electrons from nitrogen to stabilize the intermediate phosphonium salt is possible, and an Arbusov-like rearrangement is less likely to occur[51]. For these reasons aminophosphines are effective desulfurizing agents.

The second stage of the reaction involves attack of a displaced nucleophile on the phosphonium salt to evict phosphine sulfide. Disulfides are readily desulfurized because the initially displaced sulfide ion (an excellent leaving group) is also a very powerful nucleophile. If desulfurization reactions are to provide a new technique for carbon-carbon bond formation, a carbanion must be generated which can fulfill the dual role of leaving group and nucleophile.

2. DISCUSSION *

Carbanions can be stabilized by conjugation with a carbon-oxygen double bond[52]. Accordingly, a number of β-ketosulfides 24 were

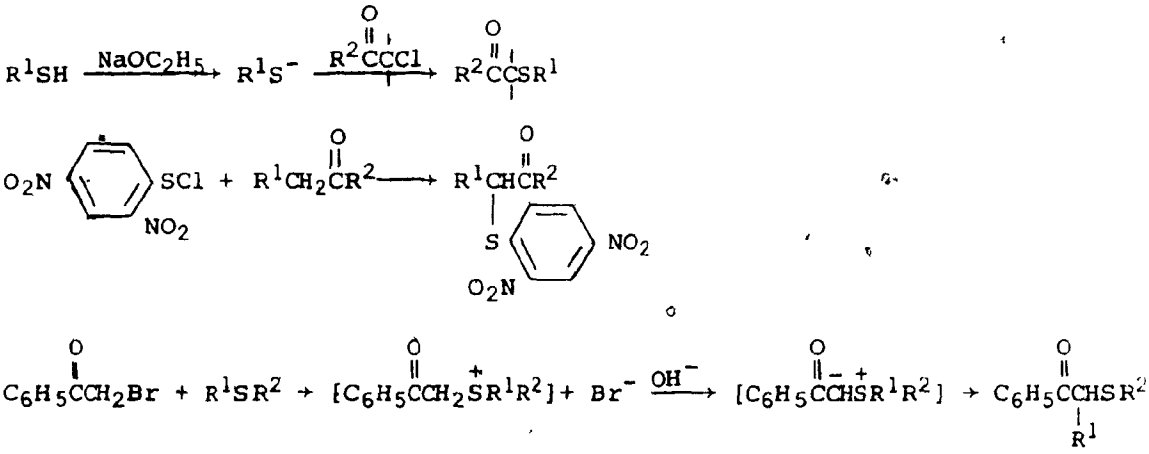


24

prepared and their reaction with tris(dimethylamino)phosphine (6a) examined.

β-Ketosulfides

Several syntheses for these compounds have been reported: the reaction of mercaptide ion with α-haloketones[53,54], the treatment of sulfenyl halides with ketones[55], the decomposition of dialkylphenacyl sulfonium salts with base[56,57], and the reduction of β-ketosulfoxides with sodium metabisulfite[58].



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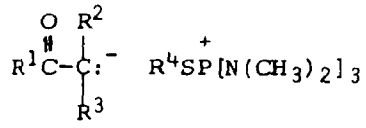
*The work in this and following sections has been published[91].

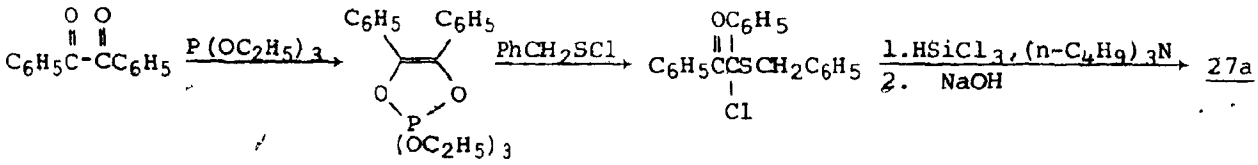
Previous work[23-32] suggested that the proposed desulfurization reaction would probably involve a phosphonium salt intermediate 26.



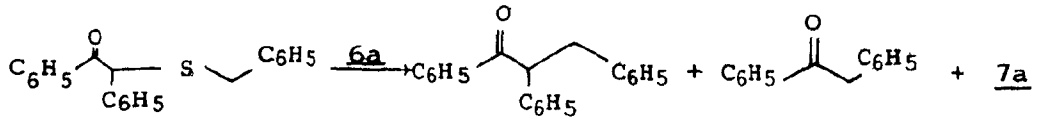
26

In order to facilitate displacement of the carbanion of 26, a phenyl group was used at R^2. It appeared that a benzyl moiety at R^4 might encourage easy displacement of tris(dimethylamino)phosphine sulfide (7a). Therefore, α-benzoyl-α-phenylmethyl benzyl sulfide (27a) was prepared.

Most methods of preparation of β-ketosulfides give poor yields or are limited in scope. Fortunately 27a can be prepared in good yield from simple starting materials by a method recently developed in our laboratory[59].

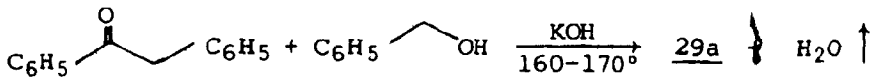


This compound was heated with phosphine 6a in a variety of solvents. Vapor phase chromatographic analysis indicated that desoxybenzoin ($C_6H_5COCH_2C_6H_5$, 28) was the principal product of an extremely slow reaction. However, in the absence of solvent, the starting materials were consumed in less than one hour to give three products as analyzed by quantitative gas chromatography: 1-benzoyl-1,2-diphenylethane (29a) (69%), desoxybenzoin (28) (22%), and tris(dimethylamino)phosphine sulfide (7a) (86%).



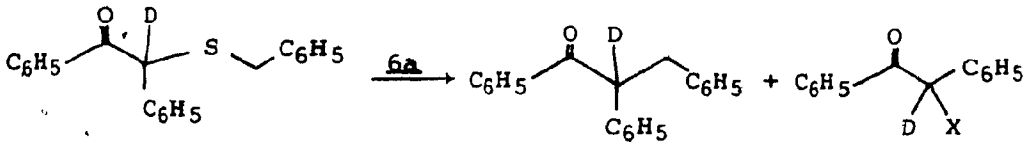
27a 29a 28

The target molecule 29a was subsequently isolated in 43% yield, identical in every respect to an authentic sample prepared by the benzylation of desoxybenzoin[60].



In the reaction of β-ketosulfide 27a with phosphine 6a, it appears that the ionic intermediate 26a, (R_1, R_2 = C_6H_5, R_3 = H , R_4 = $CH_2C_6H_5$) does indeed form and is partially diverted by proton abstraction to give desoxybenzoin (28). To test the hypothesis that the proton is abstracted from the carbon atom adjacent to the carbonyl group, 27b was required. A sample of 27a was therefore recrystallized from EtOD to which a trace of sodium had been added. The absence of a methyne signal (δ 4.72) in the nmr of the resulting material indicates that this proton is the most acidic.

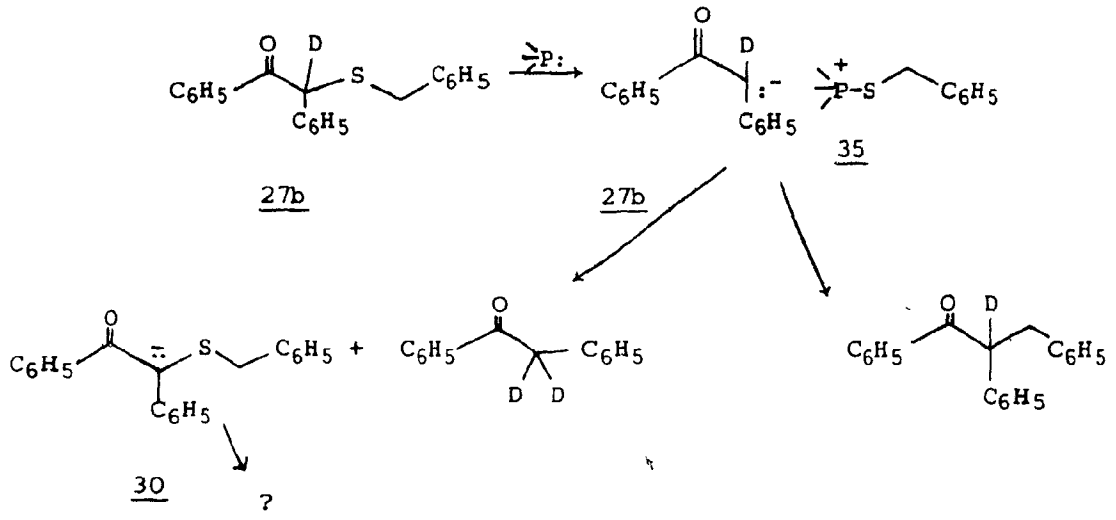
This material (27b) was treated with 6a. Careful chromatography of the product mixture gave, as expected, desoxybenzoin (28), which was 80% deuterated in the benzylic position (nmr).



27b 29b X = D 60%

X = H 40%

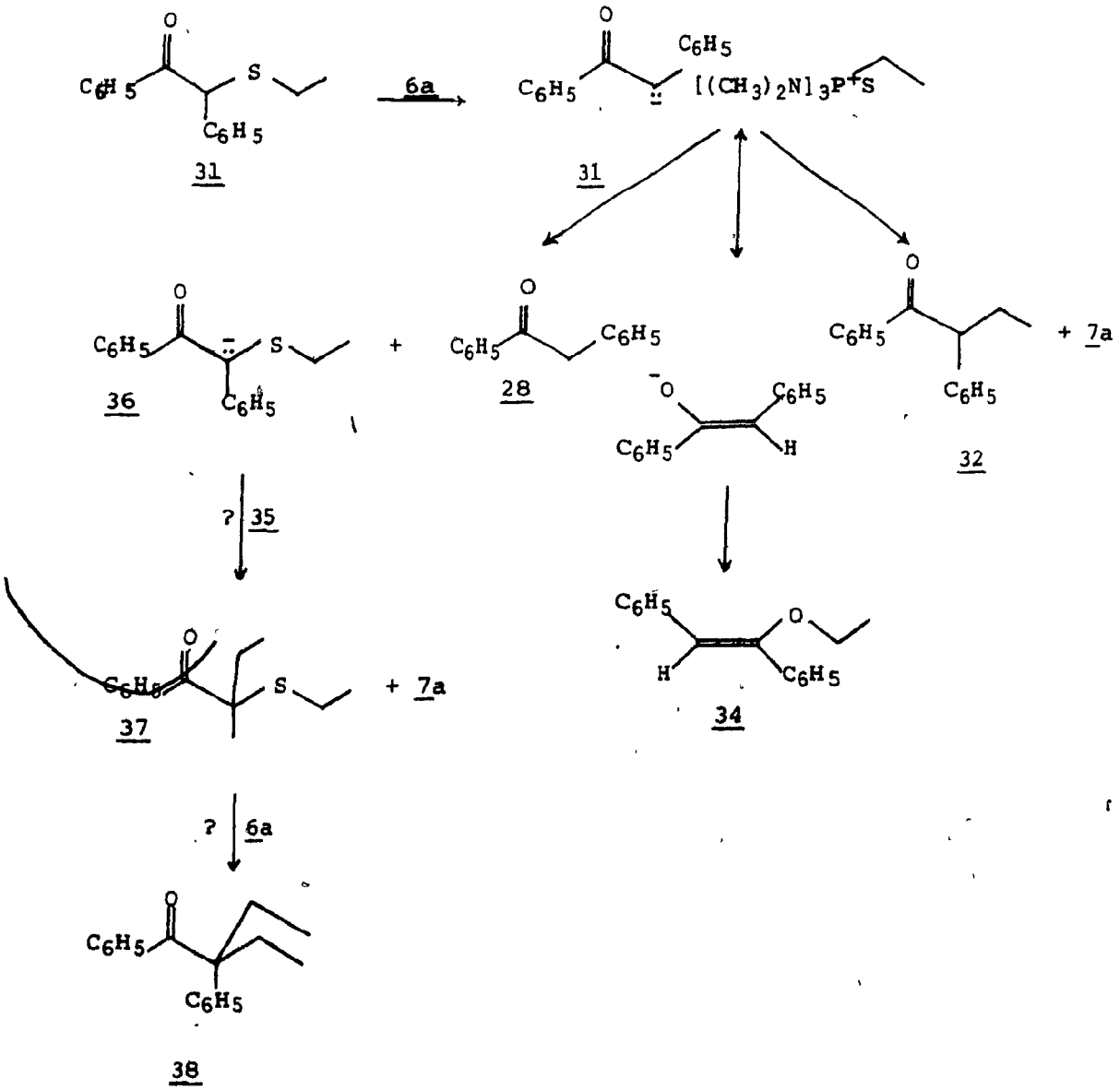
This indicates that the carbanion of salt 26a preferentially removes the atom from the position between the carbonyl group and the sulfur atom, even if this requires cleavage of a stronger C-D bond.



The fate of anion 30 is open to speculation since no products were isolated that might account for this material.

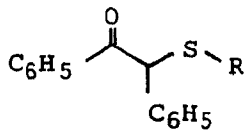
To determine whether alkylative coupling could occur for a β-ketosulfide which did not have R^4 = benzyl in 24, α-benzoyl-α-phenylmethyl ethyl sulfide (31) was prepared and treated with aminophosphine 6a. Although 1-benzoyl-1-phenylpropane (32) was formed in reasonable yield (31%) it proved difficult to isolate, since it behaves in a very similar manner (on both absorption chromatography and gas chromatography) to desoxybenzoin (28) and a third unidentified material 33. The fourth product, trans-1-ethoxy-1,2-diphenylethene (34), gives further credence to the carbanion mechanism. If intermediate 35 is formed, a variety of reaction pathways

are available. The methyne proton of 31 may be abstracted by the anion of 35 to give desoxybenzoin and anion 36. The fate of anion 36 is unclear; it might possibly be alkylated by the cation of 35 to give β-ketosulfide 37.



If the anion of 35 reacted with starting material and then were alkylated by its gegenion, the unidentified product 33 might well be ketosulfide 37 or its desulfurization product 3-benzoyl-3-phenylpentane (38). An attempt was made to prepare the former by treatment of ketosulfide 31 with ethyl bromide in the presence of ethoxide. Three compounds were formed in this reaction, all with absorption characteristics very similar to those of the starting material; separation of the mixture could not be achieved.

If the anion of 35 is not diverted by proton abstraction, it can act as an ambident anion in its reaction with the phosphonium ion. Attack by carbon yields ketone 32, whereas attack by oxygen gives enol ether 34. Investigation of the alkylation of ethyl acetoacetate with alkyl halides in the presence of base suggests that increased S_N2 activity of the alkylating agent is correlated with the proportion of C-alkylation[61,62]. Since both ethyl ketosulfide 31 and benzyl ketosulfide 27a have identical ketonic substituents attached to the sulfur atom, one might predict that 31 would give more enol ether.



27a R = $C_6H_5CH_2$

31 R = CH_3CH_2

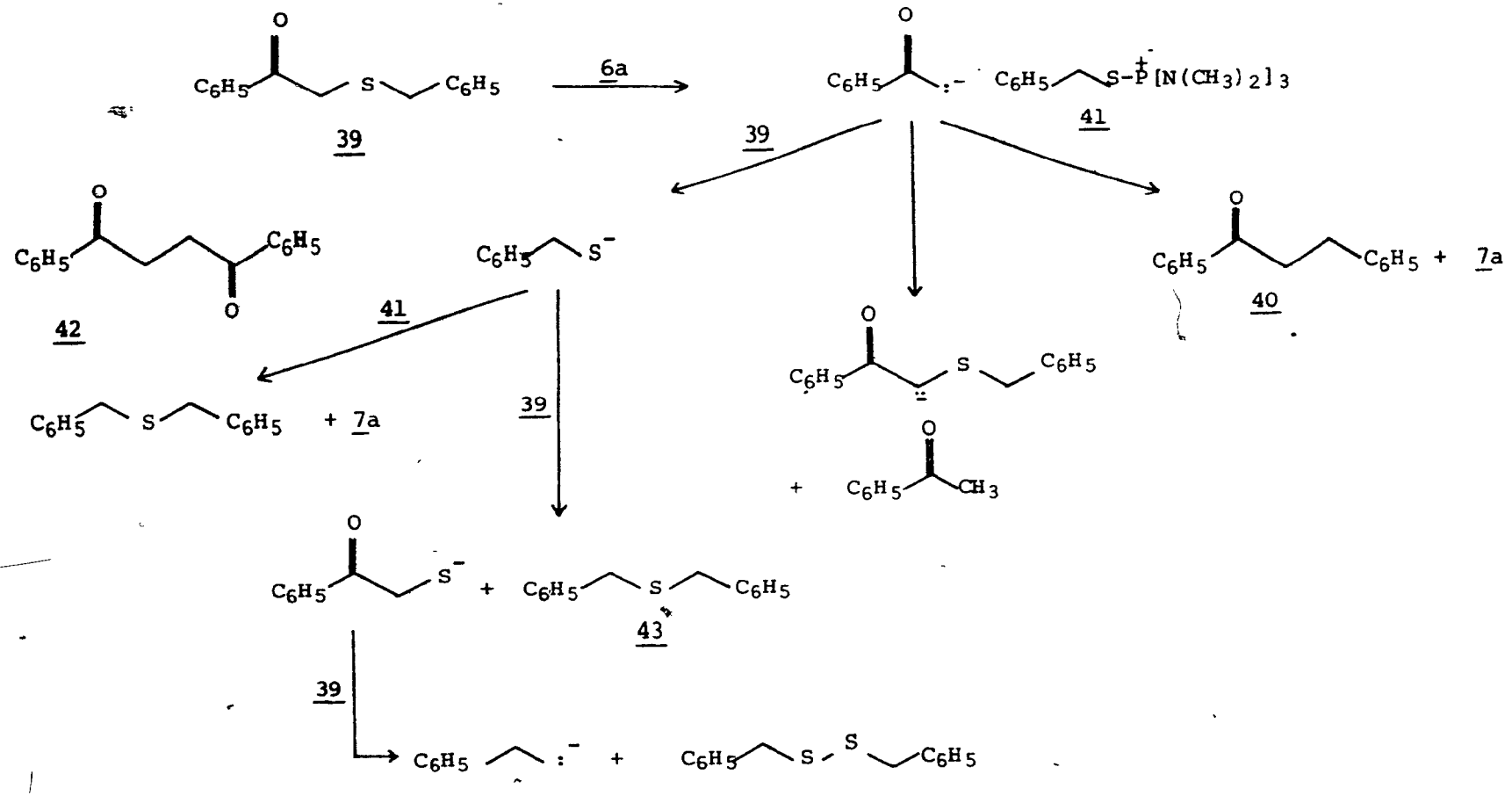
In an attempt to simplify the mixture of products in the desulfurization of 31, effects of solvent on the reaction were considered. It has been reported[63,64] that C-alkylation of ketonic anions is promoted by the use of hydroxylic solvents (such as water, polyfluorinated alcohols, or phenols). It is unlikely that the proportion of ketone 32 could be increased by the use of such solvents; instead, the anion of 35 would become irreversibly protonated, giving desoxybenzoin as the major product. Polar aprotic solvents, such as N,N-dimethylformamide or dimethylsulfoxide, tend to increase the proportion of O-alkylation[61,62]. The effect in this reaction was slight. Finally, use of volatile aprotic solvents such as benzene or p-dioxane gives slow desulfurization to form a product mixture very similar to that obtained by treatment of β-ketosulfide 31 with neat aminophosphine.

It was found that temperature has little effect on product distribution; the major effect is on reaction rate. This observation suggests that the rate-determining step is the attack of phosphorus on sulfur to give 35, or (less likely) that this step is fast and that the subsequent reactions of this intermediate all have similar thermodynamic parameters.

To test whether the α-phenyl group is required for desulfurization α-benzoylmethyl benzyl sulfide (39) was prepared and treated with aminophosphine 6a. Benzyl sulfide (43) (50%) was the only product isolable from the reaction. This ketosulfide reacted more slowly than the ketosulfides previously discussed; starting material (2%) was present even after heating for 3 hours at 150°. Acetophenone (30%) was the other major product; only a small amount of 1-benzoyl-2-phenylethane[65] (40) (5%) was produced.

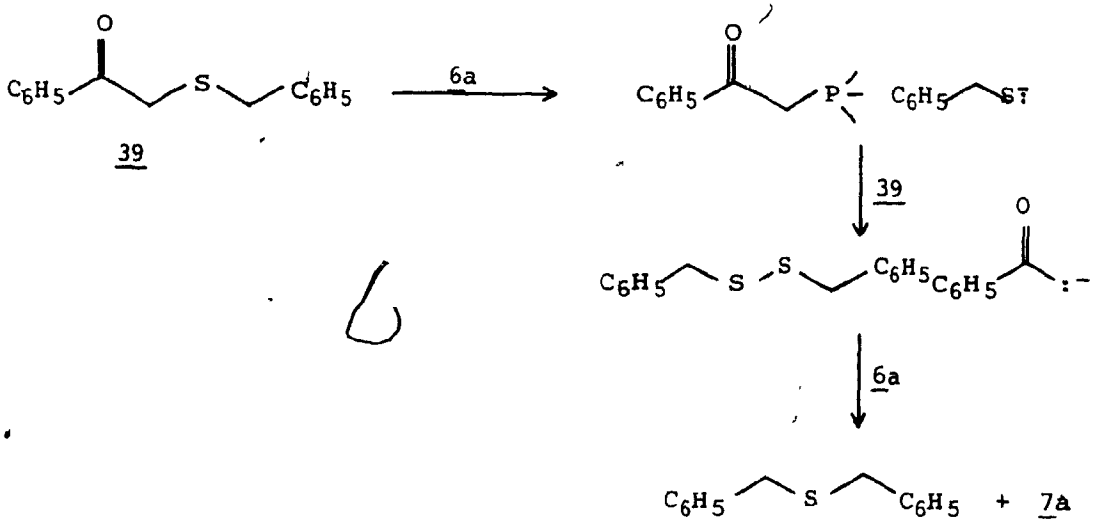
The observed products (7a, 40, and 43) could be rationalised by a mechanism similar to that invoked for the reaction of 27 and 31 with phosphine 6a (Scheme I). However, this pathway appears improbable, firstly because the anion of 41 would have to attack the starting material to displace mercaptide ion; this intermolecular reaction is not observed with the more stable desoxybenzoin anion formed from 27 and 31. Secondly, if ion pair 41 were formed, its fate should be similar to that of the corresponding ion pairs formed from these α-phenyl-β-ketosulfides; the formation of mercaptide ion from 39 should be encouraged by the presence of the α-phenyl moiety. Finally, ketone 42, which should be formed along with mercaptide ion, was not observed in the reaction mixture, precluding significant benzyl mercaptide formation by this route.

Benzyl mercaptide was shown to react with starting material 40 to give dibenzyl disulfide, which is known to desulfurize on treatment with 6a to give dibenzyl sulfide (43)[24]. A more plausible source of mercaptide ion is attack of phosphorus on carbon (Scheme II) in an S_N2 reaction analagous to that proposed for the reactions of trialkyl phosphites with aromatic thiocyanates[66]. Although this pathway contrasts both with our initial mechanism and the mechanism proposed by Borowitz[67] for the reaction of an analogous substrate, attack of phosphorus on carbon instead of sulfur explains the low yield of phosphine sulfide obtained. Such a direct substitution reaction would be encouraged by the reduction in crowding at the α-carbon atom produced by removal of the phenyl group. Removal of this group would also increase the activation energy for the attack of phosphorus on sulfur to displace the carbanion of 41, which is less stable than the anion of 26a and 35; this is probably the major factor governing the course of the reaction.



SCHEME I

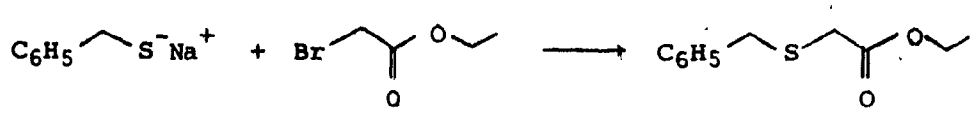
SCHEME II



Thus tris(dimethylamino)phosphine will desulfurize β-ketosulfides to give a variety of products; the nature of the reactions involved is highly dependent on the structure of the substrate. The results obtained are summarised in Table II.

β-Carbethoxysulfides

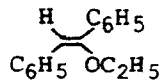
A carbanion can also be stabilized by the carbonyl group of an ester function. Ethyl-4-phenyl-3-thiabutanoate (44)[68-70] was chosen as an example of compounds that could give birth to this type of carbanion. It was prepared by the action of sodium benzyl mercaptide on ethyl bromoacetate:



44

TABLE II

The Reaction of Tris(dimethylamino)phosphine with β-Ketosulfides

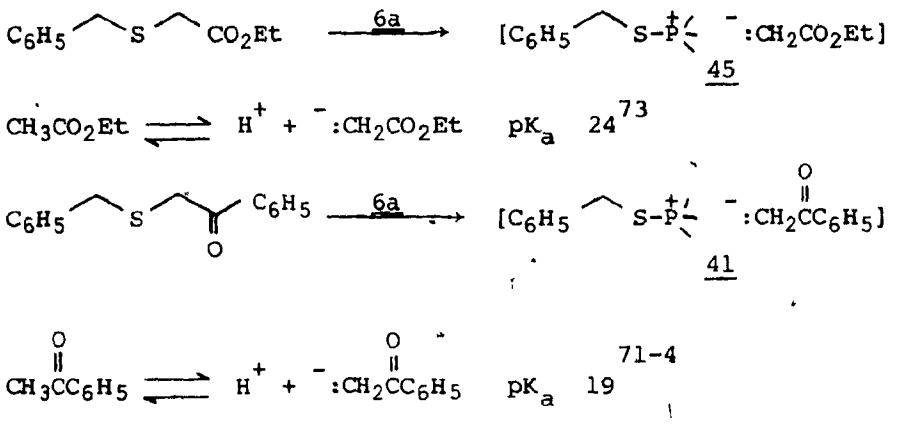
Starting Material				Products (%)					
	$R^1C(=O)CHSCH_2R^3$			$R^1C(=O)CHR^2CH_2R^3$	$C_6H_5C(=O)CH_2R^2$	$[(CH_3)_2N]_3P=S$ (7a)	Other		
number	R^1	R^2	R^3						
27a	C_6H_5	C_6H_5	C_6H_5	69[a] (43)[b]	22[a] (12)[b]	86[a]			
31	C_6H_5	C_6H_5	CH_3	31[a]	9[a]	67[a]		14[a]	unidentified material (33) 28[c]
43	C_6H_5	H	C_6H_5	5[a]	30[a]	47[a]	$(C_6H_5CH_2)_2S$	50[a]	

a- crude yield (estimated by partial isolation of product and/or quantitative vpc, nmr of impure fractions).

b- isolated pure.

c- percent of vpc integral trace.

This compound gave no reaction with neat tris(dimethylamino) phosphine (6a) even when the reaction mixture was maintained at high temperature for extended periods. The lack of reactivity of the ester can be rationalized by the relatively high pK_a associated with the anion which must be displaced by phosphine for desulfurization to occur (Table III).



The anion of 41 is more stable and is hence a better leaving group than the anion of 45. A nucleophilic substitution reaction involving attack of phosphine on the carbon atom α to the carbonyl group would be much slower for the ester than for the ketone.* Thus, the limit of the reaction of aminophosphines with sulfur-containing molecules emerges: aminophosphines will not displace groups with $pK_a \geq 20$. Where the pK_a is near 20, higher temperatures and neat reactants are usually required to effect displacement.

---

* It has been shown that α-chloroacetophenone undergoes halide exchange about eight times more rapidly than ethyl chloroacetate when treated with potassium iodide in acetone[81].

TABLE III

Reaction of Aminophosphines with RSXR

X	Product	Ref.	~pK$_a$ of RXH	Ref.	X	Product	Ref.	~pK$_a$ of RXH	Ref.
$-SO_2-$	a,b	25,26	2	75,76	-O-	a	31,32	17	2
$-\overset{O}{\overset{\|}{S}}-$	a,b	27,28	2	77	$-CH_2\overset{O}{\overset{\|}{C}}-$	b,c	-	19	71-3
-SS-	a	29	8	78	$-CH_2CO_2-$	d	-	24	73
$-N(\overset{O}{\overset{\|}{C}}R_2)$	a	30	9	79	-NR-	d	83	25	72
-S-	a	24	10	80					

a smooth desulfurization to give RXR in good yield.

b if X can provide an ambident anion (*e.g.* $-SO_2-$) more than one product may be formed.

c some desulfurization, competition from side reactions.

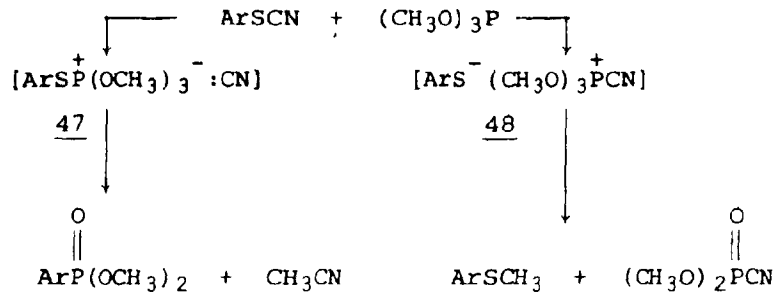
d no reaction.

The Reaction of Thiocyanates with Tris(dimethylamino)phosphines

Cyanide ion, like sulfide ion, is a good leaving group and a good nucleophile. It was thus felt that thiocyanates might readily be converted to nitriles on treatment with an aminophosphine. Early reports exist in the literature for the desulfurization of thiocyanates[82] and isocyanates[83] on treatment with trialkylphosphines, although few experimental data are given. More recently, the reactions of thiocyanates with trialkyl phosphates have been studied[66,84,85]; desulfurization accompanied by rearrangement was observed[84]. Sheppard obtained evidence that the rearrangement occurs through an ionic pathway and proposed the following mechanism:

$$(R^1O)_3P + R^2SCN \longrightarrow (R^1O)_2\overset{+}{P}SR^2 \quad \longrightarrow \quad (R^1O)_2\overset{O}{\overset{\|}{P}}SR + R^1CN$$
$$\qquad\qquad\qquad\qquad\quad \underset{O\text{-}R^1}{|} + \bar{C}N$$

Pilgram and Phillips[66], in a detailed study of the reaction of a number of aryl thiocyanates with trimethyl phosphite, found that instead of preferentially attacking sulfur to form intermediate 47, phosphorus can attack the carbon atom of the thiocyanate group, displacing a mercaptide ion to give intermediate 48.



Treatment of benzyl thiocyanate (49) with tris(dimethylamino)phosphine gave an immediate exothermic reaction which produced a deep red color, even at room temperature. Vapor phase chromatography indicated that the reaction mixture was extremely complex (at least 10 products). Preparative thin layer chromatography yielded only benzyl sulfide (44) and tris(dimethylamino)phosphine sulfide (7a) as isolable materials. A large quantity of brown oil was also obtained which contained many components. Vapor phase chromatography showed that benzyl cyanide was one of the major products.

The reaction was repeated in a variety of solvents. The yields of the major constituents of the mixture are shown below (Table IV). The rate of formation of the red color increased with the polarity of the solvent.

TABLE IV

The Reaction of Benzyl Thiocyanate with Aminophosphine 6a

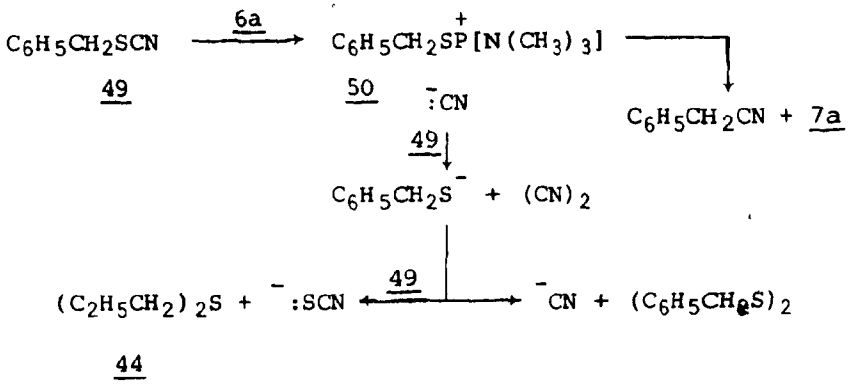
Solvent	Time[a] (min)	Products (%)[b]		
		$(C_6H_5CH_2)_2S$	$C_6H_5CH_2CN$	$[(CH_3)_2N]_3P=S$
none	40	45	9	32
acetonitrile	40	42	17	30
dichloromethane	30	25	22	38
p-dioxane	60	25	11	41
benzene[c]	130	21	6	28

a - time for the reaction mixture to attain constant composition (vpc).

b - determined by quantitative vpc.

c - reflux.

If the appearance of the red color provides an indication of the rates of the major reaction pathways, then it seems that an ionic mechanism, such as the one shown below, is in operation.



Benzyl cyanide could be formed by attack of the aminophosphine on the sulfur atom, followed by attack of the displaced cyanide ion on the intermediate phosphonium ion, in accord with the mechanisms of the other desulfurization reactions discussed. Attack of cyanide ion on this phosphonium ion may also give some isocyanide; although vpc did not rule out the existence of this compound, none was isolated.

If, instead of attacking the phosphonium ion, the cyanide ion attacks a second molecule of thiocyanate, it could displace mercaptide ion. The mercaptide ion could then attack starting material to give either the observed sulfide or dibenzyl disulfide. Again, vpc did not rule out the presence of the latter material, but it was not isolated from the reaction mixture; if formed, this compound could be desulfurized by aminophosphine to give dibenzyl sulfide[24].

Attack of 6a on the carbon atom of the thiocyano group is also possible[66]. Such an attack would lead to displacement of mercaptide ion, which could react with 49 to give dibenzyl sulfide.

3. EXPERIMENTAL

Common intermediates were obtained from commercial sources. Purification was unnecessary except where indicated in the text. Melting points were obtained on a Gallenkamp apparatus and are uncorrected.

Thin layer chromatographic analyses were performed on Eastman chromatographic sheets 6060 (silica gel with fluorescent indicator on poly(ethylene terephthalate) support; polyvinyl alcohol binder). Solvent systems used are indicated in the text.

Gas chromatographic analyses (vpc) were performed on an F & M Model 5750 Research Chromatograph equipped with a Perkin-Elmer Model 194B Printing Integrator. Two 6' x 1/8" stainless steel columns were used - 10% silicon gum rubber UC-W98 on Diaport-S (80-100 mesh) and SE-30 ultraphase (10% by weight) on Chromosorb W AW/DMCS (80-100 mesh).

Refractive indices were measured on a Carl Zeiss 38341 Refractometer at room temperature.

Infrared spectra were recorded on a Perkin-Elmer Model 257 Grating Infrared Spectrophotometer. Spectra were calibrated with the 3027 cm^{-1} and 1601 cm^{-1} bands of a polystyrene film reference.

Nuclear magnetic resonance (nmr) spectra were recorded on a Varian Associates T-60 Spectrophotometer. All data are given in parts per million relative to TMS (used as an internal standard). Solvents used are indicated in the text.

Mass spectra were recorded on an AEI-MS-902 Mass Spectrometer equipped with a direct insertion probe.

Preparation of β-Ketosulfides

α-Benzoyl-α-phenylmethyl Benzyl Sulfide (28a) was prepared by the method of Harpp and Mathiaparanam[59]; mp and mmp 70-71°; identical in all respects to an analytical sample kindly provided by Dr. P. Mathiaparanam.

α-Benzoyl-α-phenylmethyl Ethyl Sulfide (32) was prepared in a similar manner, mp and mmp 78-79.5°, identical in all respects (tlc, vpc, ir, and nmr) to a sample provided by Dr. P. Mathiaparanam.

α-Benzoylmethyl Benzyl Sulfide (40) was prepared by a modification of the method of Long[54]. Sodium hydroxide (2.0g, 0.05 mol) was dissolved in 50% aqueous ethanol (40 ml). Benzenethiol (6.2g, 0.05 mol) was added with shaking, followed by bromoacetophenone (10.0g, 0.05 mol). The mixture grew warm and a tan suspension was formed. After refluxing for one hour, the tan solid was removed by filtration and crystallized from ethanol to give a pale brown solid. Recrystallization gave colorless plates, mp 88-90° (lit.[54] mp 87°) (8.5g, 70%).

The Action of Tris(dimethylamino)phosphine on β-Ketosulfides

α-Benzoyl-α-phenylmethyl Benzyl Sulfide

(a) In the presence of a solvent

Refluxing a solution of α-benzoyl-α-phenylmethyl benzyl sulfide (28a) (0.318g, 1.0 mmol) and pre-distilled tris(dimethylamino)phosphine (6a) (0.16g, 1.0 mmol) in benzene or p-dioxane (1 ml) for 8 hours gave small amounts of desoxybenzoin as the major product (qualitative vpc). A similar result was obtained with dichloromethane, stirring for 24 hours at room temperature or refluxing for 12 hours.

(b) Without solvent

α-Benzoyl-α-phenylmethyl benzyl sulfide (28a) (1.00g, 3.2 mmol) and tris(dimethylamino)phosphine (6a) (0.510g, 3.2 mmol) were heated on an oil bath at 120°. After 30 minutes all starting material had been consumed (vpc). The mixture was then chromatographed on silica gel (60-100 mesh) using hexane (100 ml), hexane-dichloromethane mixtures (9:1, 100 ml; 4:1, 100 ml; 3:2, 500 ml; 1:1, 500 ml) and dichloromethane (100 ml) as eluents. The fractions collected were monitored by vpc. Separations were not completely efficient; however, combination of the first eluents and crystallization (ethanol) gave 1-benzoyl-1,2-diphenylethane (30a) (0.39g, 43%) as colorless needles, mp and mmp 119-120°; lit. mp 120-121°[60,86-88]. It was identical in all respects (vpc, tlc, ir, nmr) with an authentic sample. A later fraction was crystallized from aqueous ethanol to afford 0.075g (12%) of desoxybenzoin (29), mp and mmp 55-56°, identical in all respects to an authentic sample.

α-Benzoyl-α-deutero-α-phenylmethyl Benzyl Sulfide (28b)

β-Ketosulfide 28a (2.0g, 6.4 mmol) was crystallized from deuteroethanol (EtOD) to which a trace of sodium had been added. The product was dissolved in carbon tetrachloride (10 ml); the resultant solution was filtered and evaporated to give, after recrystallization (EtOH), the title compound 28b (1.4g, 70%) as colorless needles, mp 74-76°, with no detectable absorption in the nmr spectrum at δ 4.72, suggesting quantitative deuteration at the α-position.

A portion of this material (0.79g, 2.5 mmol) was mixed with tris(dimethylamino)phosphine (6a) (0.456g, 2.8 mmol) and heated on an oil bath at 150° for one hour. The resulting mixture was chromatographed to give: (a) 1-benzoyl-1-deuterio-1,2-diphenylethane (30b) (0.389g, 55%), after crystallization (EtOH) mp 121-123°, mmp with non-deuterated material 121-122°; identical to 30a by tlc and vpc; (b) $C_6H_5COCH_2C_6H_5$ (0.045g, 9%), mp 47-51°, pure by tlc (CCl_4) and vpc, containing 80% deuterium at the benzylic position (nmr, CCl_4); (c) a mixture of these two materials (0.130g) (tlc, vpc); and (d) tris(dimethylamino)phosphine sulfide (7a) (0.340g, 81%), identified by vpc and nmr.

α-Benzoyl-α-phenylmethyl Ethyl Sulfide (32)

α-Benzoyl-α-phenylmethyl ethyl sulfide (32) (0.128g, 0.5 mmol) and tris(diethylamino)phosphine (6a) (varying amounts) were mixed and heated on an oil bath for various periods of time at different temperatures. Virtually constant yields of 7a, 33, 34 and 35 were obtained in a reaction that was complete in about 10 min. (vpc).

The reaction was also examined using benzene, dioxane and dimethylformamide as solvents (1 ml) and 1 mmol of each of the starting materials. Yields varied only slightly with the solvent.

Isolation of Products

α-Benzoyl-α-phenylmethyl ethyl sulfide (32) (640 mg, 2.5 mmol) and tris(dimethylamino)phosphine (6a) (450 mg, 2.7 mmol) were heated on an oil bath at 150° for one hour. The resulting mixture was then chromatographed on silica gel (60-100 mesh, 60g) using hexane (500 ml) and

hexane-dichloromethane mixtures (9:1, 2 ℓ; 4:1, 2 ℓ; 7:3, 1 ℓ; 3:2, 1 ℓ; and 1:1, 1 ℓ) as eluents. The fractions collected were monitored by vpc. Separations were not completely efficient; however, the first fraction, a colorless oil (80 mg), was pure by tlc (hexane) and vpc; ν_{max} (liq. film) 2978, 1638, 1604, 1689, 1497, 1452, 1120 (v. broad), 925, 772 and 700 cm^{-1}; nmr gave signals (CCl_4) at δ 1.8-2.8 (multiplet, 10 H), 3.8 (singlet, 1 H), 6.1 (quartet, 2 H), and 8.7 (triplet, 3 H); ms showed P^+ at 224. This information indicates that the material is an enol ether, $C_6H_5CH = C(C_6H_5)OC_2H_5$. Identification of a trans-band in the ir[89] at 925 cm^{-1} suggests that this compound is trans-1-ethoxy-1,2-diphenylethylene (35)(14%). The second fraction was rechromatographed to give a sample of 1-benzoyl-1-phenylpropane 33 (61 mg, 11%) (vpc, tlc, nmr), after crystallization (EtOH) mp and mmp 49-52°: lit. 57°[88], 58°[90]); a mixture of 33 and 34 (160 mg) (vpc, tlc) was also obtained. Ketone 33 was also present in the next two fractions (vpc, tlc, nmr). Tris(dimethylamino)phosphine sulfide (7a) (327 mg, 67%) was isolated in a further fraction; pure by vpc and tlc.

α-Benzoylmethyl Benzyl Sulfide

α-Benzoylmethyl benzyl sulfide (40) (2.42g, 10 mmol) and tris(dimethylamino)phosphine (6a) (1.80g, 11 mmol) were heated on an oil bath at 150° for three hours. The resulting mixture was chromatographed on silica gel (60-100 mesh) (250g) using as solvents hexane (1.5 ℓ), hexane/dichloromethane mixtures (1:10, 1 ℓ; 1:9, 1 ℓ; 3:17, 1 ℓ; 1:4, 1 ℓ; 3:7, 1 ℓ; 2:3, 1 ℓ; 1:1, 1 ℓ; 7:3, 1 ℓ), dichloromethane (1 ℓ), chloroform (1 ℓ), ethyl acetate (1 ℓ) and methanol (1 ℓ). Efficient

separation proved impossible; however dibenzyl sulfide (540g, 50%) was isolated as yellow prisms, mp and mmp 47-49°, identical in all respects (tlc/benzene, vpc, ir, nmr) to an authentic sample of the sulfide.

Further fractions were obtained containing acetophenone, dibenzyl disulfide, 1-benzoyl-2-phenylethane (41)[65], starting material, and traces of other unidentified materials (vpc, tlc/cyclohexane or benzene, nmr).

Tris(dimethylamino)phosphine sulfide (7a) (911 mg, 47%) was isolated in an almost pure state. Large quantities of polar material containing many unidentified components were also obtained.

Ethyl 4-Phenylthiabutyrate (45)

(a) Synthesis

Benzenethiol (6.2g, 50 mmol) was added to a stirred solution of sodium hydroxide (2.0g, 50 mmol) in 50% aqueous ethanol (40 ml). Ethyl bromoacetate(8.4g, 50 mmol) was added and the mixture refluxed for 15 minutes. The ethanol was removed by distillation and the resulting suspension was washed with ether (3 x 25 ml). Combined ether extracts were washed with water (25 ml) and dried ($MgSO_4$). The ether was removed by distillation and the residual oil distilled to give ethyl 4-phenyl-3-thiabutyrate (45) (8.4g, 80%) as a colorless oil, bp 168-174°/15 mm (lit. 110°/1 mm.[68], 183-184°/50 mm.[69], 265°/760 mm [70])n_D^{20} 1.5356 (lit. 1.5355[69], 1.5352[70]); ν_{max} 3008 (C-H str), 1745 (C=O str), 1505 (aromatic C-C str), 1135 (C-O str), and 704 (aromatic C-H bend) cm^{-1}; nmr (CCl_4) gives signals at δ 7.44 (singlet, 5 H), 4.22 (quartet, 2 H), 3.90 (singlet, 2 H), 3.03 (singlet, 2 H) and 1.26 (triplet, 3 H).

(b) Action of Tris(dimethylamino)phosphine

A mixture of sulfide 45 and aminophosphine 6a (1 mmol of each) was heated for various times at different temperatures. No reaction occurred (vpc).

Benzyl Thiocyanate

Benzyl thiocyanate (149 mg 1 mmol) and tris(dimethylamino)phosphine (163 mg 1 mmol) were mixed. An immediate reaction ensued, turning the mixture deep red. Mixing these materials in methylene chloride (1 ml) or acetonitrile (1 ml) gave a similar result. When benzene (1 ml) was used as solvent the reaction was much slower; the mixture turned yellow, orange, then red.

The methylene chloride solution obtained in this manner was separated into five fractions by preparative tlc on silica gel (solvents: cyclohexane-ethyl acetate (1:1) then benzene).

Dibenzyl sulfide, identical to an authentic sample (vpc, tlc, nmr, ir), and tris(dimethylamino)phosphine sulfide (7a) (vpc, nmr), were isolated.

The other three fractions contained many components that were not identified, as they proved inseparable.

The reaction was then repeated in a variety of solvents; the product mixtures were analyzed for dibenzyl sulfide, benzyl cyanide and 7 by quantitative vpc, as described in Chapter 5.

REFERENCES

1. F. Wöhler, Annalen der Physik und Chemie, 12, 253 (1828).
2. S. Ogawa, M. Morita, K. Donome and K. Fujisawa, Jap. Pat. 23,937 (1967): Chem. Abstr., 69, 35919 (1968).
3. F. Sondheimer and D. Rosenthal, J. Amer. Chem. Soc., 80, 3995 (1968).
4. H. Wynberg and A. Bantjes, J. Org. Chem., 24, 1421 (1959).
5. A. Schönberg, Chem. Ber., 68, 163 (1935).
6. A. Schönberg and M.Z. Barakat, J. Chem. Soc., 892 (1949).
7. C.G. Moore and B.R. Trego, Tetrahedron, 18, 205 (1962).
8. S. Hayashi, M. Furukawa, J. Yamamoto and K. Hamamura, Chem. Pharm. Bull. Jap., 15, 1310 (1967).
9. J.G. Gleason, PhD thesis, McGill University, p.13 (1970).
10. C.G. Moore and B.R. Trego, J. Chem. Soc., 4205 (1962).
11. C.G. Moore and B.R. Trego, Tetrahedron, 19, 1251 (1963).
12. H.I. Jacobson, R.G. Harvey and E.V. Jensen, J. Amer. Chem. Soc., 77, 6064 (1955).
13. R.G. Harvey, H.I. Jacobsen and E.V. Jensen, J. Amer. Chem. Soc., 85, 1618 (1963).
14. R.S. Davidson, J. Chem. Soc. (C), 2131 (1967).
15. S.B. Hartley, W.S. Holmes, J.K. Jacques, M.F. Mole and J.C. McCoubrey, Quart. Rev., 17, 204 (1963).
16. C. Walling and R. Rabinowitz, J. Amer. Chem. Soc., 81, 1243 (1959).
17. C.Walling and R. Rabinowitz, J. Amer. Chem. Soc., 79, 5326 (1957).
18. D.E. Ailman, J. Org. Chem., 30, 1074 (1965).
19. R.D. O'Brien, J. Econ. Entomol., 50, 159 (1957).

20. A.E. Arbuzov and V.M. Zoroastrova, Izvest. Akad. Nauk. SSSR, Otdel. Khim. Nauk., 789 (1952); Chem. Abstr., 47,10461, 1953.

21. K. Pilgram, D. Phillips and F. Korte, J. Org. Chem., 29, 1844 (1964).

22. K. Pilgram and F. Korte, Tetrahedron, 21, 203 (1965).

23. D.N. Harpp, J.G. Gleason and J.P. Snyder, J. Amer. Chem. Soc., 90, 4181 (1968).

24. D.N. Harpp and J.G. Gleason, J. Amer. Chem. Soc., 93, 2437 (1971) and references cited therein.

25. D.N. Harpp and J.G. Gleason, Tetrahedron Lett., 1447 (1969).

26. D.N. Harpp, J.G. Gleason and D.K. Ash, J. Org. Chem., 36, 322 (1971).

27. J.E. McCormick and R.S. McElhinney, J. Chem. Soc., Perkin Trans. I, 2795 (1972).

28. D.N. Harpp and J.G. Gleason, unpublished results.

29. D.N. Harpp and D.K. Ash, Chem. Commun., 811 (1970).

30. D.N. Harpp and B.A. Orwig, Tetrahedron Lett., 2691 (1970).

31. D.H.R. Barton, G. Page and D.A. Widdowson, Chem. Commun., 1466 (1970).

32. D.N. Harpp and B.A. Orwig, unpublished results.

33. C.C.J. Culvenor, W. Davies and N.S. Heath, J. Chem. Soc., 282 (1949).

34. R.E. Davis, J. Org. Chem., 23, 1767 (1958).

35. N.P. Neureiter and F.G. Bordwell, J. Amer. Chem. Soc., 81, 578 (1959).

36. D.B. Denney and M.J. Boskin, J. Amer. Chem. Soc., 82, 4736 (1960).

37. D.C. Dittmer and S.M. Kotin, J. Org. Chem., 32, 2009 (1967).

38. (a) M. Roth, P. Dubs, E. Götschi and A. Eschenmoser, Helv. Chim. Acta., 54, 710 (1971).

(b) Y. Yamada, D. Miljkovic, P. Wehrli, B. Golding, P. Löliger, R. Keese, K. Müller and A. Eschenmoser, Angew Chem. Int. Ed., 8, 343 (1969).

39. R.W. Murray and M.L. Caplan, J. Amer. Chem. Soc., 91, 5358 (1969).

40. P.D. Bartlett and G.D. Mendenhall, J. Amer. Chem. Soc., 92, 210 (1970).

41. D.B. Denney, D.Z. Denney, B.C. Chang and K.L. Marsi, J. Amer. Chem. Soc., 91, 5243 (1969).

42. W. Adam, R.J. Ramirez and S.C. Tsai, J. Amer. Chem. Soc., 91, 1254 (1959).

43. F. Ramirez, N.B. Desai, B. Hansen and N. McKelvie, J. Amer. Chem. Soc., 83, 3539 (1961).

44. R. Rabinowitz and R. Marcus, J. Amer. Chem. Soc., 84, 1312 (1962).

45. P.D. Bartlett and S. Meguerian, J. Amer. Chem. Soc., 78, 3710 (1956).

46. A. Michaelis and R. Kaehne, Chem. Ber., 31, 1048 (1898).

47. A.E. Arbuzov, Zhur. Russ. Fiz. Chim. Obschestva, 38, 687 (1906).

48. G.A. Aksnes and D. Aksnes, Acta. Chem. Scand., 18, 38 (1964).

49. A.J. Burn and J.I.G. Cadogen, Chem. and Ind. (London), 736 (1963).

50. R.G. Pearson, H. Sobel and J. Songstad, J. Amer. Chem. Soc., 90, 319 (1968).

51. R.F. Hudson, "Structure and Mechanism in Organo-Phosphorus Chemistry" Academic Press, New York, 1965, p. 137.

52. See for example J. March "Advanced Organic Chemistry: Reactions, Mechanisms and Structure", McGraw-Hill, New York, 1968, p.142ff.

53. T.C. Whitner, Jr. and E.E. Reid, J. Amer. Chem. Soc., 43, 638 (1921).

54. L.M. Long, J. Amer. Chem. Soc., 68, 2159 (1946).

55. C. Rappe, "Mechanisms of Reactions of Sulfur Compounds", Intra-Science Research Foundation, Vol. 4 (1969), p.95

56. H. Böhme and W. Krause, Chem. Ber., 82, 426 (1949).

57. F. Krollpfeiffer and H. Hartmann, Chem. Ber., 83, 90 (1950).

58. G.A. Russell and E.T. Sabourin, J. Org. Chem., 34, 2336 (1969).

59. D.N. Harpp and P. Mathiaparanam, J. Org. Chem., 37, 1367 (1972).

60. S. Miyano and Y. Sako, Chem. Pharm. Bull. (Tokyo), 13, 1372 (1965).

61. W.J. LeNoble and J.E. Puerta, Tetrahedron Lett., 1087 (1966).

62. W.J. LeNoble and H.F. Morris, J. Org. Chem., 34, 1969 (1969).

63. N. Kornblum, P.J. Berrigan and W.J. LeNoble, J. Amer. Chem. Soc., 82, 1257 (1960).

64. N. Kornblum, P.J. Berrigan and W.J. LeNoble, J. Amer. Chem. Soc., 85, 1141 (1963).

65. R.Adams, J.W. Kern and R.L. Schriner, "Organic Syntheses", Collect. Vol. I, H. Gilman and A.H. Blatt, Eds., John Wiley & Sons, New York, N.Y. 1964, p.101.

66. K. Pilgram and D.D. Philips, J. Org. Chem., 30, 2388 (1965).

67. I.J. Borowitz and R. Virkhaus, J. Amer. Chem. Soc., 85, 2183 (1963).

68. K. Schlogl, F. Wessely and H. Woidich, Monatch Chem., 87, 425 (1956).

69. A. Ghavveau and R. Mathis-Noel, Ann. Fac. Sci. Univ. Toulouse Sci. Math. Sci. Phys., 25, 147 (1961): Chem Abstr. 60, 11885 (1964).

70. C. Berse and G. Dupuis, Can. J. Chem., 43, 2174 (1965).

71. J.B. Conant and G.W. Wheland, J. Amer. Chem. Soc., 54, 1212 (1932).

72. W.K. McEwan, J. Amer. Chem. Soc., 58, 1124 (1936).

73. R.G. Pearson and R.L. Dillon, J. Amer. Chem. Soc., 75, 2439 (1953).

74. R.E. Dessy, W. Kitching, T. Psarras, R. Salinger, A. Chen and T. Chivers, J. Amer. Chem. Soc., 88, 460 (1966).

75. R.R. Coates and D.T. Gibson, J. Chem. Soc., 442 (1940).

76. P. Rumpf and J. Sadet, Bull. Soc. Chim.Fr., 450 (1958): Chem. Abstr. 52, 14290 (1958).

77. Estimated value.

78. D.N. Harpp and D.K. Ash, unpublished results.

79. D.N. Harpp and T.G. Back, unpublished results.

80. J. Maurin and R.A. Paris, Compt. Rend., 232, 2428 (1951): Chem. Abstr. 45, 8857 (1951).

81. J.B. Conant, W.R. Kirner and R.E. Hussey, J. Amer. Chem. Soc., 47, 488 (1925).

82. A.W. Hofmann, Ann. Chem. Pharm., Suppl. 1, 53 (1861).

83. A.W. Hofmann, Ber., 3, 766 (1870).

84. W.A. Sheppard, J. Org. Chem., 26, 1460 (1961).

85. J. Michalski and J. Wieczorkowski, Bull. Acad. Polon. Sci., Classe 3, 4279 (1956); Chem. Abstr., 51, 4266 (1957).

86. F. Klingemann, Justus Liebigs Ann. Chem., 275, 50 (1893).

87. H. Fiesselmann and J. Ribka, Chem. Ber., 89, 27 (1956).

88. E.J. Cragoe Jr., A.M. Pietruszkiewicz and C.M. Robb, J. Org. Chem., 23, 971 (1958).

89. S.I. Miller, J. Amer. Chem. Soc., 78, 6091 (1956).

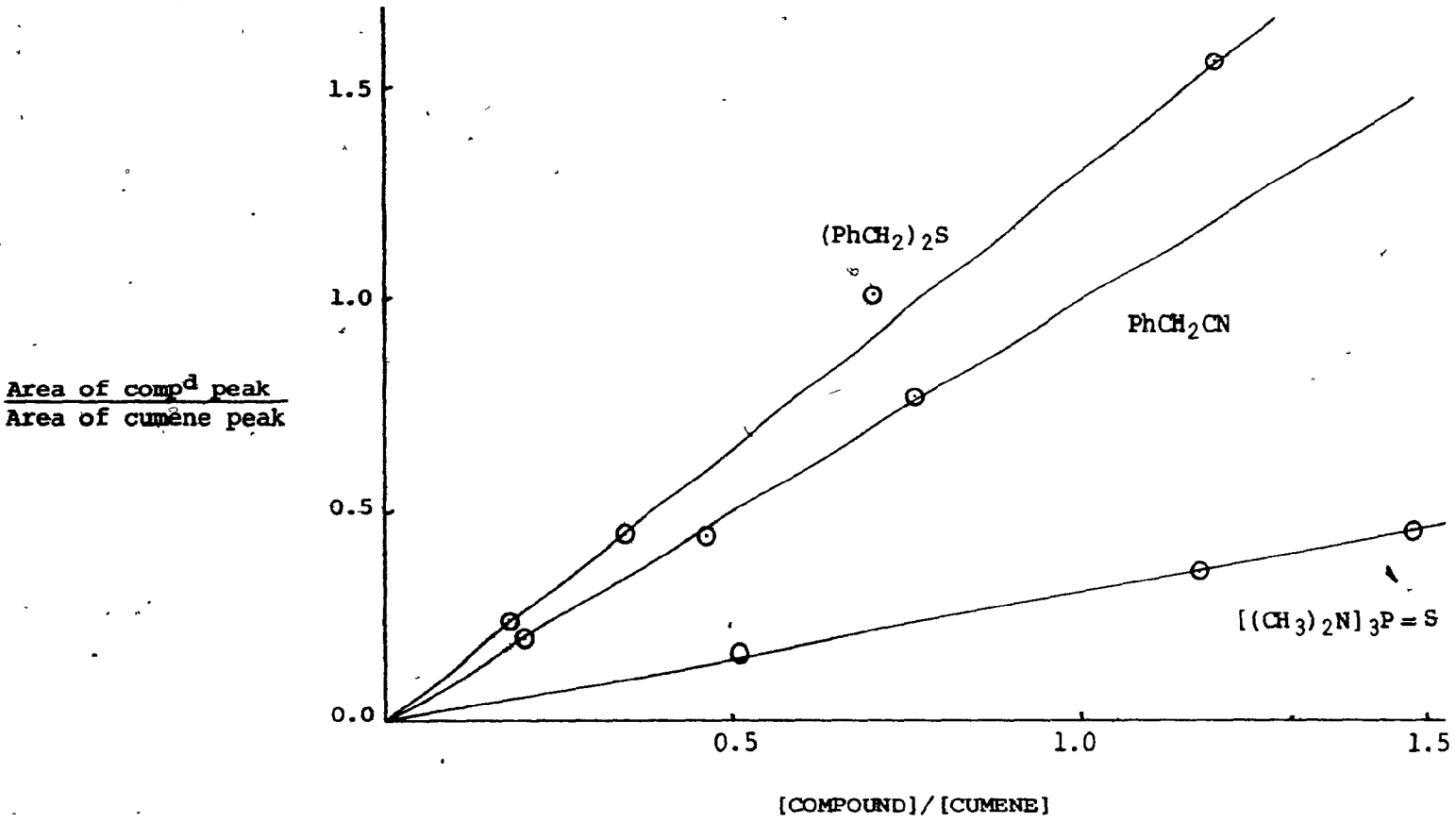
90. V. Meyer and L. Oelkers, Ber., 21, 1297 (1888).

91. D.N. Harpp and S.M. Vines, J. Org. Chem., 39, 647 (1974).

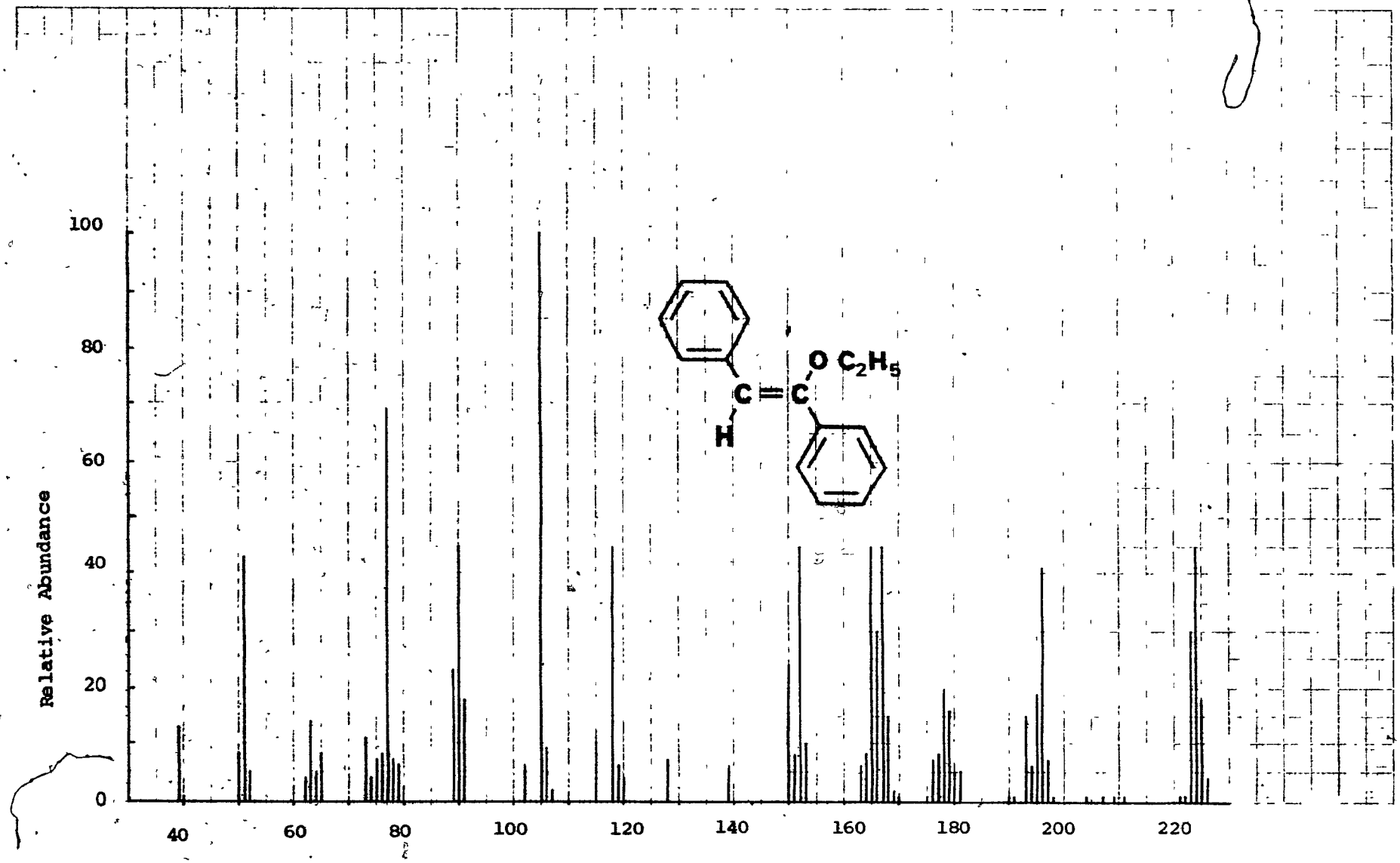
5. CALIBRATION OF THE GAS CHROMATOGRAPH

To determine the composition of the mixtures produced by reaction of thiocyanate with tris(dimethylamino)phosphine, the gas chromatograph was calibrated, using cumene as an internal standard. The response factors varied considerably with the flow rates of the gases, but were consistent if these were not altered. Typical calibration curves are shown in Figure I.

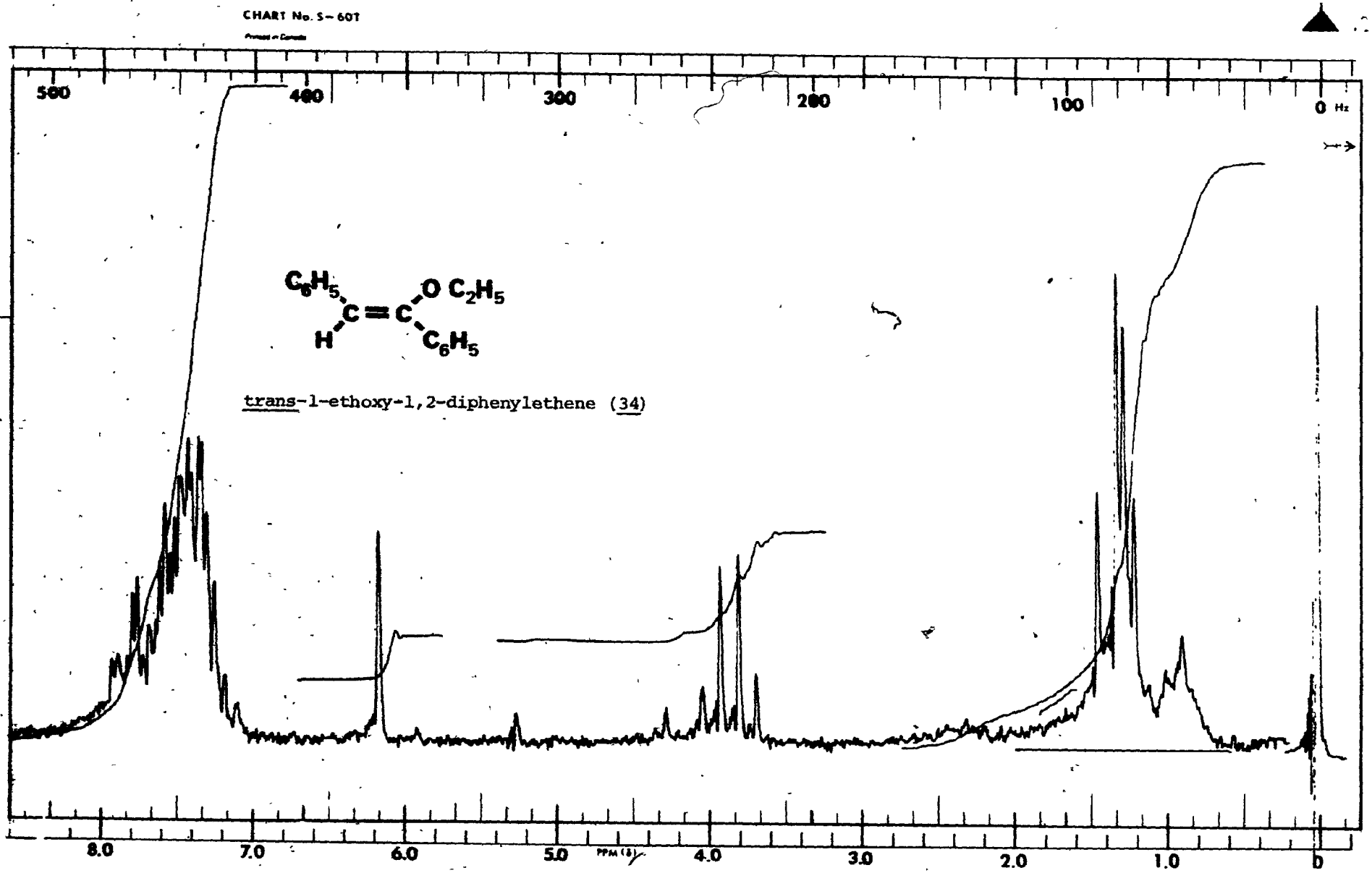
FIGURE I. Standardization of Gas Chromatograph



6. SPECTRA OF TRANS-1-ETHOXY-1,2-DIPHENYLETHENE



trans-1-ethoxy-1,2-diphenylethene (34)



trans-1-ethoxy-1,2-diphenylethene (34)

SUMMARY AND CLAIMS TO ORIGINAL RESEARCH

1. It has been demonstrated that tris(dimethylamino)phosphine desulfurizes a variety of β-ketosulfides in variable yields.

2. Phosphonium salt intermediates have been implicated in the reactions, which produce a variety of products, including ketones and enol ethers.

3. The scope of this type of the desulfurization reaction involving RSXR with aminophosphines has been determined; the phosphine will not desulfurize molecules with leaving groups of $pK_a \geq 20$.

4. It has also been demonstrated that benzyl thiocyanate is readily desulfurized by the aminophosphine in a highly complex reaction to afford benzyl cyanide and dibenzyl disulfide as the major products.

PART II

THE SYNTHESIS OF CHIRAL SULFUR COMPOUNDS

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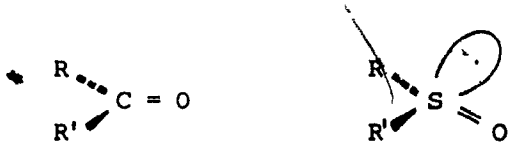
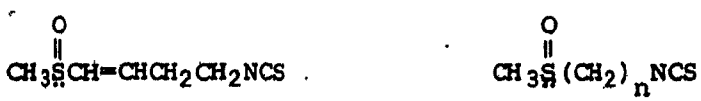
THE SYNTHESIS OF CHIRAL SULFUR COMPOUNDS

1. INTRODUCTION

Unlike carbon, sulfur has a number of stable oxidation states; divalent, tetravalent and hexavalent states of sulfur are all known. Tetravalent sulfur forms compounds that differ in their stereochemistry from the corresponding carbon compounds; while the carbonyl group is planar, the sulfoxide moiety is tetrahedral as the



lone pair of electrons on the sulfur atom acts as a fourth group attached to the central atom. Thus, the sulfoxide moiety can give rise to asymmetry in a molecule. The first known natural product in which optical activity results from chirality of an atom other than carbon was sulforaphene (1), a mustard oil isolated from the seeds of the black raddish (Raphanus sativus var. alba L.)[1]. Iberin (2, n=3)[2], sulforaphane (2, n=4)[3], and higher homologues containing five[4,5], six[6],



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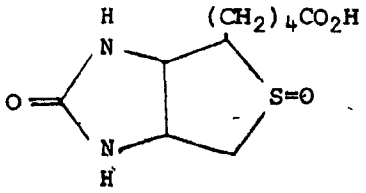
eight[7], nine[8], or ten[9] methylene groups have also been isolated from plant sources. All these compounds are levorotatory and exhibit similar optical rotatory dispersion curves[10]. Since an X-ray analysis of the thiourea derivative of natural (-)-iberin shows that the configuration at the sulfur atom is R, this configuration has been assigned to all the sulfoxide-isothiocyanates[11].

Other naturally occurring sulfoxides include biotin sulfoxide (3), found among the metabolites of Aspergillus niger and other penicilia[12,13], aliin (4, R = CH_2=$CHCH_2$-) found in garlic[14-17] and onion[20], cysteine methyl sulfoxide (4, R = CH_3-) isolated from cabbage[19], turnip[20,21] and other vegetables[19], and the cyclic sulfoxide 5 isolated



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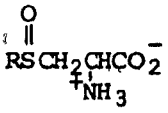

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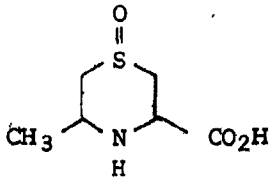

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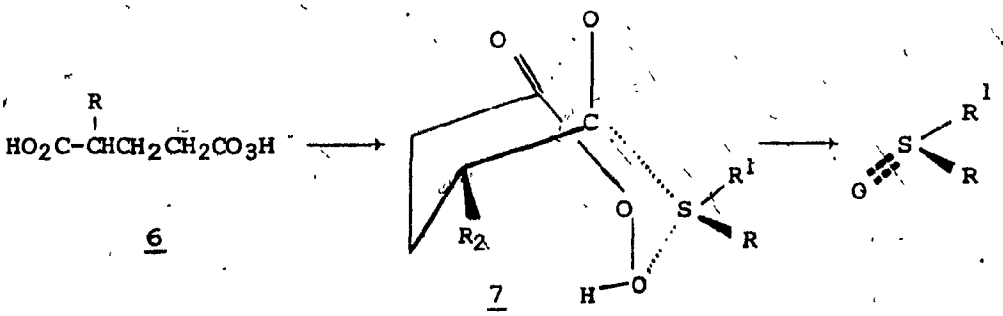
from onion[18,21]. The irritant principle of the onion is thought to be the sulfene, thiopropanal-S-oxide (CH_3CH_2CH=S=O), formed by the action of the enzyme allinase on cysteine S-(1-propenyl) sulfoxide[18,22].

Synthesis of Chiral Sulfoxides

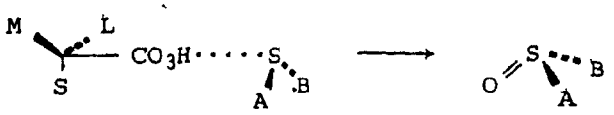
The standard method for the preparation of sulfoxides involves the oxidation of sulfides. Of the many reagents that have been used for this oxidation, sodium periodate[23,24] and 1-chlorobenzotriazole[25] are preferred since the problem of overoxidation to the sulfone is usually avoided. Diaryl sulfoxides may be prepared by oxidation with N-bromosuccinimide[26], but this reagent cleaves the C-S bond of alkyl sulfides[27].

A group of Yugoslavian workers demonstrated that oxidation of sulfides with γ-substituted monoperglutaric acids (6) produces sulfoxides possessing a small amount of optical activity[28,29]. They explained this optical induction by invoking a cyclic transition state (7) in which the substituent on the peracid and the bulkier group on the sulfide (R^1) prefer equatorial positions[29].



Italian workers led by Montanari showed that such partial stereospecific syntheses were not limited to oxidations with monoperglutaric acids[30-32], and proposed a mechanism[33] inspired by the work of Cram[34] and Prelog[35]. They argued that the product formed

depends on the relative sizes of the groups S (small), M (medium) and L (large) attached to the peracid, as well as the relative sizes of the groups on the sulfide. If the peracid attacks perpendicular to the sulfide molecule, transition state 8 or 9 will be preferred



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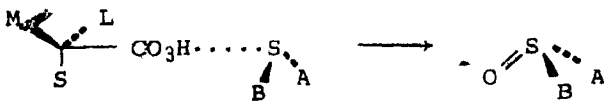

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depending on the relative sizes of the substituents, and hence the predominant configuration of the product can be predicted[33,36,37].

Mislow[38,39] took exception to these arguments, citing discrepant results and reminding that even a blind stab at the configuration of the sulfoxides has a 50% chance of being correct. After further studies of the reaction with a wide variety of peracids[32,40,41] Montanari replied that in every case where solvation effects and electrostatic interactions could be discounted with certainty, his theory predicts the correct configuration for the sulfoxides.

Although these reactions invariably give sulfoxides in greater than 80% yield, the products always have low optical purity[42-44]. Higher optical purities can be obtained by performing the reaction at low

temperatures, but optical purities over 10% are unusual[40,41]. Material of higher optical purity is obtained in lower yield (9-61%) when an aralkyl sulfide is oxidized in a culture of Aspergillus niger or with the insoluble material obtained by extracting the mold with acetone[45-47].

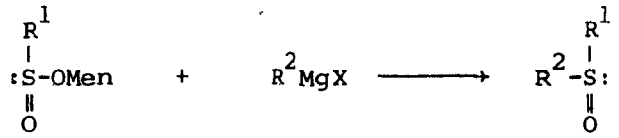
Sulfoxides of low optical purity (~6%) have also been obtained by the oxidation of sulfides with iodine in the presence of a chiral catalyst[48a]. Comparable optical induction has been observed in the electrochemical oxidation of sulfur with a "chiral electrode"[48b].

Several techniques exist for the optical enrichment of racemic sulfoxides. Partial oxidation with optically active peracids[49] or Aspergillus niger[50] and partial reduction with chiral thiols[51] or phosphorus thioacids[52a] give low yields of material with varying degrees of optical purity. Kagan has successfully employed chiral acid chlorides to help partially resolve sulfoxides[52b].

Sulfoxides have been resolved using platinum complexes[53,54]. A more elegant technique involves the preferential inclusion of one enantiomer into a chiral host molecule such as a β-cyclodextrin[55a]. Photochemical oxidation of sulfides using a chiral sensitizer preferentially gives one isomer[55b,c].

Optically pure sulfoxides were first prepared by Andersen[56,57]. Treatment of a menthyl sulfinate ester (10, R^2 = menthyl) with a Grignard reagent, according to the method of Gilman[58], gave a sulfoxide of high optical purity. Mislow and co-workers subsequently confirmed the high

stereospecificity of the reaction, demonstrating that inversion occurs at sulfur[38,59].



Other diastereomeric sulfinyl derivatives such as sulfinamides (11)[60,61] and heterocycles (12)[62] have also been treated with

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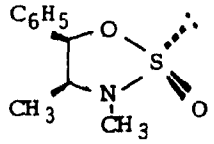


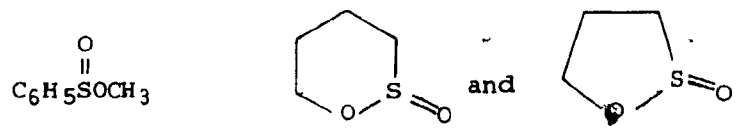
12

organometallic reagents, but none appears to have displaced sulfinate esters as the preferred precursors to chiral sulfoxides.

While this valuable synthetic technique can, in certain instances, give high yields of sulfoxide, close scrutiny of the literature reveals that the yield depends greatly on the structure of the target sulfoxide. Diaryl sulfoxides and aryl benzyl sulfoxides can often be prepared in good yield, usually greater than 80% and 70-84% respectively[38,63,64]. Yields of aralkyl sulfoxides appear to be more variable. Andersen obtained ethyl p-tolyl sulfoxide in 62% yield[56]; he also found that although reaction of menthol methylsulfinate with phenylmagnesium bromide gave a 91% yield of menthol, only a 60% yield of the crude methyl phenyl

sulfoxide was obtained[65]. Mislow and co-workers prepared a number of aralkyl sulfoxides[38]; only the yield for i-propyl p-tolyl sulfoxide is reported (22%). Methyl i-propyl sulfoxide and allyl methyl sulfoxide were also prepared, but no yields are given, suggesting that these are low*.

The simple sulfinate ester 13 and the cyclic sulfinate esters 14 and 15 were chosen as models for a study of this Grignard reaction.



13 14 15

Although these substrates differ somewhat from the menthyl esters, they should enable us to explore possible side-reactions in the reaction of sulfinate esters with Grignard reagents, and should give a clue to the problems that can arise. Analysis of the product mixtures showed that the reactions are complex. These compounds can give sulfoxides, but conditions must be very carefully selected, otherwise considerable quantities of sulfides and other impurities are produced. These impurities often remain tenaciously with the sulfoxide, making separation difficult and therefore severely limiting the synthetic utility of the reaction.

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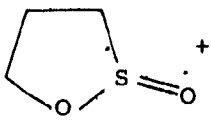
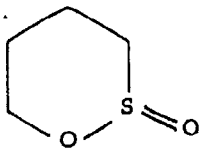
* An interesting indirect approach to the synthesis of chiral dialiphatic sulfoxides has recently been reported. Chiral aralkyl sulfoxides will react with an alkyl lithium to give dialiphatic sulfoxides; however neither the product yields nor optical purities is dependably high[66,67].

The nature of the sulfide formed as a by-product appears to depend on the structure of the intermediate sulfoxide and on the quantity of Grignard present. If the sulfoxide contains a phenyl group and a two-fold or greater excess of organomagnesium reagent is used, the sulfide formed generally corresponds in structure to the sulfoxide:

e.g.  + C_6H_5MgBr ⟶ $C_6H_5S(CH_2)_3OH$

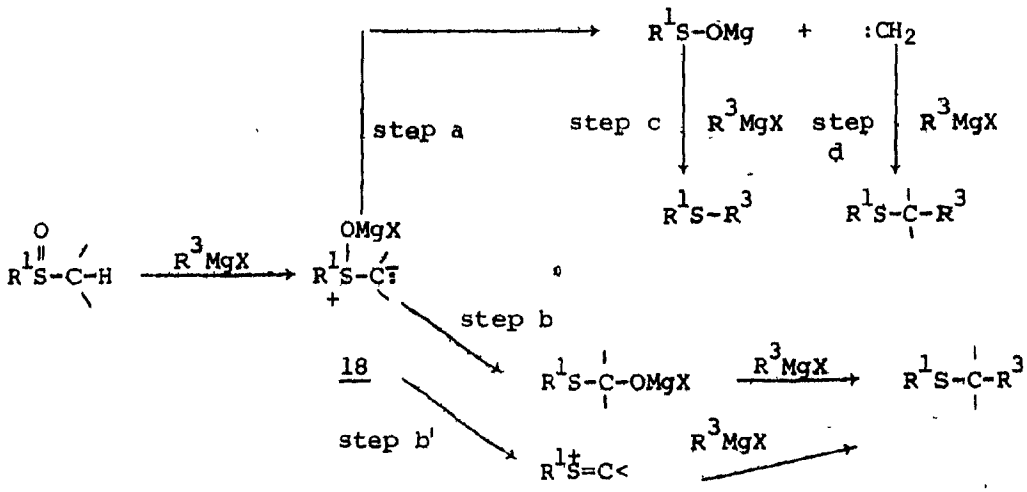
15 16

In other cases a sulfide corresponding to double addition of the Grignard reagent is observed:

e.g.  + CH_3MgBr ⟶ $CH_3CH_2S(CH_2)_4OH$

14 17

The reaction of sulfoxides with Grignard reagents has been shown to be exceedingly complex[69-72]; many products are formed, including sulfides of the type 16 and 17. Manya and co-workers[71,72] explained the formation of these compounds by proposing an intermediate sulfonium methylide 18 which can either eject a carbene fragment (step a) or rearrange in a similar manner to that proposed in the Pummerer rearrangement[73] (step b). Such an intermediate (18) could be present in the Grignard-sulfinate ester reaction.



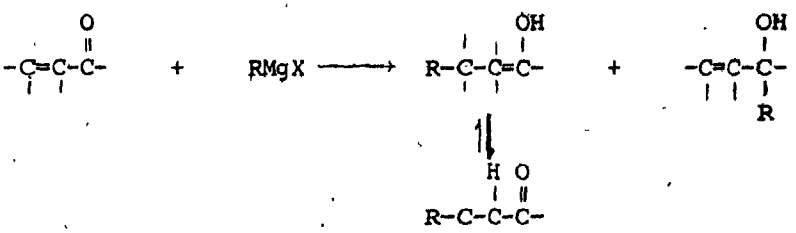
The sulfide corresponding in structure to the sulfoxide could then be formed from the sulfenate intermediate produced in step a. If the carbene fragment adds to this magnesium salt before step c, then the double addition product will be formed as shown in step d. The double addition product is the same as that produced by rearrangement of the sulfonium methylide 18 (step b) or the more probable elimination from 18 (step b'), followed by addition of the Grignard.

Lithium Organocuprates

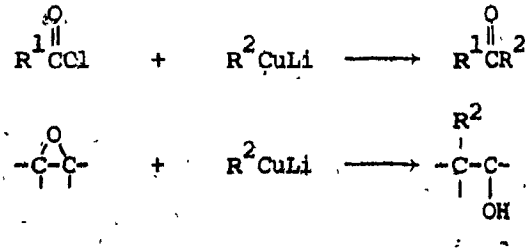
For many years copper-catalyzed reactions were unwittingly carried out by chemists using copper vessels for their reactions. The first stoichiometric organocopper reagents were prepared by Gilman, who isolated methylcopper while studying the catalysis of Grignard reactions by salts of copper and other heavy metals[74]. It is difficult to prepare pure methyl copper and other reagents with the stoichiometry RCu[75]. In contrast, ethereal solutions of compounds with the stoichiometry R_2CuLi can easily be made by adding two equivalents of organolithium reagent

to one equivalent of cuprous halide; the reaction is often self-indicating, obviating the need to standardize the lithium reagent[76].

Organocopperlithium reactions often parallel Grignard reactions, but the former are usually more specific. Thus, while Grignard reagents will add to an α,β-unsaturated ketone to give a mixture of the 1,2- and 1,4-products, the organocopper reagents give only the 1,4 addition product[77].



This selectivity has been exploited in the synthesis of ketones from acyl chlorides[78], and of alcohols from epoxides[79].



In this way materials which are unstable towards Grignard reagents can be isolated[79,80].

It was thought that the selectivity of the organocopperlithium reagents might apply to their reaction with sulfinate esters. If these reagents would convert sulfinate esters to optically pure sulfoxides without subsequent reduction, they would usefully improve the Andersen synthesis.

2. RESULTS AND DISCUSSION

Synthesis of Sulfinate Esters

Sulfinate esters can be prepared from a sulfinic acid and an alcohol in the presence of pyridine or potassium carbonate[81]. It has been reported that hydrochloric acid will catalyze the esterification[82] or hydrolysis[83] of sulfinate esters, as occurs with the corresponding carboxylate esters. The uncatalyzed esterification proceeds if water is removed by azeotropic distillation[84].

$$R^1SOH + R^2OH \longrightarrow R^1SOR^2 + H_2O$$

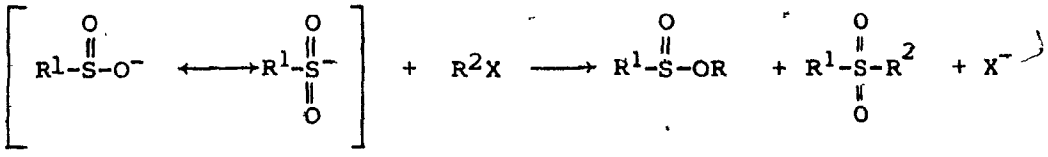
The esterification can also be effected with the coupling agent N,N'-dicyclohexylcarbodiimide (19)[85].

$$ArSOH + C_6H_{11}N{=}C{=}NC_6H_{11} \longrightarrow ArSOC(NC_6H_{11})(NHC_6H_{11}) \xrightarrow{ROH} RSOR + O{=}C(NHC_6H_{11})_2$$

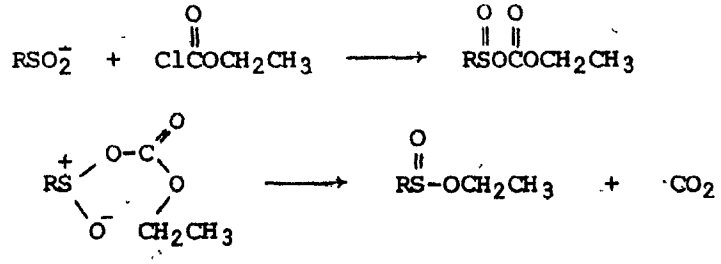
19

Methyl esters of arenesulfinic acids can be prepared by treatment of the sulfinic acid with diazomethane[86].

Nucleophilic attack of the sulfinate ion on alkylating agents could, in principle, give the sulfinate ester. However, in most cases the bidentate nature of this ion results in the formation of sulfone as the sole product, or a mixture of sulfone and the sulfinate ester[87].

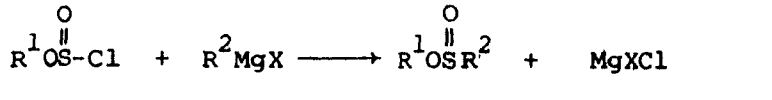


The reaction of the sulfinate anion with ethyl chloroformate[82] is a useful exception.



In a similar vein, sulfinate ions react with an alkyl chlorocarbonate in the presence of an alcohol to give the sulfinate ester containing the alkoxide group derived from the alcohol solvent[88].

Sulfinate esters are formed in several other reactions. Treatment of alkyl chlorosulfinates (20) with Grignard reagents[89], oxidation of disulfides[90,91] or thiols[92] with lead tetraacetate, thermal decomposition of sulfites[93-95], ozonolysis of sulfenate esters (21)[96], and cleavage of t-butyl sulfoxides with N-halosuccinimides[97] all give sulfinate esters.



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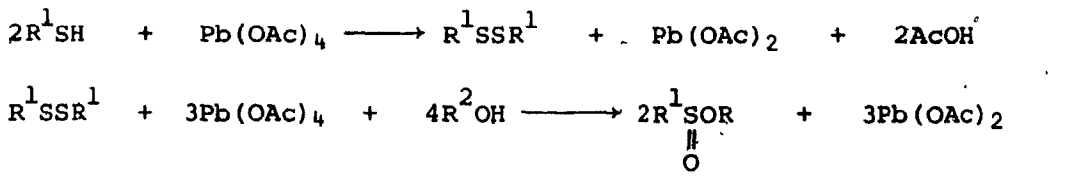

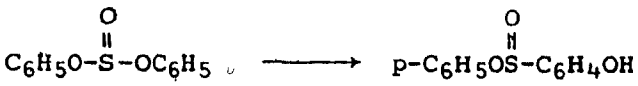

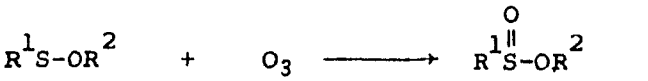

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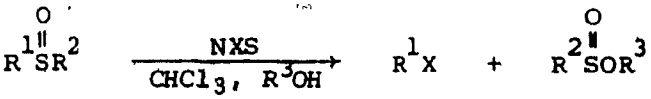
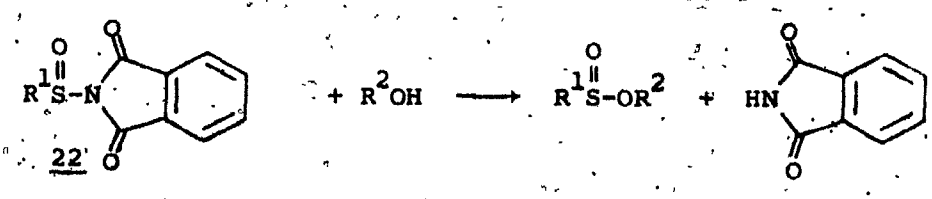


None of these reactions, however, gives good yields of sulfinate ester from readily available starting materials. A method developed by Douglass[98] in which a sulfinyl chloride reacts with an alcohol does not suffer from these drawbacks, although the sulfinyl chlorides are unstable and must be reacted *in situ*. A convenient and stable source of the sulfinyl moiety is provided by the sulfinyl phthalimides (22), a series of reagents developed by Harpp and Back[100,101]. These compounds react with alcohols or alkoxide ions to give sulfinate esters in near quantitative yield[101].



22

Reaction of Sulfinate Esters with Organocopperlithium Reagents*

The literature examination in the previous section shows that the Andersen synthesis is the best approach to optically pure sulfoxides. However, as yields obtained are often low, there is ample scope for improvement. If the poor yields in these syntheses can be ascribed to reduction of the sulfoxides, then simple sulfinate esters should provide good models for a study of lithium organocuprates as replacements for the Grignard reagents. Use of simple sulfinates as models has the further advantage in that a direct comparison can be made with the product analyses obtained previously for the Grignard reactions[68].

Methyl benzenesulfinate (13) was prepared by treatment of diphenyl disulfide with chlorine in the presence of acetic acid, followed by methanolysis of the intermediate sulfinyl chloride[98].

$$C_6H_5SSC_6H_5 + 2CH_3COOH + 3Cl_2 \longrightarrow C_6H_5\overset{O}{\overset{\|}{S}}Cl + 2CH_3\overset{O}{\overset{\|}{C}}Cl + 2\ HCl$$

$$C_6H_5\overset{O}{\overset{\|}{S}}Cl + CH_3OH \longrightarrow C_6H_5\overset{O}{\overset{\|}{S}}OCH_3$$

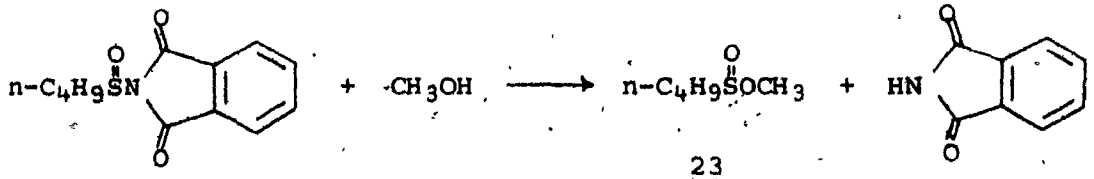
13

This sulfinate ester was treated with various quantities of lithium dimethylcuprate. After hydrolysis, analysis of the mixtures by vpc or nmr showed the presence of methyl phenyl sulfoxide and methyl phenyl sulfide, together with varying amounts of starting material. Altering

*This study, combined with a study of the reactions of sulfinate esters and Grignard reagents, has been submitted for publication[68].

the reaction times and temperatures indicated that an optimum yield of the sulfoxide was produced in a rapid reaction by treating one mole of the sulfinate with two moles of the organometallic reagent at low temperature (0° or below). Distillation of this mixture gave the sulfoxide in 59% yield, more than twice the yield of sulfoxide obtained from the Grignard reaction under optimum conditions (see below). The material was pure by tlc and vpc and indistinguishable from a sample of the sulfoxide prepared by oxidation of the sulfide. The sulfinate ester was not totally consumed if less than two moles of organometallic reagent were used.

Treatment of the sulfinate ester with lithium diethylcuprate or lithium diphenylcuprate gave sulfoxide as the major product (Table I). Similar results were obtained with samples of methyl n-butanesulfinate (23) prepared through the sulfinyl chloride[98] or the sulfinylphthalimide[101], and



23

with the sultines 14 and 15, prepared from the thiosulfonates 24 and 25 by desulfurization with tris(diethylamino)phosphine[102,103].

TABLE I Reaction of Sulfinate Esters with Lithium Organocuprates

$$R^2\overset{O}{\overset{\|}{S}}OR^3 + R^1_2CuLi \rightarrow R^2\overset{O}{\overset{\|}{S}}R^3 \text{ and other products}$$

Sulfinate Ester	$C_6H_5\overset{O}{\overset{\|}{S}}OCH_3$ (13)			$n\text{-}C_4H_9\overset{O}{\overset{\|}{S}}OCH_3$ (23)			14			Others			
R^1	Reaction Temp (°C)	Product	Yield (%)	Reaction Temp (°C)	Product	Yield (%)	Reaction Temp (°C)	Product	Yield (%)	Sulfinate Ester	Reaction Temp (°C)	Product	Yield (%)
CH_3-	0	$C_6H_5\overset{O}{\overset{\|}{S}}CH_3$[a]	59	0	$nC_4H_9\overset{O}{\overset{\|}{S}}CH_3$[a]	50	0	$CH_3\overset{O}{\overset{\|}{S}}(CH_2)_4OH$[b] (58)	59	10 R^2=C_6H_5	0	$C_6H_5\overset{O}{\overset{\|}{S}}CH_3$[c]	22
										R^3=p$CH_3(C_6H_4)$		$C_6H_5SCH_3$[c]	53
C_2H_5-	-78	$C_6H_5\overset{O}{\overset{\|}{S}}CH_2CH_3$[d]	36										
nC_4H_9-	-40	$C_6H_5SnC_4H_9$[a]	36	0	no isolable products								
				-30	$n\text{-}C_4H_9\overset{O}{\overset{\|}{S}}nC_4H_9$[c]	15							
				-78	$n\text{-}C_4H_9\overset{O}{\overset{\|}{S}}nC_4H_9$[d]	52							
C_6H_5-	0	$C_6H_5\overset{O}{\overset{\|}{S}}C_6H_5$[e]	50	-78	$C_6H_5SnC_4H_9$[a]	64	0	$C_6H_5\overset{O}{\overset{\|}{S}}(CH_2)_4OH$[f] (57)	32	15	0	$C_6H_5\overset{O}{\overset{\|}{S}}(CH_2)_3OH$[f] (56)	52
	-78	$C_6H_5\overset{O}{\overset{\|}{S}}C_6H_5$[e]	48										

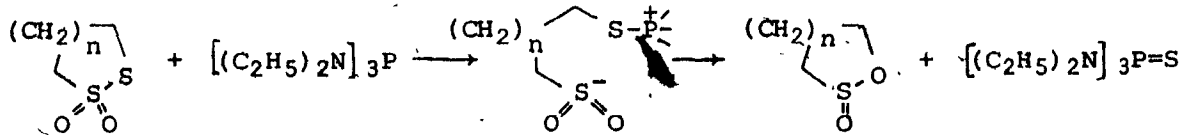
a - purified by distillation; b - purified by preparative tlc (silica, chloroform);

c - purified by column chromatography (silica, ethyl acetate) then Kugelrohr distillation at 100°/1 mm Hg;

d - purified by column chromatography (silica, ethyl acetate), distillation, then rechromatographed (dry column alumina) with benzene-pyridine (19:1) or 1,4-dioxane;

e - purified by column chromatography (silica, hexanes then chloroform);

f - purified by column chromatography (silica, ethyl acetate-cyclohexane (4:1), then methanol).



24, n=2

25, n=3

14, n=2

15, n=3

In most cases the yield of isolated sulfoxide was greater than that formed in the corresponding Grignard reaction. Furthermore, the organocopper reagents are more selective, and hence the sulfoxide will tolerate an excess. Treatment of 13 with a four molar excess of lithium dimethylcuprate gives methyl phenyl sulfoxide in 43% yield. The best yield of sulfoxide obtained from the corresponding Grignard reaction is 27%; treatment of 13 with 3.3 moles of Grignard reagent gives only sulfide.

The reaction of 23 with lithium di-n-butylcuprate clearly shows that sulfoxide formation is favoured at low temperatures; the reaction yielded over 50% of the target sulfoxide at -78°, although no product could be isolated at 0°.

Formation of Sulfides

In contrast with the Grignard reaction, sulfide formed by addition of two alkyl groups is not a significant product; in most cases less sulfide corresponding in structure to the sulfoxide was formed.

The reaction of 13 with lithium di-n-butylcuprate and 27 with lithium diphenylcuprate gave anomalous results; in both cases n-butyl phenyl sulfide was formed and no sulfoxide could be detected.

The sulfides could be formed by reduction of the sulfoxides in a manner similar to that proposed for the Grignard reactions. However, a pathway involving a sulfonium methylide intermediate (18) is unlikely since double addition products are not observed.

To determine unequivocally whether sulfide could arise from the sulfoxide, a number of sulfoxides were treated with lithium organocuprates. Most of the required sulfoxides could be prepared by oxidation of the sulfide with sodium periodate[24]. This reagent does not oxidize n-butyl phenyl sulfide; n-butyl phenyl sulfoxide was obtained from the sulfide by oxidation with m-chloroperbenzoic acid[104,105]. Treatment of the sulfoxides with lithium organocuprates (Table II) showed that reduction of the sulfoxide could not account for all the sulfide formed. For example, after treatment of n-butyl phenyl sulfoxide with lithium di-n-butylcuprate for an hour, 11% of the sulfoxide could be recovered, whereas only sulfide could be isolated from a 15 minute reaction with the sulfinate at the same temperature.

The sulfinate ester might be partially converted to the sulfenate ester (21), which could then react with the organometallic reagent to give

$$R^1\overset{O}{\overset{\|}{S}}OR^2 + R^3_2CuLi \longrightarrow R^1SOR^2 \xrightarrow{R^3_2CuLi} R^1SR^3$$

21

TABLE II Reaction of Sulfoxides with Lithium Organocuprates

$$R^1\overset{O}{\overset{\|}{S}}R^2 + R^3_2CuLi$$

Sulfoxide (1 mole)	$(R^3)_2CuLi$ R^3	Number of moles	Temp. (°C)	Time (hr)	Products $R^1\overset{O}{\overset{\|}{S}}R^3$	Others	(% Yield)
$C_6H_5\overset{O}{\overset{\|}{S}}C_6H_5$	C_6H_5-	2	0	3	94	-	
$nC_4H_9\overset{O}{\overset{\|}{S}}C_6H_5$	nC_4H_9-	2	-40	1	11	$nC_4H_9SC_6H_5$	80
$CH_3\overset{O}{\overset{\|}{S}}C_6H_5$	CH_3-	2	0	3	49[a]	$CH_3SC_6H_5$	11
						$C_6H_5\overset{O}{\overset{\|}{S}}CH_2CH_2\overset{O}{\overset{\|}{S}}C_6H_5$[a] (26)	10
						$C_6H_5SCH_2CH_2SC_6H_5$ (27)	3
$nC_4H_9\overset{O}{\overset{\|}{S}}CH_3$	CH_3-	2	0	3	88		

a – isolated as sulfone.

the sulfide. Methyl benzenesulfenate (21, $R^1=C_6H_5$, $R^2=CH_3$) prepared by the method of Lecher[106], reacted rapidly and smoothly with lithium dimethylcuprate to give methyl phenyl sulfide in good yield. However, this pathway does not permit an explanation of the anomalous reactions that produce n-butyl phenyl sulfide (Table I).

Two interesting by-products were isolated in low yield from the reaction of methyl phenyl sulfoxide with lithium dimethylcuprate. These were 1,2-di(phenylsulfinyl)ethane (26, $R=C_6H_5$) isolated as the disulfone, and 1,2-di(phenylthio)ethane (27, $C_6H_5SCH_2CH_2SC_6H_5$). Enantiomeric disulfoxides 26 have previously been prepared in good yield by the copper-promoted dimerization of the α-carbanion 28[107].

$$RS(O)CH_3 \xrightarrow[\text{base}]{\text{strong}} RS(O)CH_2^- \quad (28) \xrightarrow[\text{salt}]{\text{Cu}} RS(O)CH_2CH_2S(O)R \quad (26)$$

Aryl Sulfinate Esters

In the reactions of sulfinate esters with organocopper reagents, considerable quantities of material remain unaccounted for. While 94% of a sample of diphenyl sulfoxide could be recovered after treatment with lithium diphenylcuprate for an extended period of time (Table II), it proved impossible to isolate the sulfoxide in yields greater than 50% from the reaction of methyl benzenesulfinate (13) with lithium diphenylcuprate. The only other organic material isolated in these reactions was biphenyl, a decomposition product of the lithium and copper-lithium reagents. The sulfinate ester might be reacting with the organocopper reagent in the following way:

$$R^1S(O)OR^2 \ (10) + R^3_2CuLi \longrightarrow R^1SO^- \ (29) + R^2\text{-}R^3 + R^3Cu$$

If this occurs, the sulfinate anion (29) would be difficult to detect in the complex mixture of inorganic salts produced in the reaction. Treatment of a sulfinate ester in which R^2 is an aryl group (*e.g.* 10) with an organocopper reagent should give a higher yield of sulfoxide than that obtained with the corresponding alkyl ester. However, reaction of p-tolyl benzenesulfinate (10, R^1=C_6H_5, R^2=p-$CH_3C_6H_4$-) with lithium dimethylcuprate gave methyl phenyl sulfoxide in low yield (22%). This may merely reflect the instability of the aryloxy sulfinate esters. Although it proved possible to prepare p-tolyl benzenesulfinate in good yield by the reaction of phenyl sulfinylphthalimide with the sodium salt of p-cresol, the ester decomposed on standing overnight at -20°;

$$NaH + p\text{-}CH_3C_6H_4OH \longrightarrow p\text{-}CH_3C_6H_4O^-Na^+$$

$$p\text{-}CH_3C_6H_4O^-Na^+ + C_6H_5SN(C_8H_4O_2) \longrightarrow C_6H_5SOC_6H_4CH_3\text{-}p$$

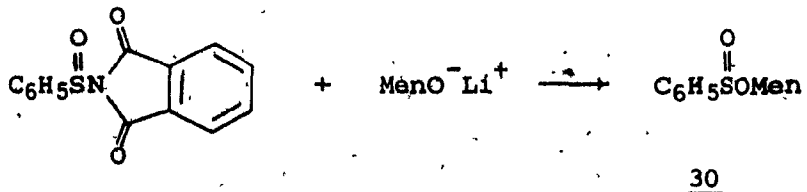
attempts to distil or chromatograph it also caused its decomposition to a brown tar. This observation is corroborated by Baarschers and Krupay[108], who unsuccessfully attempted to prepare phenyl methanesulfinate (10, R^1=CH_3, R^2=C_6H_5).

Stereochemistry

It has been shown that organocopper reagents are more convenient than Grignard reagents, and that they give higher yields of sulfoxide on reaction with sulfinate esters. If the reactions are stereospecific,

then they would be the preferred reagents for the synthesis of chiral sulfoxides.

(-)-Menthyl (-)-(S)-benzenesulfinate (30) was prepared by treatment of phenyl sulfinylphthalimide with lithium menthoxide.



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Treatment of this material with lithium dimethylcuprate gave methyl phenyl sulfoxide (16%) with a high degree of optical activity ($[\alpha]_D$ = 134°). Vapor phase chromatography indicated that the sulfoxide was only 95% pure despite extensive purification. The sulfoxide had been isolated by open column chromatography; further purification was accomplished by thin layer chromatography followed by Kügelrohr distillation. Reported values of the optical rotation of methyl phenyl sulfoxide, prepared from a pure diastereomer of a sulfinyl compound, vary from 128°[62] to 149°[109]. While this may reflect in part the degree of stereospecificity of the reactions invoked, it must also be an indication of the problems which arise in removing impurities from the sulfoxides, which are often hygroscopic oils or solids with low melting points.

Numerous reports in the literature describe methods of identifying sulfoxides. These couple with our results to reflect the perversity of these compounds when most classical methods of separation are attempted. When chromatographed on silica or alumina, sulfoxides

tend to 'tail'[110,111] and separation by vapor phase chromatography is not usually feasible since they often decompose rapidly above 100°[112-4]. Pure samples can only be obtained after painstaking chromatographic separations coupled with repeated distillation. This seemed to be an ideal problem to which the modern technique of high efficiency liquid chromatography (helc) could be addressed.

Helc offers four modes of separaton:-

Normal phase chromatography in which the nonpolar moving phase elutes material from a polar stationary phase (usually silica or alumina).

Reversed phase chromatography in which a polar solvent elutes material from a nonpolar stationary phase (in modern packing materials, this stationary phase is often silica to which hydrocarbon groups are bonded).

Gel permeation chromatography (gpc) in which molecules are separated according to size in a partially crosslinked, irregular gel.

Ion exchange chromatography, a technique used to separate very polar materials.

Although samples of sulfoxides could be separated on normal phase columns, it was found that this technique was limited to very small loadings, otherwise serious 'tailing' occurred. This evidence confirmed that normal phase chromatography (on silica or alumina) is not ideally suited to the purification of these mixtures. Examination of these materials by gpc showed the presence of high molecular weight impurities; perhaps these partially cause the 'tailing' phenomenon.

Reversed phase chromatography of a reaction mixture containing sulfoxide on C_{18}-Porasil (silica to which C_{18} hydrocarbons have been bonded) gave a major symmetrical peak on elution with tetrahydrofuran-water mixtures (3:1 to 20:1); the presence of other minor materials was usually indicated by the ultra-violet detector. Analysis of the sulfoxides was eventually accomplished under these conditions, which gave symmetrical peaks for analytical work and clean samples of the sulfoxides from preparative runs.

A careful reading of the literature suggested that (-)-menthyl (-)-(S)-p-toluenesulfinate should be far easier to isolate than the corresponding phenyl compound (20). Treatment of this material with lithium organocuprates showed that a stereospecific reaction occurs, giving moderate yields of sulfoxide, with inversion at sulfur (Table III). Thus this reaction constitutes a more efficient, convenient route to chiral sulfoxides.

Treatment of (-)-menthyl (-)-(S)-p-toluenesulfinate with lithium di-n-butylcuprate gave a mixture that was complex. Menthol was the only component that was isolated and identified. This result is in accord with those obtained when methyl benzenesulfinate reacts with this reagent.

Sulfinimides

The Andersen synthesis might be further improved by supplanting the menthol sulfinate esters with other diastereomeric sulfinyl derivatives. Sulfinimides (22), a potential source of such reagents, would have several advantages over the esters. The sulfinimides can conveniently be

TABLE III

Reaction of Menthyl Sulfinates with Lithium Organocuprates; Synthesis of Chiral Sulfoxides

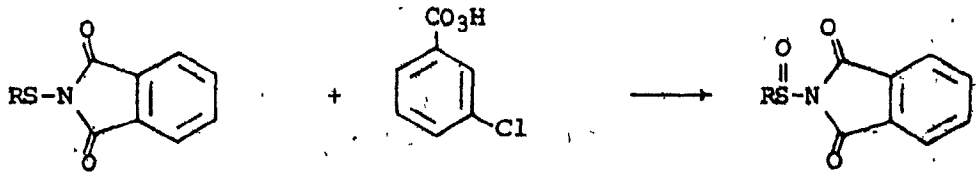
$$R^1\overset{O}{\overset{\|}{S}}OMen + R^3CuLi \longrightarrow R^1\overset{O}{\overset{\|}{S}}R^3$$

R^1	R^3	Yield %	$[\alpha]_D$	$[\alpha]_D^{lit}$	Optical purity %
C_6H_5	CH_3	16	+ 133.9°	+ 146°[a]	96
$pCH_3C_6H_4$	CH_3	55	+ 143.2°	+ 145.5°[b]	99
$pCH_3C_6H_4$	C_6H_5	59	+ 21.8°	+ 22°[a]	100

a - Highest value in the same solvent.

b - For literature values, see experimental section page 119.

prepared from readily available thioimides* (31) by oxidation with m-chloroperbenzoic acid[100]. The thioimide intermediates (31) appear



31 22

to have an indefinite shelf life (several years) in contrast to the menthol sulfinate esters. (The melting point of a pure sample of menthol p-toluenesulfinate decreased from 104-106° to 82-92° after six months in an airtight vial; during this period the sample turned brown and developed an odor of menthol). Another advantage of the sulfinimides is that they are usually solids with high melting points; in contrast, the esters of low molecular weight sulfinic acids are often oils that are difficult to purify[62].

A further advantage of sulfinimides is that the imide function is a better leaving group than the alkoxide ion from a sulfinate ester or the amide ion from either a sulfinamide (11) or the heterocyclic system 12. Resolution of a sulfinimide with a chiral centre in the imide moiety might allow formation of sulfoxides under milder conditions (lower temperatures and shorter reaction times), thus minimizing reduction. In addition, this better leaving group could expedite the

* A greater degree of consistency would be achieved if compounds having the structure 31 were called sulfenimides. However, this term has been used to denote compounds with the formula RS-NH-SR. In order to avoid confusion compounds having the structure 31 are best named N-(alkyl or arylthio)imides[115].

synthesis of optically pure sulfinate esters and sulfinamides with sulfur as the sole chiral centre. Sulfinate esters of very low optical purity (1-2%) have been prepared by the transesterification of a menthol ester with a non-chiral alcohol[81], or by oxidation of a sulfenate ester with a chiral peracid[116,117]. Hydrolysis of methanesulfinyl chloride under mild conditions gives a crystalline sulfinic acid containing sulfur atoms of only one chirality (by X-ray crystallography), but attempts to carry out a stereospecific esterification of this material failed[118]. More recently sulfinate esters of higher optical purity (10-45%) have been prepared by reaction of a sulfinyl chloride with achiral alcohols in the presence of optically active tertiary amines[119]. Sulfinate esters can be partially resolved by inclusion into β-cyclodextrins[120]; this technique is limited, since in most cases material of low optical purity is obtained. In addition, the β-cyclodextrins catalyze hydrolysis of these esters.

The reactions of a number of sulfinimides with lithium organocuprates were examined (Table IV) to determine whether they were cleaner than the sulfinate ester reactions. The sulfinimides were prepared by oxidation of the corresponding thioimides[101]. These were prepared from the sulfenyl chlorides by a modification of the method of Kittleson[121-123] (thiophthalimides) or by a modification of the procedure of Abé and co-workers[124] (thiosuccinimides):

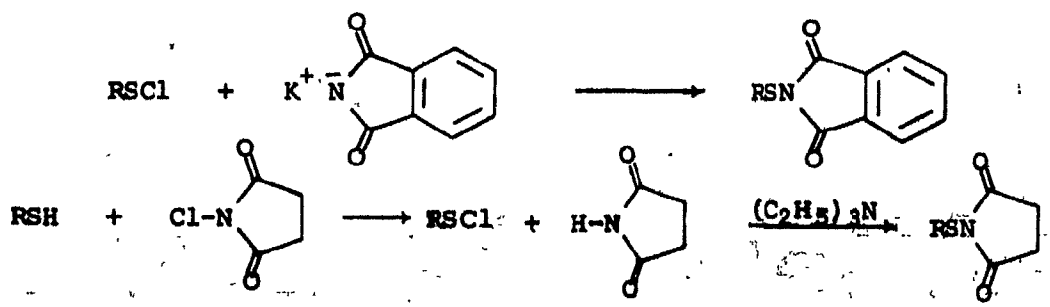
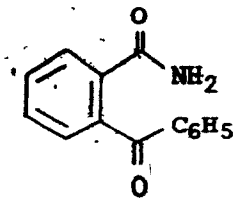


TABLE IV

Reaction of Sulfinimides with Lithium Organocuprates

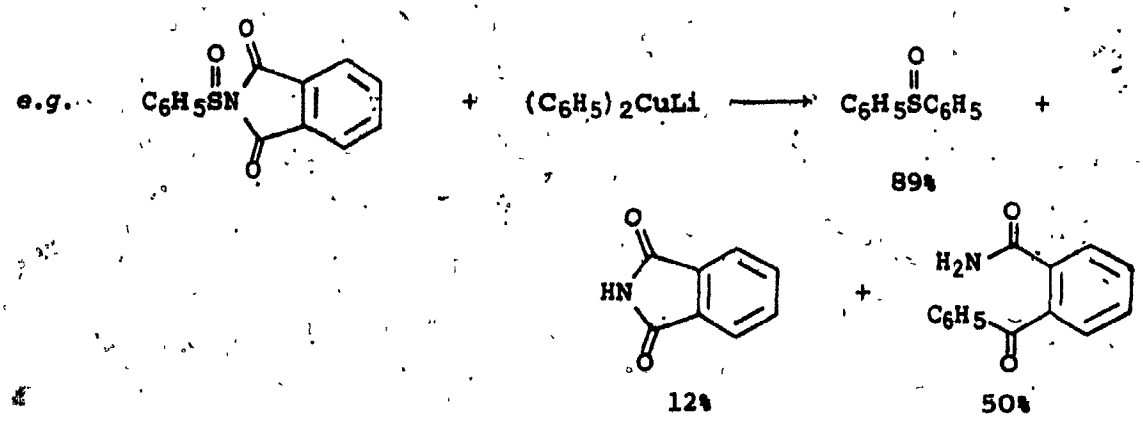
$$R^1\overset{O}{\overset{\|}{S}}\text{-Imide} + R^2_2CuLi$$

R^1	Imide	R^2	Temp (°C)	Yields (%) $R^1\overset{O}{\overset{\|}{S}}R^2$	Imide	R^1SR^2	Others
C_6H_5	Phthalimide	CH_3	0			17	
		C_6H_5	-40	89	12		 50
C_6H_5	Succinimide	CH_3	0	24	17	14	
			-78	90			
		C_6H_5	-78	75			$C_6H_5\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}NH_2$ 10
		n-C_4H_7	-78	80		14	
$C_6H_5CH_2$	Succinimide	CH_3	0	29		2	

Although treatment of N-(phenylthio)succinimide with lithium dimethylcuprate gave poor yields (24%) of methyl phenyl sulfoxide at 0°, reaction at -78° gave a 90% yield of the crude sulfoxide which was readily purified by distillation or column chromatography.

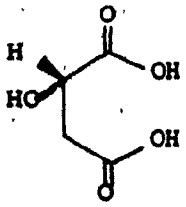
In all cases examined (Table IV), yields of sulfoxide were found to be higher than those obtained from sulfinate ester. n-Butyl phenyl sulfoxide, which was not obtained from reaction of sulfinate esters with organocopper reagents, was produced in greater than 50% yield from phenyl or butysulfinimides.

Only minor amounts of sulfide were produced in these reactions. The major by-product was an amide arising from ring opening of the imide. This reaction does not appear to reduce the yield of sulfoxide.



Chiral Imides

If the reaction of a lithium organocuprate with a sulfinimide is to provide a route to chiral sulfoxides, an optically active imide must be incorporated into a series of sulfinimides. A variety of chiral imides derived from alkyl or aryl succinic acids are described in the literature, but in most cases the succinic acid precursors are commercially available only as the racemic mixture which must be resolved by repeated crystallization of their strychnine or brucine salts[125,126]. This procedure is not compatible with the practical requirement that the chiral imide be available in large quantities. According to a recent report[127], optically pure malic acid (32) and tartaric acid (33) can be converted to their imides; these acids are commercially available, since they can be obtained from natural sources.



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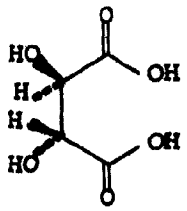

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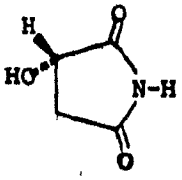

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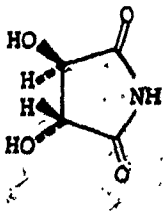
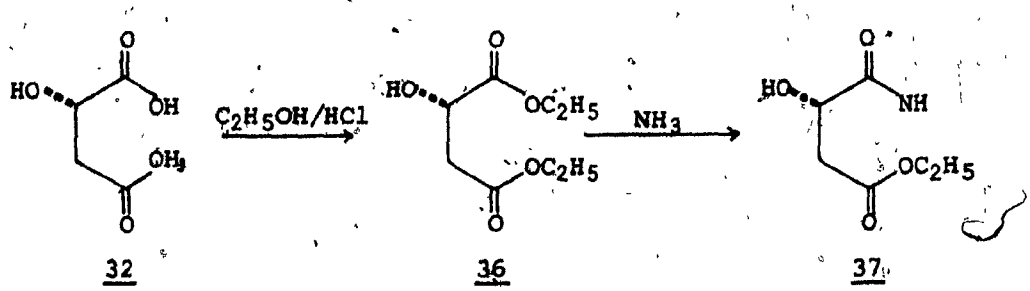


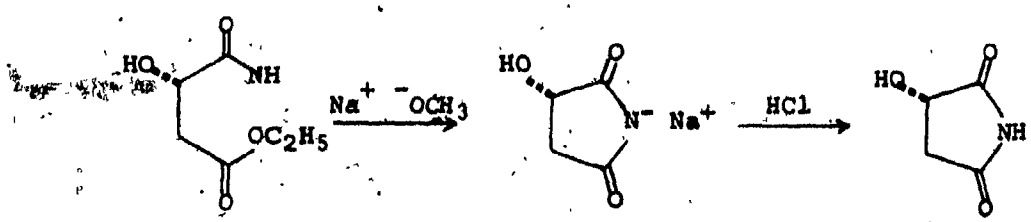
35

(-)-(S)-malimide (34) is prepared by treatment of an amido ester of (-)-(S)-malic acid (32) with sodium methoxide in benzyl alcohol. A literature dredge revealed that Pasteur had prepared the amido ester precursor β-ethyl-α-(-)-(S)-malamate (37) by treating diethyl malate (36) with ammonia[128]. This reaction yielded only 8-15% of the amido ester; the remaining ester could be recovered and recycled. A more

convenient one-step synthesis of the imide 34 (from the diester 36) was developed. A methanolic solution of the diester (36) is treated



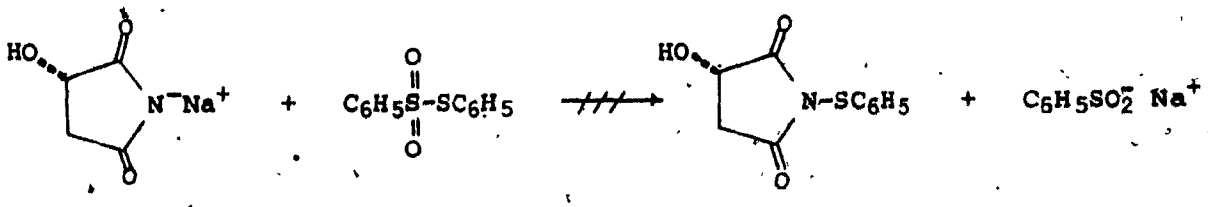
32 36 37



37 38 34

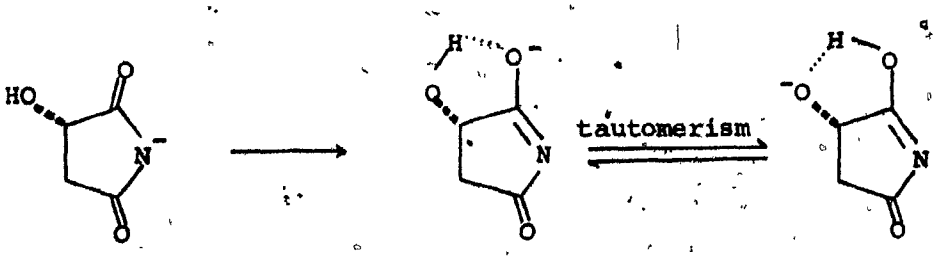
with ammonia in the presence of methoxide: acidification gives imide 34 in 56% yield, after purification.

Treatment of the sodium salt 38 with phenyl sulfenyl chloride[121-123] gave no thioimide. Neither did treatment of malimide (34) with a sulfenyl chloride in the presence of triethylamine, although a wide variety of thioimides have been synthesized under these conditions[129]. An unsuccessful attempt was made to prepare N-(phenylthio)malimide by treatment of the sodium salt 38 with phenyl benzenethiosulfonate (39) at high temperature (150°), in imitation of a synthesis of sulfenamides[130].

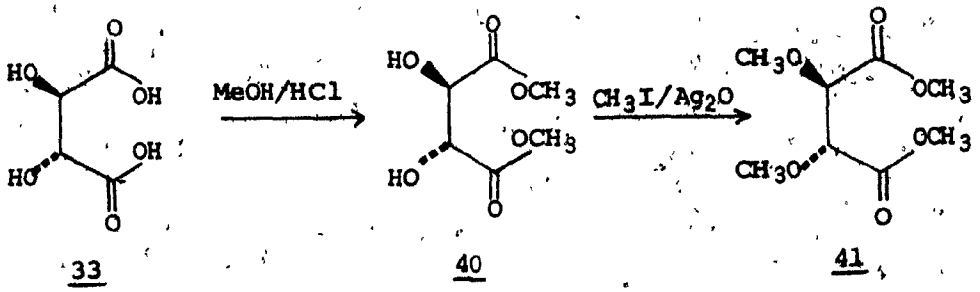


38 39 59

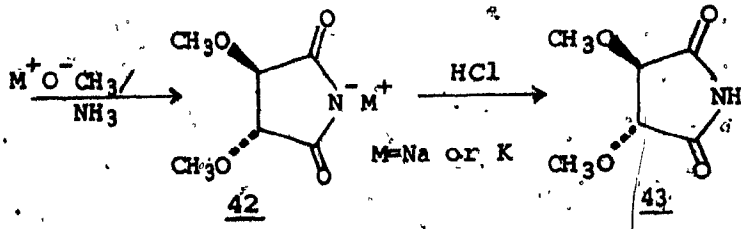
The cause of the unreactivity of (S)-malimide and its salts must involve the hydroxyl group. This moiety could aid in the delocalization of negative charge from nitrogen by stabilizing the neutral nitrogen forms by hydrogen bonding or outright tautomerism.



The dimethyl ether of (R)-tartrimide (43) is a known compound[131,132] for which these interactions are not possible. (R)-Tartaric acid (33) was esterified by the method of Fischer[133], the diester 40 was converted to the diether 41 by treatment with methyl iodide and silver oxide[134]. The resulting material was cyclized with methoxide and ammonia to give the salt 42, which could be converted to the free imide if desired. The free imide, its potassium salt or its sodium salt could be prepared in 72-80% yield based on (R)-tartaric acid.

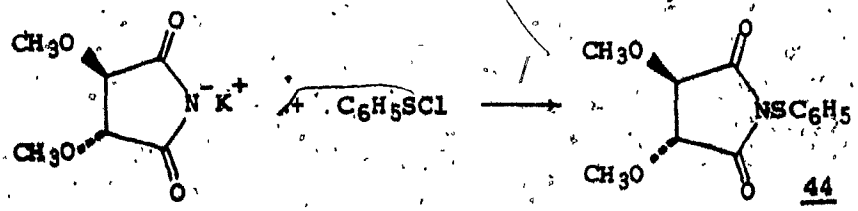


33 40 41



42 43

The sodium salt of (R)-2,3-dimethoxysuccinimide (42, M=Na) would not react with phenyl sulfenyl chloride to give the thiomide 44. Treatment of the imide 43 with triethylamine, followed by sulfenyl chloride[129] gave N-(phenylthio)-(R)-2,3-dimethoxysuccinimide (44) in very poor yield (4%); diphenyl disulfide was the major product (65%). Improved yields of 44 were obtained by addition of triethylamine to a mixture of sulfenyl chloride and the imide (64%) or by treatment of the potassium salt of the imide (42, M=K) with sulfenyl chloride (55-60%).



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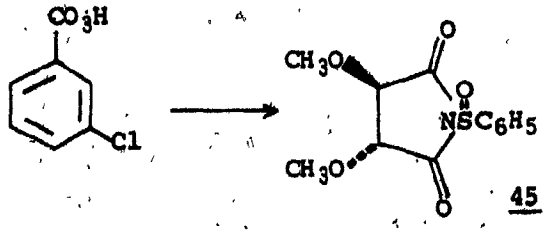
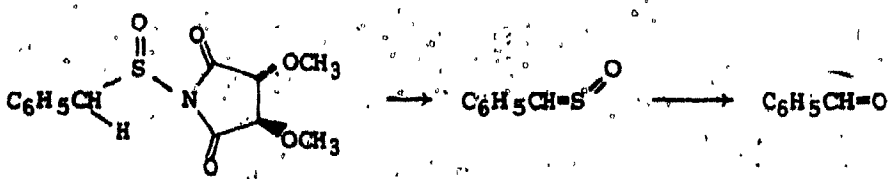


45

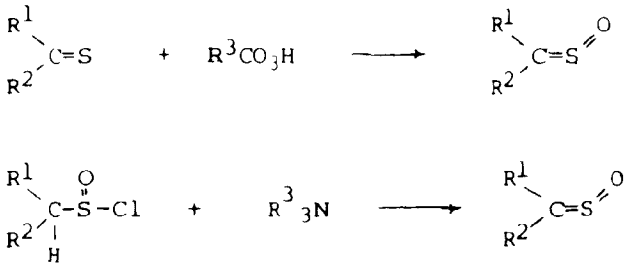
Oxidation of 44 with m-chloroperbenzoic acid gave N-(phenylsulfinyl)-(R)-2,3-dimethoxysuccinimide (45) as a solid with a broad melting range (120-137°) which was not significantly sharpened by repeated crystallization. The optical rotation of the sample was similarly unaffected. The identity of 45 was confirmed spectroscopically; in addition, treatment of 45 with methanol gave methyl benzenesulfinate (13) (80%), and treatment with lithium dimethylcuprate at 0° gave sulfoxide in a yield comparable with that from the analogous sulfinyl succinimide and phthalimide compounds (*cf.* Table IV). The sulfinate ester and sulfoxide so obtained had no significant optical activity. These properties of 45 can be explained by considering it a mixture of two diastereomers which are not separable by crystallization.

N-(Benzylsulfinyl)-(R)-2,3-dimethoxysuccinimide (46) was prepared by the same route as 45. Although the oxidation step proceeded in good yield (88%), the condensation step again gave only a moderate yield of the thioimide (53%). Attempts to crystallize 46 failed. In solution it decomposed even at -20° to give (R)-2,3-dimethoxysuccinimide (43). The solid was stable for longer periods at -20°, but after a few days it had turned pink and had developed the characteristic odour of benzaldehyde. The presence of benzaldehyde was confirmed by high-efficiency liquid chromatography. The material might decompose through a sulfine intermediate (47).



46 47

In recent years Zwanenburg and others have shown that sulfines have a rich and varied chemistry[135-149]. If sulfine 47 is indeed the major decomposition product of sulfinimide 46, these dimethoxyimide derivatives might constitute a useful entry to them. The major routes to these compounds require acidic[135-142] or basic conditions[135,136,143-145], whereas the decomposition of the sulfinimides



occurs under neutral conditions.

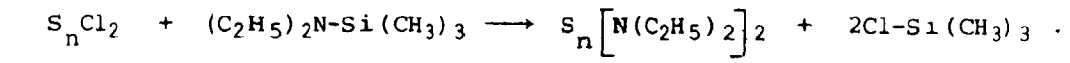
The Synthesis of Thioimides

In the previous section it has been shown that (S)-malimide and (R)-2,3-dimethoxysuccinimide can be prepared in excellent yield from the readily available (S)-malic and (R)-tartaric acids. Preliminary experiments indicate that the procedure will also give (S)-2-methoxysuccinimide from (S)-malic acid. Thus (S)-malimide, (R)-tartrimide and their ether derivatives are readily available. Since a wide variety of sulfenyl chlorides can be prepared from the disulfide by treatment with chlorine[119,129,150,151] or sulfuryl chloride[152], a variety of diastereomeric sulfinimides should be preparable.

In contrast, the yields of thioimide obtained under any one set of conditions can vary wildly. For example, phenyl sulfenyl chloride will react with phthalimide or succinimide in the presence of triethylamine to give the thioimides in 95% and 75% yield respectively[129]. Under the same conditions reactions with (S)-malimide and (R)-2,3-dimethoxysuccinimide were less successful. Similarly, attempts to prepare N-(n-butylthio)succinimide failed under conditions that were viable for other alkyl and aryl succinimides*. It thus appears that the yield of thioimide can change drastically with small changes in the structure of either the hydrocarbon or the imide moiety. A less fickle reaction would improve access to the thioimides.

Silicon-nitrogen bonds are cleaved in reactions with compounds containing carbon-chlorine bonds[153].

Abel and Armitage[154] showed that this reaction also applies to a variety of covalent sulfur-chlorine compounds:



Treatment of an imide with an excess of hexamethyldisilazane (48) at a temperature just below the melting point of the imide gives the

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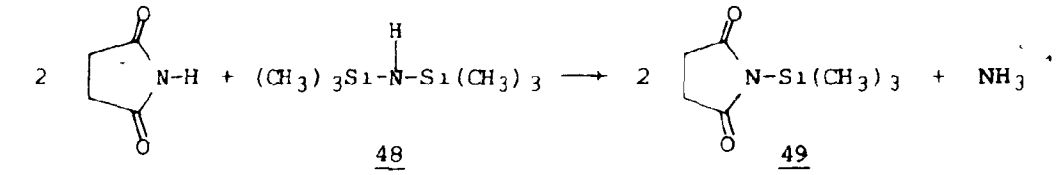
* Although many simple N-(alkyl and arylthio)succinimides are described in the literature[124,129], N-(n-butylthio)succinimide is conspicuously absent.

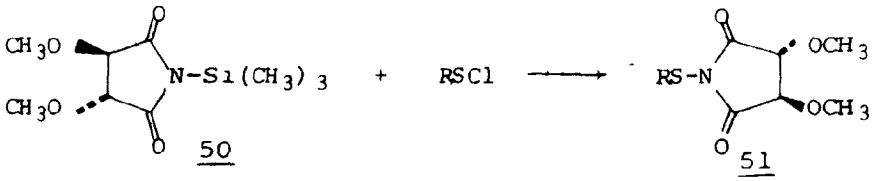
N-(trimethylsilyl)imide in good yield[153-5].



48 49

N-(trimethylsilyl)succinimide (49) was shown to react with sulfenyl chlorides to give thioimides in yields greater than 60%.

Nmr analysis of the mixtures produced by reaction of benzyl or p-toluenesulfenyl chlorides with N-(trimethylsilyl)-(+)-(R)-2,3-dimethoxysuccinimide (50), either at room temperature or at elevated temperatures, suggested the presence of the thioimides (51) together with some imide. Attempts to purify the thioimides by crystallization



50 51

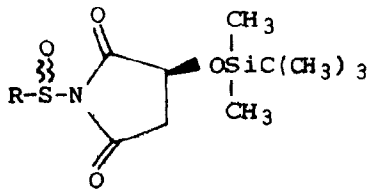
were unsuccessful and column chromatography yielded only imide and disulfide.

These results are probably a result of the properties of the dimethoxyimide, since this will provide a better leaving group than succinimide, owing to the presence of the two electronegative methoxy groups. If previous experience is valid, it should be possible to improve the purity of the crude product by modifying the reaction conditions, thus making a final purification by crystallization possible. Thus these results do not eclipse the promise of the organosilicon reagents to provide an improved route to thioimides.

3. FUTURE PROSPECTS

A versatile route to diastereomeric sulfinimides is now available. Perhaps a series of these compounds will be amenable to resolution by crystallization. If the mixtures all prove to be recalcitrant, a variety of techniques are available which should induce some stereoselectivity into the formation of the sulfinimides. When one of the two diastereomers predominates in a mixture, separation often becomes facile.

It is possible that some stereoselectivity will be observed when a less symmetric imide than (R)-2,3-dimethoxysuccinimide is incorporated into the sulfinimide (*e.g.* (S)-2-methoxysuccinimide). If this imide will not suffice, then perhaps a more bulky substituent than the methoxy group might provide the key. The synthesis of a series of N-substituted t-butyldimethylsilyloxysuccinimides (52) could be useful in this regard.



52

If the effect of a large group is not sufficient, stereoselectivity might be increased by the use of a chiral peracid[28-33,36-41,115,116] or an enzyme[45-47] for the oxidation of the thioimides.

Reaction of a sulfinyl chloride with menthol gives a preponderance of one of the possible diastereomers[38,39,156,157]. Similarly, reaction of sulfinyl chlorides with achiral alcohols in the presence of a chiral amine gives a sulfinate ester with some induced optical activity[119]. Perhaps the reaction of a sulfinyl chloride with a chiral imide (either directly, or through a more controlled reaction involving the silyl imide) will give an excess of one of the diastereomers.

If none of these approaches work, recent developments in high-efficiency liquid chromatography may make separation possible. Sulfinimides decompose when chromatographed on silica or alumina, but might be stable on newly developed packing materials in which the hydroxyl functions of silica have been replaced by nitrile functions.

4. EXPERIMENTAL

Common intermediates were obtained from commercial sources. Purification of these was unnecessary except where indicated. Melting points were obtained on a Gallenkamp apparatus and are uncorrected.

Vapor phase chromatographic analyses (vpc) were performed on an F & M Model 5750 Research Chromatograph equipped with a Perkin-Elmer Model 194B Printing Integrator. Four 6' x 1/8" stainless steel columns were used - 10% silicon gum rubber UC-W98 on Diaport-S (80-100 mesh), SE-30 ultraphase (10% by weight) on chromosorb W AW/DMCS 80-100 mesh, 10% apiezon L on chromosorb W AW/DMCS 80-100 mesh, and 10% carbowax 400 on chromosorb W AW/DMCS.

Thin layer chromatographic analyses (tlc) were performed on Eastman Chromatographic sheets 6060 (silica gel with fluorescent indicator) or 6063 (alumina with fluorescent indicator). Solvent systems are indicated in the text. Preparative thin layer separations were carried out on glass plates 20cm x 20 cm coated with a 0.75 mm layer of silica gel HF-254 (acc. to Stahl). Refractive indices were measured on a Carl Zeiss 38341 Refractometer at room temperature. Specific gravities were measured with a 2 ml pycnometer also at room temperature.

High-efficiency liquid chromatographic analyses were performed on a Waters Associates High Speed Chromatograph equipped with a Model 6000 pump, a U6K loop injector, differential ultraviolet (254 and 280 cm^{-1}) and refractive index detectors, and a Hewlett-Packard Electronic 196 dual pen recorder. Columns, solvent systems and flow rates are indicated in the text.

Infrared spectra were recorded on Perkin-Elmer Model 257 or Unicam SP1000 grating infrared spectrometers. Spectra were calibrated with 3027 and 1601 cm^{-1} bands of a polystyrene film reference.

Nuclear magnetic resonance spectra (nmr) were recorded on a Varian Associates T-60 spectrophotometer. All data are recorded in parts per million relative to tms (used as an internal standard).

Mass spectra were recorded on an AEI-MS-902 Mass spectrometer equipped with a direct insertion probe.

Microanalyses were performed by Organic Microanalyses, Montreal.

Optical rotations were measured on a Perkin Elmer model 141 automatic polarimeter.

Synthesis of Sulfinate Esters

Methyl Benzenesulfinate (12)[98]

Thiophenol (30.0 g, 273 mmole), glacial acetic acid (16.4 g, 273 mmole) and methylene chloride (35 ml) were mixed in a 500 ml three-necked flask fitted with a mechanical stirrer, a condenser with a drying tube, a thermometer and a gas inlet tube. The flask was cooled to -10°, and the contents were chlorinated.* The mixture turned pink and then to a straw color that did not change on further addition of chlorine.

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* For full details and discussion of this reaction, see P. Mathiaparanam, Ph.D. Thesis, McGill University 1972.

Acetyl chloride, hydrogen chloride and the solvent methylene chloride were removed by allowing the mixture to warm to room temperature, heating to 70° at atmospheric pressure and, after cooling to 10°, to 70° (20 mm) until the evolution of volatile matter had virtually ceased.

The mixture was then cooled to -30° in a dry ice/acetonitrile slush bath and methanol (13.9 ml, 344 mmol) was added dropwise. The mixture was transferred to a distillation flask and gently heated under reduced pressure to 70° (20 mm); this temperature was maintained until evolution of hydrogen chloride had practically stopped. The crude ester was cooled, diluted with ether (50 ml) and treated with aniline (5 g). After allowing a few minutes for any benzenesulfonyl chloride to react, the mixture was washed with water (50 ml), dilute hydrochloric acid (2 x 50 ml) and then water (50 ml). A portion of the first acid wash liberated aniline on basification with dilute aqueous sodium hydroxide solution, indicating that all the sulfonyl chloride in the ester had been destroyed. The organic solution was dried ($MgSO_4$), the ether was removed, and the residue was distilled to give methyl benzenesulfinate (13) as a colorless oil (35-40%), pure by vpc and tlc (silica/benzene), bp 65-67°/0.5 mm (lit[98,99,101], bp 88-89°/0.3 mm, 47.5-51.0°/0.2 mm, 43-45°/0.07 mm), n_D^{25} 1.5425 (lit[98] n_D^{25} 1.5437), showing ir ν_{max} at 1498 (aromatic c — c str) and 1137 cm^{-1} (S=O str) and nmr absorptions at δ 7.37 - δ 7.80 (5H multiplet) and δ 3.37 (3H singlet).

Methyl n-Butanesulfinate (23)

Method A: The sulfinate ester could be prepared from n-butanethiol *via* the sulfinyl chloride as described above (yield 75%).

Method B:[101] N-(n-butylsulfinyl)phthalimide (5.02 g, 20 mmol), prepared as described in the section on sulfinimides, was added to a solution of sodium methoxide (1.42 g, 20 mmol) in methanol (40 ml). After 30 min of stirring at room temperature, the methanol was evaporated *in vacuo*. The residue was stirred vigorously with pentane (60 ml) which was subsequently decanted. The pentane extraction was repeated several more times and the washings were combined and evaporated to give the methyl n-butanesulfinate as a colorless oil (yield: 75-80% after distillation).

Both procedures gave the sulfinate ester (23) as a colorless oil bp 69°/9 mm (lit[98,101] bp 69-70°/10 mm, 84-5°/12 mm), n_D^{26} 1.4430 (lit[98,101] n_D^{25} 1.4438, 1.4430) showing ν_{max} 1135 cm^{-1} (S=O str) and nmr absorptions at δ 3.82 (3H singlet), δ 2.5-3.0 (2H multiplet), δ 1.2-2.1 (4H multiplet) and δ 0.8-1.2 (3H multiplet).

1,2-Oxathiane 2-oxide (14)[103]

1,2Dithiane 1,1-Dioxide (24)

A solution of 1,4-butanedithiol (45.8 g, 375 mmol) in glacial acetic acid (250 ml) was cooled in an ice bath and a solution of 35% aqueous hydrogen peroxide solution (125 ml, 1000 mmol) in glacial acetic acid (125 ml) was added slowly to prevent the reaction mixture temperature

rising above 15°. The mixture was stirred overnight. The solvent was removed under vacuum and the residue was extracted with chloroform (5 x 50 ml). The chloroform extracts were reduced to 100 ml, washed with saturated aqueous sodium bicarbonate solution (50 ml), then water (50 ml). After drying this solution ($MgSO_4$), the solvent was removed at reduced pressure. Scratching the resultant oil after cyclohexane had been added gave 1,2-dithiane 1,1-dioxide (24) as a colorless solid (27.1 g, 48%) mp 49-53° (lit[158,103] mp 54.5-55°, 54-56°).

1,2-Oxathiane 2-Oxide (14)

Tris(diethylamino)phosphine (17.9 g, 110 mmol) was added slowly to a stirred solution of 1,2-dithiane 1,1-dioxide (24) (15.2 g, 100 mmol) in dry benzene (60 ml). An immediate exothermic reaction occurred to give an oil which slowly redissolved to give a clear golden yellow solution. After stirring for 5 hours the solvent was removed under vacuum and the residue fractionally distilled to give a clear oil bp 48-49°/0.15 mm. This oil was redistilled from sulfur (0.5 g) to give 1,2-oxathiane 2-oxide (14) (10 g, 83%) as a colorless oil bp 58-60°/0.25 mm (lit[103] bp 60-61°/0.1 mm) n_D^{23} 1.4867 (lit[103] n_D^{25} 1.4862), ir (film) 1125 cm^{-1} (S=O str).

1,2-Oxathiolane 2-Oxide (15)[103]

1,3-Propanedithiol (27.0 g, 250 mmol) was oxidized with hydrogen peroxide (78 ml, 750 mmol) as described in the previous section to give 1,2-dithiolane 1,1-dioxide (25) as an oily solid (10.6 g, 33%). This

material was dissolved in dry benzene (50 ml) and treated with tris(diethylamino)phosphine (20.8 g, 92 mmol) to give 1,2-oxathiolane 2-oxide (15) as a colorless oil, pure by vpc (5.6 g, 67%) bp 40-43°/0.2 mm (lit[103] bp 48-49°/0.2 mm), n_D^{25} 1.4859 (lit[103] n_D^{25} 1.4862); ir shows ν_{max} at 1105 cm^{-1} (S=O str), nmr shows absorptions at δ 4.55 (multiplet, 2H) and δ 1.45 (multiplet, 4H).

p-Tolyl Benzenesulfinate (10, R^1= C_6H_5, R^2=p-$CH_3C_6H_4$)

p-Cresol (2.16 g., 2.0 mmol) was added to a stirred suspension of sodium hydride (0.84 g of a 58% suspension in paraffin oil (2.0 mmol)) in pentane (100 ml). The salt was washed well (pentane) and then suspended in carbon tetrachloride. Phenyl sulfinylphthalimide (22, R^1=C_6H_5)[101] (5.42 g, 2.0 mmol) was added and the mixture was stirred for 1 hour. The mixture was filtered and the solvent removed to give p-tolyl benzenesulfinate as a colorless oil (4.30 g, 93%), pure by tlc (silica, benzene R_f=0.6); nmr ($CDCl_3$) gave signals at δ 8.8-7.5 (miltiplet, 5H) δ 7.3 (singlet, 4H) and δ 2.2 (singlet, 3H). The compound decomposed exothermically to give a red polymeric tar when distillation was attempted; decomposition also occurred when the compound was stored overnight at -20°.

Synthesis of Lithium Organocuprates[158]

Cuprous Iodide

Cuprous iodide as purchased from Alfa Chemical Co. or Fisher Scientific Co. was a brown or black powder. A sample (10 g) was stirred with a solution of potassium iodide (98 g) in water (75 ml). After addition of decolorizing carbon (0.25 g) the solution was filtered into water (250 ml). The suspension was allowed to settle, decanted and washed well with water, absolute ethanol and hexanes. The cuprous iodide (a white powder) was dried under vacuum.

Lithium Organocuprates

Purified cuprous iodide (1.9 g, 10 mmol) was placed in a three-necked flask, fitted with two dropping funnels with equilibrating side arms, and a magnetic stirrer. The apparatus was flame-dried under a stream of prepurified nitrogen. Anhydrous ether (10 ml) was added, and the stirred suspension was cooled to the required temperature. The alkyl or aryl lithium was then added dropwise.

Lithium Dimethylcuprate

This compound was prepared at or below 0°. On addition of the first drops of methyl lithium an intense yellow coloration (methyl copper) was produced; then as further addition of methyl lithium was continued a colorless or light tan solution was produced (after addition of 20 mmol). This end point could be titrated easily with methyl lithium.

Lithium Diethylcuprate

This was prepared at or below -30°. After addition of two equivalents of ethyl lithium a black solution resulted. This end point was very difficult to detect.

Lithium di-n-butylcuprate

The preparation was carried out at or below -30°. The initial bright yellow color lasted until about half the butyl lithium was added; this changed to a bright blue solution which turned red at the end point.

Lithium Diphenylcuprate

This was prepared at or below 0°. The suspension initially turned bright yellow, then a red brown color until one equivalent of the phenyl lithium had been added. The solution then started turning green. After addition of two equivalents of phenyl lithium a dark green or black solution was obtained.

Synthesis of Sulfides

n-Butyl methyl sulfide, diphenyl sulfide and methyl phenyl sulfide were all available from commercial sources.

Method A: Ethyl phenyl sulfide, phenyl propan-3-ol sulfide (53) and butan-4-ol phenyl sulfide (55) were prepared by the following method[159]. To the ice-cold alkyl mercaptan was added with stirring a 25% aqueous solution of sodium hydroxide (1.25 moles). To the resulting clear

solution the chloroalkanol was added at such a rate that the reaction temperature did not exceed 60°. Stirring was continued at room temperature for four hours, after which the organic layer was taken up in ether, washed with 25% sodium hydroxide and water. After drying ($MgSO_4$) the residue was fractionally distilled under reduced pressure. The yields and properties of the sulfides are summarized in Table V.

Method B: n-Butyl phenyl sulfide and butan-4-ol methyl sulfide (54) were prepared by the following method[160]. Sodium (2.3 g, 100 mmol) was dissolved in ethanol (50 ml) and the thiol was added (n-butanethiol was added dropwise; methanethiol, prepared from methyl isothiourea sulfate as described below, was bubbled slowly through the solution) The chloroalkanol (100 mmol) was added and the resultant mixture was refluxed briefly. After filtration to remove sodium chloride, the solvent was flash-evaporated and the residue distilled to give the sulfides whose yield and properties are found in Table V.

Method C: Di-n-butyl sulfide was prepared by reduction of the sulfoxide with sodium bisulfite[161]. n-Butyl sulfoxide (4 g, 25 mmol) was added to a solution of sodium bisulfite (16 g, 150 mmol) in water (40 ml) and the mixture was heated on a steam bath for 48 hours. The mixture was cooled and extracted several times with chloroform. The solution was dried ($MgSO_4$) and evaporated to give crude sulfide that was purified by vacuum distillation (Table V).

TABLE V. Preparation and Properties of Sulfides[a]

Name	Method of prep.	Yield (%)	Boiling Point (°C/mm Hg)	n_D/temp.	Analytical and Spectral Data
di-n-butyl sulfide	C	70	70-2/12 lit 187/760[162] 91-91.5/10[163]	1.4509/25 lit 1.45297/20[162] 1.4532/30[163]	
ethyl phenyl sulfide	A	70	92-96/0.5 lit 123/12[164] 90/10[165], 98/22[166] 102-4/15[167]		
n-butyl phenyl sulfide	B	74	120-2/18 lit 117/15[166] 78-83/2.3[168] 123-9/25[169]	1.5423/25 lit 1.5472/21[166] 1.5432/28[168] 1.5312/25[169]	
phenyl propan-3-ol sulfide (53) $C_6H_5S(CH_2)_3OH$	A	71	105/0.1 lit 134-5/2[170] 155-9/8[171]		ir ν_{max} (film): 3340 (O-H str), 2910 and 2810 (C-H str), and 1060 cm^{-1}. ms: 120 (P^+) and 87 amu ($CH_3CH_2SCH_2^+$, base peak). Anal.calcd. for $C_9H_{12}OS$: C, 64.28; H, 7.14; S, 19.04. Found: C, 64.53; H, 7.19; S, 19.04

a - All sulfides were pure by tlc (silica, hexanes) and vpc, and had nmr spectra consistent with their structures.

TABLE V (continued)

Name	Method of prep.	Yield (%)	Boiling Point (°C/mm Hg)	n_D/temp.	Analytical and Spectral Data
butan-4-ol methyl sulfide (54) $CH_3S(CH_2)_4OH$	B	48	103-5/10 lit 81-5/3[159]		ir ν_{max}(film):3340 (O-H str), 2910 and 2850 (C-H str), 1055 (C-O str) and 1030 (C-S str) cm^{-1}. ms: 120 (P^+), 102 (P^+-H_2O) and 61 ($CH_3SCH_2^+$) amu.
butan-4-ol phenyl sulfide (55) $C_6H_5S(CH_2)_4OH$	A	78	112/0.1 lit 150/6[172] needles mp 24°[173]		ir ν_{max}(film): 3380 (O-H str), 2950 and 2870 (C-H str), 1060 (C-O str) and 1030 cm^{-1} (C-S str). ms: 182 (P^+), 164 (P-H O), 123 ($C_6H_5SCH_2^+$) 110 ($C_6H_5SH^+$), 91 ($C_7H_7^+$) and 77 amu ($C_6H_5^+$). Anal. calcd. for $C_{10}H_{14}OS$: C, 70.07; H, 6.58; S, 23.35. Found: C, 70.24; H, 6.67; S, 23.36.

Synthesis of Methanethiol[160]

Methyl Isothiouronium Sulfate[174]

Thiourea (78 g, 1 mol) and water (70 ml) were placed in a 1 litre round-bottomed flask. On addition of dimethyl sulfate (69 g, 0.55 mol) the mixture grew warm and a clear yellow solution was produced. The mixture was refluxed vigorously for one hour then cooled. Ethanol (100 ml) was added, the copious crystalline precipitate was filtered, then washed with ethanol (2 x 50 ml). Evaporation of the mother liquor to a paste, addition of ethanol and filtration gave a second crop of the material which was combined with the first crop of methyl isothiouronium sulfate (total yield 107 g, 78%) mp 243° with decomposition.

Methanethiol

A 50 ml round-bottomed flask was fitted with a stopcock, a dropping funnel and a condenser. The end of the condenser was attached to the following assembly: an empty flask; a flask containing dilute sulfuric acid (1 volume of concentrated sulfuric acid to two volumes of water); a drying tube containing calcium chloride; an empty flask; the flask containing the reagents with which the methanethiol is to react; an empty flask; a flask containing aqueous lead acetate solution as a trap for unreacted thiol, and finally a suction pump.

A slow current of air was pulled through the apparatus by means of the suction pump. A solution of 5N aqueous sodium hydroxide solution (20 ml) was added dropwise to the methyl isothiouronium sulfate (14.8 g,

53 mmol) in the first flask. When the addition was complete, this flask was heated slowly to reflux temperature and maintained there for one hour, to complete the reaction. The material produced in this reaction was trapped in ethanolic sodium ethoxide, as described previously.

Synthesis of the Sulfoxides

Di-n-butyl sulfoxide was commercially available. The other sulfoxides were prepared by oxidation of the sulfides with sodium periodate ($NaIO_4$)[23,24] or m-chloroperbenzoic acid[104,105].

Methyl Phenyl Sulfoxide

In a 500 ml flask equipped with a magnetic stirrer were placed sodium periodate (22.5 g, 105 mmol) and water (200 ml). The mixture was stirred and cooled in an ice bath. Methyl phenyl sulfide (12.4 g, 100 mmol) was added and the mixture was stirred overnight at 0°. The suspended solid was removed by filtration, and the solution was extracted with methylene chloride (3 x 50 ml). The combined extracts were dried ($MgSO_4$) and the solvent was flash-evaporated. The residue was distilled from decolorizing charcoal (1 g) to give methyl phenyl sulfoxide (22.6 g, 89%) as a colorless oil bp 95-6°/0.5 mm (lit[24,175] 78-9°/0.1 mm, 115°/2 mm), pure by vpc and tlc (silica, benzene: ethyl acetate 5:1 R_f 0.20), n_D^{25} 1.5762 (lit[175] n_D^{25} 1.5580).

Ethyl Phenyl Sulfoxide (1.30 g, 84%) was prepared from ethyl phenyl sulfide (1.38 g, 10 mmol) as a colorless oil bp 80-2°/0.15 mm (lit[176,24] 146°/13 mm, 101-2°/1.5 mm), pure by vpc and tlc (silica, chloroform, R_f 0.46) or ethyl acetate (R_f 0.64) n_D^{22} 1.4679.

n-Butyl Methyl Sulfoxide (2.2 g, 85%) was prepared from n-butyl methyl sulfide (2.08 g, 20 mmol) as a colorless oil bp 101°/8 mm, n_D^{25} 1.4679.

Phenyl Propan-3-ol Sulfoxide, $C_6H_5S(O)(CH_2)_3OH$ (56), (1.39 g, 75%) was prepared from phenyl propan-3-ol sulfide (53) (1.68 g, 10 mmol) as a colorless oil that decomposes before boiling, purified by chromatography on alumina (eluents: chloroform then dioxane); pure by tlc (silica, ethyl acetate R_f 0.33), ms 184 (P^+), 166 ($P^+ - H_2O$), 126 ($C_6H_5OH^+$, base peak), 107 ($O{=}S(CH_2)_3OH^+$), 91 ($C_7H_7^+$) and 77 ($C_6H_5^+$) amu; ir ν_{max}(film) 3340 (O-H str), 2900 and 2815 (C-H str) and 1010 (S=O str) cm^{-1}; anal. calcd. for $C_9H_{12}O_2S$: C, 58.69; H, 6.52; S, 17.39. Found: C, 58.01; H, 6.64; S, 16.87.

Butan-4-ol Phenyl Sulfoxide, $C_6H_5S(O)(CH_2)_4OH$ (57), (1.59 g, 80%) was prepared from butan-4-ol phenyl sulfide (55) (1.83 g, 10 mmol) as a colorless oil that decomposes before boiling, purified by chromatography on silica gel (60 g; eluents: benzene (250 ml), chloroform: ethyl acetate 5:1 (300 ml), ethyl acetate (250 ml)), pure by tlc (silica, ethyl acetate R_f 0.36), ms 198 (P^+), 180 ($P^+ - H_2O$), 166 ($C_6H_5SCH{=}CH_2^+$),

107 ($HOCH_2CH_2CH_2CH_2SH_2^+$; base peak), 91 ($C_7H_7^+$) and 77 ($C_6H_5^+$) amu; ir ν_{max}(film) 3340 (O-H str), 2900 and 2815 (C-H str), 1040 (C-O str) and 1010 (S=O str) cm^{-1}; anal. calcd. for $C_{10}H_{14}O_2S$: C, 60.60; H, 7.07; S, 16.16. Found: C, 60.84; H, 7.24; S, 15.86.

Attempted oxidation of n-butyl phenyl sulfide under the same conditions gave starting material, recovered in a yield of 99.8%. Oxidation of butan-4-ol methyl sulfide (54) gave a mixture of sulfide 54 and sulfoxide 58 that could not be separated.

n-Butyl Phenyl Sulfoxide

A solution of n-butyl phenyl sulfide (4.56 g, 30 mmol) in chloroform (120 ml) was placed in a 250 ml round-bottomed flask equipped with a magnetic stirrer. The solution was stirred and cooled in an ice bath. m-Chloroperbenzoic acid (6.09 g 85% acid, 30 mmol) dissolved in chloroform (200 ml) was added dropwise. The solution was then allowed to warm up to room temperature and stirred for an additional half hour. The solution was then washed with saturated aqueous sodium bicarbonate solution, then water. After the solution had been dried ($MgSO_4$) the solvent was flash-evaporated and the crude product was chromatographed on alumina (120 g, eluent: benzene:pyridine 20:1). The resultant material was further purified by distillation to give butyl phenyl sulfoxide (2.8 g, 51%) as a colorless oil bp 99-99.5°/0.4 mm, $n_D^{26.5}$ 1.5433, $d^{26.5}$ 1.0652, $[R_L]_D^{exp}$ 53.99 (calc 53.88).

n-Butan-4-ol Methyl Sulfoxide, $CH_3S(O)(CH_2)_4OH$ (58), (1.15 g, 85%) was prepared from n-butan-4-ol methyl sulfide (54) (1.20 g, 10 mmol) as a colorless oil that decomposes before boiling, ms 136 (P^+), 119 (P^+-OH) and 64 (P^+-CH_3SOH) amu; ir ν_{max}(film) 3400 (O-H str), 2970 and 2895 (C-H str), 1068 (C-O str) and 1020 (S=O str) cm^{-1}.

Diphenyl Sulfoxide[26]

Diphenyl sulfide (18.6 g, 100 mmol) and methanol (30 ml) were placed in a three-necked flask equipped with a magnetic stirrer, a condenser and a thermometer. N-Bromosuccinimide (17.8 g, 100 mmol) was added in 5 g portions. The mixture was stirred at a temperature below 10° for one hour. The mixture was stirred overnight to give a yellow solution that was evaporated and stirred with ether (200 ml). The resulting solid was removed by filtration (succinimide, 8.3 g, mp 124-6°) and the filtrate was evaporated to give the crude product. Crystallization of this material from hexanes:benzene (3:2) gave diphenyl sulfoxide (5.2 g, 26%) as a colorless solid mp 66-8° (lit[177-9] 70.0-70.5°), pure by vpc and tlc (silica, chloroform R_f 0.64).

Reaction of Sulfinate Esters with Lithium Organocuprates

The sulfinate ester (10 mmol) in anhydrous ether (40 ml) was added dropwise to the organocopper reagent under a stream of prepurified nitrogen. The mixture was stirred and then hydrolyzed with saturated ammonium chloride solution (50 ml). After stirring for 15 min at room temperature, the mixture was filtered and both the copper salts and the aqueous layer were washed well with chloroform-tetrahydrofuran (1:1). The organic extracts were dried ($MgSO_4$) and evaporated to give an oil that was worked up as indicated below. All products were identified by comparison to authentic samples. The results are summarized in Table I.

Methyl Benzenesulfinate (13)

Treatment of the sulfinate ester 13 (3.12 g, 20 mmol) with lithium dimethylcuprate (40 mmol) at 0° for one hour gave a yellow oil that was purified by distillation to give methyl phenyl sulfoxide (1.65 g, 59%). Treatment of the ester 13 (10 mmol) with a large excess of lithium dimethylcuprate (10 mmol) again gave the sulfoxide (0.67 g, 43%).

Lithium diethylcuprate (20 mmol) reacted with the ester (10 mmol) at -78° for one hour to give an oil that was chromatographed on silica (60 g; eluents: hexanes (200 ml), toluene (100 ml), chloroform (100 ml) and ethyl acetate (100 ml)) to give four fractions:-

Fraction A: A colorless oil (110 mg) containing several components (vpc, tlc (silica, hexanes)).

Fraction B: A colorless oil containing ethyl phenyl sulfide (168 mg, 12%) as the major component (tlc, vpc, nmr).

Fraction C: A red oil containing methyl benzenesulfinate (13) (219 mg, 16%) as the major component (tlc, vpc, nmr).

Fraction D: A yellow oil containing ethyl phenyl sulfoxide as the major component (tlc, vpc, nmr).

Fraction D was distilled at 80-2°/0.15 mm to give the product that was further purified by chromatography on alumina (eluent: benzene:pyridine 19:1), yielding ethyl phenyl sulfoxide (560 mg, 36%) as a colorless oil.

Reaction of 13 (10 mmol) with lithium di-n-butylcuprate at -78° for one hour gave a red oil that was distilled to give n-butyl phenyl sulfide (600 mg, 36%) as a pale yellow oil.

Treatment of ester 13 (10 mmol) with lithium diphenylcuprate for one hour at -40° gave an orange oily solid, that was chromatographed on silica (120 g; eluents: hexanes and chloroform) to give two fractions:-

Fraction A: Biphenyl (1.37 g) mp and mmp 67-9°. Addition of phenyl lithium to ammonium chloride solution, followed by extraction with ether, gave a solution containing the same material (vpc, tlc (silica, hexanes)).

Fraction B: A solid that was crystallized from benzene:hexanes (2:3) to give diphenyl sulfoxide (970 mg, 48%).

The reaction was repeated at -78° for one hour to give an oil that was chromatographed on silica (60 g; eluents: toluene (100 ml), chloroform (25 ml), chloroform (250 ml), ethyl acetate (100 ml) and methanol (100 ml)) to give six fractions:-

Fraction A: Biphenyl (tlc, vpc).

Fraction B: An oil that was shown to be ester 13 (86 mg, 6%)(tlc, vpc, nmr).

Fraction C: An orange oil (521 mg) containing the sulfoxide (tlc, vpc).

Fraction D: A colorless oil (567 mg) containing the sulfoxide (tlc, vpc).

Fraction E: An orange oil (81 mg) containing the sulfoxide (tlc, vpc).

Fraction F: A foul-smelling oil (5 mg) containing many components (vpc, tlc (silica, chloroform)).

Fractions C, D and E were recombined and chromatographed on alumina (60 g; eluent: chloroform) to give diphenyl sulfoxide as a colorless solid mp 62-4° (970 mg, 48%).

Methyl n-Butanesulfinate (23)

Treatment of the sulfinate ester 23 (1.36 g, 10 mmol) with lithium dimethylcuprate (20 mmol) for one hour at 0° gave an orange oil that was distilled to give n-butyl methyl sulfoxide (600 mg, 50%).

Reaction of ester 23 (10 mmol) with lithium di-n-butylcuprate (20 mmol) for one hour at 0° gave a complex mixture. The experiment was repeated with the same result. Nmr analysis indicated that the mixture contained a small amount of the sulfoxide, but none was isolated. Distillation of the mixture (1.5 g) gave a major fraction bp 93-5°/ 0.175 mm (1.0 g) that contained many components.

The reaction was repeated at -30° to give a brown oil that was chromatographed on silica (eluents: toluene, chloroform and ethyl acetate) to give three fractions:-

Fraction A: A brown oil (150 mg) containing ester 23 and di-n-butyl sulfide as the major components (vpc, tlc).

Fraction B: A pale yellow oil (100 mg) containing many components (vpc, tlc (silica, benzene)).

Fraction C: A pale yellow oil (400 mg) containing n-butyl sulfoxide as the major constituent (tlc, nmr). This material was rechromatographed (alumina, eluent dioxane) to give the pure sulfoxide (210 mg, 15%).

The reaction was again repeated at -78° (one hour) to give an oil that was distilled in an attempt to purify the sulfoxide; the distillate (bp 54-93°/0.10 mm) was chromatographed on silica (60 g, eluents: chloroform (250 ml), ethyl acetate (250 ml)) to give an ethyl acetate fraction containing the sulfoxide (vpc, tlc). Rechromatography on alumina (eluent: benzene:pyridine 19:1) gave di-n-butyl sulfoxide (822 mg, 52%).

Treatment of the ester 23 (10 mmol) with lithium diphenylcuprate (20 mmol) yielded a yellow oil that was shown by vpc to have two major components. This was chromatographed on silica (60 g, eluents: hexanes, toluene:ethyl acetate 5:1, toluene:ethyl acetate 1:6) to give three fractions:-

Fraction A: Biphenyl as a solid mp 62-4°, mmp 66-68° (850 mg).

Fraction B: A pale yellow oil that was distilled to give n-butyl phenyl sulfide (1.05 g, 64%) (vpc, tlc).

Fraction C: A yellow oil containing many components (150 mg) (vpc, tlc).

1,2-Oxathiane 2-Oxide (14)

Reaction of the sulfinate ester 14 (1.20 g, 10 mmol) with lithium dimethylcuprate (20 mmol) gave a pale yellow oil containing one major component (tlc). The oil was washed with ether to give butan-4-ol methyl sulfoxide (58) (800 mg, 59%) as a pale yellow oil that could be further purified by preparative tlc (eluent: chloroform).

Reaction of cyclic ester 14 (10 mmol) with lithium diphenylcuprate at 0° for one hour gave a brown solid that was shown by tlc (silica, chloroform or ethyl acetate) to contain large quantities of biphenyl, some butan-4-ol phenyl sulfide (55) and a small amount of butan-4-ol phenyl sulfoxide (57), along with many trace materials. The experiment was repeated at -78° to give a mixture that was chromatographed on silica (60 g, eluents: toluene (100 ml), ethyl acetate:cyclohexane 4:1 (200 ml), ethyl acetate (200 ml) and methanol (250 ml) to give four fractions:-

Fraction A: Biphenyl as a colorless solid which after crystallization (pentane) showed mp and mmp 67-9°.

Fraction B: A brown oil (145 mg) containing many components (tlc, chloroform).

Fraction C: A brown oil (278 mg) containing many components (tlc, chloroform).

Fraction D: n-Butan-4-ol phenyl sulfoxide (57) as a colorless oil (639 mg, 32%) (tlc).

1,2-Oxathiolane 2-Oxide (15)

Reaction of sulfinate ester 15 (1.06 g, 10 mmol) with lithium diphenylcuprate (20 mmol) at -78° for one hour gave a material that was chromatographed on alumina (60 g, eluents: chloroform and dioxane) to give three fractions:-

Fraction A: A red solid (1 g) that was mainly biphenyl (tlc, vpc).

Fraction B: A colorless oil containing mainly starting material (tlc, vpc) (25 mg, 2%).

Fraction C: Phenyl propan-3-ol sulfoxide (36) (960 mg, 52%) as a very pale yellow oil (tlc, nmr).

p-Tolyl Benzenesulfinate (10), $R^1=C_6H_5$, $R^2=p\text{-}CH_3C_6H_4$)

A sample of the sulfinate ester prepared from phenyl sulfinylphthalimide (22, $R^1=C_6H_5$, 20 mmol) was treated with lithium dimethylcuprate (40 mmol) for one hour at 0°. The resultant oil was chromatographed on silica (60 g, eluents: hexanes (300 ml), benzene:ethyl acetate 5:1 and ethyl acetate (200 ml each)), to give three fractions:-

Fraction A: Diphenyl disulfide (180 mg, 8%) as colorless needles mp 65-8°, pure by tlc (silica, hexanes, R_f 0.63) and vpc.

Fraction B: p-Cresol (1.15 g, 53%) as a brown oil, identified by tlc (silica, benzene, R_f 0.37) and nmr.

Fraction C: A pale yellow oil that was purified by Kugelrohr distillation (105°/1 mm) to give methyl phenyl sulfoxide (300 mg, 22%), identical to an authentic sample (tlc, vpc).

Reaction of Sulfoxides with Lithium Organocuprates

The sulfoxide (10 mmol) was treated with the organocopper reagent for an extended period of time. The results obtained are summarized in Table II. In each case the organic materials were isolated in a similar manner to that described for the sulfinate ester reactions.

Diphenyl Sulfoxide

This material gave an oil that was chromatographed on silica (60 g) to give biphenyl and starting material (1.9 g, 94%).

n-Butyl Phenyl Sulfoxide

This gave the sulfide as the major product in a mixture (1.5 g), a portion of which (250 mg) was separated into two fractions by high efficiency liquid chromatography (Porasil, 2 x 2' x 3/8", methylene chloride:acetonitrile 9:1, 9 ml/min):-

Fraction A: A colorless oil identified as n-butyl phenyl sulfide (200 mg, 80%), pure by nmr, tlc and vpc.

Fraction B: A colorless oil, pure by tlc and helc, identified (nmr, ir) as n-butyl phenyl sulfoxide (30 mg, 12%).

Methyl Phenyl Sulfoxide

This gave a mixture of materials (1.4 g) that was partially separated by chromatography on silica (60 g, eluents (200 ml fractions): hexanes, hexane:methylene chloride 19:1, 9:1, 8:2, 4:1, methylene chloride and methanol). In this way four fractions were obtained:-

Fraction A: Methyl phenyl sulfide (138 mg, 11%) as a colorless oil identical to an authentic sample (nmr, tlc, ir, vpc).

Fraction B: 1,2-di(phenylthio)ethane (27) (69 mg, 3%) as a colorless oil that solidified to needles on standing mp and mmp 70-2° (lit[182,183] 65°, 69°).

Fractions C and D: were both oils. They were dissolved in glacial acetic acid and oxidised with potassium permanganate(3% aqueous). 1,2-Di(phenylsulfonyl)ethane was filtered off and purified by chromatography on silica (eluent: benzene:ethyl acetate 5:1) to give a sample mp 182.5°, mmp 182-4° (lit[184,185] 179.5-180°). Methyl phenyl sulfone (685 mg, 49%) was isolated by extraction of the oxidised mixture with chloroform; the combined chloroform extracts were dried ($MgSO_4$) and evaporated to give the sulfone as a colorless solid mp and mmp 83-6° (lit[181,181] 88°).

n-Butyl Methyl Sulfoxide

This gave a pale yellow oil (1.05 g, 88%) that was shown by vpc to be starting material.

Preparation of Sulfones

Methyl Phenyl Sulfone

Method A: Hydrogen peroxide (22.8 g, 30% aqueous solution, 200 mmol) was added to a flask containing methyl phenyl sulfide (12.4 g, 100 mmol). After it had been stirred for one hour a vigorous exothermic reaction occurred to give a clear golden homogeneous solution. This solution was refluxed for four hours, treated with decolorising charcoal, filtered, diluted with water (200 ml) and cooled to give methyl phenyl sulfone (11.6 g, 76%), mp 87-9° (lit[180,181] 88°), pure by vpc and tlc (silica, methylene chloride R_f 0.74).

Method B: Methyl phenyl sulfide (1.24 g, 10 mmol) was dissolved in glacial acetic acid (10 ml). A solution of potassium permanganate (3% aqueous) was added dropwise until a drop of the solution applied to a piece of filter paper no longer gave a purple coloration. Sodium busulfite solution was then added dropwise to dissolve the manganese dioxide. The solution was then extracted well with chloroform, the extracts were combined, dried ($MgSO_4$) and evaporated to give pale yellow needles (1.4 g, 90%) that were dissolved in water and treated with decolorising charcoal to give methyl phenyl sulfone as colorless needles mp and mmp 87-9°.

1,2-Di(phenylsulfonyl)ethane (26)

1,2-Di(phenylthio)ethane (27)

A solution of sodium ethoxide (50 mmol) was prepared from sodium (1.15 g) and ethanol (50 ml). Benzenethiol (5.51 g, 50 mmol) was added followed by 1,2-dibromoethane (4.7 g, 25 mmol). The mixture was refluxed briefly, filtered while hot, then reduced in volume until crystallization occurred. The product was filtered off and recrystallized from ethanol to give 1,2-di(phenylthio)ethane (27) (3.7 g, 30%) mp 70-2° (lit[182,183] 65°, 69°), pure by tlc (silica, hexanes R_f 0.39) with nmr absorptions at δ 7.02 (10H, singlet) and δ 2.92 (4H, singlet).

1,2-Di(phenylsulfonyl)ethane (26)

1,2-Di(phenylthio)ethane (1.23 g, 5 mmol) was dissolved in glacial acetic acid (5 ml) and treated with excess potassium permanganate (3% aqueous). After treating with sodium bisulfite solution the crude product was filtered off and crystallized from aqueous ethanol to give 1,2-di(phenylsulfonyl)ethane (26) (1.1 g, 71%) as colorless needles mp 182-4° (lit[184,185] 179.5-180°), pure by tlc (silica, benzene R_f 0.20) showing nmr peaks at δ 6.95-7.62 (10H, singlet) and δ 3.27 (4H, singlet).

Methyl Benzenesulfenate (21, $R^1=C_6H_5$, $R^2=CH_3$)

Synthesis

A solution of dibenzyl disulfide (21.8 g, 100 mmol) in carbon tetrachloride was cooled to 0-5°. Sulfuryl chloride (13.5 g, 110 mmol) was added and the mixture was stirred for 0.5 hr. The solvent was flash-evaporated, and the residue was distilled to give phenyl sulfenyl

chloride (19.8 g, 69%) bp 43-8°/1.5 mm (lit[106] 58-60°/3 mm).

Phenyl sulfenyl chloride (19.8 g, 137 mmol) was treated with sodium methoxide (152 mmol) prepared by dissolving sodium (3.5 g) in methanol (200 ml) at 0°. The mixture was allowed to warm up to room temperature, filtered and evaporated to give an oil that gave two fractions on distillation (bp 78-81°/4 mm and 93°/4.5 mm). The lower boiling fraction was redistilled to give methyl benzenesulfenate (5.3 g, 27%) bp 95°/6 mm (lit[106] 88-9°/0.4 mm), n_D^{26} 1.5508, d^{26} 1.1081, $[R_L]_D$ exp 40.75 (calc 40.89).

Reaction of Methyl Benzenesulfenate with Lithium Dimethylcuprate

The sulfenate ester (1.4 g, 10 mmol) was treated with lithium dimethylcuprate (20 mmol) at 0° for one hour. Distillation afforded a sample of methyl phenyl sulfide (1.08 g, 87%) pure by vpc and tlc (silica, hexanes or carbon tetrachloride), and identical to an authentic sample by nmr and ir.

Synthesis of Chiral Sulfoxides

Menthyl Sulfinate Esters

(-)-Menthyl (-)-(S)-Benzenesulfinate (30)

A commercial solution of n-butyl lithium (100 mmol) was slowly added to a solution of menthol (15.6 g, 100 mmol) in petroleum ether (bp 30-60°, 500 ml). The clear solution was flash-evaporated and the residue was dissolved in carbon tetrachloride (300 ml). N-(phenylsulfinyl)phthalimide (27.1 g, 100 mmol) was added and the mixture was stirred overnight. The mixture was filtered and the filtrate was evaporated to give a pale yellow oil (20 g), that contained one main component (tlc, silica, chloroform R_f 0.77). The oil was dissolved in chloroform and filtered through a silica column (60 g) to remove most of the impurities. After several attempts, the resultant oil was crystallized from methanol (-78°) to give a colorless solid, mp 25° (4.0 g). This was recrystallized twice from pentane to give (-)-menthyl (-)-(S)-benzenesulfinate as colorless needles, mp 51-2° (lit[156] 49-51°), $[\alpha]_D$ -205.5° (c 2.4 acetone) (lit[156,140] -205.5°, -206.1° (c 2.0 acetone)).

Attempts to obtain a second crop of material from the mother liquors were unsuccessful. They were evaporated, dissolved in methanol and treated with gaseous hydrogen chloride. The resulting solution could not be induced to crystallize despite many attempts at a variety of concentrations and temperatures.

(-)-Menthyl (-)-(S)-p-Toluenesulfinate

Sodium p-Toluenesulfinate[186]

Water (600 ml) was placed in a 2 ℓ beaker and heated to 70°. Zinc dust (80 g, 2.75 atom) was added, followed by powdered p-toluenesulfonyl chloride (100 g, 1.3 mol, in 5 g portions). The temperature rose to about 80° during the addition. The mixture was stirred for a further 10 min, then heated to 90° and made strongly alkaline by the addition of 12 N sodium hydroxide (50 ml) followed by 10 g portions of sodium carbonate. Considerable frothing occurred at this stage.

The mixture was filtered and the cake of solids was transferred to a beaker and heated slowly with 1000 ml water until the mixture started to froth vigorously. The mixture was again filtered, the filtrates were combined and the mixture was evaporated to a volume of 200 ml. The mixture was cooled in an ice bath and the crystals were filtered to give sodium p-toluenesulfinate (49.2 g, 53%) as large flat colorless crystals that were air-dried.

p-Toluenesulfinyl chloride[187]

Sodium p-toluenesulfinate (42.8 g, 200 mmol) was powdered and added in small portions (over a period of 15 min) to thionyl chloride (179 g, 109 ml, 2 mol; bp 76°) in a 250 ml round-bottomed flask. A vigorous reaction produced hydrogen chloride and sulfur dioxide. A calcium chloride tube was attached to the flask to protect the straw-coloured liquid from the atmosphere. After 2 hours the excess thionyl chloride was removed by distillation at reduced pressure (15 mm) and a temperature below 50°. Ether (50 ml) was added and the mixture

was again distilled. A further portion of ether (50 ml) was added, to be removed by distillation, giving a viscous oil containing a suspended granular solid. The crude sulfinyl chloride was dissolved by three successive treatments with ether (50 ml, 30 ml and 30 ml respectively) which were decanted from the residue. Removal of the ether from the combined filtrates gave the sulfinyl chloride as a pale yellow oil that was distilled to give p-toluenesulfinyl chloride as an orange oil (31 g, 89%), bp 74°/0.1 mm.

(-)-Menthyl (-)-(S)-p-toluenesulfinate[188]

p-Toluenesulfinyl chloride (19.1 g, 110 mmol) and (l)-menthol (17.2 g, 110 mmol) were dissolved in ether (275 ml) in a 2 ℓ three-necked flask fitted with a magnetic stirrer, an addition funnel with an equilibrating side-arm, and a Vigreux column. Pyridine (17.7 ml, 220 mmol) was rapidly added to the well-stirred solution. After the initial reaction had subsided (~1 min), a drying tube (silica gel) was placed on the Vigreux column. The mixture was stirred overnight and then filtered. The ether solution was washed well with water (4 x 25 ml), dilute hydrochloric acid (4 x 25 ml) then water (50 ml). After drying ($MgSO_4$), this solution was evaporated under reduced pressure until crystals began to appear. The solution was then kept at −20° overnight.

The resulting crystals were collected to give the product as colorless prisms (16.4 g). A second and third crop (4.3 g, 4.8 g) were obtained by treating the mother liquor with hydrogen chloride and storing the solution at -20°.

The three crops were combined and recrystallized twice from acetone to give (-)-menthyl (-)-(S)-p-toluenesulfinate (21.5 g, 71%), mp 102-4.5° (lit[188,38] 108-9°, 105-6°) $[\alpha]_D$ -210° (c 2.0, acetone) (lit[188,38] -210°, -198°)

When freshly prepared this material had no detectable odour. After storing for six months in an airtight vial this material turned brown and developed an odour of menthol. Its melting point had dropped to 82-92°.

Reaction of Menthyl Sulfinate Esters with Lithium Organocuprates

The sulfinate ester was treated with the organocopper lithium reagent as previously described. The crude sulfoxide was isolated by chromatography on silica using hexane-chloroform and then chloroform-acetone mixtures as eluents. The fractions collected were monitored by vpc and/or tlc. The results obtained are summarised in Table III.

Methyl Phenyl (+)-(R)-Sulfoxide

(-)-Menthyl (-)-(S)-benzenesulfinate (1.4 g, 5 mmol) was treated with lithium dimethylcuprate (10 mmol) to give a mixture of menthol and the sulfoxide (vpc). This was chromatographed on silica (30 g), to give a yellow oil (228 g, 16%) containing mainly sulfoxide with a small amount of menthol (vpc, nmr). The sulfoxide was purified by Kugelröhr distillation, followed by preparative tlc (silica, eluent:

ethyl acetate) and a final Kugelrohr distillation, to give a sample of methyl phenyl (+)-(R)-sulfoxide that was 95.2% pure (vpc), $[\alpha]_D$ (c 1.305 ethanol) +133.9° (lit[40,60,62,109] +146° (ethanol), +137° (ethanol), ±°128.5° (ethanol), +149° (solvent not stated)).

Methyl p-Tolyl (+)-(R)-Sulfoxide

(-)-Menthyl (-)-(S)-p-toluenesulfinate (3.1 g, 10 mmol) was treated with lithium dimethylcuprate (20 mmol) to give a complex mixture that was chromatographically separated yielding four fractions:-

Fraction A: An oily mixture (153 mg) containing several components (tlc, vpc).

Fraction B: Starting material (1.24 g, 41%) mp and mmp 102-4°.

Fraction C: Menthol (507 mg, 55%) identified by vpc and helc (C_{18}-Porasil, tetrahydrofuran:H_2O 1:1).

Fraction D: An oil (573 mg, 63%) containing one major component.

Fraction B was shown to contain a small amount of high molecular weight material that was removed by helc (4 x μ-styrogel, tetrahydrofuran). The remaining menthol was then removed by reversed phase chromatography on C_{18}-Porasil (2 x 2' x 3/4", tetrahydrofuran:H_2O 1:1). The major component of the mixture was then purified by a second reversed phase chromatograph under similar conditions (tetrahydrofuran:H_2O 1:10 as eluent), to give methyl p-toluene (+)-(R)-sulfoxide as a pale yellow oil that solidified to colorless needles on standing, showing ir absorption at 1050 cm^{-1} (S=O str), and nmr absorptions at δ 7.1-7.7 (4H, quartet), δ 2.66 (3H, singlet) and

δ 2.45 (3H, singlet). This material was further purified by a repetition of the last step of the purification to give a sample (503 mg, 55%) mp 74-6° (lit[38,62] 73-4.5°, 75-6°), $[\alpha]_D$ +143.2 (c 2.0 ethanol) (lit[38] +141° (ethanol), +145.5 (acetone)*).

Phenyl p-Tolyl (+)-(R)-Sulfoxide

(-)-Menthyl (-)-(S)-p-toluenesulfinate (3.1 g, 10 mmol) was treated with lithium diphenylcuprate (20 mmol). A procedure similar to that used for the methyl compound using tetrahydrofuran:H_2O 1:3 for the final step gave phenyl p-tolyl (+)-(R)-sulfoxide as colorless needles (1.27 g, 59%), mp 91-3° (lit[38,57,63] 91-2.5°, 92-3°, 90-2°), $[\alpha]_D$ +21.8 (c 2.0, acetone) (lit[38,57,63] +21.1°, +22°, +21.6°).

Attempted Synthesis of n-Butyl p-Tolyl Sulfoxide

(-)-Menthyl (-)-(S)-p-toluenesulfinate (3.1 g, 10 mmol) was treated with lithium di-n-butylcuprate (20 mmol). Analysis of the reaction mixture by vpc or helc shows the presence of many materials from which the only readily-isolable compound was menthol (0.83 g, 53%).

* Other values appearing in the literature are +182.4°[62] (c 2.13 acetone) measured at 5460 Å, and +156° (ethanol)[189] with no melting point or other physical properties stated.

Synthesis of Sulfinimides

Thiophthalimides[123]

Sulfuryl chloride (13.5 g, 100 mmol) was added to a stirred solution of the disulfide (100 mmol) in carbon tetrachloride (200 ml) at 0-5°. Three drops of triethylamine were added, then the mixture was stirred for 30 min. This solution was added to a suspension of potassium phthalimide (37 g, 200 mmol) in carbon tetrachloride (400 ml) and the mixture was allowed to warm up to room temperature. After stirring overnight the solvent was removed and the residue was crystallized from either ethanol or chloroform-hexanes.

N-(Phenylthio)phthalimide mp and mmp 158-61° (lit[129] 160-1°) and N-(n-butylthio)phthalimide mp and mmp 67-9° (lit[129] 65-6°) were prepared.

Thiosuccinimides

A solution of the mercaptan (500 mmol) in methylene chloride (200 ml) was added dropwise to a stirred solution of N-chlorosuccinimide (67.8 g, 500 mmol) in methylene chloride (300 ml) at 0-5°. After 10 min the solution turned red or orange. Triethylamine (52.5 g, 530 mmol) was added dropwise; during this addition the colour of the mixture faded. The mixture was allowed to warm up to room temperature. After stirring for 10 minutes, the mixture was washed thoroughly with water, dried ($MgSO_4$) and evaporated to give the crude thioimide. This was purified by crystallization from ethanol.

N-(Phenylthio)succinimide mp 114-6° (lit[109,124] 116°, 117-7.5°) and N-(benzylthio)succinimide mp 164° (lit[124,190] 164-5°, 165-6°) were prepared.

An attempt to prepare N-(n-butylthio)succinimide gave an orange oil that contained mainly n-butyl sulfide (vpc). In another experiment the reaction solution was washed well with water; examination of the solution by nmr suggested the presence of the thioimide. The solution was evaporated to give an oil containing disulfide and another material (tlc, silica, benzene, R_f 0.30). Attempts at distillation or chromatography (silica, benzene) yielded only disulfide.

Sulfinimides

The thioimides (10 mmol) were dissolved in methylene chloride (40 ml) and the solution was cooled to 0-5°. m-Chloroperbenzoic acid (2.03 g, 85%, 10 mmol) in methylene chloride (20 ml) was added over a period of at least 20 minutes. The mixture was stirred at room temperature for a further 30 minutes, then evaporated. Ether (30 ml) was added and the mixture was stirred vigorously for 5 minutes. The insoluble material was removed by filtration, washed with a small amount of ether and dried to give the crude sulfinimide. This was purified by crystallization from methylene chloride-ether.

N-(Phenylsulfinyl)phthalimide, mp and mmp 150-3°, N-(n-butylsulfinyl)phthalimide, mp and mmp 87-8°, N-(phenylsulfinyl)succinimide (83%), mp 101-3°, ir ν_{max} 1115 and 1140 cm^{-1} (S=O str), nmr δ 7.3-8.0 (multiplet, 5H) and δ 2.65 (singlet, 4H),

ms 88 (base peak), 100 with P^+ at 223.0280 ± 5 ppm (calc for $C_{10}H_9NO_3$: 223.0303), and N-(benzylsulfinyl)succinimide (94%), mp 118-23° with decomposition, ir ν_{max} 1120 and 1150 cm^{-1} (S=O str), nmr δ 7.34 (singlet, 5H) δ 4.17 (singlet, 2H) and δ 2.73 (singlet, 4H), ms shows base peak at 91 with P^+ at 237.0448 ± 2 ppm (calc for $C_{11}H_{11}NO_3S$:237.0459), were prepared.

The Reaction of Sulfinimides with Lithium Organocuprates

Sulfinimide (10 mmol)was dissolved in tetrahydrofuran (40 ml) and added dropwise to a solution of the lithium organocuprate (prepared from cuprous iodide (3.8 g, 20 mmol) in anhydrous ether (20 ml)). The mixture was hydrolyzed with saturated aqueous ammonium chloride (50 ml) after it had been stirred for 5 min. The resultant mixture was filtered and the organic layer was separated. The solid and the aqueous solution were washed well with tetrahydrofuran:chloroform 1:1. The organic solutions were combined, washed well with saturated aqueous sodium chloride, dried ($MgSO_4$) and evaporated. The resulting material was chromatographed on silica (100 g) using as eluents (200 ml fractions) hexanes, hexanes:chloroform 9:1, 3:1, 1:1, 1:3; chloroform, chloroform: acetone 9:1, 3:1, 1:1 and acetone. The fractions were monitored by tlc and vpc as applicable. The results obtained are shown in Table III.

Reaction of N-(phenylsulfinyl)phthalimide with lithium dimethylcuprate at 0° gave methyl phenyl sulfide (17%) that was pure by vpc and tlc after distillation.

Treatment of N-(phenylsulfinyl)succinimide with lithium dimethylcuprate under similar conditions gave a low yield of the sulfoxide (24%). Sulfide (14%) was again isolated, along with a small amount of the imide (17%). When the reaction was repeated at -78° the sulfoxide became the major product (90%); this was purified by rechromatography of the initial oil on μ-styragel (eluent tetrahydrofuran) followed by a final helc purification on silica (2 x 2' x 3/8" Porasil A, chloroform + 1% ethanol).

Treatment of N-(phenylsulfinyl)succinimide with lithium diphenylcuprate gave a mixture that was resolved into three major fractions by the preliminary chromatograph:-

Fraction A: Biphenyl, mp and mmp 66-68°.

Fraction B: A dark oil (1.552 g) containing diphenyl sulfoxide (tlc); this was chromatographed (μ-styrogel, tetrahydrofuran, 0.5 ml/min) to give the sulfoxide as a pale yellow oil (1.378 g, 68%) that was further purified (helc, 2 x 2' x 3/8" Porasil A, chloroform: isooctane 3:1) to give the product mp and mmp 68-70°.

Fraction C: A pale blue solid (176 mg) that was purified by hepc (4 x μ-styragel, 0.7 ml/min tetrahydrofuran) to give a colorless solid (121 mg, 7%) mp 118-20°, which was shown by ms to be 2-benzoylpropionamide (lit[191,192] mp 125°).

N-(Phenylsulfinyl)phthalimide, when treated similarly, gave only two fractions. The first of these was biphenyl. The other (2.511 g) was rechromatographed on μ-styragel to give two fractions:-

Fraction A: Mainly one component (tlc, silica, chloroform:acetonitrile 17:3, R_f 0.38) shown by ir and ms to be 2-benzoylbenzamide, mp 154-7° (lit[193,194] 160°, 165°) after crystallization from benzene.

Fraction B: An oily yellow solid that was stirred with chloroform: isooctane 1:5 and filtered to give 2-benzoylbenzamide as colorless needles, mp 144-8°. The solution was evaporated to give the sulfoxide, mp and mmp 67-9°.

Treatment of N-(benzylsulfinyl)succinimide with lithium dimethylcuprate gave a mixture from which benzyl methyl sulfoxide and benzyl methyl sulfide were isolated. The sulfide (48 mg, 2.4%) was pure by vpc after hepc (2 x 2' x 3/8", C_{18} Porasil, tetrahydrofuran:water 1:20). The sulfoxide (623 mg, 29%) was purified by helc (4 x μ-styrogel, tetrahydrofuran followed by 2 x 2' x 3/8", C_{18} Porasil, tetrahydrofuran: water 1:3).

Synthesis of Diastereomeric Sulfinimides

(-)-(S)-Malimide

Diethyl (-)-(S)-malate (36)

Hydrogen chloride was bubbled slowly through a solution of malic acid (50 g) in ethanol (200 ml) for 5 min. The mixture was heated on a steam bath for one hour, by which time the reaction was complete (nmr). The solvent was flash-evaporated and the residue was

distilled to give diethyl (-)-(S)-malate (36) (74-6%) bp 119°/7 mm Hg (lit[195,196] 103-5°/2-3 mm, 128°/10 mm), $[\alpha]_D$ = -9.63° (lit[197-9] -10.18, -10.44, -10.465), n_D^{23} 1.4328 (lit[195] n_D^{25} 1.4340), d^{23} 1.1208, $[R_L]^D_{exp}$ 43.7 (calc 43.5).

β-Ethyl-α-(-)-(S)-malamate (37)

Ammonia was bubbled through a stirred sample of diethyl (-)-(S)-malate (50 g). After one hour the oil was cooled to -20°. The crystalline precipitate was filtered and washed with a small amount of ether. Crystallization from chloroform-ether gave β-ethyl-α-(-)-(S)-malamate (37) (3.5 g, 8%), mp 107-8° (lit[201] 102-3°, $[\alpha]_D$ (c 2.5, MeOH) 44.9° (lit[201] 43.8°).

Nmr analysis indicated that the oil remaining was starting material containing a small amount of the amido-ester (37).

Sodium (-)-(S)-Malimate (38)

Sodium (460 mg, 20 matom) was dissolved in methanol (20 ml). The methanol was removed under vacuum, then β-ethyl-α-(-)-(S)-malamate (37) (1.61 g, 10 mmol) dissolved in benzyl alcohol (10 ml) was added. The mixture was stirred at 0.025 mm for one hour. The gelatinous precipitate was filtered and washed with ether to give sodium (-)-(S)-malimate (38) (1.20 g, 88%), $[\alpha]_D$ -59.4°.

Acidification with gaseous hydrogen chloride of a suspension of this material in dioxane, followed by removal of solvent, gave an oil that solidified to give sticky crystals. Chromatography on silica

(eluent: ethyl acetate) gave a sample of (-)-(S)-malimide (34), mp 97-8° (lit[127] 96-7°), $[\alpha]_D$ -91.1° (c 1.025, MeOH) (lit[127] -90.6°).

(-)-(S)-Malimide (34)

In a three-necked round-bottomed flask equipped with a gas dispersing tube, a dropping funnel and a dry ice condenser, dimethyl (-)-(S)-malate (41) (4 g, 1.94 mmol) was dissolved in absolute methanol (150 ml). Ammonia was allowed to bubble gently through the solution for 25 min, then the warm flask was cooled in an ice-cold water bath, and sodium methoxide (prepared from sodium (632 mg, .0275 gatom) in methanol (20 ml)) was added dropwise over a period of 45 min. During that time the bath was allowed to warm gradually to about 20°. The dropping funnel was rinsed with absolute methanol (5 ml). The flow of ammonia was stopped after 2.5 hr, but the stirring was continued for a further 30 min at 20°. The methanol was then partially removed at reduced pressure until the volume was reduced to 50 ml. The slurry was acidified with dry gaseous hydrogen chloride (checked with pH paper) and then the remaining solvent was removed on the rotovap.

The white solid was taken up in acetone (100 ml), which dissolved the free imide. Sodium chloride was filtered off, washed with acetone (10 ml); the acetone solutions were combined, evaporated to dryness and the resulting yellow oil (3.6 g) dried *in vacuo* at room temperature for 1.5 days.

Chromatographing this material on silica gel (eluent:ethyl acetate) gave a sample of (-)-(S)-malimide (34) (1.60 g, 56%) identical to that described above.

(+)-(R)-2,3-Dimethoxysuccinimide (43)

Dimethyl (+)-(R)-Tartrate (40)

(R)-Tartaric acid (100 g) was dissolved in methanol (400 ml) and dry hydrogen chloride gas was passed until 20 g had been absorbed. The mixture was allowed to stand for 45 min then refluxed for an hour to give, after removal of the solvent at reduced pressure, dimethyl (+)-(R)-tartrate (40) (121 g, 102%), bp 166°/17 mm, 159°/12 mm. A sample that had been purified by distillation gave one peak on vpc and showed n_D^{25} 1.4520, d^{25} 1.3344, $[R_L]_D^{25}$ 35.99 (calc 36.74), $[\alpha]_D$ +2.719 (lit[202] +2.14°).

Dimethyl (+)-(R)-2,3-dimethoxysuccinate (41)

Dimethyl (+)-(R)-tartrate (40) (59.3 g, 333 mmol), silver oxide (231 g, 1 mol) and methyl iodide (282 g, 2 mol) were mixed in a 2 ℓ flask with a reflux condenser attached. A vigorous reaction ensued that was moderated by cooling on ice. The reaction subsided and the mixture was refluxed for 4 hr; during this period the silver oxide turned from brown to purple, and then whitish. The mixture was washed well with ether, the ether solutions were combined and the residue was distilled after removal of the ether to give dimethyl (+)-(R)-2,3-dimethoxysuccinate (41), bp 137-8°/8 mm, $[\alpha]_D^{24}$ +102.3 (c 10.97 benzene) (lit[202,203] +104.7°, c 10.01 benzene).

(+)-(R)-2,3-dimethoxysuccinimide (43)

Treatment of dimethyl (R)-2,3-dimethoxysuccinate (41) with ammonia in the presence of sodium methoxide, as described for the synthesis of imide 34, gave crude (+)-(R)-2,3-dimethoxysuccinimide (3.09 g, 99%), that was recrystallized from chloroform-hexanes to give colorless needles, mp 108-10° (lit[131,132] 108-10°, 111°), $[\alpha]_D^{17}$ + 225.5° (c 1.5 acetone), optical purity 95.5% (lit[131] 235.5°, c 1.6 acetone).

Potassium (+)-(R)-2,3-dimethoxysuccinimide (42)

This was prepared in a manner similar to sodium (-)-(S)-malimate using potassium in place of sodium for the preparation of the methoxide. After the reaction was complete, the solvent was evaporated to give the product 42 as a colorless powder (80-90%) that was washed well with ether.

(-)-(A)-2-Methoxysuccinimide

In a manner similar to that described in the previous section, (-)-(S)-malic acid was converted to dimethyl (-)-(S)-malate (77%), bp 94-7°/0.015 mm (lit[205,206] 110-2°/7 mm, 90-2/2 mm), $[\alpha]_D$ -10.2° (acetone c 8.33) (lit[204,206] -16°, -8.9° (methanol, c 6.37)). This material was converted to dimethyl (-)-(S)-2-methoxysuccinate, bp 72°/0.005 mm (lit[207] 108-12°/11 mm), $[\alpha]_D$ -48.68° (acetone c 6.23) (lit[207] -47.8° (acetone c 3.047). Cyclisation of this material gave (-)-(S)-2-methoxysuccinimide as a colorless solid mp 65-7°; anal. found: 46.32%C, 5.25%H, 10.68%N; calc for $C_5H_7NO_3$: 46.51%C, 5.46%H, 10.85%N.

Synthesis of N-(Phenylthio)-(-)-(S)-Malimide (59, R=C_6H_5)

Method A: A solution of phenyl sulfenyl chloride (5 mmol, prepared from diphenyl disulfide (545 mg,2.5 mmol) and sulfuryl chloride (338 mg, 2.5 mmol) in carbon tetrachloride (2.5 ml)) was added to a stirred suspension of sodium (-)-(S)-malimate (38) (685 mg, 5 mmol) in carbon tetrachloride (7.5 ml). The mixture was stirred overnight and then filtered. The residue was washed well with chloroform, the organic solutions were combined and evaporated to give an oil that solidified on cooling. Nmr, tlc (silica, hexanes) and vpc showed that this was mainly diphenyl disulfide (521 mg, 96%).

Similar results were obtained when the reaction was repeated with dichloromethane as solvent.

Method B: The procedure was repeated using (-)-(S)-malimide (34) (575 mg, 5 mmol) and triethylamine (530 mg, 5.05 mmol) in place of the salt (38). Again, most of the diphenyl disulfide was recovered. Similar results were obtained if 10.1 mmol triethylamine were used in this reaction.

Method C: Sodium (S)-malimide (685 mg, 5 mmol) was added to a stirred solution of phenyl benzenethiosulfonate (39) (1.25 g, 5 mmol) in ether (20 ml). After 4 hours tlc (benzene) indicated that no reaction had occurred. The solvent was replaced by dimethoxyethane. Tlc and nmr indicated that no reaction had occurred after the mixture had been heated to 150° for several hours.

Synthesis of Phenyl Benzenethiosulfonate (39)[200]

m-Chloroperbenzoic acid (20.3 g, 85% pure, 100 mmol) dissolved in chloroform (200 ml) was added dropwise to a solution of phenyl disulfide (10.9 g, 50 mmol) in chloroform (500 ml) at 0-5°. The yellow mixture became cloudy after stirring for about an hour. The mixture was allowed to warm up to room temperature and stirred overnight. The solution was washed with saturated aqueous sodium bicarbonate solution and then evaporated to give phenyl benzenethiosulfonate (39) (12.0 g, 96%) as a pale yellow oil. Dissolving this oil in petroleum ether (500 ml) and cooling to -20° gave the product as a crystalline solid, mp 46-8° (lit[200] 43-44.5°).

Attempted Synthesis of N-(Phenylthio)-(+)-(R)-2,3-dimethoxysuccinimide (44)

Method A: Sodium (+)-(R)-2,3-dimethoxysuccinimide (18.1 g, 100 mmol) was treated with benzenesulfenyl chloride, prepared from diphenyl disulfide (10.9 g, 50 mmol) and sulfuryl chloride (6.25 g, 50 mmol). After stirring for three hours the mixture was still bright orange, suggesting that the desired reaction had not occurred. The mixture was filtered and tlc showed that the filtrate contained diphenyl disulfide as the major component.

Method B: (+)-(R)-2,3-dimethoxysuccinimide (8.3 g, 52.5 mmol) and triethylamine (2.6 g, 52.2 mmol) were dissolved in carbon tetrachloride (200 ml) and cooled in an ice bath. Benzenesulfenyl chloride prepared

from diphenyl disulfide (5.7 g, 26 mmol) and sulfuryl chloride (3.5 g, 26 mmol) was added slowly. The orange solution of the sulfenyl chloride rapidly gave way to a yellow color. The solution was evaporated and chromatographed on silica to give diphenyl disulfide (3.7 g, 65%), and N-(phenylthio)-(+)-(R)-2,3-dimethoxysuccinimide (44) (550 mg, 4%) mp and mmp 112-4°.

Method C: Triethylamine (20 mmol) was added to a solution of imide 43 (20 mmol) and benzenesulfenyl chloride (20 mmol) in carbon tetrachloride (200 ml) at 0-5°. The mixture was stirred for one hour, filtered then evaporated. The residue was crystallized from chloroform-hexanes to give thioimide 44 (64%), mp and mmp 113-115°.

Method D: Potassium (+)-(R)-2,3-dimethoxysuccinimide (15.4 g, 78 mmol) was added to a solution of benzenesulfenyl chloride prepared from diphenyl disulfide (9.07 g, 42 mmol) and sulfuryl chloride (5.62 g, 42 mmol). The mixture was stirred overnight, filtered and evaporated to give an oil that was crystallized from chloroform-hexanes to give a pale yellow solid. This was recrystallized from ethanol to give N-(phenylthio)-(+)-(R)-2,3-dimethoxysuccinimide (44) (11.4-12.4 g, 55-60%) as colorless needles, mp 115-7.5°, $[\alpha]_D^{17}$ +179.1° (c 1.32 acetone), pure by tlc (silica, benzene, R_f 0.40), showing nmr absorptions at δ 7.8-8.4 (5H, multiplet), δ 4.64 (2H, singlet) and δ 4.13 (6H, singlet) ms shows peaks at 45, 65, 73, 77, 88 (base peak), 91, 109, 121, 129, 218, 267 (P^+), ir ν_{max} 1117 cm^{-1} (S=O str), with anal: C 53.56; H 5.02; S 5.33; N 11.80. Calc. for $C_{12}H_{13}SNO_4$: C 53.93; H 4.87; S 5.02; N 11.90.

N-(Phenyl-(±)-Sulfinyl)-(+)-(R)-2,3-dimethoxysuccinimide (45)

A solution of m-chloroperbenzoic acid (2.08 g, 10 mmol) in methylene chloride (25 ml) was added over a period of 20 min to a solution of thioimide 44 (2.67 g, 10 mmol) in methylene chloride (25 ml) at 0-5°. The mixture was allowed to warm up to room temperature and stirred for a further hour before the solvent was removed at reduced pressure and the residue was stirred with dry ether (25 ml). The resultant solid was washed with dry ether (10 ml) to give N-(phenyl-(±)-sulfinyl)-(+)-(R)-2,3-dimethoxysuccinimide (45) (1.54 g, 54%), mp 120-37°, showing ms peaks at 77 ($C_6H_5^+$), 88 ($C_5H_4S^+$), 125 ($C_6H_5S^+{=}O$) and 283.0510 (P^+, calc. for $C_{12}H_{13}NO_3S$ 283.0514), ir ν_{max} shows S=O stretch at 1115 cm^{-1}, and $[\alpha]_D$ +148.1°.

Recrystallization of this material from methylene chloride-ether gave material mp 129-49°, $[\alpha]_D^{25}$ +154.3° (1.17 g) with a second crop mp 124-144°, $[\alpha]_D^{25}$+153.4°.

Treatment of a sample of 45 (100 mg) with methanol under reflux for one hour gave a solution that was evaporated and extracted with pentane (5 ml) to give a solution of methyl benzenesulfinate (50 mg, 79%), that was pure by tlc and vpc (identical with an authentic sample) and showed $[\alpha]_D^{17}$ +3.18°. This rotation can be explained by the presence of 1.1% imide as an impurity.

Treatment of a sample of 45 (1.42 g, 5 mmol) with lithium dimethylcuprate (10 mmol) at 0° for one hour gave a mixture that was worked up in the usual manner to give methyl phenyl sulfide (260 mg, 42%), methyl phenyl sulfoxide (116 mg, 17%), and (+)-(R)-2,3-dimethoxysuccinimide (252 mg, 32%), all identical with authentic samples. The sulfoxide showed $[\alpha]_D$ - 3.9° .

N-(Benzyl-(±)-sulfinyl)-(+)-(R)-2,3-dimethoxysuccinimide (46)

N-(Benzylthio)-(+)-(R)-2,3-dimethoxysuccinimide

Benzyl sulfenyl chloride (50 mmol) was treated with potassium (+)-(R)-2,3-dimethoxysuccinimide (19.7 g, 100 mmol) as described for the corresponding phenyl compound, to give N-(benzylthio)-(+)-(R)-2,3-dimethoxysuccinimide as colorless needles, mp 65-6° (ethanol), $[\alpha]_D^{17}$ +231.2 (acetone c 1.009), ms shows peaks at 45, 65, 85, 88, 91 (base peak), 122 (base peak), 160, 281 (P^+), ir ν_{max} 1112 cm^{-1} (S=O str).

Synthesis of N-(Benzyl-(r)-sulfinyl)-(+)-(R)-2,3-dimethoxysuccinimide(46)

Oxidation of the thioimide (10 mmol) with m-chloroperbenzoic acid gives benzyl-(r)-sulfinyl-(R)-2,3-dimethoxysuccinimide (6.4 g, 89%) mp 89-97°.

Attempts to crystallize this material from methylene chloride-ether yielded only imide, identical to an authentic sample. Even at -20° the sulfinimide solution decomposed over a period of several days to give imide. A sample of the material (200 mg) was dissolved in deuterochloroform (2 ml) and allowed to stand for 48 hr. A crystalline solid was precipitated and the solution turned pale orange. Hexanes were added and the precipitate was filtered off. Nmr and ir showed this precipitate to be (+)-(R)-2,3-dimethoxysuccinimide (118 mg, 97%). The mother liquor was evaporated to give a residue that smelled of benzaldehyde. The presence of the latter material was confirmed by helc (hexanes, μ-porasil).

Synthesis of Thioimides *via* Organosilicon Intermediates

N-Trimethylsilylsuccinimide (49)

A 1000 ml three-necked flask equipped with a mechanical stirrer, condenser and mercury seal, was charged with succinimide (198 g, 2 mol), hexamethyldisilazane (48) (242 g, 1.5 mol), and imidazole (2-3 g, 1-2% based on succinimide). The mixture was gently refluxed for 12 hr while a gentle stream of dry nitrogen was bubbled through the reaction mixture to help expel the ammonia produced and maintain anhydrous conditions. The product was distilled from the reaction mixture to give N-trimethylsilylsuccinimide (49) bp 97-8°/4 mm, 112-4°/12 mm (lit[208] 120°/18 mm), showing nmr absorptions at δ 2.59 (singlet, 4H) and δ 0.35 (singlet, 9H).

N-trimethylsilyl-(+)-(R)-2,3-dimethoxysuccinimide

In a similar manner, a sample of (+)-(R)-dimethoxysuccinimide (1.366 g, 8.6 mmol) was treated with hexamethyldisilazane (25 ml) at 90° under a constant stream of nitrogen. The imide dissolved after 15 min. The heating was continued overnight; then the mixture was allowed to cool. No imide was precipitated at this stage, indicating that the reaction was complete. Excess hexamethyldisilazane was removed at reduced pressure and the residue was distilled to give N-trimethylsilyl-(+)-(R)-2,3-dimethoxysuccinimide (1.766 g, 90%) as a colorless hygroscopic oil, bp 98-100°/1 mm $[\alpha]_D$ +193.7°, nmr shows absorptions at δ 3.88 singlet, 2H), δ 3.53 (singlet, 6H) and δ 0.40 (singlet, 9H).

N-(Phenylthio)succinimide

Diphenyl disulfide (1.09 g, 5 mmol) and trimethylsilylsuccinimide (0.585 mg, 5 mmol) were dissolved in carbon tetrachloride (20 ml) and placed in a bath at 80° for 24 hr. At the end of this time the solvent was removed to give a solid (1.72 g) mp 96-106°. Crystallization of this material (ethanol) gave N-(phenylthio)succinimide (1.4 g, 68%) mp and mmp 113-5°.

Under similar conditions benzyl sulfenyl chloride gave N-(benzylthio)succinimide (1.2 g, 54%) mp and mmp 160-2°.

Treatment of n-butanesulfenyl chloride with the organosilicon reagent gave an oil that contained a trace of disulfide and imide (tlc benzene). Nmr and ms analysis showed the main component was N-(n-butylthio)succinimide (1.39 g, 74%). Repeated attempts at crystallization failed and distillation gave only disulfide as did chromatography attempts on silica or alumina.

REFERENCES

1. H. Schmid and P. Karrer, Helv. Chim. Acta, 31, 1017 (1948).
2. O.E. Schultz and R. Gmelin, Arch. Pharm., 287, 404 (1954); Chem. Abstr., 51, 14562 (1957).
3. H. Schmid and P. Karrer, Helv. Chim. Acta., 31, 1497 (1948).
4. A. Kjaer and R. Gmelin, Acta. Chem. Scand., 10, 1100 (1956).
5. O.E. Schulz and W. Wagner, Z. Naturforsh, 11B, 417 (1956).
6. B.W. Christensen and A. Kjaer, Acta. Chem. Scand., 17, 846 (1963).
7. A. Kjaer and B.W. Christensen, Acta. Chem. Scand., 12, 833 (1956).
8. A. Kjaer and R. Gmelin, Acta. Chem. Scand., 10, 1358 (1956).
9. A. Kjaer, R, Gmelin and R.B. Jensen, Acta. Chem. Scand., 10, 1614 (1956).
10. W. Klyne, J. Day and A. Kjaer, Acta. Chem. Scand., 14, 215 (1960).
11. K.K. Cheung, A. Kjaer and G.A. Sim, Chem. Commun., 100 (1965).
12. L.D. Wright, E.L. Cressom, J. Valiant, D.E. Wolf and K. Folkers, J. Amer. Chem. Soc., 76, 4163 (1954).
13. L.D. Wright and E.L. Cresson, J. Amer. Chem. Soc., 76, 4156 (1968).
14. C.J. Cavallito, J.S. Buck and C.M. Suter, J. Amer. Chem. Soc., 66, 1952 (1944).
15. A. Stoll and E. Seebeck, Helv. Chim. Acta., 32, 197 (1949).
16. A. Stoll and E. Seebeck, Helv. Chim. Acta., 34, 481 (1951).
17. A. Stoll and E. Seebeck, Advances in Enzymol., 11, 377 (1951).
18. A.I. Virtanen and C.G. Spare, Suomen Kemistilehti, 34, 72 (1961); Chem. Abstr., 56, 10585 (1962).
19. C.J. Morris and J.F. Thompson, J. Amer. Chem. Soc., 78, 1605 (1956).

20. C.J. Morris and J.F. Thompson, Chem. and Ind. (London), 951 (1955).

21. A.I. Virtanen and E.J. Matikrala, Acta Chem. Scand., 13, 623 (1959).

22. M.H. Brodnitz and J.V. Pascale, J. Agr. Food Chem., 19, 269 (1971).

23. N.J. Leonard and C.R. Johnson, J. Org. Chem., 27, 282 (1962).

24. C.R. Johnson and J.E. Keiser, Org. Syn., 46, 78 (1966).

25. W.D. Kingsbury and C.R. Johnson, Chem. Commun., 365 (1969).

26. W. Tagaki, K. Kikukawa, K. Ando and S. Oae, Chem. Ind. (London), 1624 (1964).

27. S. Oae, Y. Ohnishi, S. Kozuka and W. Tagaki, Bull. Chem. Soc. (Japan), 39, 364 (1966).

28. K. Balenovic, N. Bregant and D. Francetic, Tetrahedron Lett., No. 6, 20 (1960).

29. K. Balenovic, I. Bregovec, D. Fracetic, I. Monkovic and V. Tomasic, Chem. Ind. (London), 469 (1961).

30. A. Mayr, F. Montanari and M. Tramontini, Gazz. Chim. Ital , 90, 739 (1960); Chem. Abstr., 55, 16460 (1961).

31. A. Mayr, F. Montanari and M. Tramontini, Ricerca Sci., 30, 746 (1960); Chem. Abstr., 55, 1499 (1961).

32. F Montanari, Tetrahedron Lett., 3367 (1965).

33. A. Maccioni, F. Montanari, M. Secci and M. Tramontini, Tetrahedron Lett., 607 (1961).

34. D.J. Cram and F.A. Abd Elhafez, J. Amer. Chem. Soc., 74, 5828 (1952).

35. V. Prelog, Bull. Soc. Chim., 987 (1956).

36. A. Maccioni, Boll. Sci. Fac. Chim. Ind. Bologna, 23, 41 (1965); Chem. Abstr.,63, 8239 (1965).

37. G. Barbieri, U. Folli, F, Montanari and G. Torre, *ibid.*, 23, 47 (1965); Chem. Abstr., 63, 8224 (1965).

38. K. Mislow, M.M. Green, P. Laur, J.T. Melillo, T. Simmons and A.L. Ternay Jr., J. Amer. Chem. Soc., 87, 1958 (1965).

39. K. Mislow, M.M. Green and M. Raban, *ibid*,, 87, 2761 (1965).

40. U. Folli, D.Iarossi, F. Montanari and G. Torre, J. Chem. Soc. (C), 1317 (1968).

41. G. Barbieri, V. Davoli, I Moretti, F. Montanari and G. Torre, J. Chem. Soc. (C) 731 (1969).

42. D. Iarossi and A. Pinetti, Boll. Sci. Fac. Chim. Ind. Bologna, 27, 221 (1969); Chem. Abstr., 72, 131811 (1970).

43. U. Folli and D. Iarossi, Gazz. Chim. Ital., 99, 1306 (1969); Chem. Abstr., 72, 110969 (1970).

44. U. Folli, D. Iarossi and G. Torre, Ric. Sci., 38, 914 (1968); Chem. Abstr., 71, 3099 (1969).

45. R.M. Dodson, N. Newman and H.M. Tsuchiya, J. Org. Chem., 27, 2707 (1962).

46. B.J. Auret, D.R. Boyd and H.B. Henbest, Chem. Commun., 66 (1966).

47. B.J. Auret, D.R. Boyd, H.B. Henbest and S. Ross, J. Chem. Soc. (C), 237 (1968).

48a. T. Higushi, I.H. Pitmanand, K.H. Gensch, J. Amer. Chem. Soc., 88, 5676 (1966).

b. L.J. Miller, personal communication.

49. U. Folli, D. Iarossi and F. Montanari, J. Chem. Soc. (C), 1372 (1968).

50. B.J. Auret, D.R. Boyd and H.B. Henbest, J. Chem. Soc. (C), 2374 (1968).

51. K.Balenovic and N. Bregnant, Chem. and Ind. (London), 1577 (1964).

52a. M. Mikolajczyk and M. Para, Chem. Commun., 1192 (1969).

b. S. Juge and H.B. Kagan, Tetrahedron Lett., 2733 (1975).

53. J. Tsuji, Advan. Org. Chem., 109 (1969).

54. A.C. Cope and E.A. Caress, J. Amer. Chem. Soc., 88, 1711 (1966).

55a. M. Mikolajczyk, J. Drabowicz and F. Cramer, Chem. Commun.,317 (1971).

b. G. Balavoine, S. Juge, H.B. Kagan, Tetrahedron Lett., 4159 (1973).

c. H.B. Kagan, G. Balavoine,and A. Moradpour, J. Mol. Evol. 4, 41 (1974).

56. K.K. Andersen, Tetrahedron Lett., 93 (1962).

57. K.K. Andersen, W. Gaffield, N.E. Papanikolau, J.W. Foley and R.I. Perkins, J. Amer. Chem. Soc., 86, 5637 (1964).

58. H. Gilman, J. Robinson and N.J. Beaber, J. Amer. Chem. Soc., 48, 2715 (1926).

59. M. Axelrod, P. Bickart, J. Jacobus, M.M. Green and K. Mislow, J. Amer. Chem. Soc., 90, 4835 (1968).

60. J. Jacobus and K. Mislow, Chem. Commun., 253 (1968).

61. S. Colonna, R. Giovani and F. Montanari, Chem. Commun., 865 (1968).

62. F. Wudl and T.B.K. Lee, J. Amer. Chem. Soc., 95, 6349 (1973).

63. H. Hope, U. de la Camp, G.D. Homer, A.W. Messing and L.H. Sommer, Angew Chem. Int. Ed., 8, 612 (1969).

64. C.J.M. Stirling, J. Chem. Soc., 5741 (1963).

65. K.K. Andersen, J. Org. Chem., 29, 1953 (1964).

66. L.P. Lockard, W. Schroeck and C.R. Johnson, Synthesis, 485 (1973).

67. T. Durst, M.J. LeBelle, R. Van den Elzen and K.C. Tin, Can. J. Chem., 52, 761 (1974).

68. D.N. Harpp, S.M. Vines, J.P. Montillier and T.H. Chan, submitted for publication.

69. H. Potter: Abstracts 137th A.C.S Meeting, April 1960, p.30.

70. R. Oda and K. Yamamoto, J. Org. Chem., 26, 4679 (1961).

71. P. Manya, A. Sekera and P. Rumpf, Compt. Rend. Acad. Sci. (Paris) (C), 264, 1196 (1967).

72. P. Manya, A. Sekera and P. Rumpf, Tetrahedron, 26, 467 (1970).

73. C.R. Johnson, J.C. Sharp and W.G. Phillips, Tetrahedron Lett., 5299 (1967).

74. H. Giman, R.G. Jones and L.A. Woods, J. Org. Chem., 17, 1630 (1952).

75. G. Costa, A. Camus, L. Gatti and N. Marsich, J. Organomet. Chem., 5 568 (1966).

76. C.R. Johnson and G.A. Dutra, J. Amer. Chem. Soc., 95, 7777 (1973).

77. G.H. Posner, Org. React., 19, 1 (1972).

78. G.H. Posner and C.E. Whitten, Tetrahedron Lett., 4647 (1970).

79. B.C. Hartman, T. Livinghouse and B. Rickborn, J. Org. Chem., 38 4346 (1973).

80. C.R. Johnson, R.W. Herr and D.M. Wieland, J. Org. Chem., 38, 4263 (1973).

81. H. Phillips, J. Chem. Soc., 127, 2552 (1925).

82. R. Otto and A. Sossing, Chem. Ber., 18, 2493 (1885).

83. C.A. Bunton and B.N. Hendry, Chem. Ind. (London), 466 (1970).

84. A.J.H. Houssa, J. Kenyon and H. Phillips, J. Chem. Soc., 1700 (1929).

85. Y. Miyaji, H. Minato and M. Kobayashi, Bull. Chem. Soc. Japan, 44 862 (1971).

86. F. Arndt and H. Scholz, Ann., 510, 62 (1934).

87. C.J.M. Stirling, Int. J. Sulfur Chem., Part B, 6, 277 (1971).

88. M. Kobayashi and M. Terao, Bull. Chem. Soc. Japan, 39, 1292 (1966).

89. P. Carré and D. Libermann, Compt. Rend, 200, 2086 (1935).

90. L. Field, C.B. Hoelzel, J.M. Locke and J.E. Lawson, J. Amer. Chem. Spc., 83, 1256 (1961).

91. L. Field, C.B. Hoelzel and J.M. Locke, J. Amer. Chem. Soc., 84, 847 (1962).

92. L. Field and J.E. Lawson, J. Amer. Chem. Soc., 80, 838 (1958).

93. D. Libermann and A. Rouaix, C.R. Acad. Sci. Paris, 226, 2157 (1948); Chem. Abstr., 45, 1532 (1951).

94. D. Libermann, Bull. Soc. Chim. Fr., C., 141 (1951).

95. P. Carré and D. Libermann, C.R. Acad. Sci. Paris, 200, 2086 (1935); Chem. Abstr., 29, 6206 (1935).

96. F. Jung and T. Durst, Chem. Commun., 4 (1973).

97. D. Barnard, J. Chem. Soc., 4547 (1957).

98. I.B. Douglass, J. Org. Chem., 30, 633 (1965).

99. J.W. Wilt, R.G. Stein and W.J. Wagner, J. Org. Chem., 32, 2097 (1967).

100. D.N. Harpp and T.G. Back, Tetrahedron Lett., 5313 (1972).

101. D.N. Harpp and T.G. Back, J. Org. Chem., 38, 4328 (1973).

102. D.N. Harpp, and J.G. Gleason, Tetrahedron Lett., 1447 (1969).

103. D.N. Harpp, J.G. Gleason and D.K. Ash, J. Org. Chem., 36, 322 (1971).

104. D.J. Brown and P.W. Ford, J. Chem. Soc. (C), 2720 (1969).

105. G.A. Russell and L.A. Ochrymowycz, J. Org. Chem., 35, 2106 (1970).

106. H. Lecher, Chem. Ber., 58, 413 (1925).

107. C.A. Maryanoff, B.E. Maryanoff, R. Tang and K. Mislow, J. Amer. Chem. Soc., 95, 5839 (1973).

108. W.H. Baarschers and B.W. Krupay, Can. J. Chem., 51, 156 (1973).

109. J. Jacobus and K. Mislow, J. Amer. Chem. Soc., 89, 5228 (1967).

110. V. Horak and J. Pecka, J. Chromatog., 14, 97 (1964).

111. H.W. Prinzler, H. Tauchmann and C. Tzscharricke, J. Chromatog., 29, 151 (1967).

112. N. Grabowsky, Ann., 175, 348 (1875).

113. D.W. Emerson, A.P. Craig and I.W. Potts, Jr., J. Org. Chem., 32, 102 (1967).

114. R.A.W. Johnstone and I.D. Entwhistle, Chem. Ind.(London), 324 (1966).

115. N.Kharasch, S.J. Potempa and H.L. Wehrmeister, Chem. Rev., 39, 269 (1946).

116. L. Sargramora, P. Koch, A. Garbesi and A. Fava, Chem. Commun., 985 (1967).

117. E. Ciuffarin, M. Isola and A. Fava, J. Amer. Chem. Soc., 90, 3594 (1968).

118. F. Wudl, D.A. Lighter and D.J. Cram, J. Amer. Chem. Soc., 89, 4099 (1967).

119. M. Mikolajczyk and J. Drabowicz, Chem. Commun., 547 (1974).

120. M. Mikolajczyk and J. Drabowicz, Tetrahedron Lett., 2379 (1972).

121. A.R. Kittleson, U.S. Patent 2,553,270 (1951); Chem. Abstr., 45, 6792 (1951).

122. F. Klivenyi, J. Szabo and E. Vinkler, Acta. Chim. Acad. Sci. Hung., 6, 373 (1965); Chem. Abstr., 51, 1882 (1957).

123. T.G. Back, Thesis, McGill University, Montreal 1974, p.45.

124. Y. Abé, T. Nakabayashi and J. Tsurugi, Bull. Chem. Soc. Jap., 46 1898 (1973).

125. H. Wren and H. Williams, J. Chem. Soc., 109, 572 (1916).

126. M. Naps and I.B. Johns, J. Amer. Chem. Soc., 62, 2450 (1940).

127. H.R. Dave and M.K. Hargreaves, Chem. Commun., 743 (1967).

128. M.L. Pasteur, Ann. de Chem. et de Physique, 3, 38, 457 (1852).

129. M. Behforouz and J.E. Kerwood, J. Org. Chem., 34, 51 (1969).

130. J.E. Dunbar and J.H. Rogers, J. Org. Chem., 31, 2842 (1966).

131. C.R. Young, J. Chem. Soc., 105, 1228 (1914).

132. Th. Pasternak and J. Ph. Susz, Helv. Chim. Acta, 39, 2032 (1956).

133. E. Fischer and A. Speier, Ber., 28, 3252 (1895).

134. T. Purdie and J.C. Irvine, J. Chem. Soc. Trans., 79, 957 (1901).

135. B. Zwanenburg and J. Strating, Quart. Rep. Sulfur Chem., 5, 79 (1970).

136. G. Opitz, Angew Chem. Int. Ed., 6, 107 (1967).

137. J. Strating, L. Thijs and B. Zwanenburg, Tetrahedron Lett., 65 (1966).

138. B. Zwanenburg, L. Thijs and J. Strating, Tetrahedron Lett., 3453 (1967)

139. B. Zwanenburg, L. Thijs and J. Strating, Tetrahedron Lett., 2871 (1968).

140. B. Zwanenburg, L. Thijs and J. Strating, Tetrahedron Lett., 4461 (1969).

141. B.F. Bonini, G. Maccagnani, A. Wagenaar, L. Thijs and B. Swanenburg, J. Chem. Soc. Perkin Trans. I, 2490 (1972).

142. B. Zwanenburg, A. Wagenaar, L. Thijs and J. Strating, J. Chem. Soc., Perkin Trans. I, 73 (1973).

143. J.F. King and T. Durst, J. Amer. Chem. Soc., 85, 2676 (1963).

144. J.F. King and T. Durst, Tetrahedron Lett., 585 (1963).

145. W.A. Sheppard and J. Dieckmann, J. Amer. Chem. Soc., 86, 1891 (1964).

146. W.G. Phillips and K.W. Rats, J. Org. Chem., 37, 3818 (1972).

147. C.G. Vernier and C.G. Gibbs, Tetrahedron Lett., 2293 (1972).

148. B. Zwanenburg, L. Thijs, J. Broens and J. Strating, Rec. Trav. Chim. Pays-Bas, 91, 443 (1972).

149. E. Wedekind, D. Schenk and R. Strüsser, Chem. Ber., 56, 633 (1923).

150. W.A. Schulze, G.H. Short and W.W. Crouch, Ind. Eng. Chem., 42, 916 (1950).

151. L.B. Douglas, R.K. Bromer and F.T. Martin, J. Amer. Chem. Soc., 74, 5770 (1952).

152. D.N. Harpp and T.G. Back, unpublished results.

153. L. Birkofer, P. Richter and A. Ritter, Chem. Ber., 93, 2804 (1960).

154. E.W. Abel and D.A. Armitage, J. Chem. Soc., 3122 (1964).

155. D.N. Harpp and K. Steliou, unpublished results.

156. H.F. Herbrandson and R.T. Dickenson, Jr., J. Amer. Chem. Soc., 81, 4102 (1959).

157. R.E. Estep and D.F. Tavares, Int. J. Sulfur Chem., 8, 279 (1973).

158. C.R. Johnson, Personal communication.

159. R.M. McCurdy and J.H. Prager, J. Polymer Science (A), 2, 1185 (1964).

160. W. Windus and P.R. Shildneck, Org. Syn. Collected Vol. II, p. 345, John Wiley & Sons, N.Y. (1966).

161. C.R. Johnson, C.C. Bacon and J.J. Rigau, J. Org. Chem., 37, 919 (1972).

162. A.I. Vogel and D.M. Cowan, J. Chem. Soc., 16 (1943).

163. R.D. Obelentsev, S.V. Netupskaya, A.V. Mashkina and L.K. Gladkova, Isvest. Vostock Filialov. Acad. Nauk. SSSR, No. 10, 60 (1957); Chem. Abstr., 53, 273 (1959).

164. H. Brintzinger and H. Ellwanger, Chem. Ber., 87, 300 (1954).

165. H. Reinheckel and D. Jahnke, Chem. Ber., 99, 1718 (1966).

166. T, Mukaiyama and M. Ueki, Tetrahedron Lett., 3429 (1967).

167. A. Cerniani and G. Modena, Gazz. Chim. Ital., 89, 834 (1959); Chem. Abstr., 54, 22446 (1960).

168. W.E. Parham and R.F. Motter, J. Amer. Chem. Soc., 81, 2146 (1959).

169. J.R. Campbell, J. Org. Chem., 27, 2207 (1962).

170. W.R. Kirner and G.H. Richter, J. Amer. Chem. Soc., 51, 3409 (1929).

171. S. Searles, J. Amer. Chem. Soc., 73, 4515 (1951).

172. T. Nambara and N. Matsuhisa, Yakugaku Zasshie, 83, 642 (1963); Chem. Abstr., 59, 7411 (1963).

173. G.M. Bennett and F. Heathcoat, J. Chem. Soc., 273 (1929).

174. P.R. Shildneck and W. Windus, Org. Syn. Collected Vol. II, p. 411, John Wiley & Sons, N.Y. (1966).

175. I.B. Douglass and B.S. Farah, J. Org. Chem., 23, 805 (1958).

176. H. Böhme, H. Fischer and R. Frank, Ann., 563, 54 (1949).

177. E. Colby and C.S. McLoughlin, Chem. Ber., 20, 195 (1887).

178. F. Kraft and R.E. Lyons, Chem. Ber., 29, 441 (1896).

179. A. Rosenheim and L. Singer, Chem. Ber., 37, 2154 (1904).

180. M. Michael and A. Palmer, J. Amer. Chem. Soc., 6 254 (1884).

181. R. Otto and A. Artmann, Ann., 284, 301 (1880).

182. F. Ewerlöf, Ber. 4, 716 (1871).

183. E.V. Bell and G.M. Bennett, J. Chem. Soc., 3189 (1928).

184. R. Otto, Ber., 13, 1272 (1880).

185. R. Otto, J. Prakt. Chem., 2, 30, 174 (1884).

186. F.C. Whitmore and F.H. Hamilton, Org. Syn. Collected Vol. I, p. 492, John Wiley & Sons, N.Y. (1967).

187. F. Kurzer, Org. Syn. Collected Vol. IV, p. 937, John Wiley & Sons, N.Y. (1967).

188. R.E. Estep and D.F. Tavares, Int. J. Sulfur Chem., 8, 279 (1973).

189. K. Mislow, M. Axelrod, D.R. Rayner, H. Gotthardt and G.S. Hammond. J. Amer. Chem. Soc., 87, 4958 (1965).

190. K.H. Büchel and A. Conte, Chem. Ber., 100, 1248 (1967).

191. F. Tiemann, Ber., 24, 4065 (1891).

192. J. Biedermann, Ber., 24, 4074 (1891).

193. C. Beis, Compt. Rend., 139, 62 (1904).

194. C. Graebe and F. Ullmann, Ann., 291, 11 (1896).

195. H. Adkims and K.R. Billi, J. Amer. Chem Soc., 70, 3124 (1948).

196. Y. Tsuzuki, K. Tanabe, K. Okamoto and M. Fukubayashi, Bull. Chem Soc. Jap., 39, 1387 (1966).

197. E. Fischer and A. Sepier, Ber., 28, 3255 (1895).

198. H. Reitter, Zeitschrifte für Physikalische Chem., 36, 129 (1901).

199. L. Henry, Ann., 156, 177 (1870).

200. J.L. Kice and T.E. Rogers, J. Amer. Chem. Soc., 96, 8015 (1974).

201. K. Lutz, Chemisches Zentralblatt, 1900 II, 1013

202. T. Purdie and W. Barbour, J. Chem. Soc. (Trans.) 79, 971 (1901).

203. T. Purdie and J.C. Irvine, J. Chem. Soc. (Trans.) 79, 957 (1901).

204. I.Listowsky, G.Avigod and S.England, J. Org. Chem., 35, 1080 (1970).

205. A.S. Sadykov and N.I. Salit Uzbecksk. Khim. Zh. 6, 68 (1962); Chem. Abstr. 59, 432 (1963).

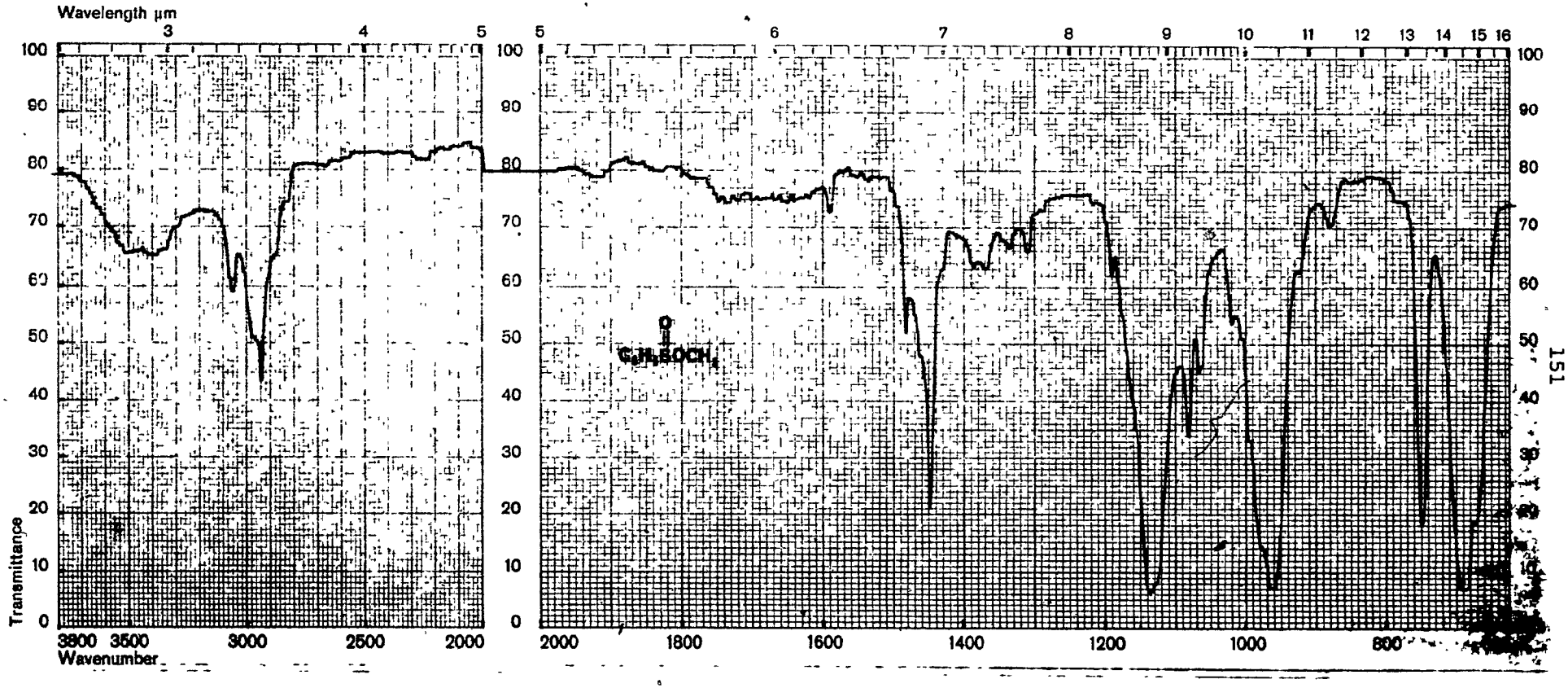
206. H. Arakawa, Naturwischenshaften, 50, 441 (1962); Chem. Abstr., 59, 7419 (1963).

207. A. Lardon and T. Reichstein, Helv. Chim. Acta, 32, 2003 (1949).

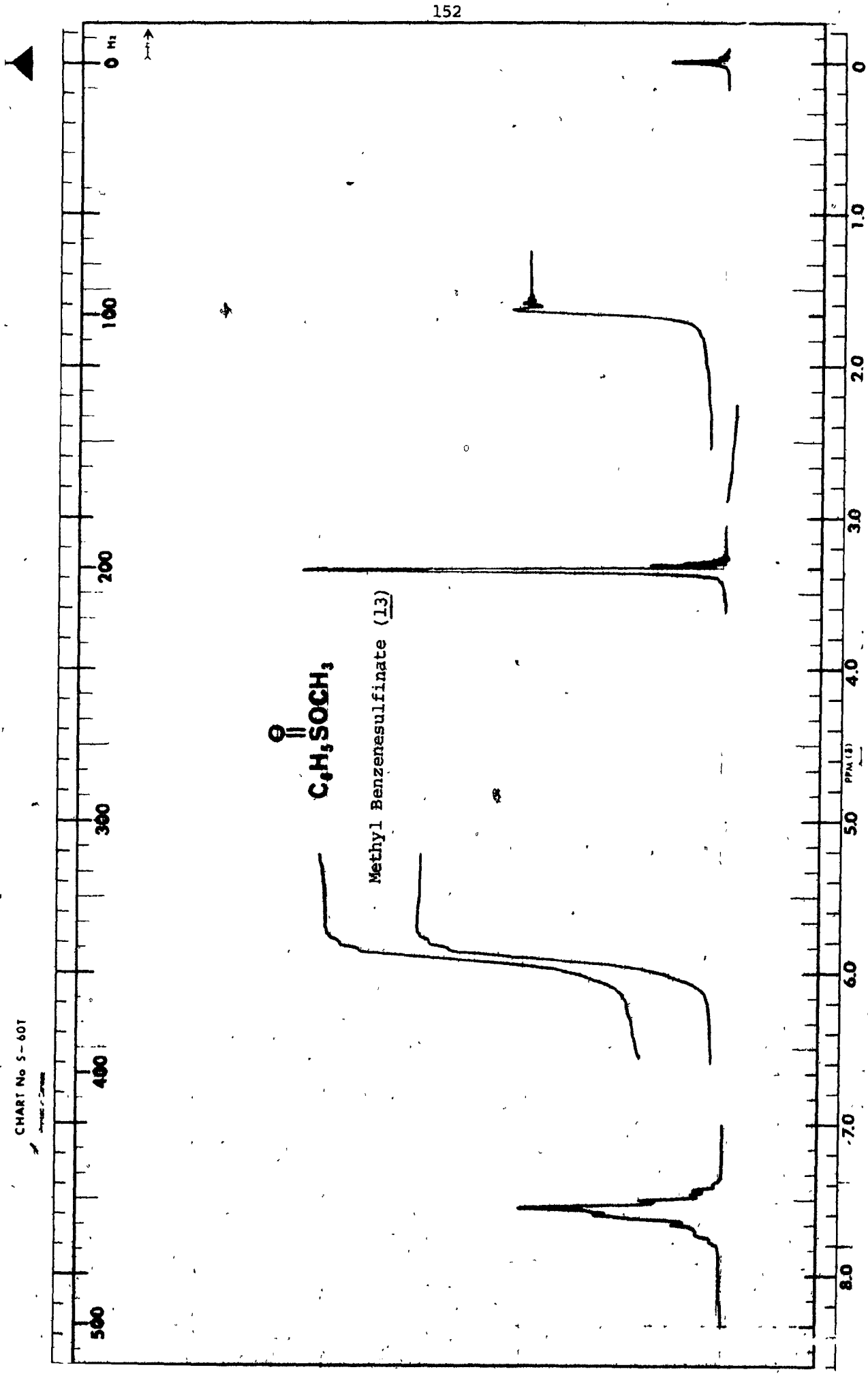
208. H. Sakurai, A. Hosomi, J. Makajima and M. Kumada, Bull. Chem. Soc. Jap., 39, 2263 (1966).

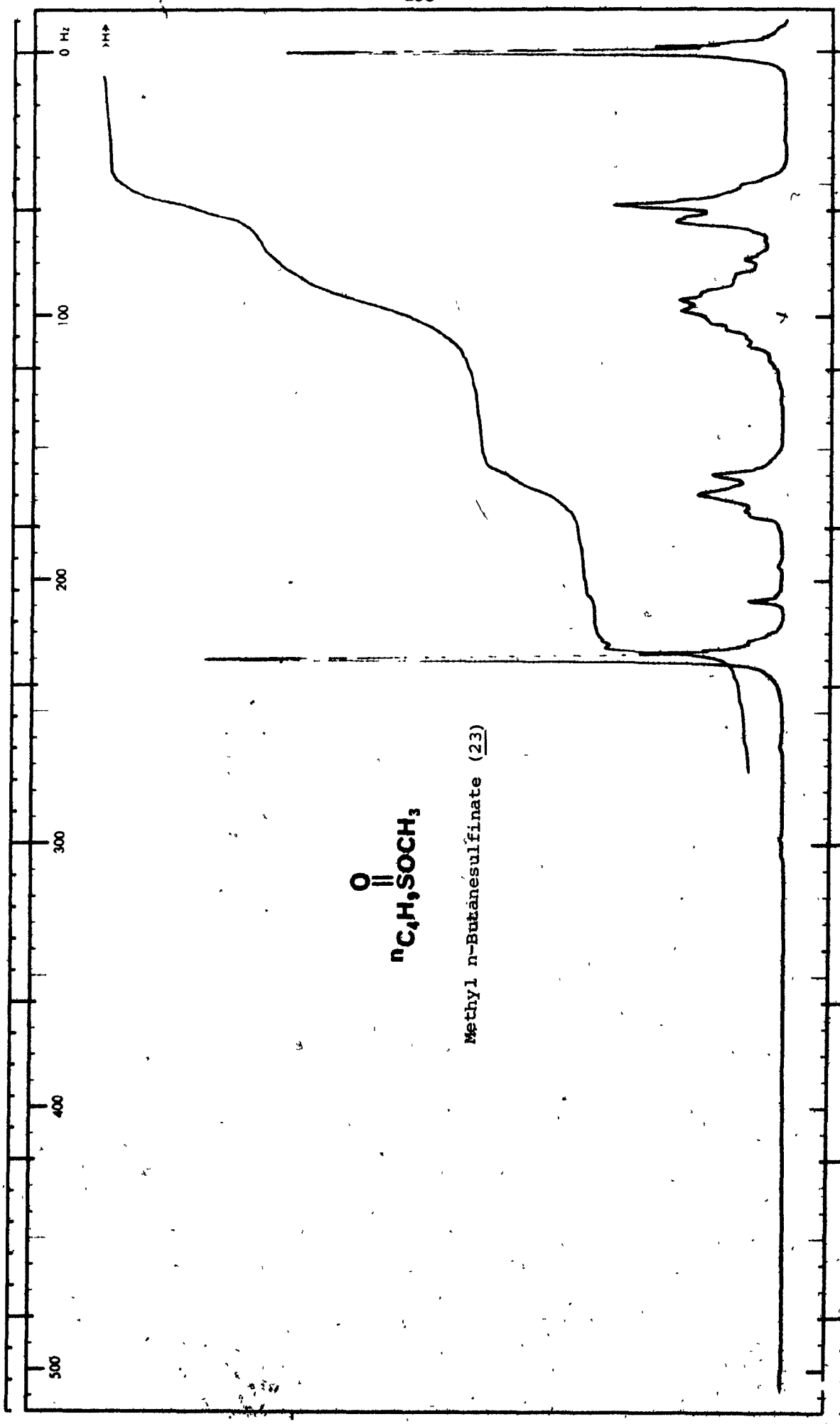
6 SPECTRA

SULFINATE ESTERS



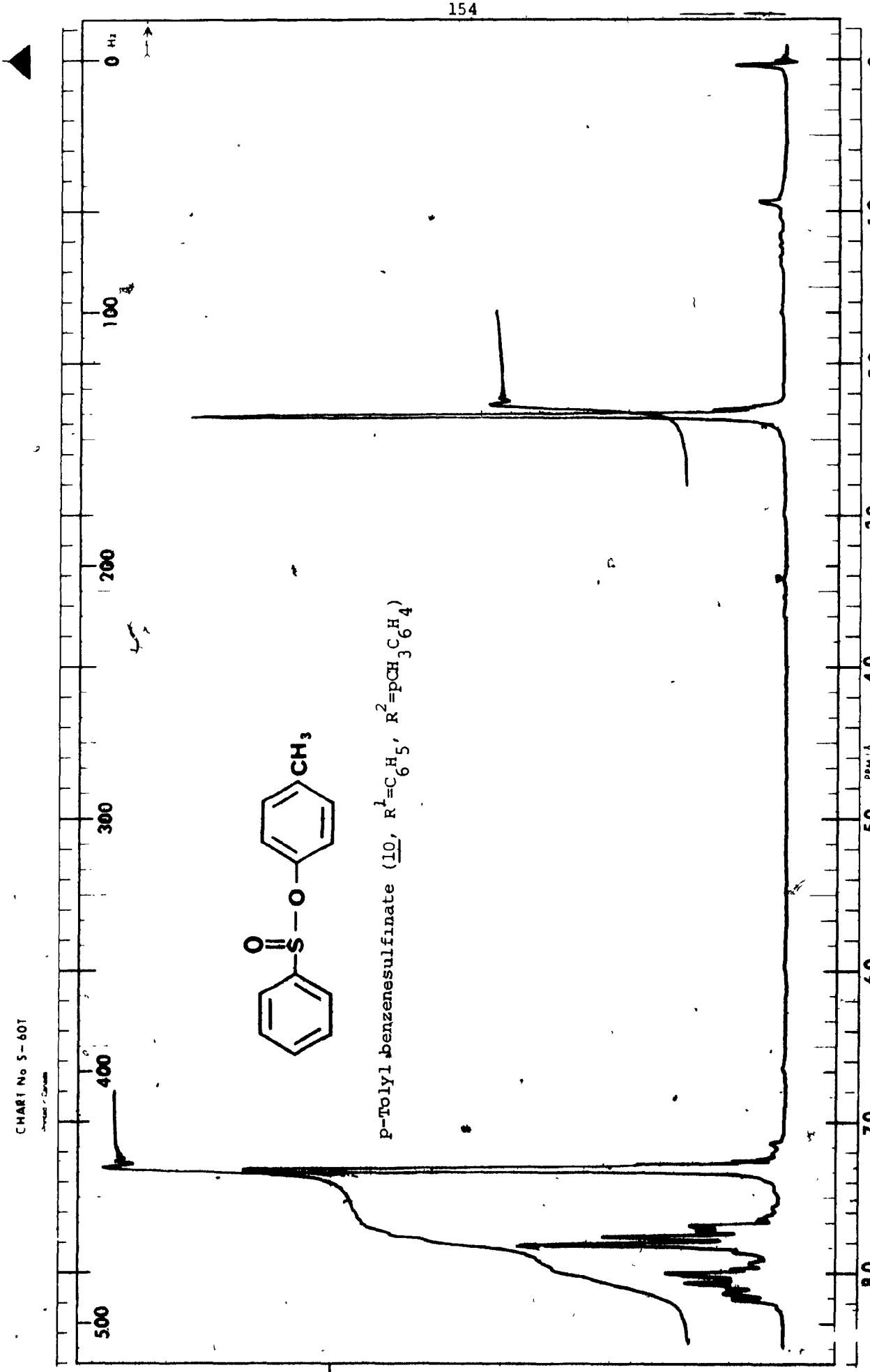
Methyl Benzenesulfinate (13)


Methyl Benzenesulfinate (13)
$C_6H_5SOCH_3$
CHART No 5-60T
PPM (δ)
0
100
200
300
400
500
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0



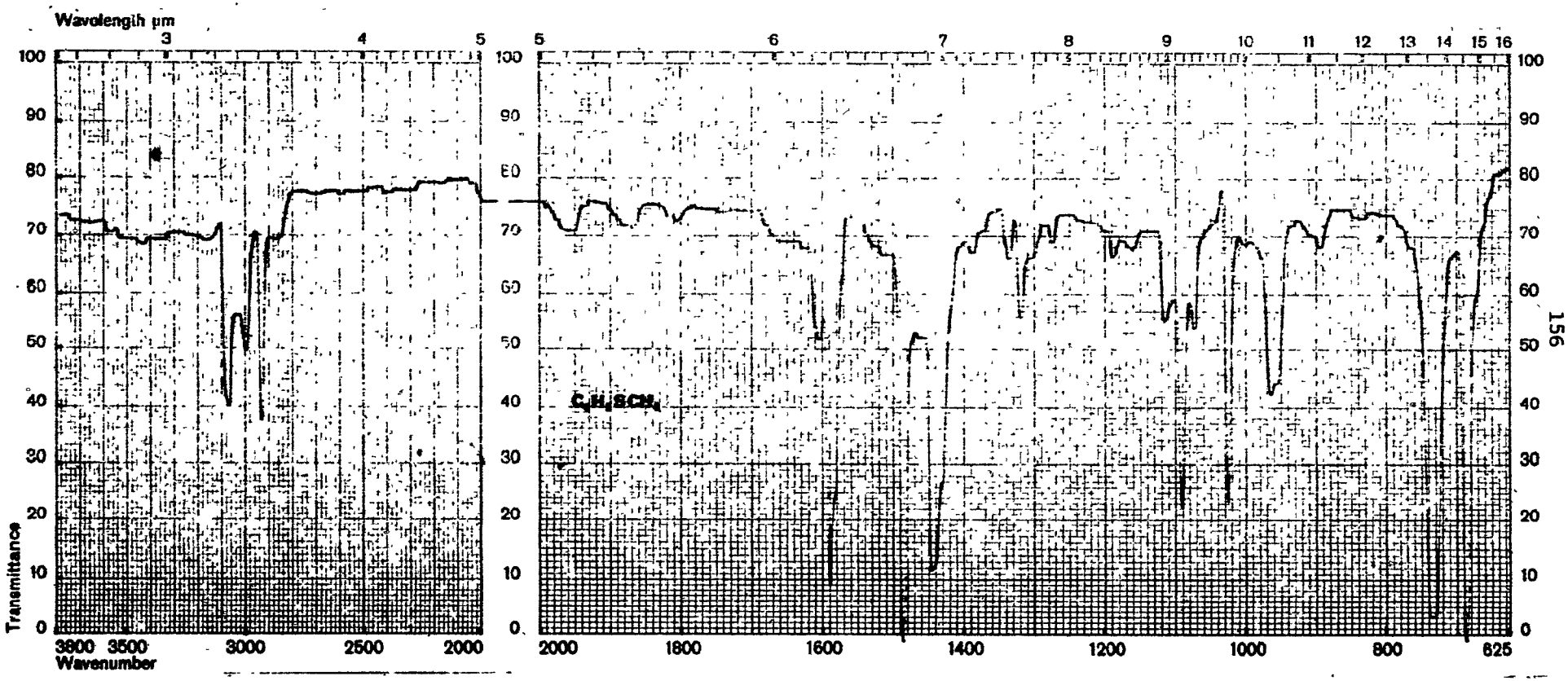
Methyl n-Butanesulfinate (23)

$$n\text{C}_4\text{H}_9\text{SOCH}_3$$



p-Tolyl benzenesulfinate (10, $R^1=C_6H_5$, $R^2=pCH_3C_6H_4$)

SULFIDES



Methyl Phenyl Sulfide

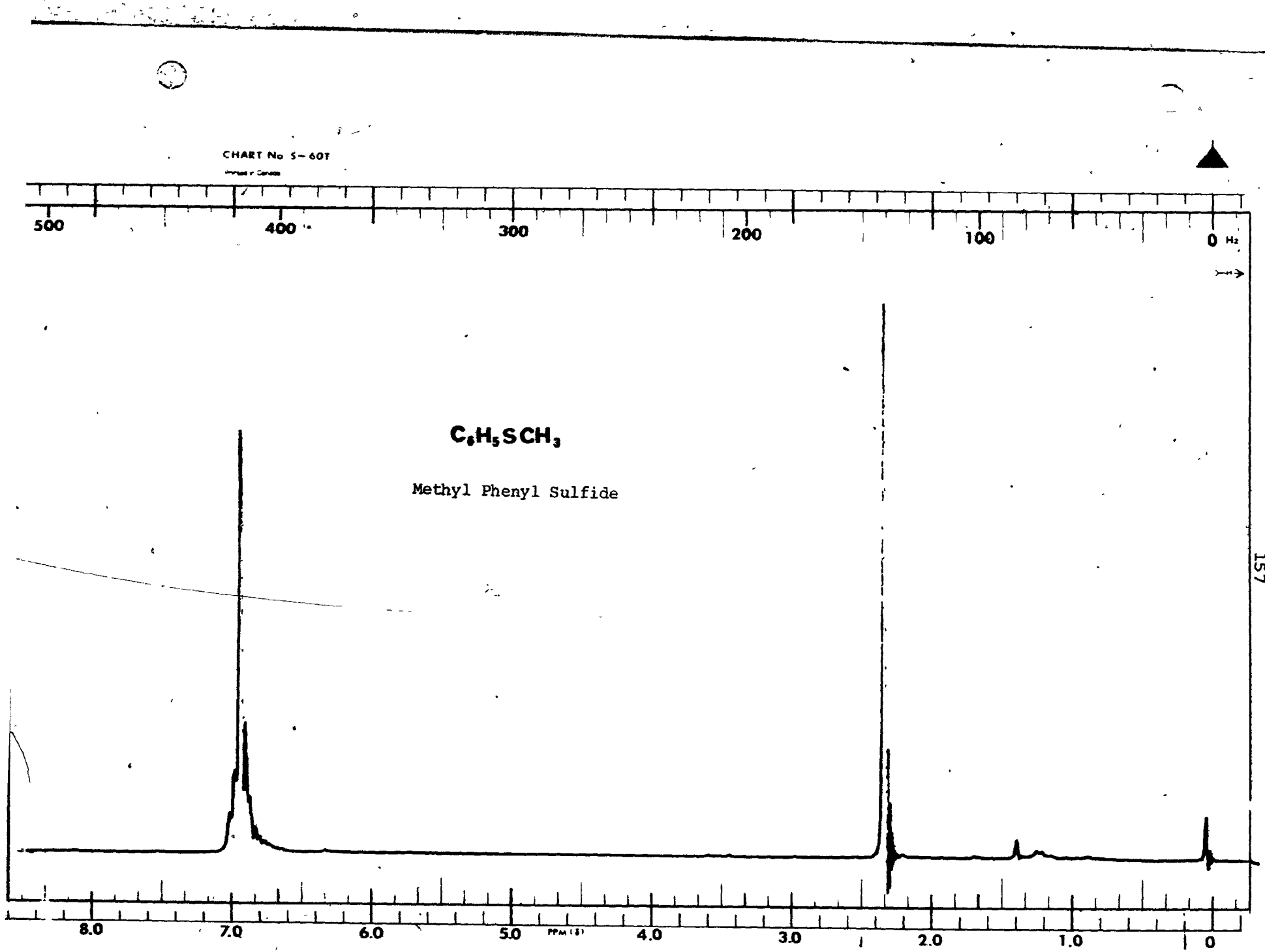
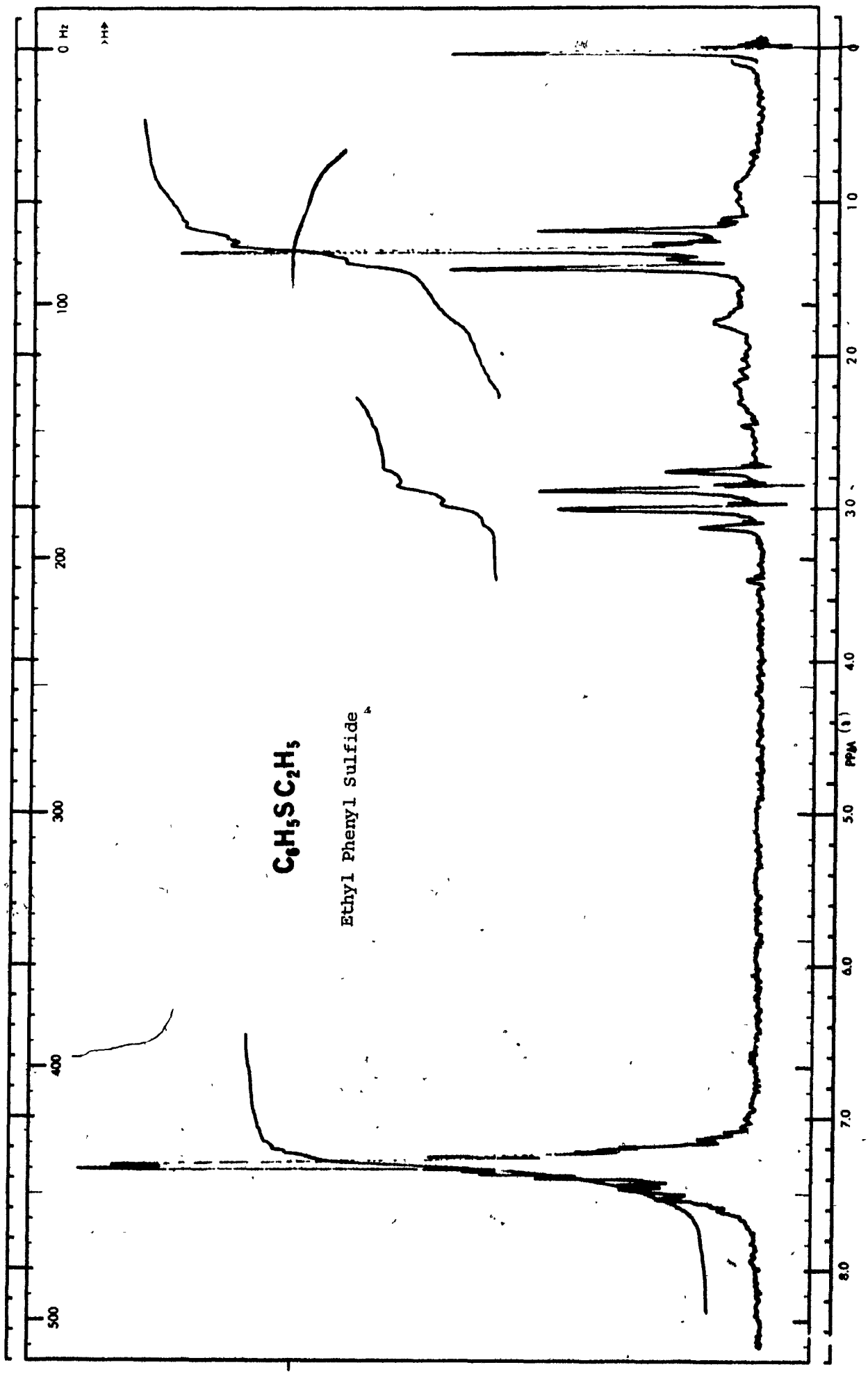


CHART No 5-60T
500
400
300
200
100
0 Hz
$C_6H_5SCH_3$
Methyl Phenyl Sulfide
8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0


0 Hz
100
200
300
400
500
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
PPM (δ)
$C_6H_5SC_2H_5$
Ethyl Phenyl Sulfide

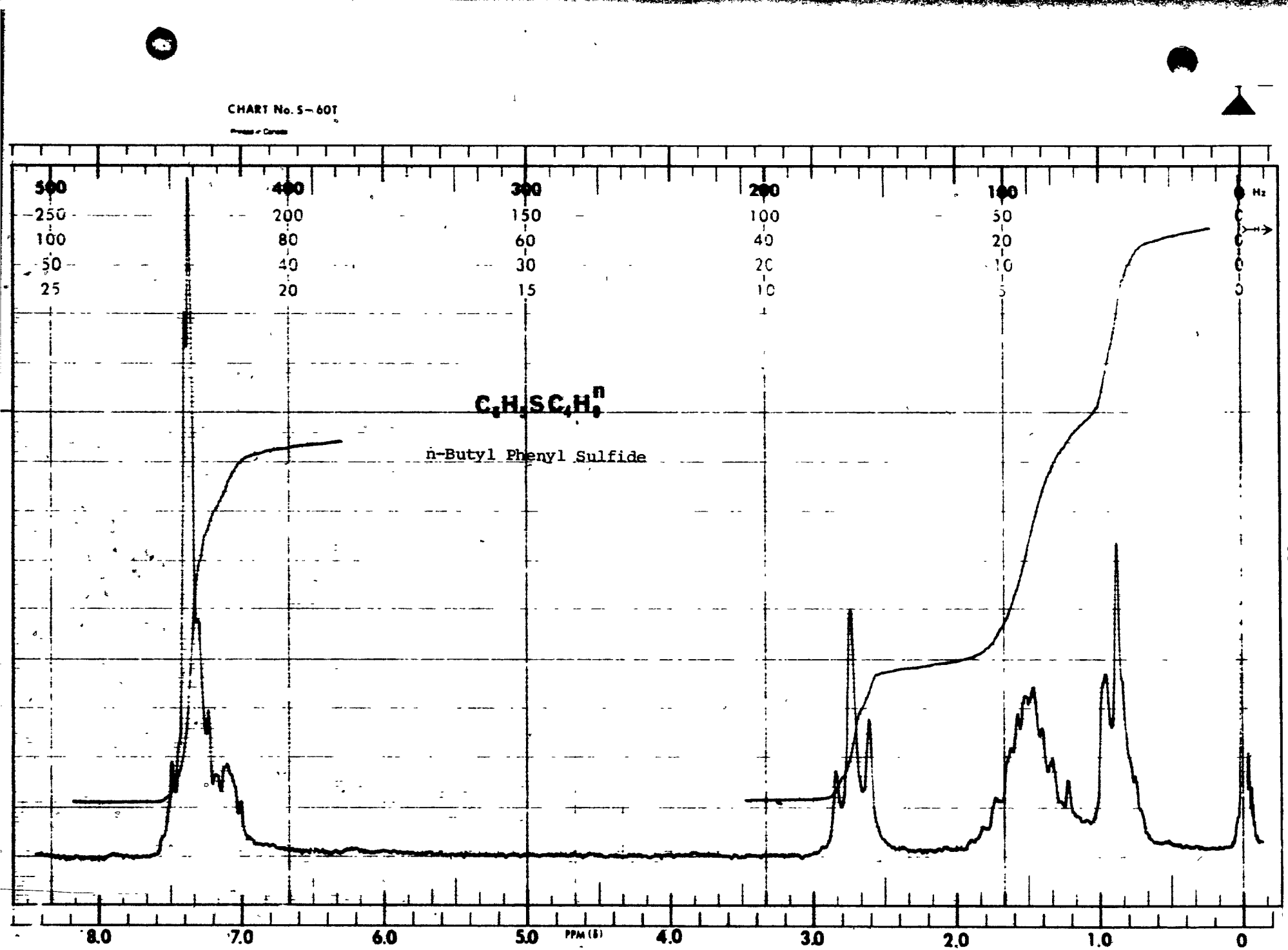


CHART No. 5-60T
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400
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200
100
Hz
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200
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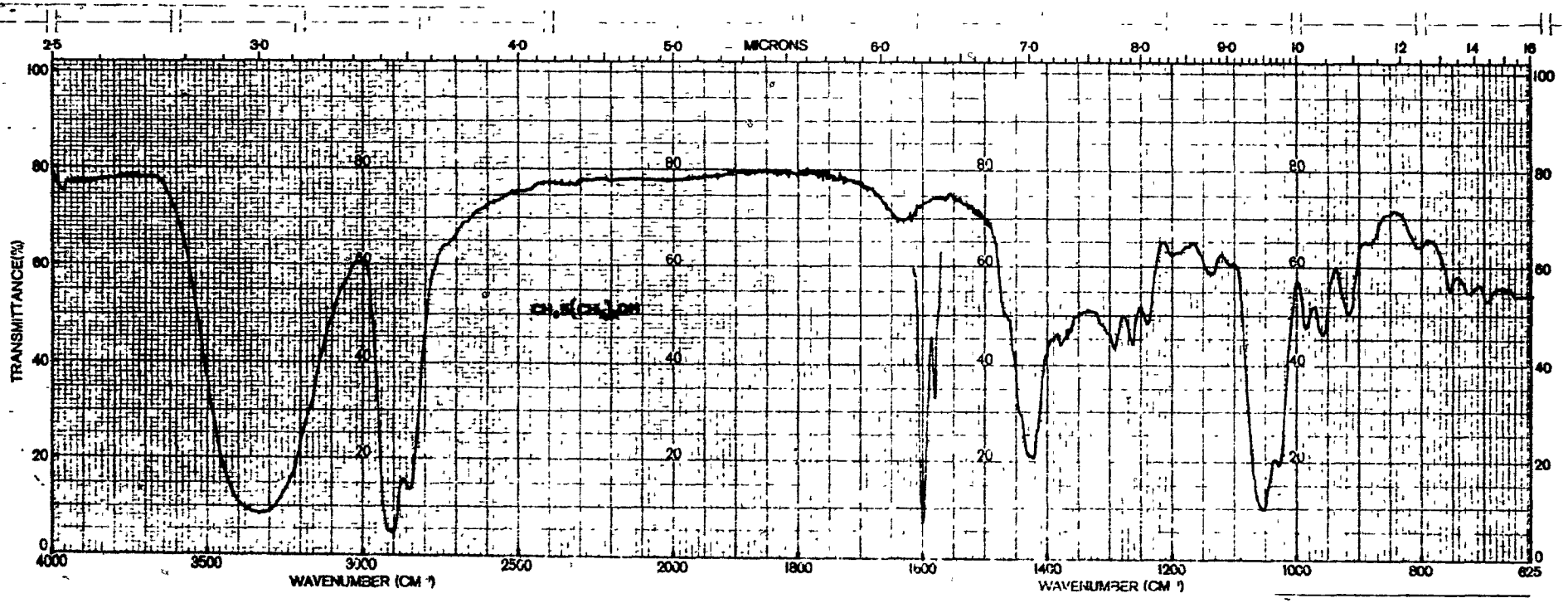
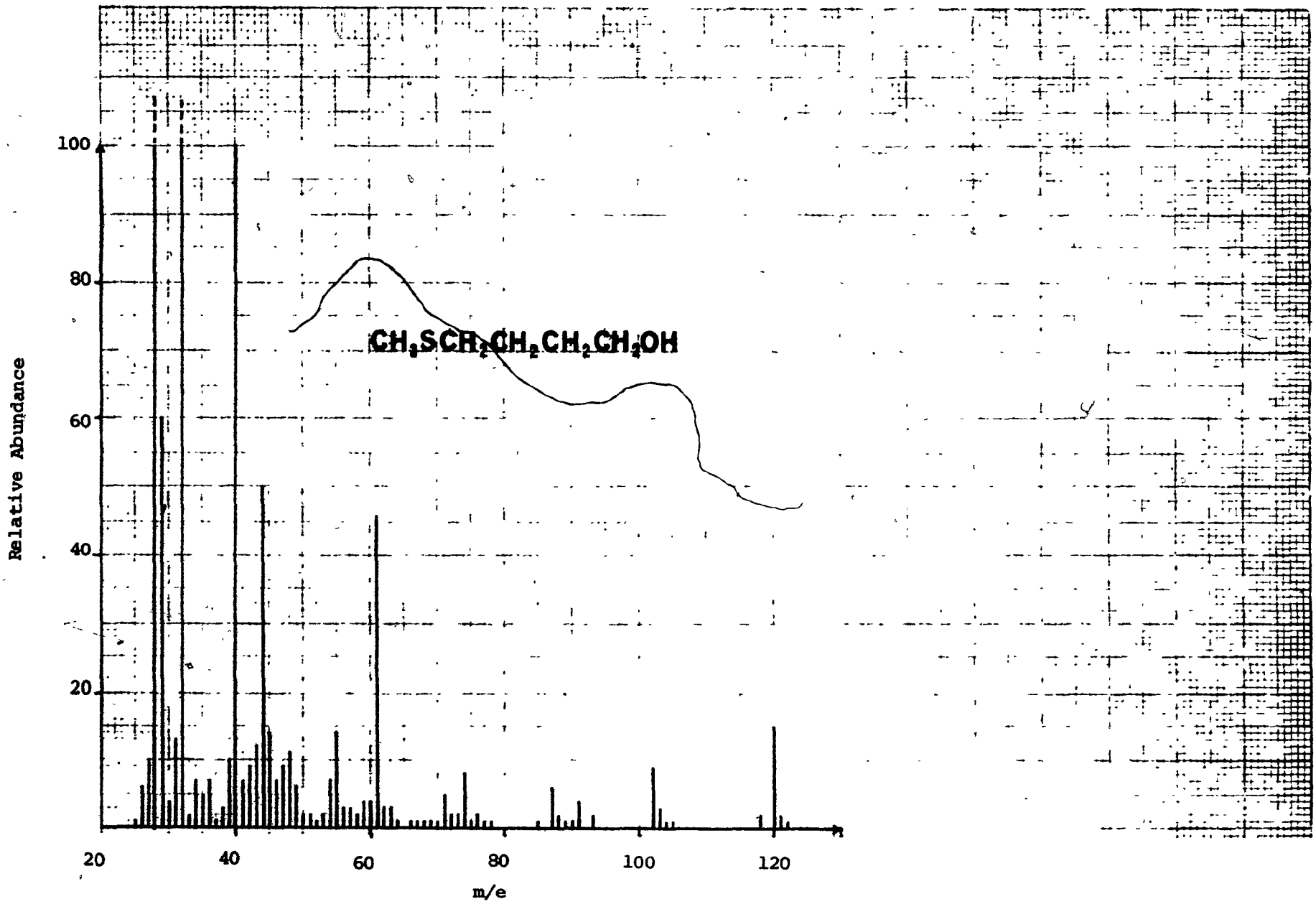
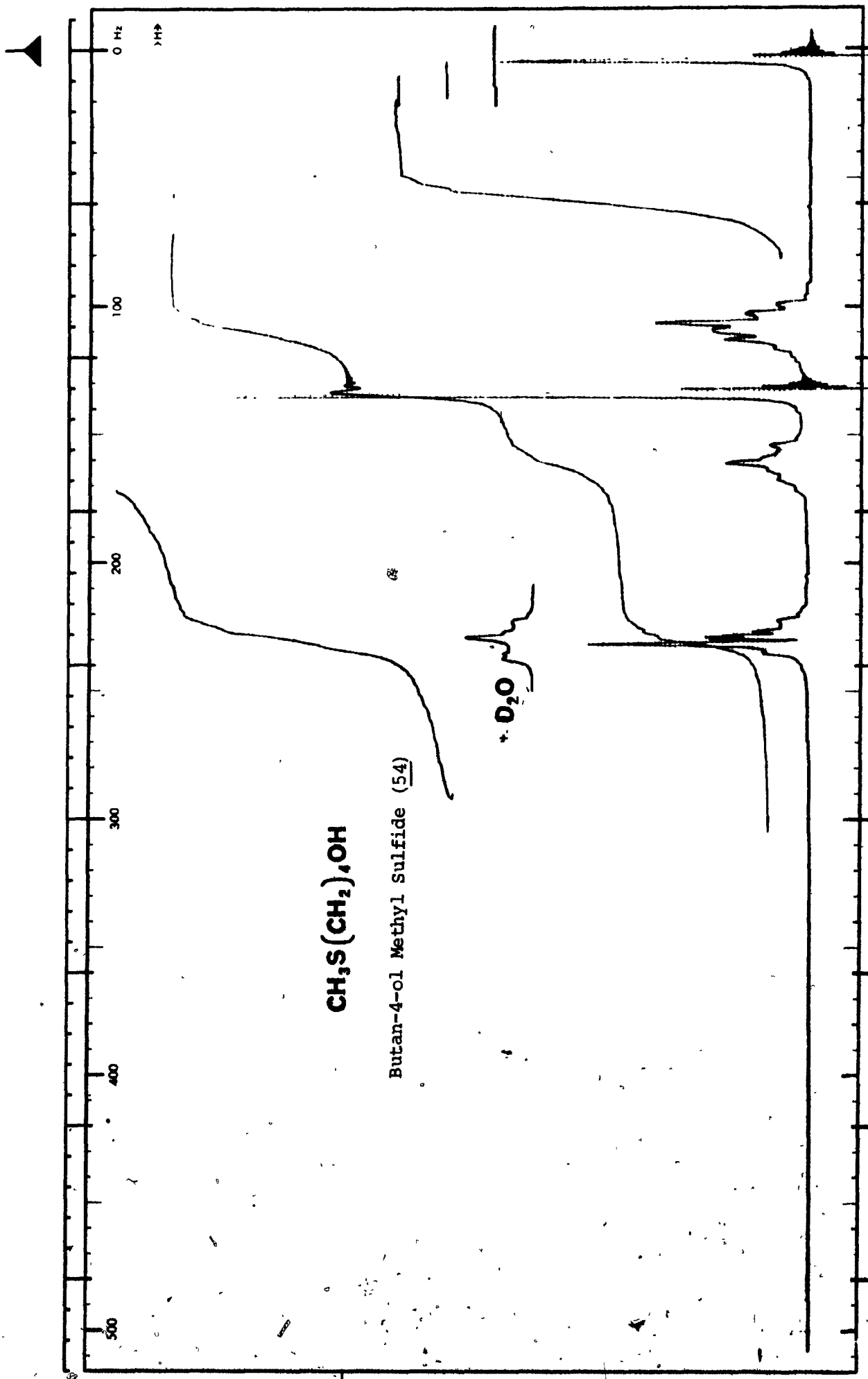
100
50
100
80
60
40
20
50
40
30
20
10
25
20
15
10
5
0
$C_6H_5SC_4H_9^n$
n-Butyl Phenyl Sulfide
8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0

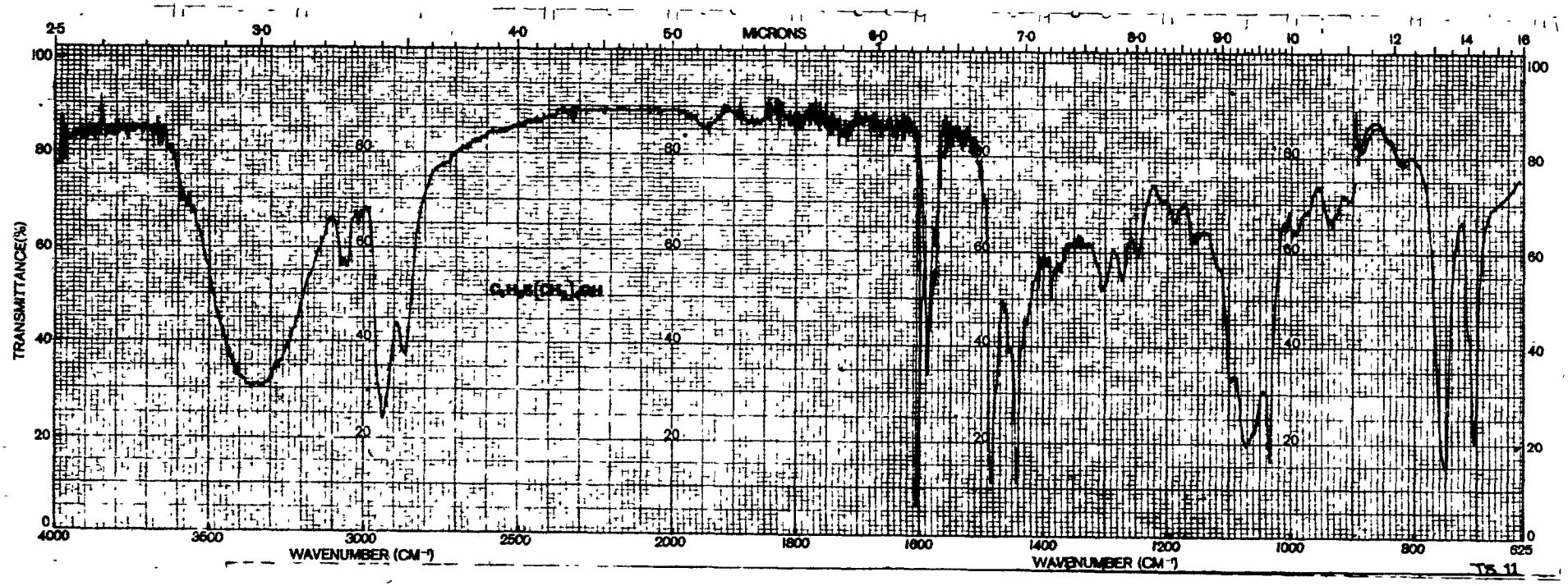


Butan-4-ol methyl sulfide (54)

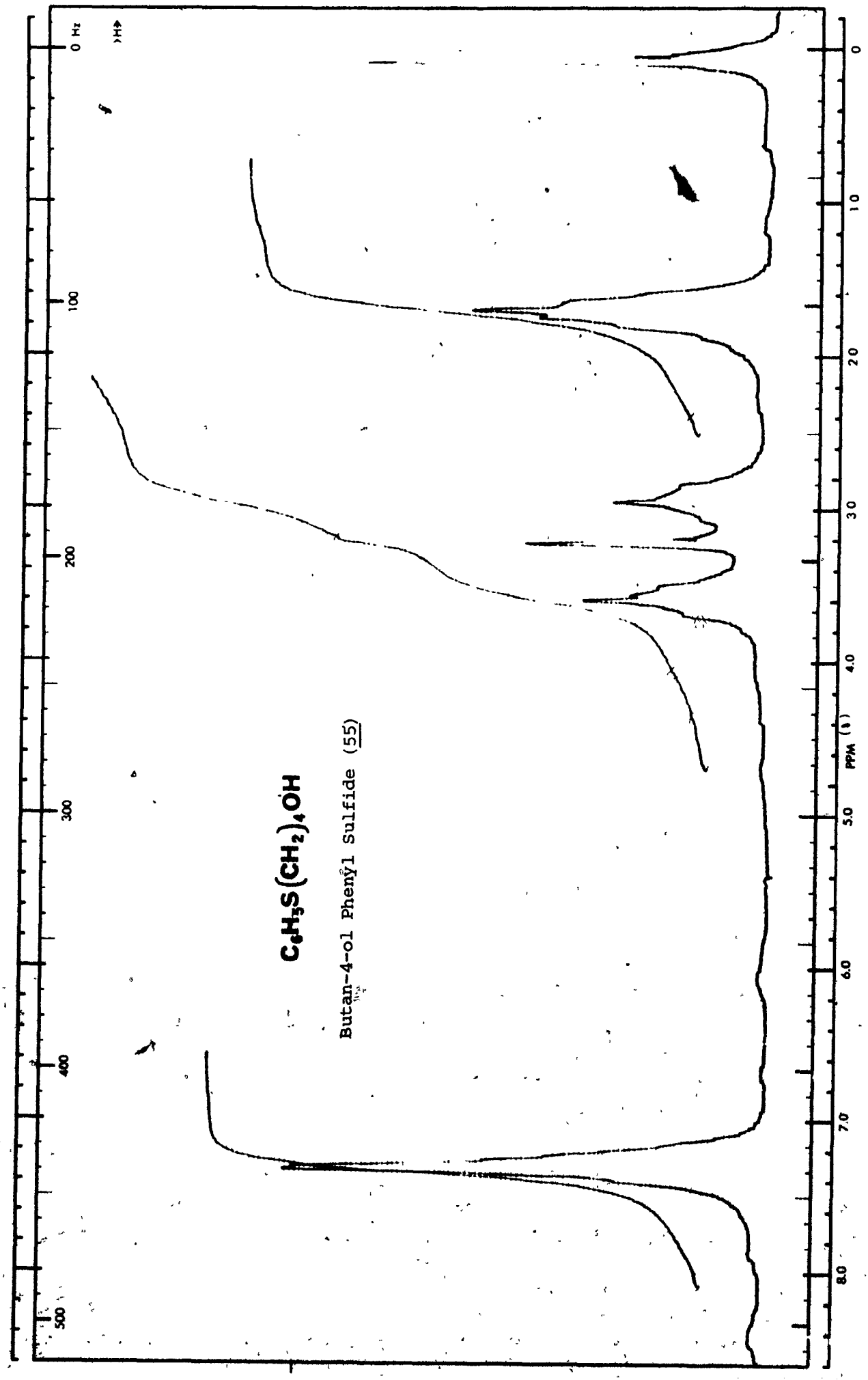


Butan-4-ol Methyl Sulfide (54)

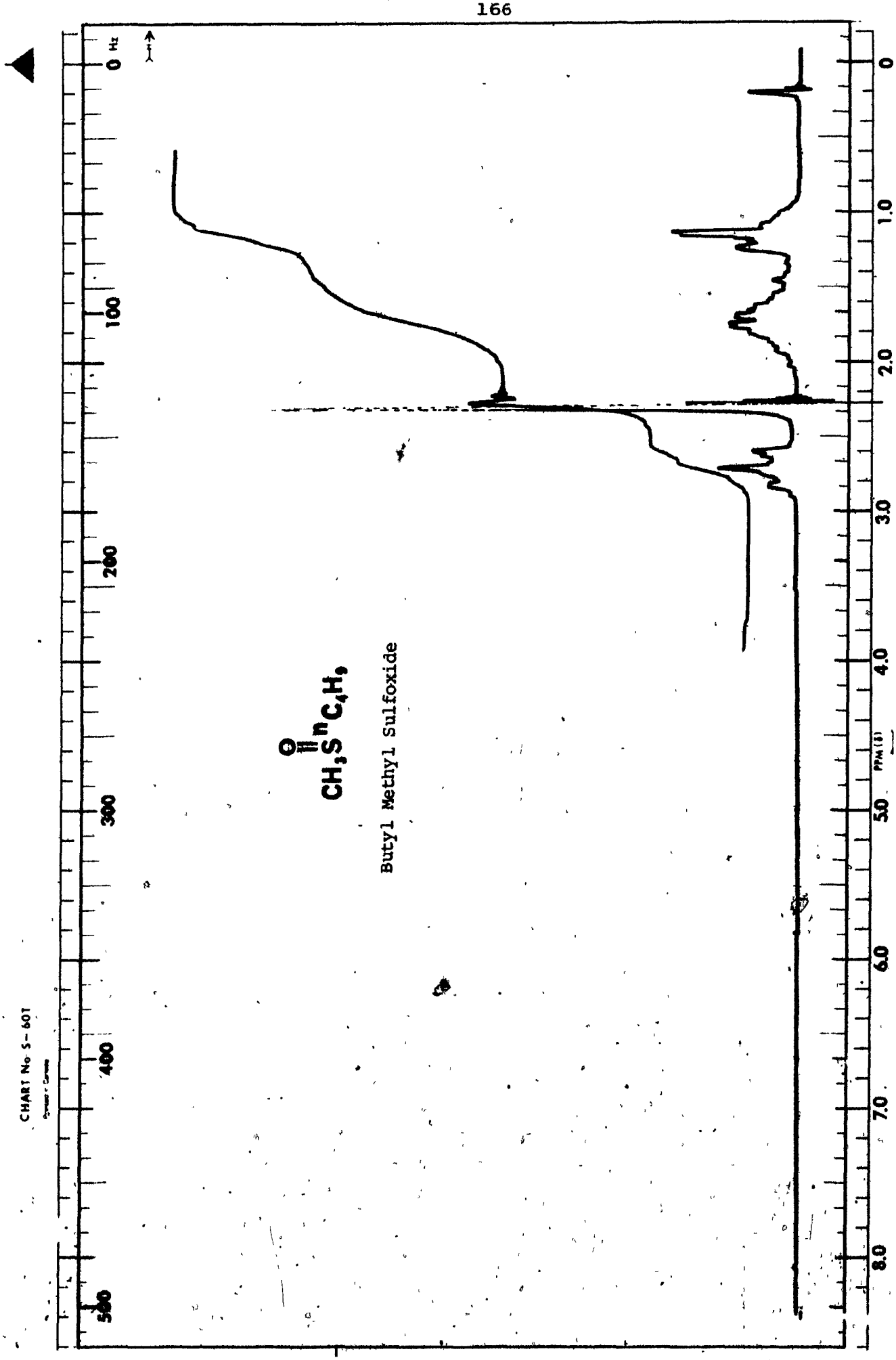

0 Hz
100
200
300
400
500
0
10
20
30
40
50
60
70
80
PPM (δ)
$CH_3S(CH_2)_4OH$
Butan-4-ol Methyl Sulfide (54)
D_2O

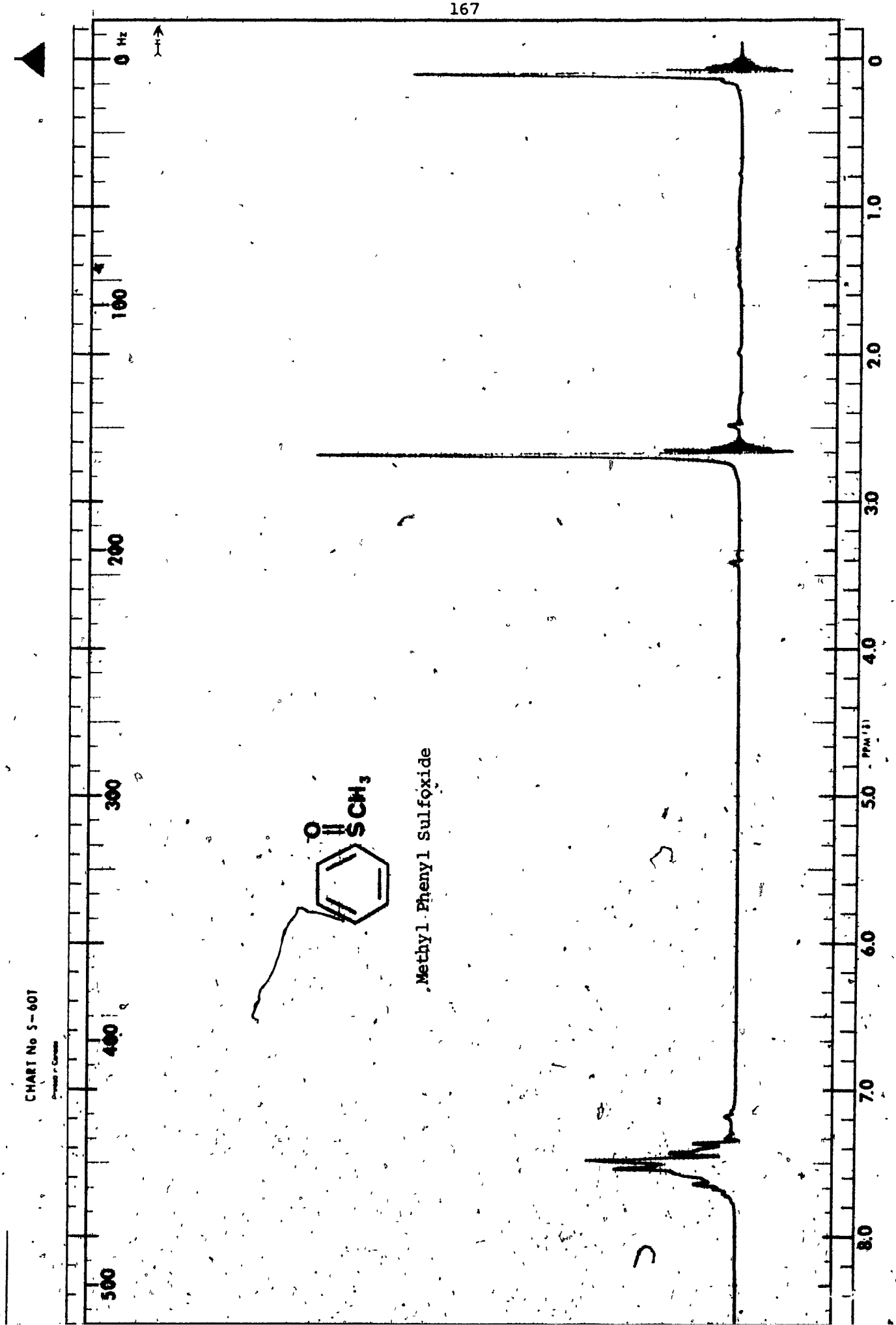


Butan-4-ol Phenyl Sulfide (55)

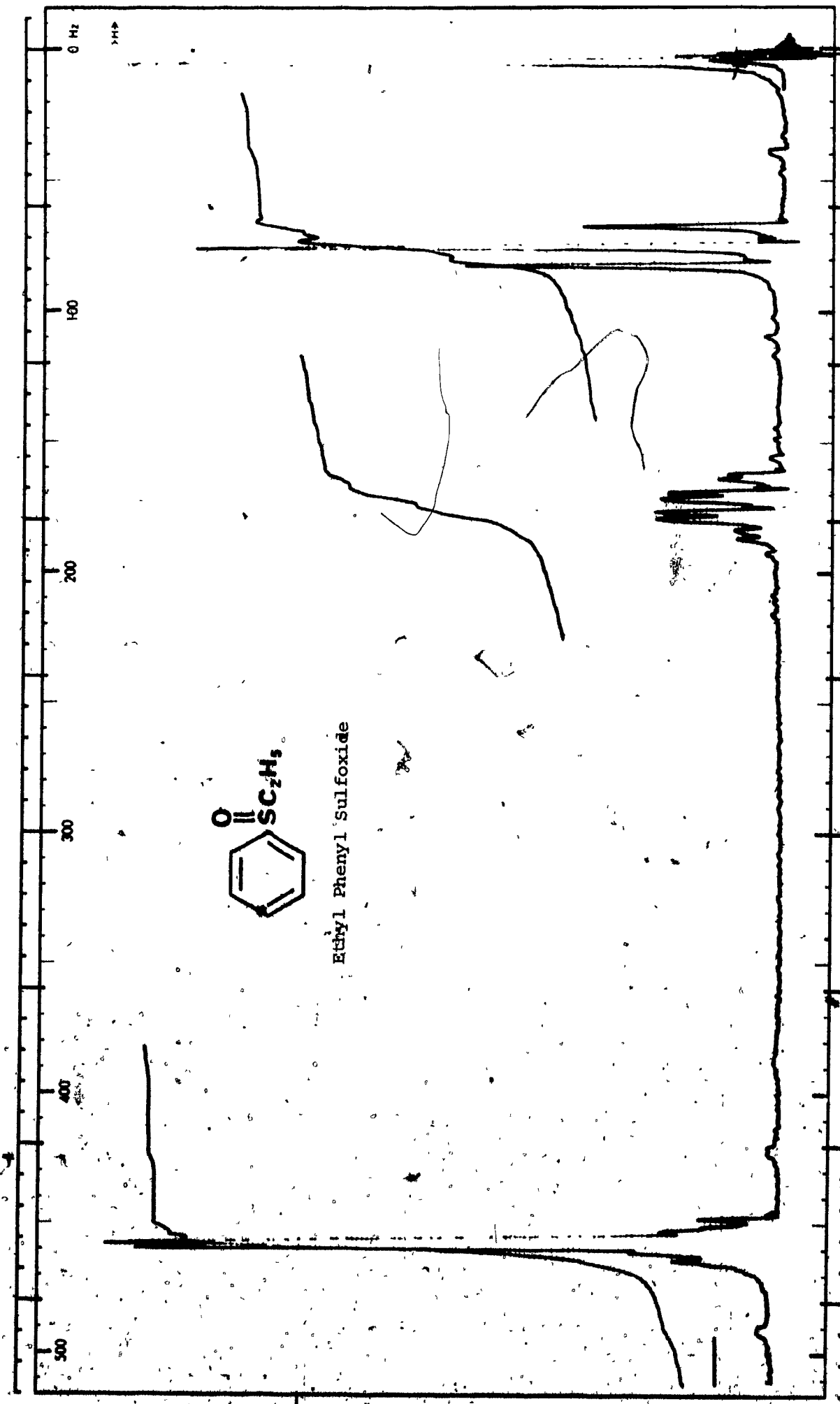

0 Hz
100
200
300
400
500
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
PPM (δ)
$C_6H_5S(CH_2)_4OH$
Butan-4-ol Phenyl Sulfide (55)

SULFOXIDES

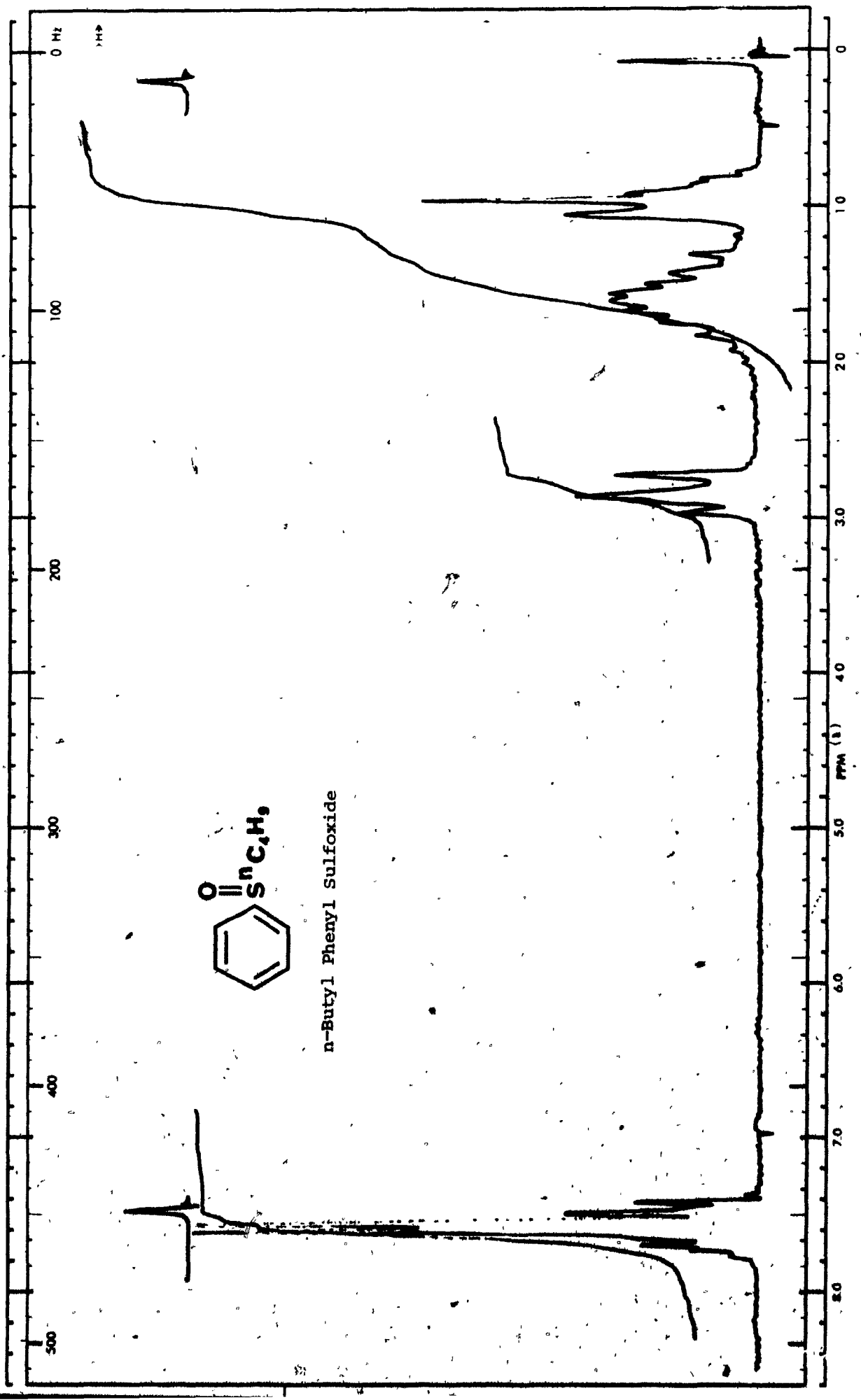

0 Hz
100
200
300
400
500
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
PPM (δ)
CHART No. S-601
O
CH3SnC4H9
Butyl Methyl Sulfoxide



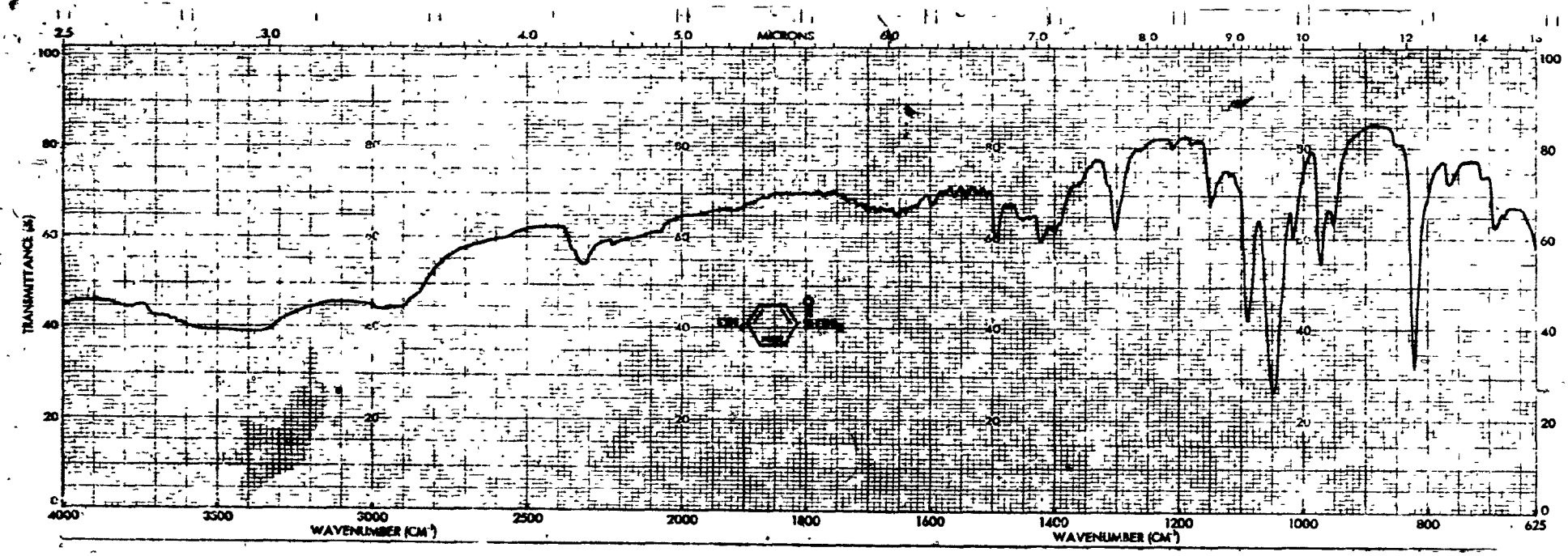
Methyl Phenyl Sulfoxide



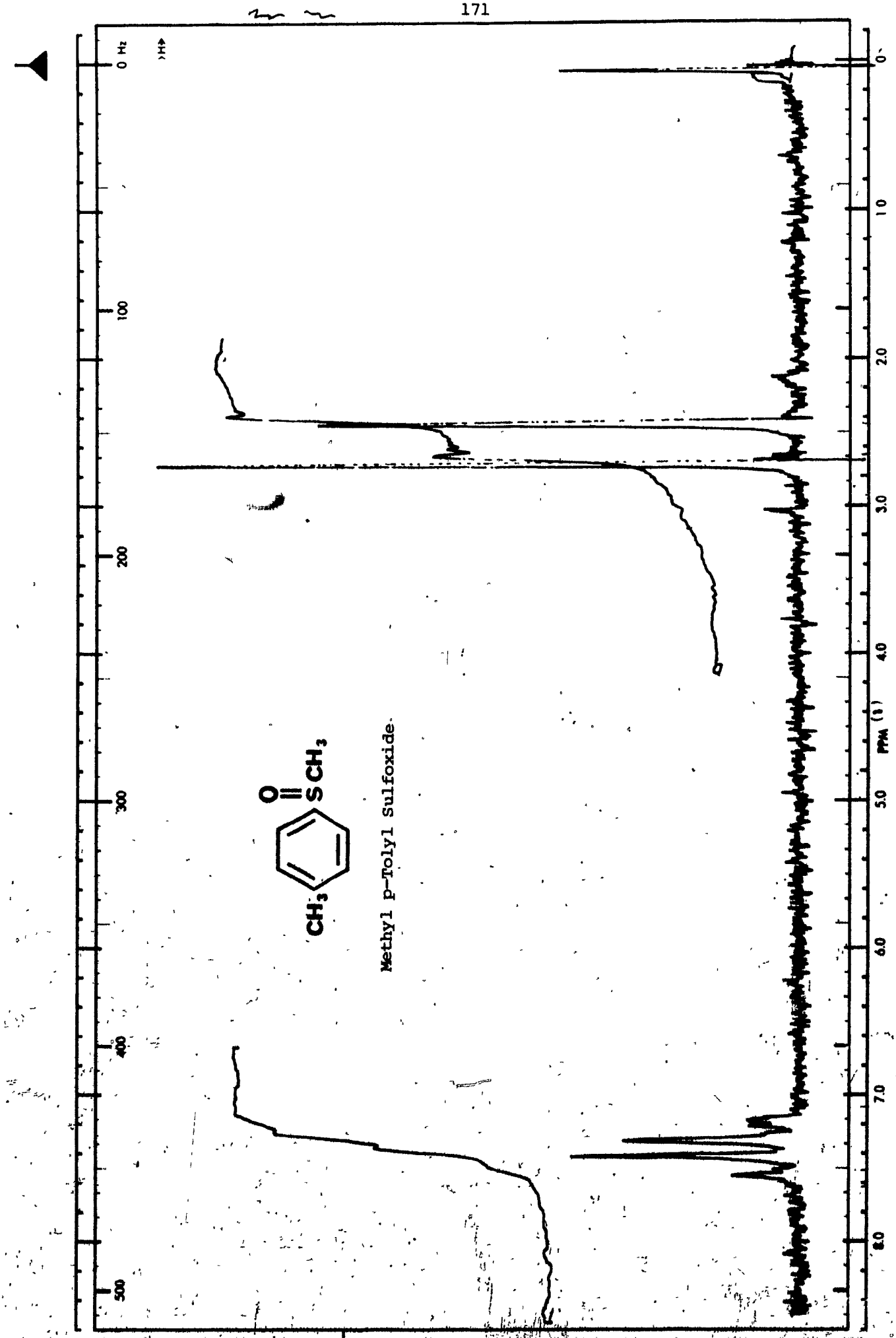
Ethyl Phenyl Sulfoxide



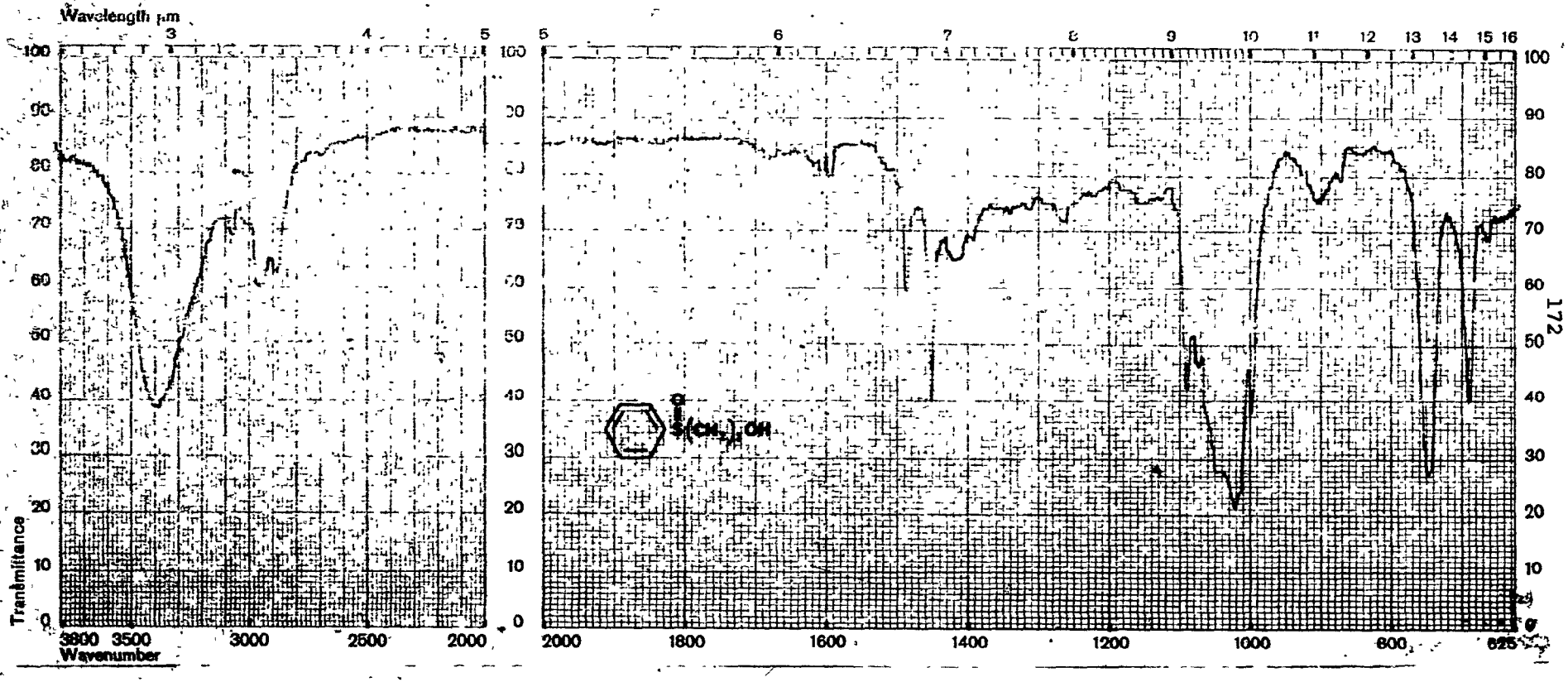
n-Butyl Phenyl Sulfoxide



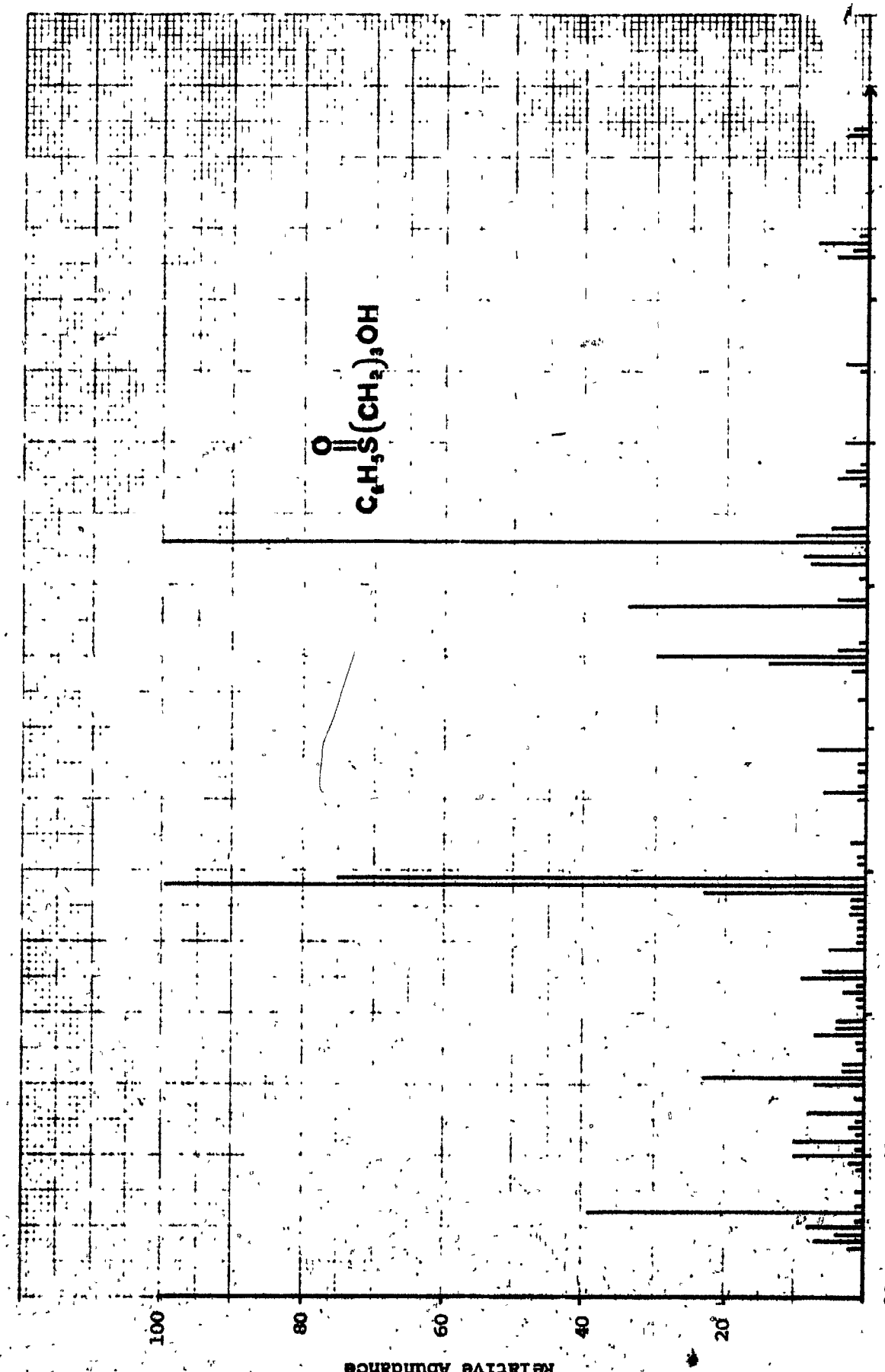
Methyl p-Tolyl Sulfoxide



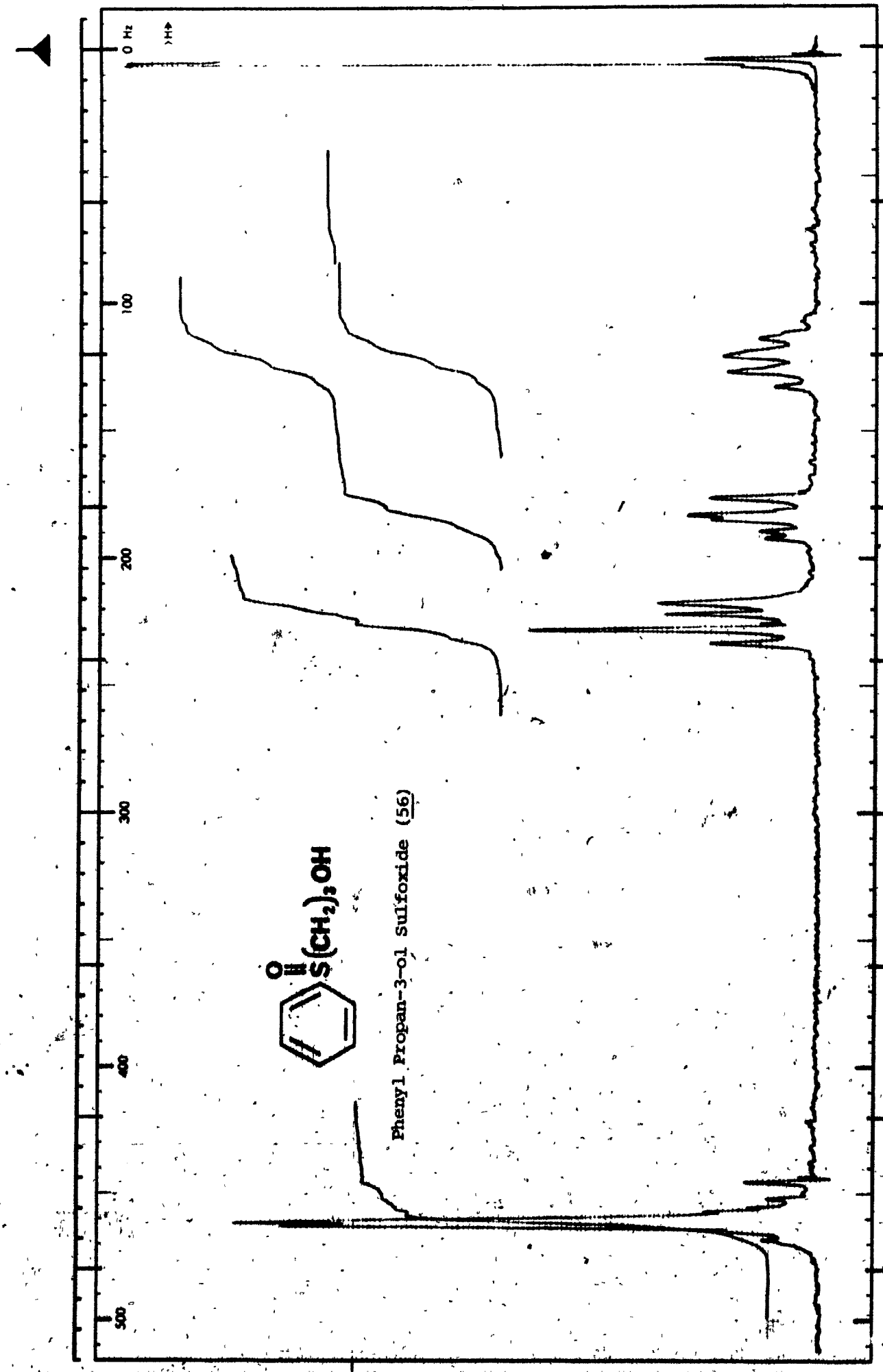
Methyl p-Tolyl Sulfoxide



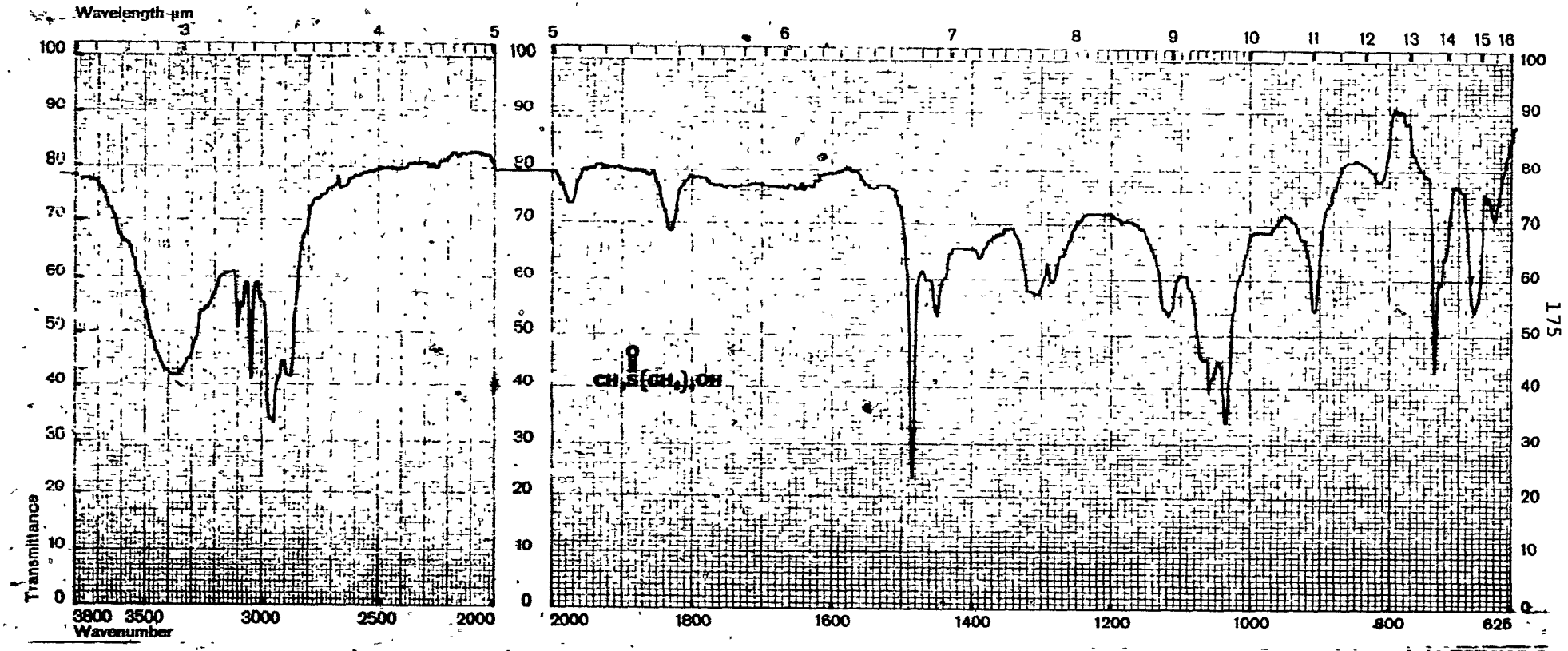
Propan-3-ol Phenyl Sulfoxide (56)



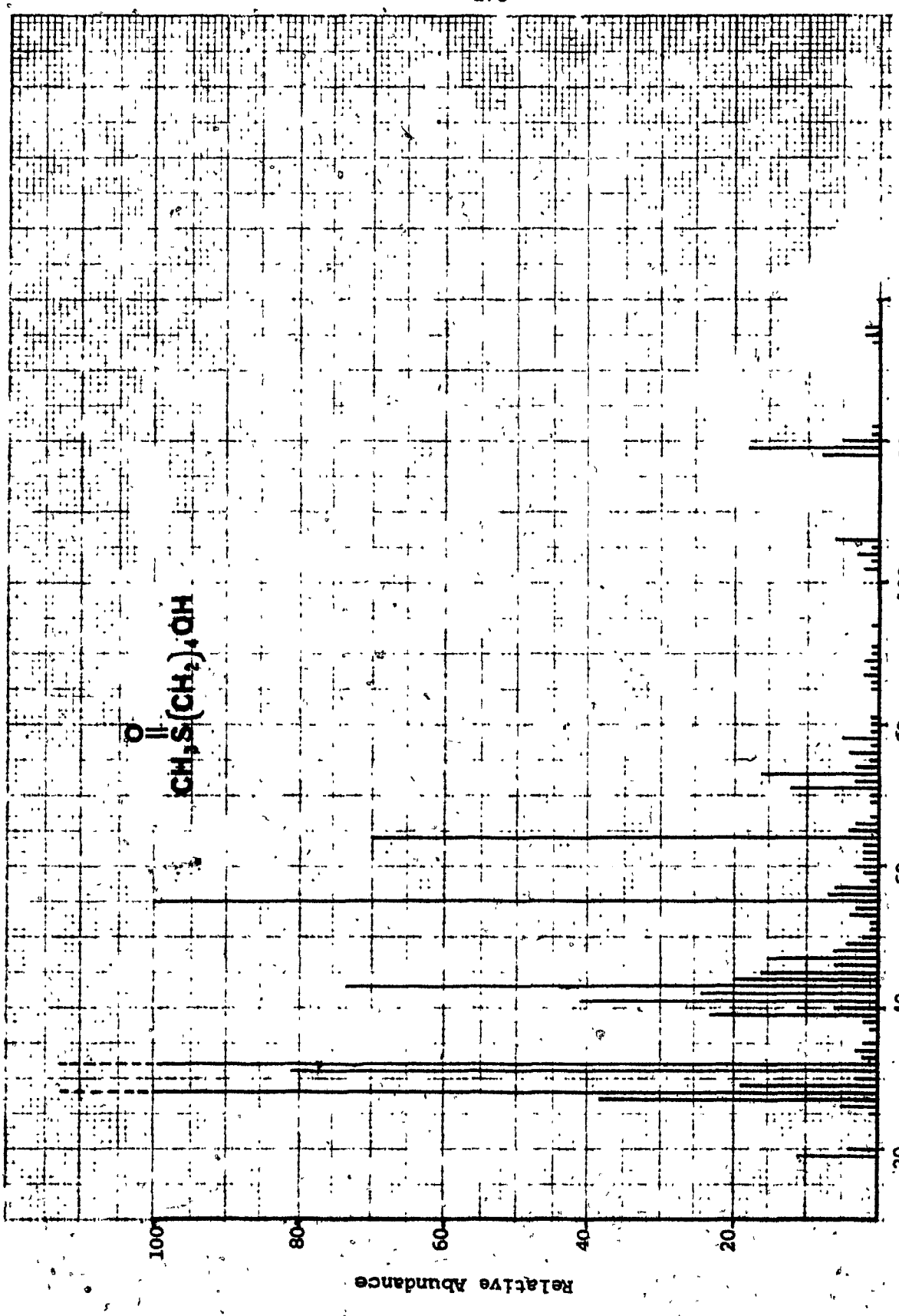
Phenyl Propan-3-ol Sulfoxide (56)



Phenyl Propan-3-ol Sulfoxide (56)

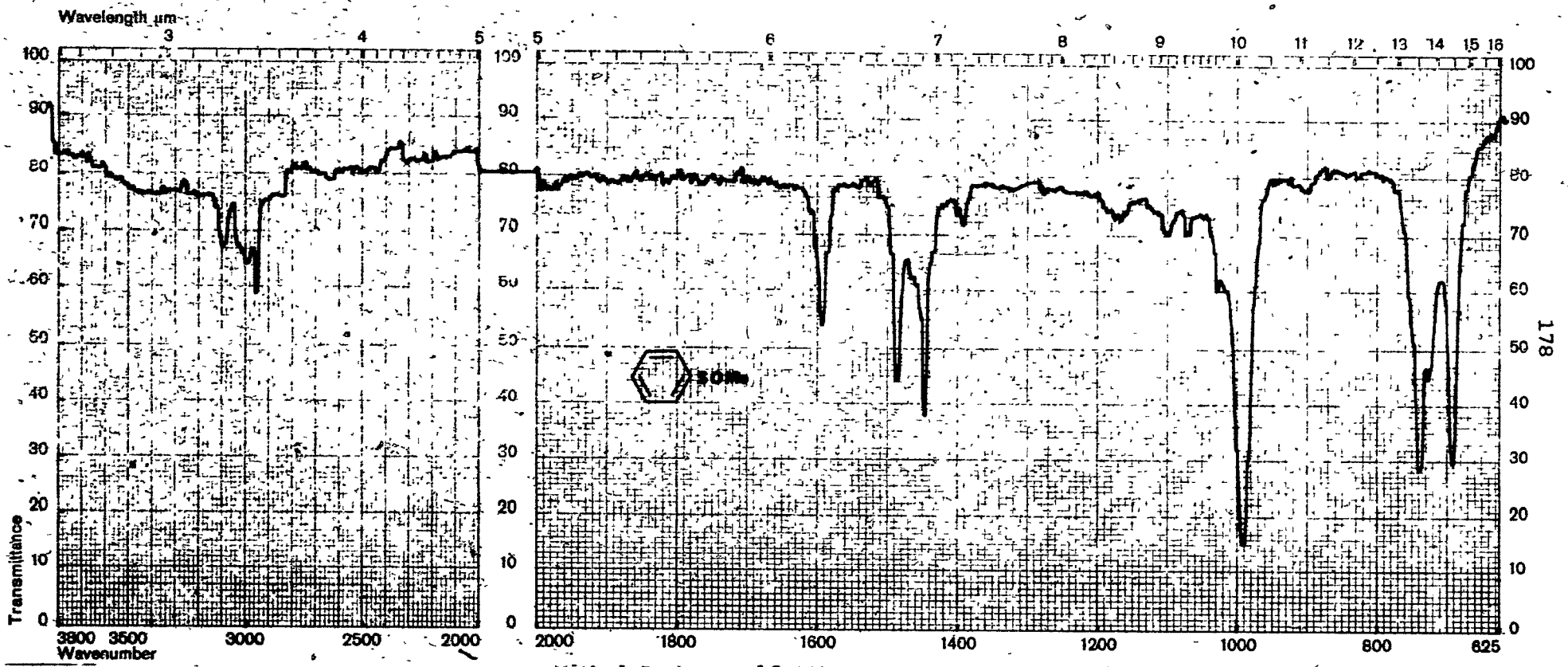


Butan-4-ol Methyl Sulfoxide (58)



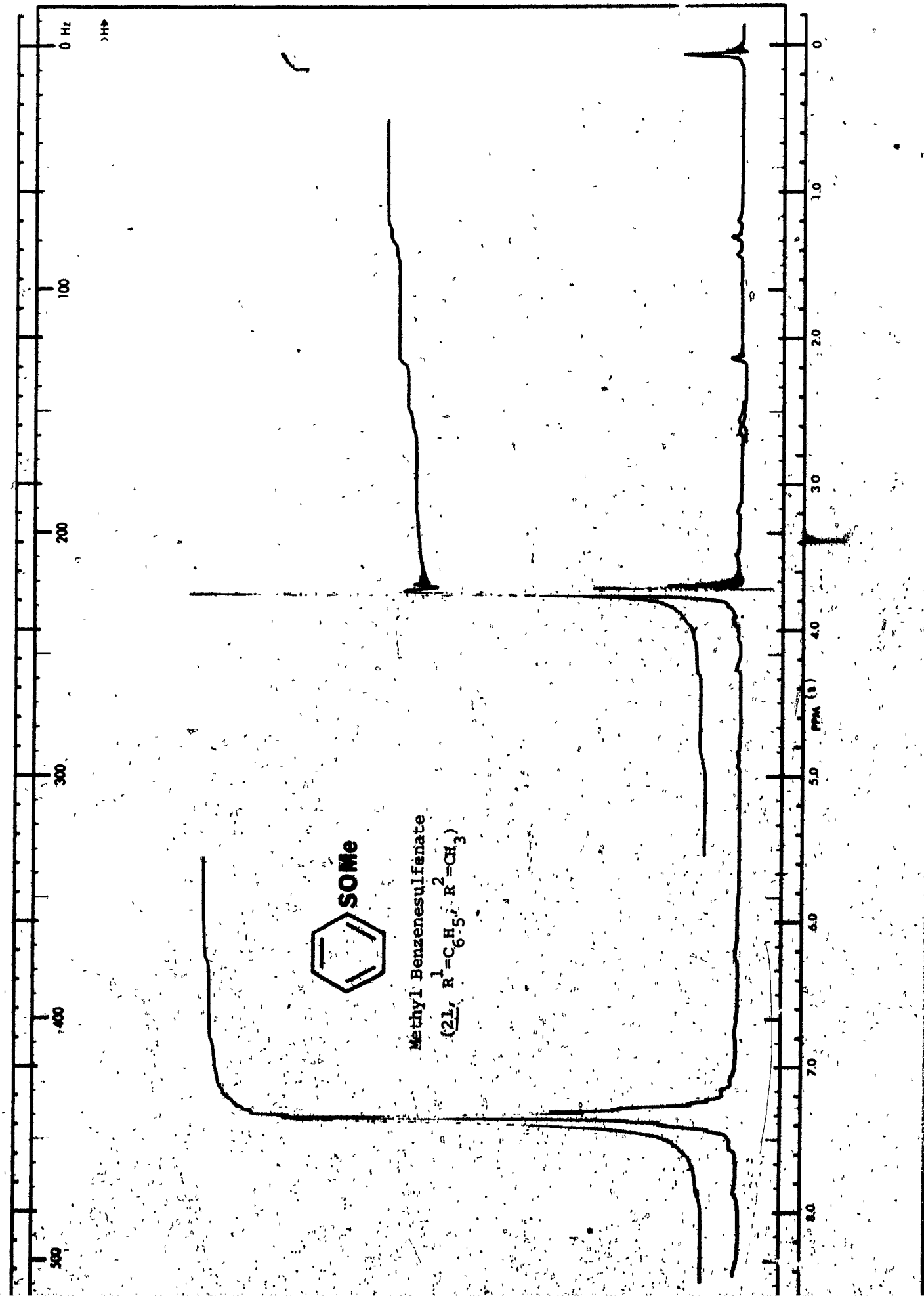
Butan-4-ol Methyl Sulfoxide (58)

METHYL BENZENESULFENATE



Methyl Benzenesulfenate

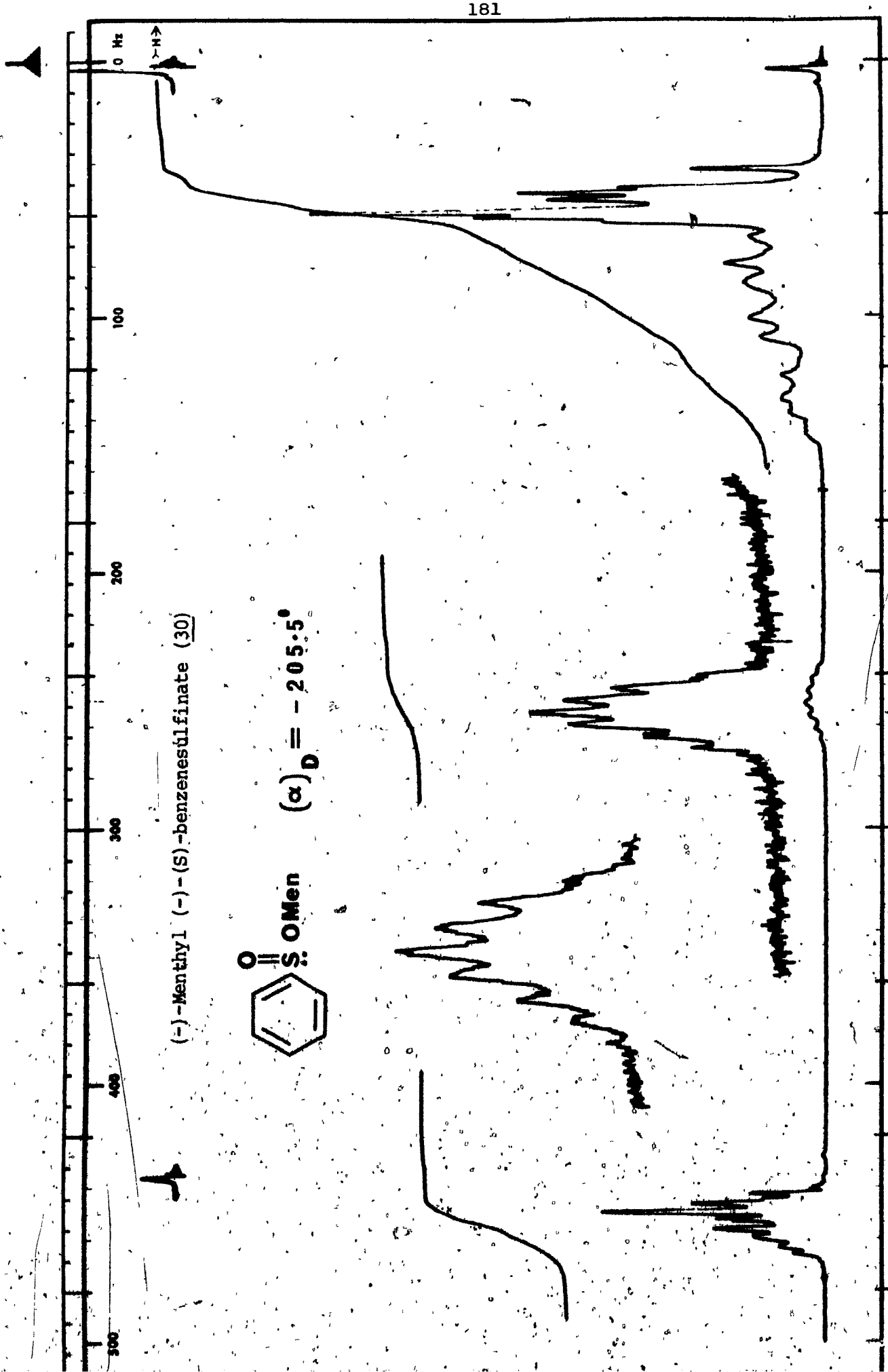
(21, $R^1=C_6H_5$, $R^2=CH_3$)



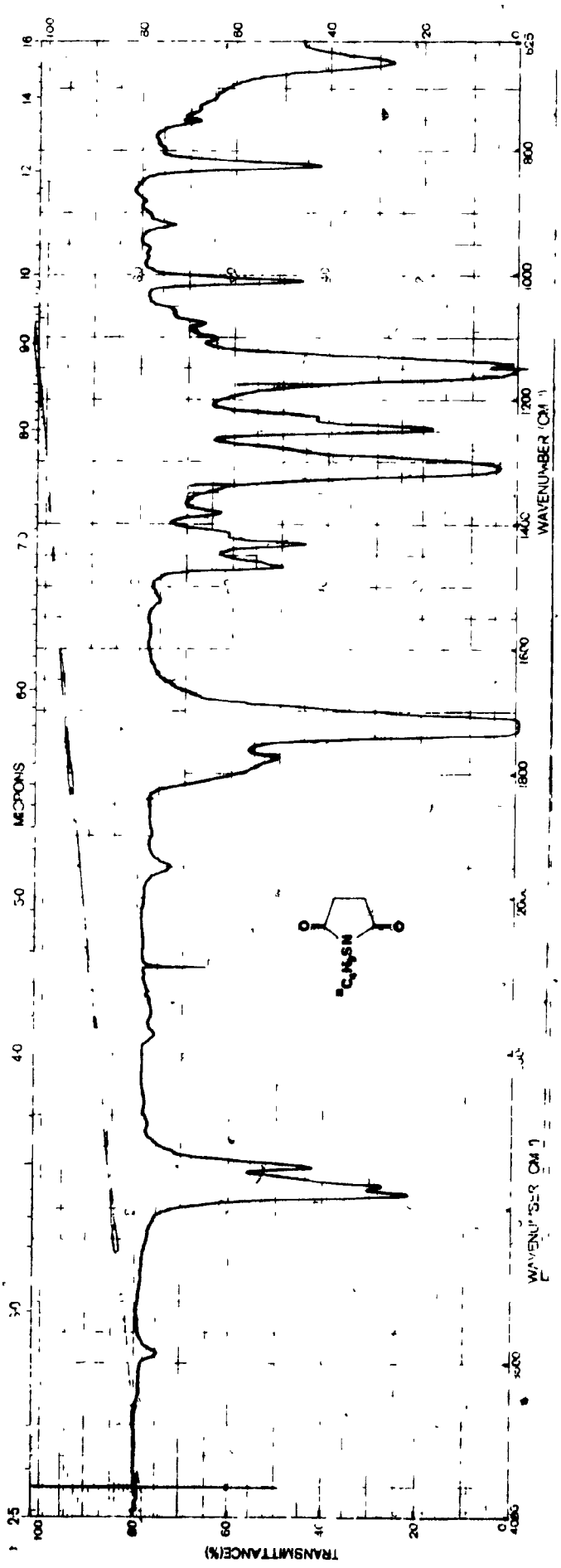
Methyl Benzenesulfinate

(21, $R^1=C_6H_5$, $R^2=CH_3$)

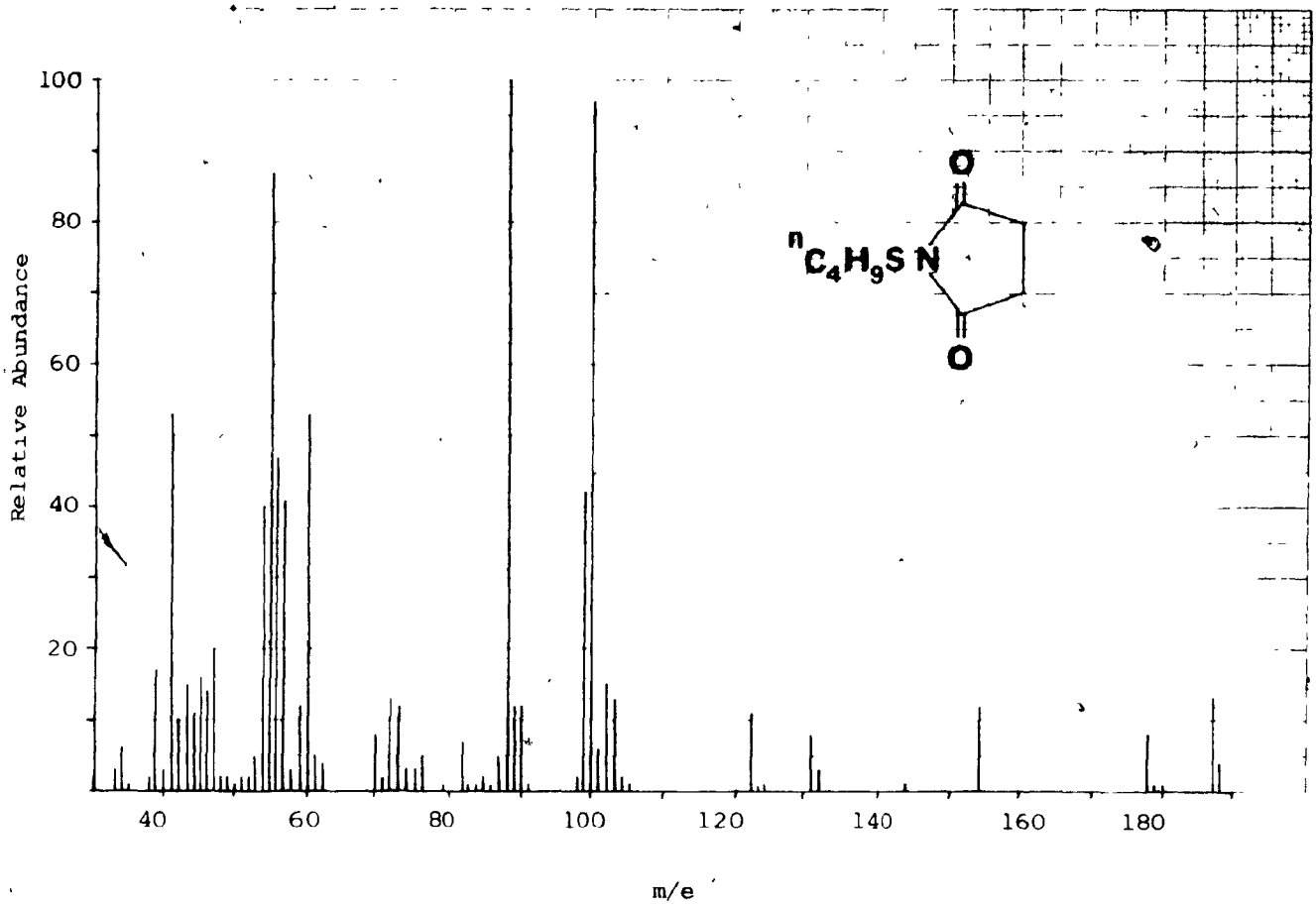
(-)-MENTHYL (-)-(S)-BENZENESULFINATE


(-)-Menthyl (-)-(S)-benzenesulfinate (30)
$(\alpha)_D = -205.5°$
OMen
0 Hz
100
200
300
400
500
PPM (δ)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

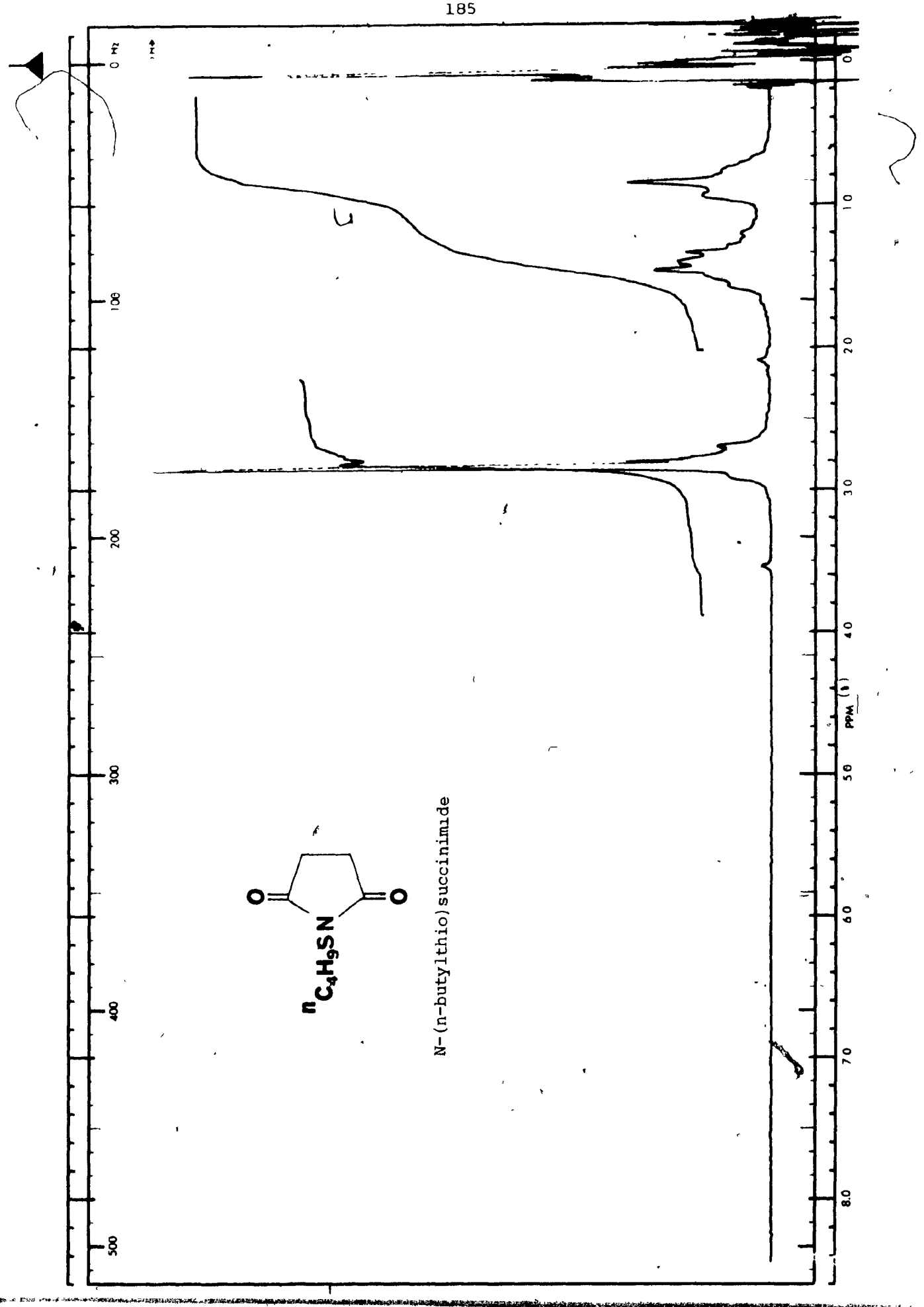
THIOIMIDES AND SULFINIMIDES



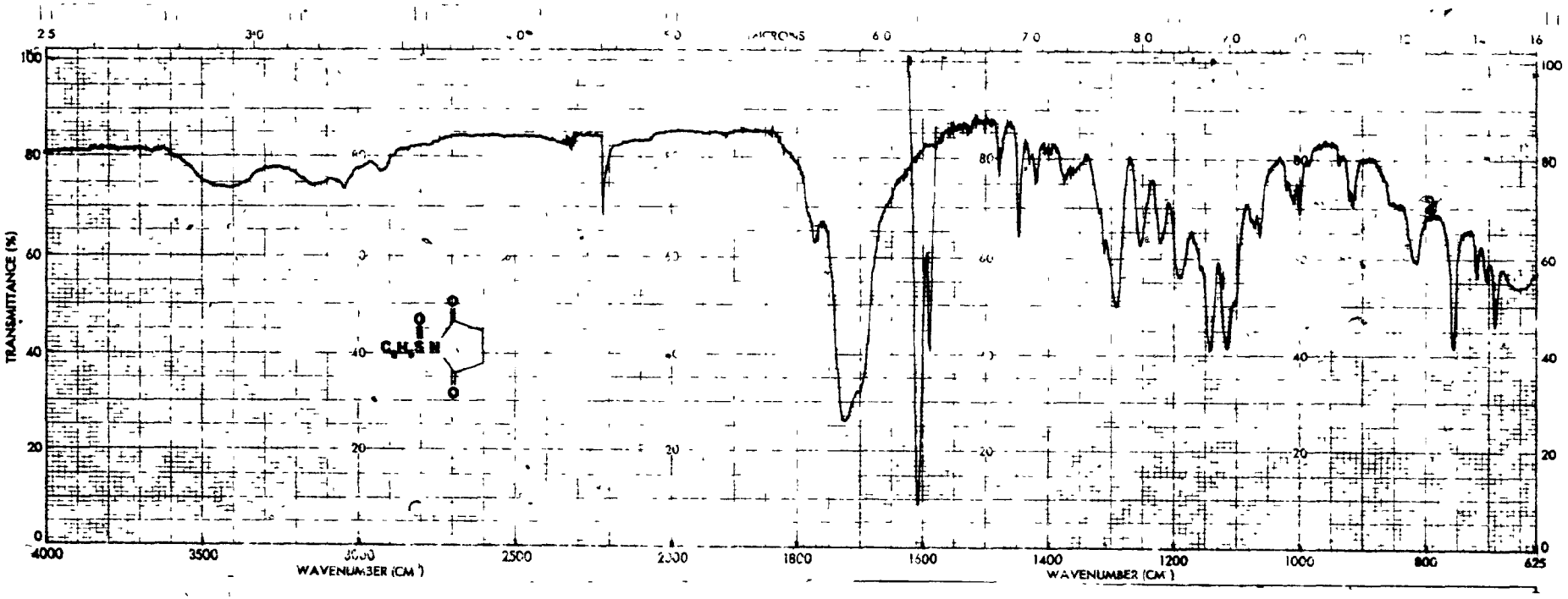
N-(n-butylthio)succinimide



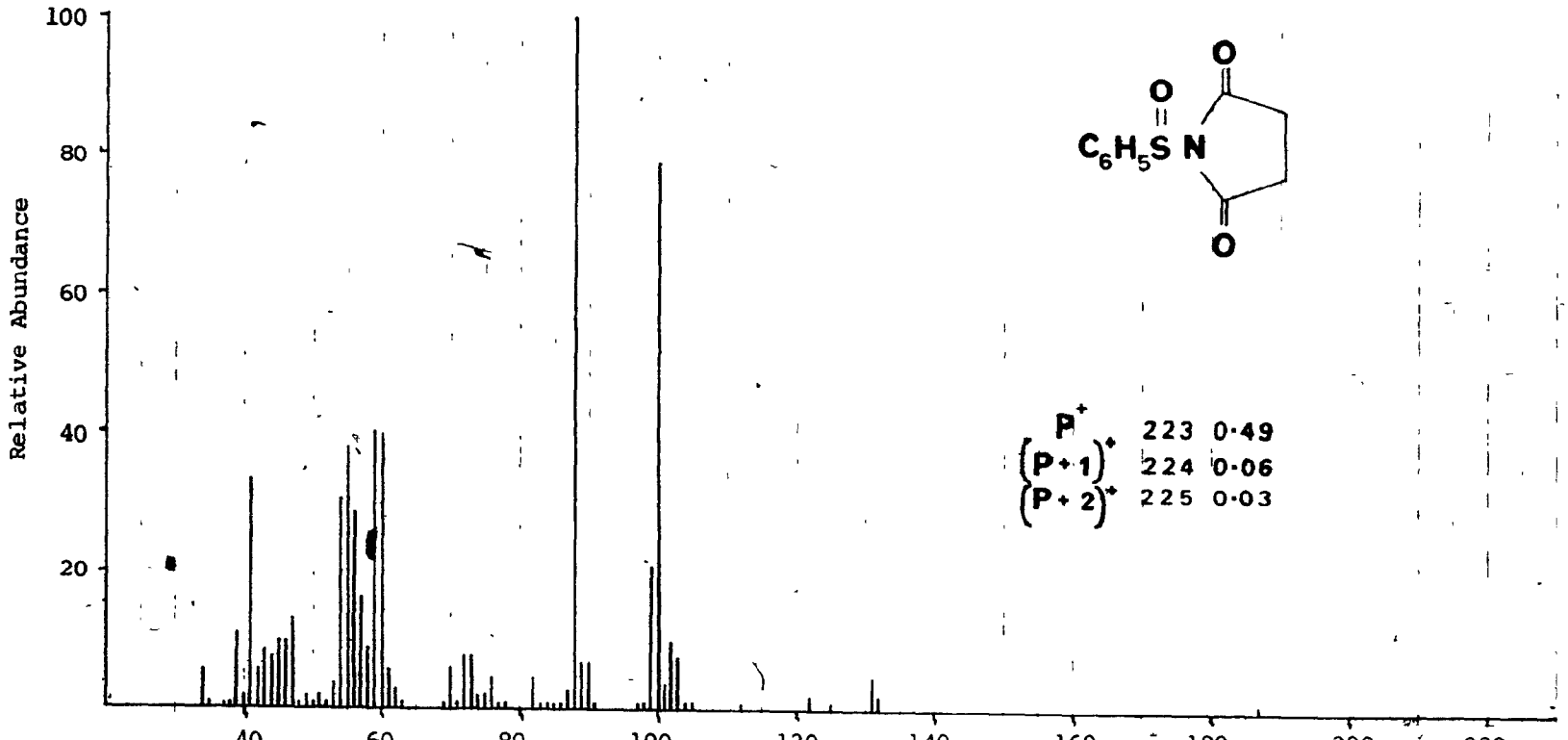
N-(n-butylthio)succinimide



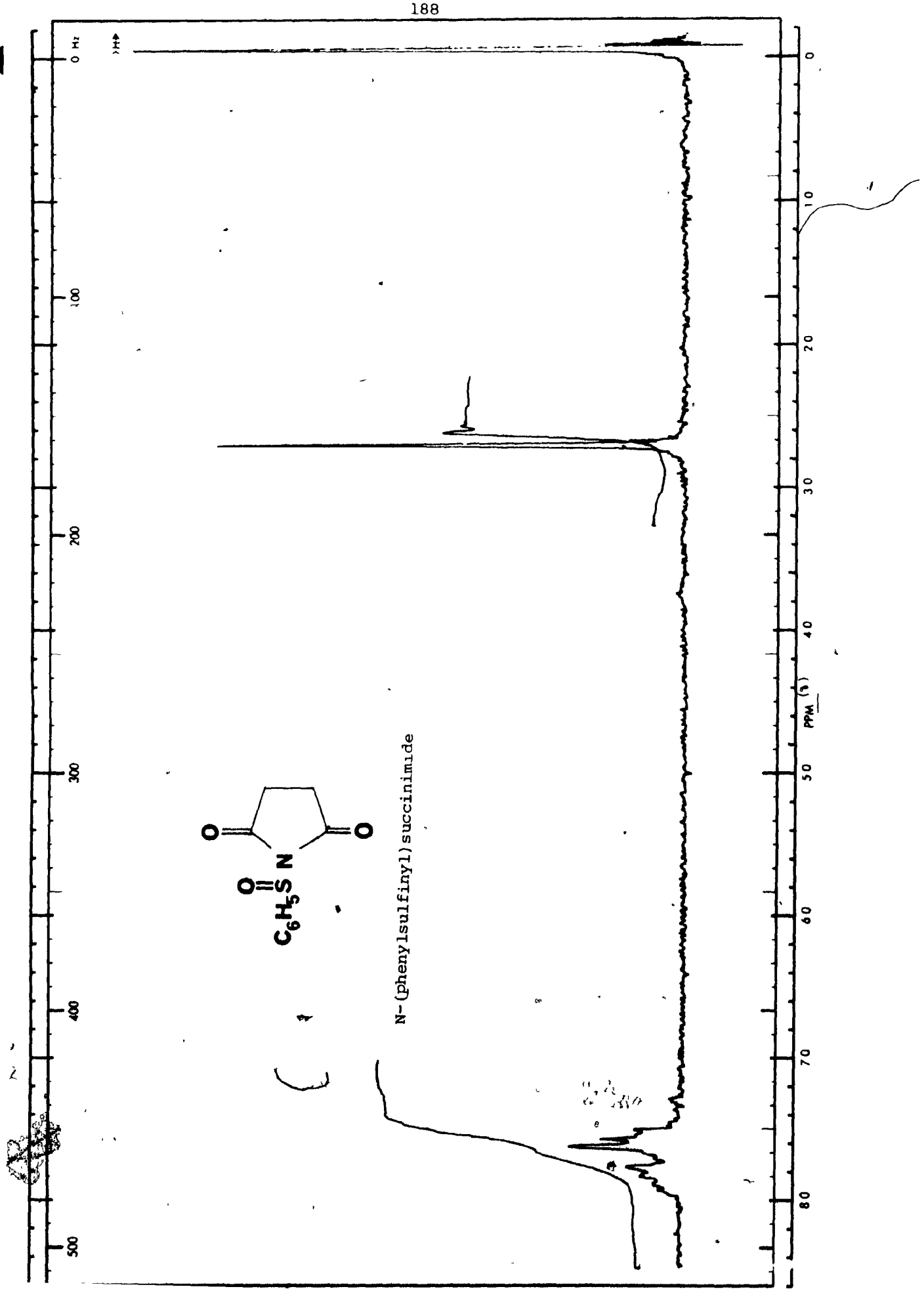
N-(n-butylthio)succinimide



N-(phenylsulfinyl)succinimide



N-(phenylsulfinyl)succinimide


0 Hz
100
200
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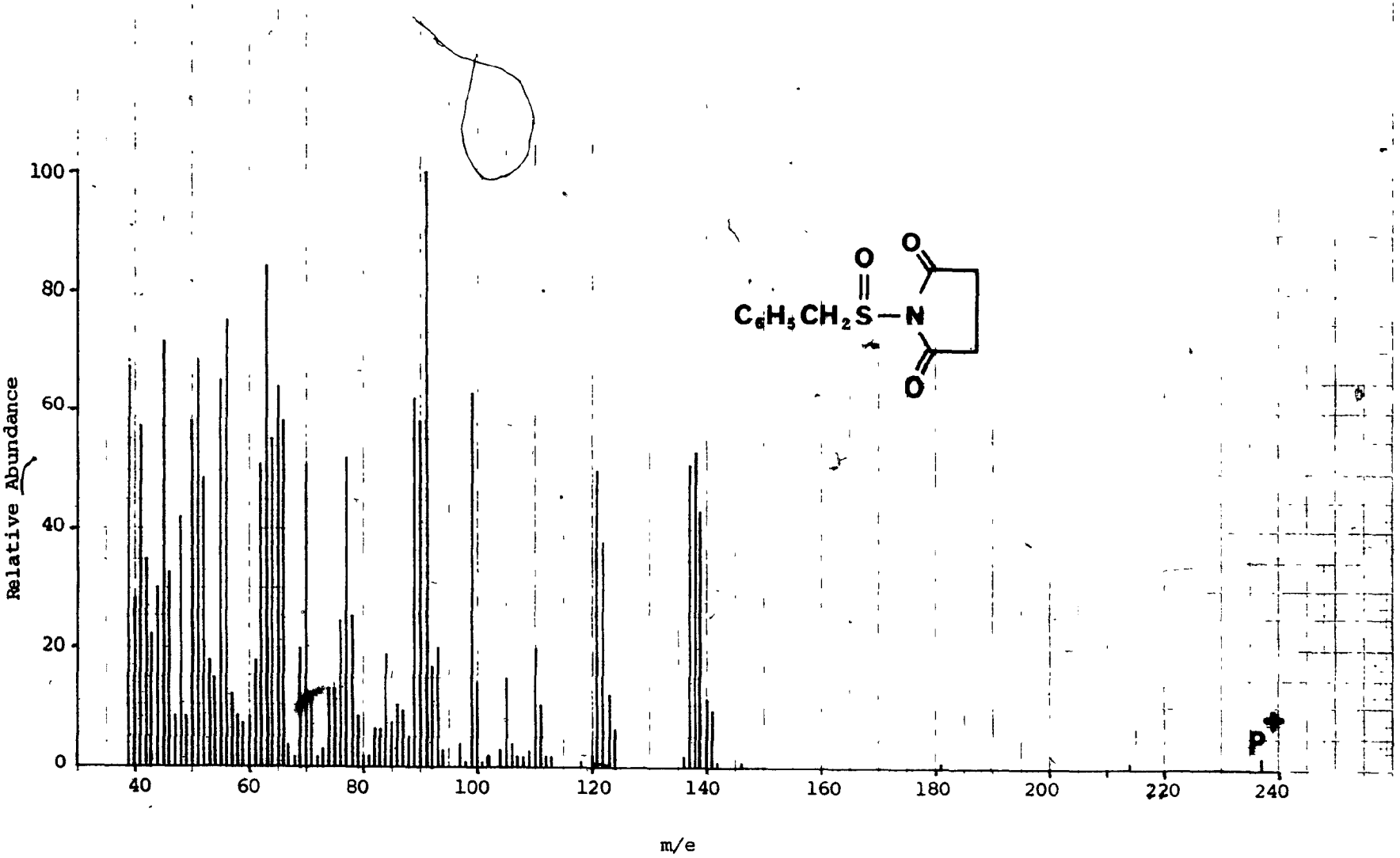
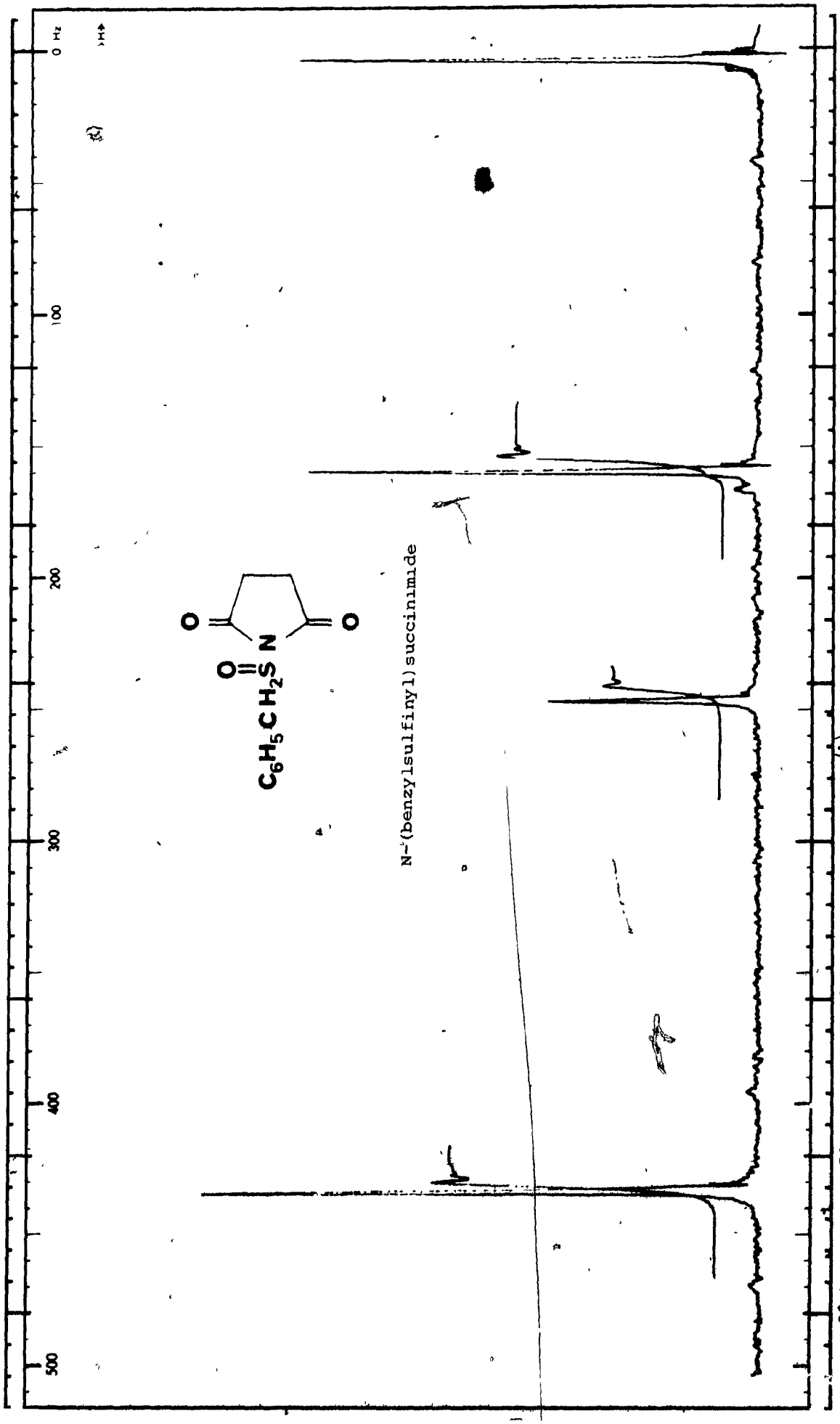
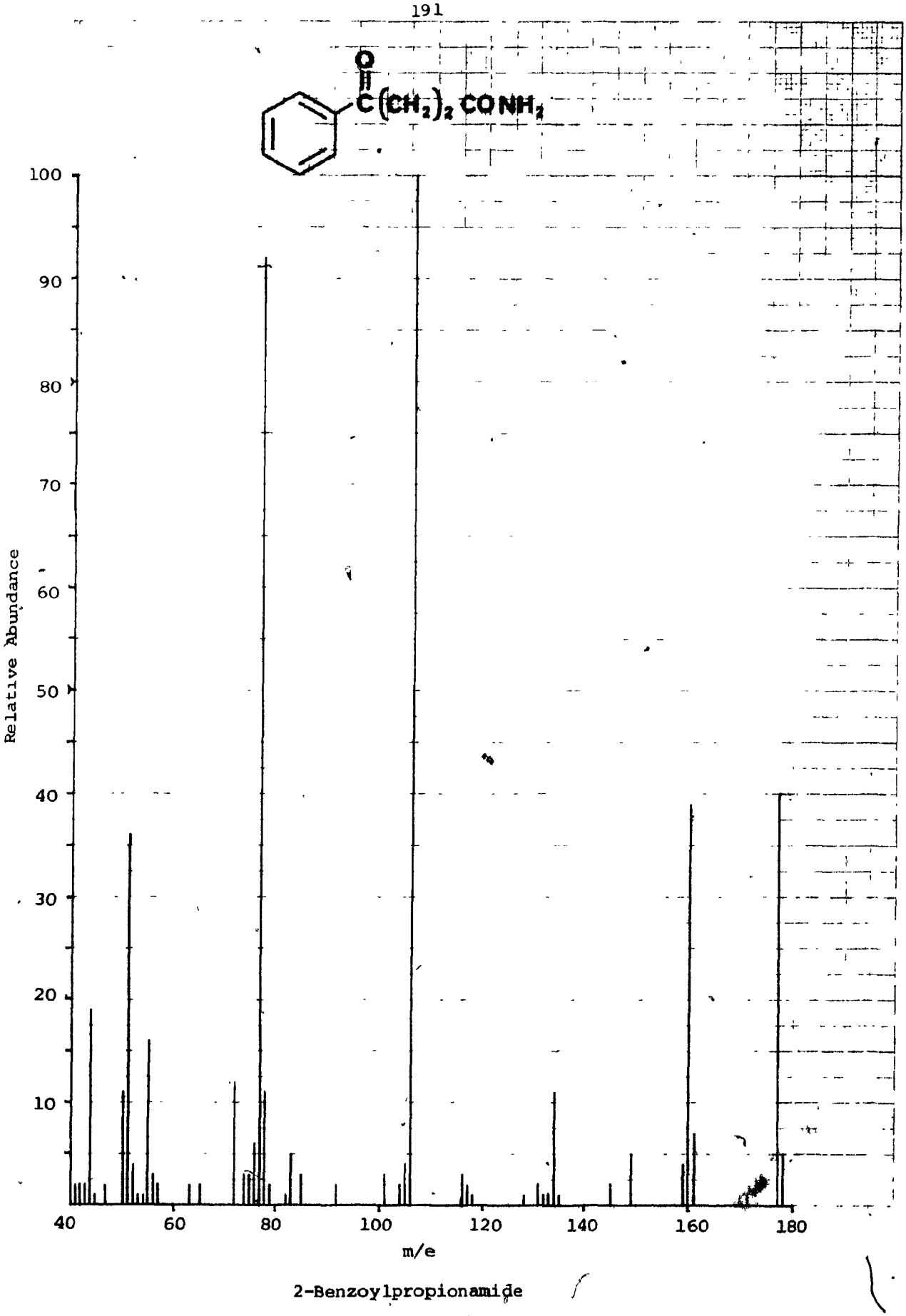
0
10
20
30
40
50
60
70
80
PPM (δ)
N-(phenylsulfinyl)succinimide
O
O
O
S
N
C6H5



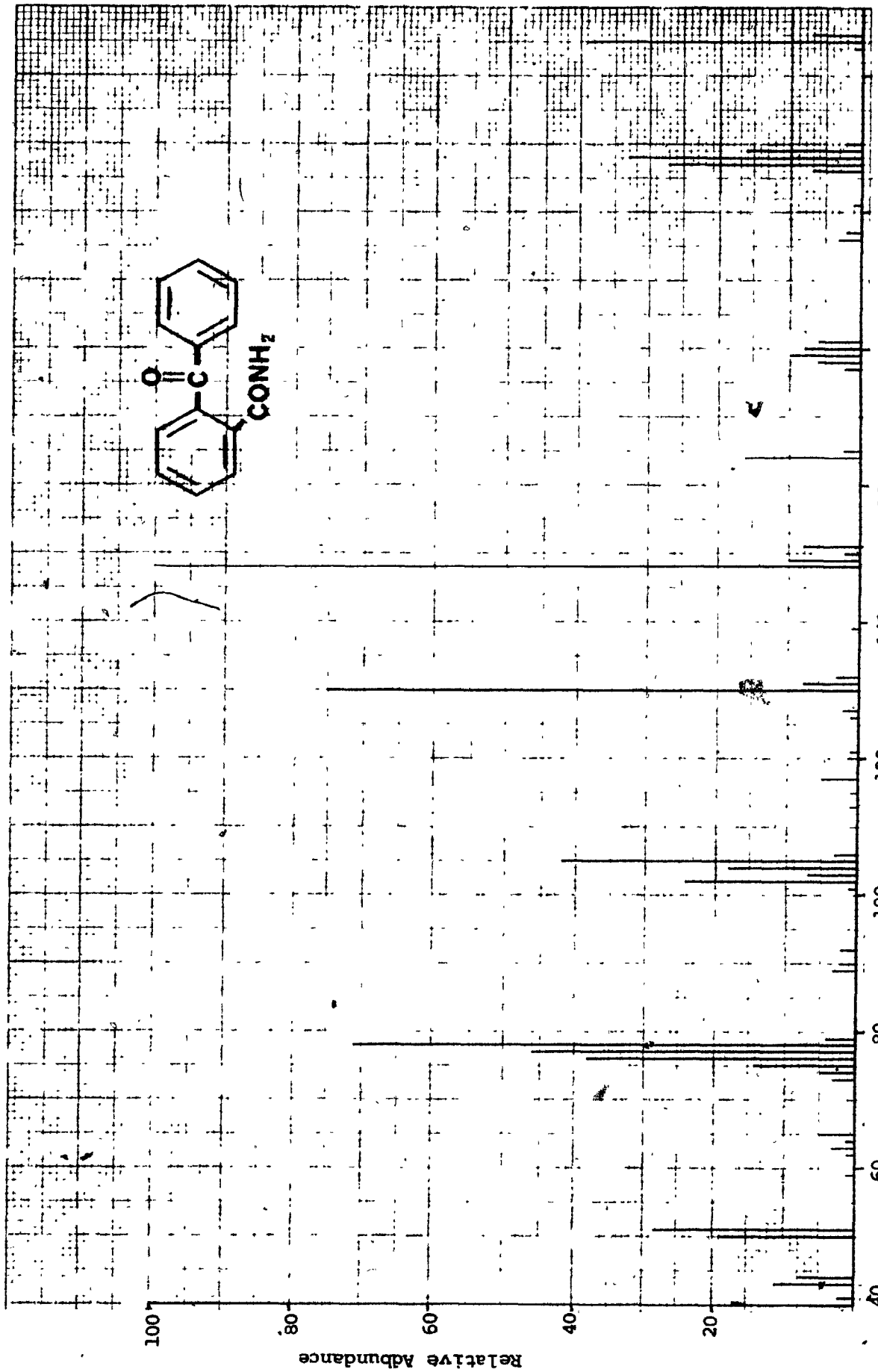
N-(benzylsulfinyl)succinimide



N-(benzylsulfinyl)succinimide

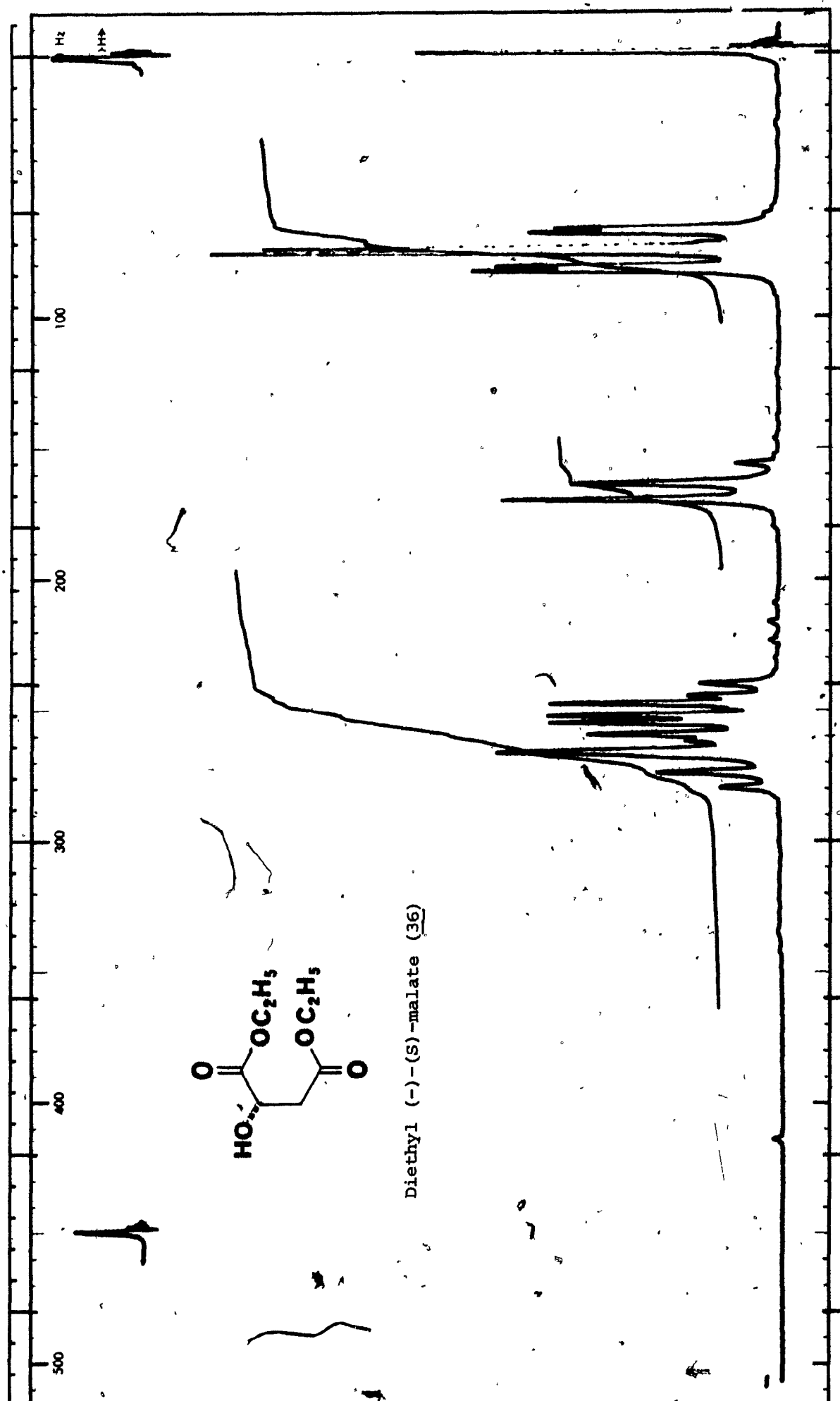


2-Benzoylpropionamide



2-Benzoylbenzamide

CHIRAL SULFINIMIDES AND PRECURSORS



Diethyl (-)-(S)-malate (36)

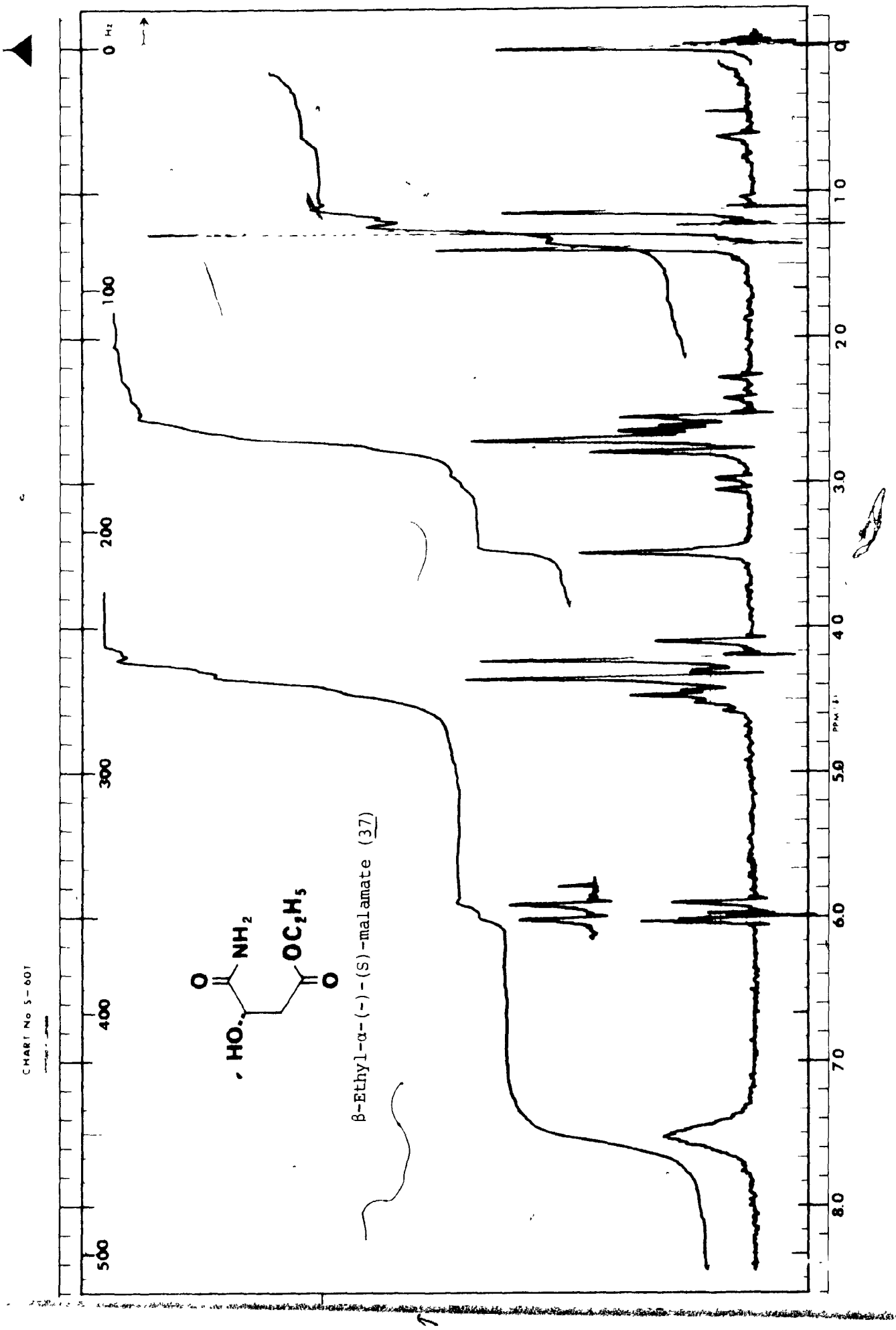
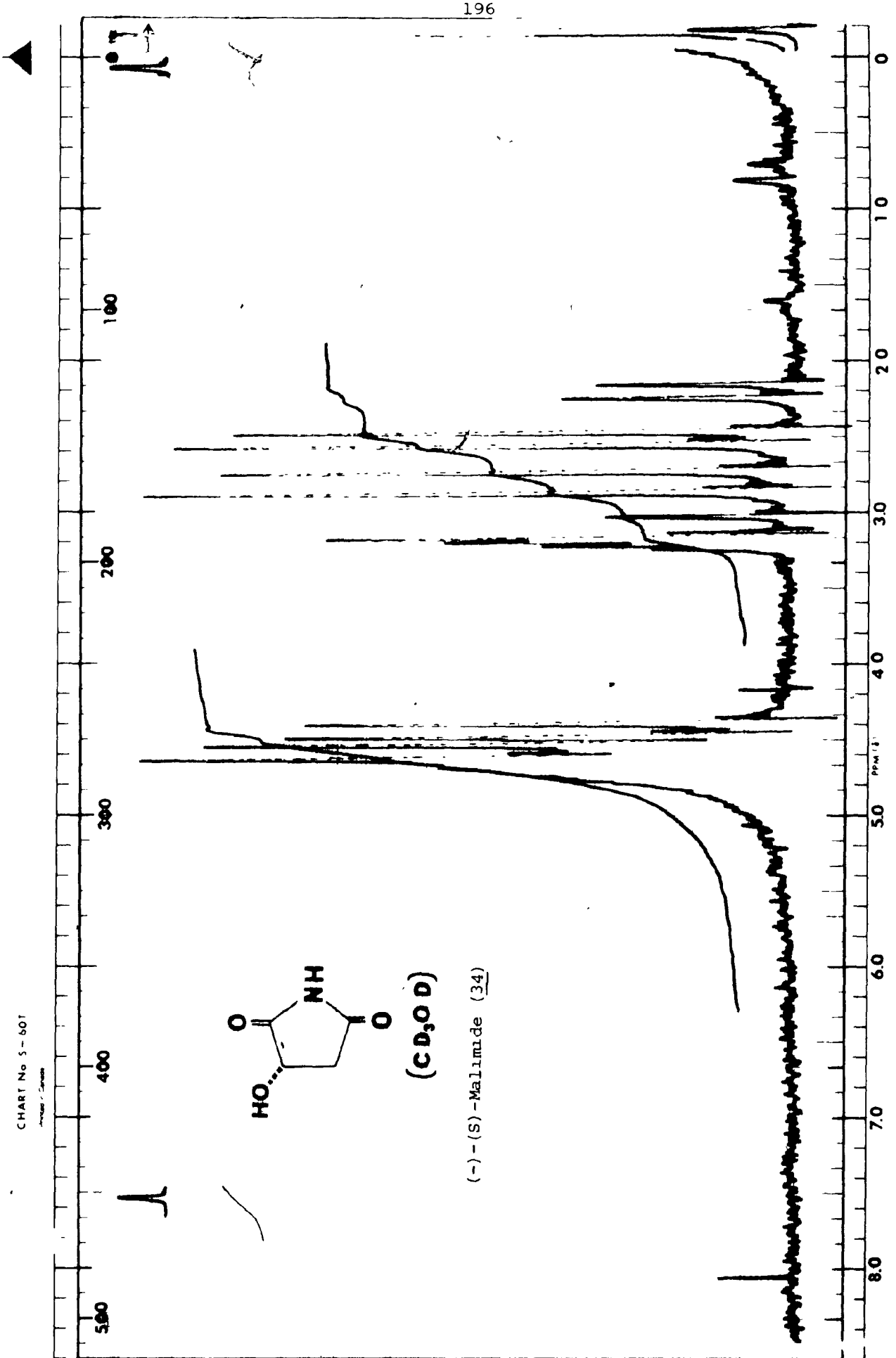
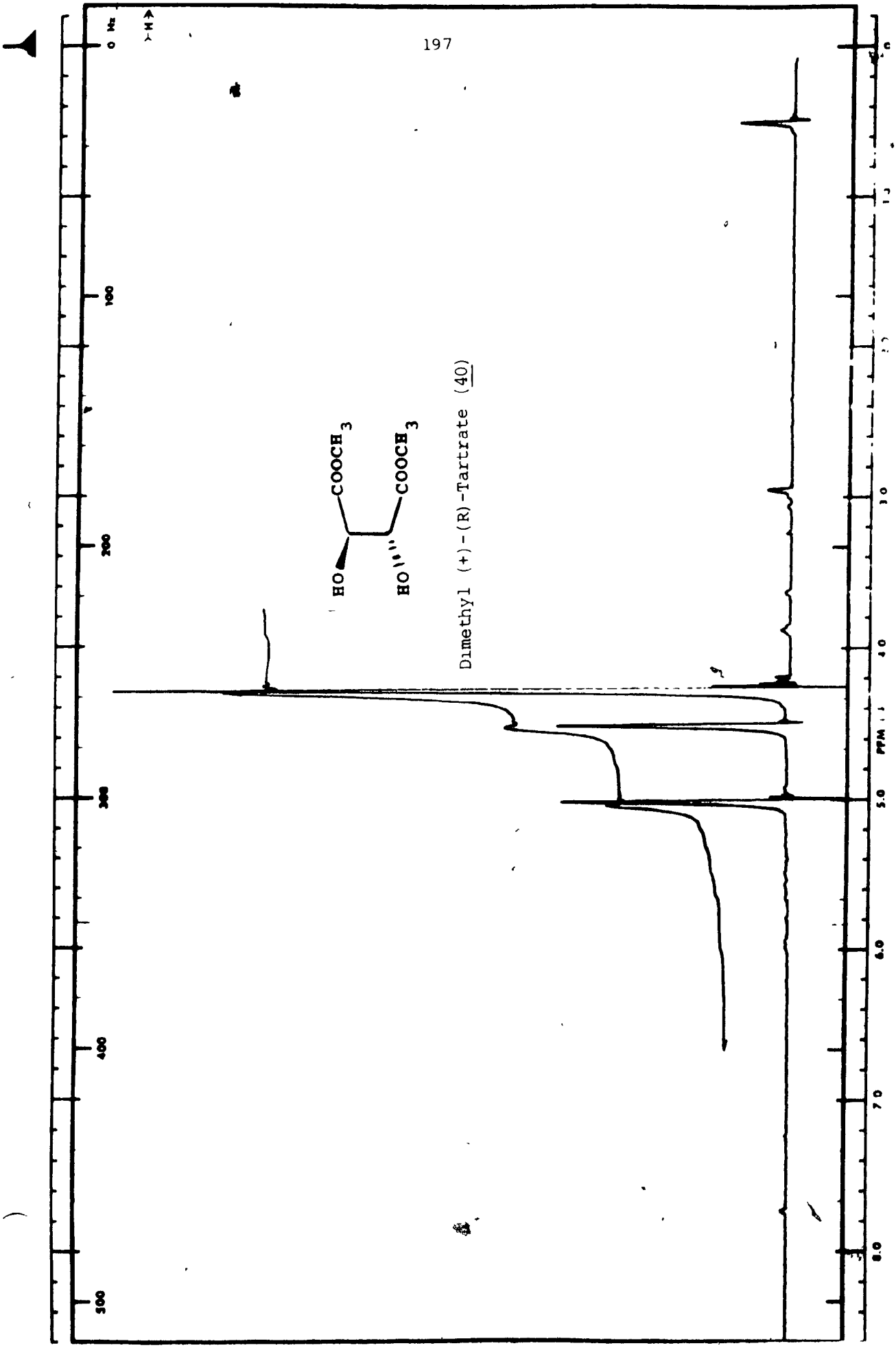
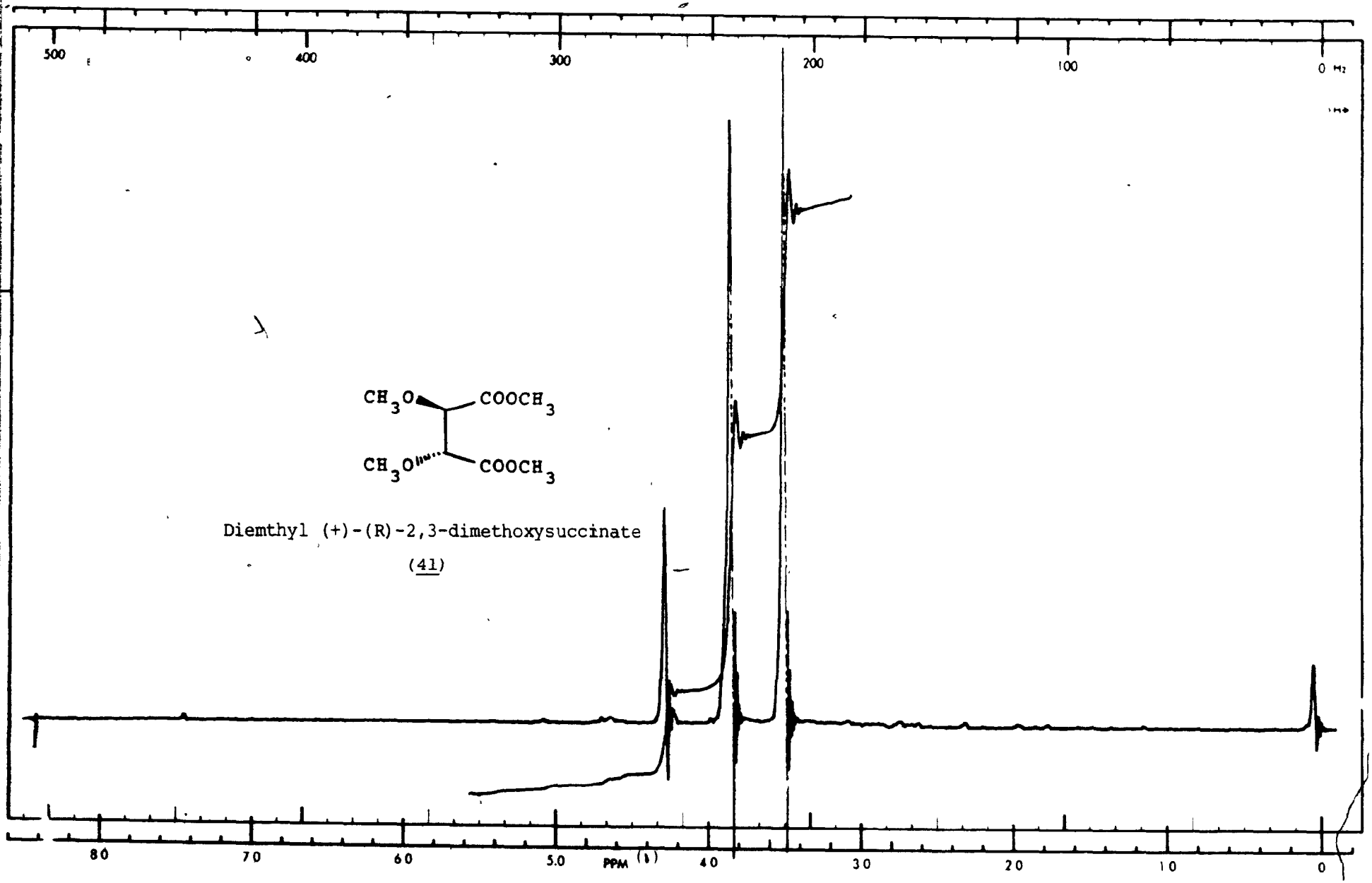


CHART No 5-601
0 Hz
100
200
300
400
500
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
PPM
NH2
OC2H5
HO
β-Ethyl-α-(-)-(S)-malamate (37)



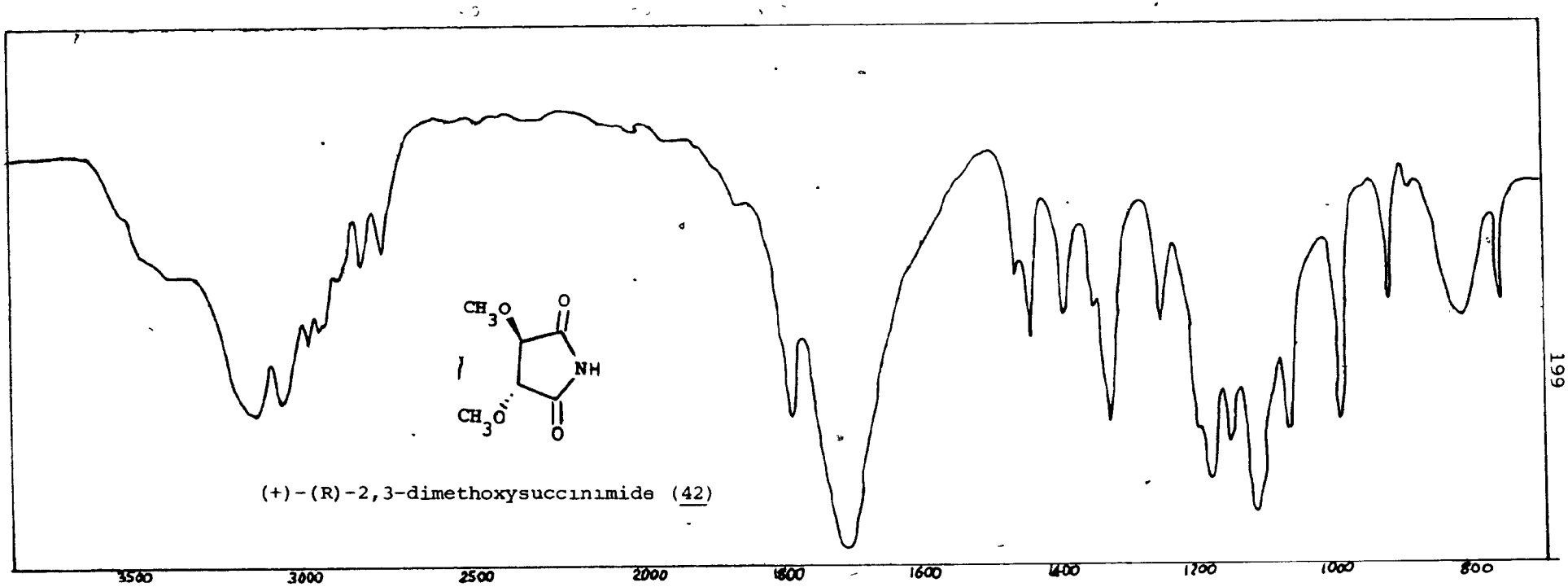
(-)-(S)-Malimide (34)


HO
COOCH3
HO
COOCH3
Dimethyl (+)-(R)-Tartrate (40)
PPM

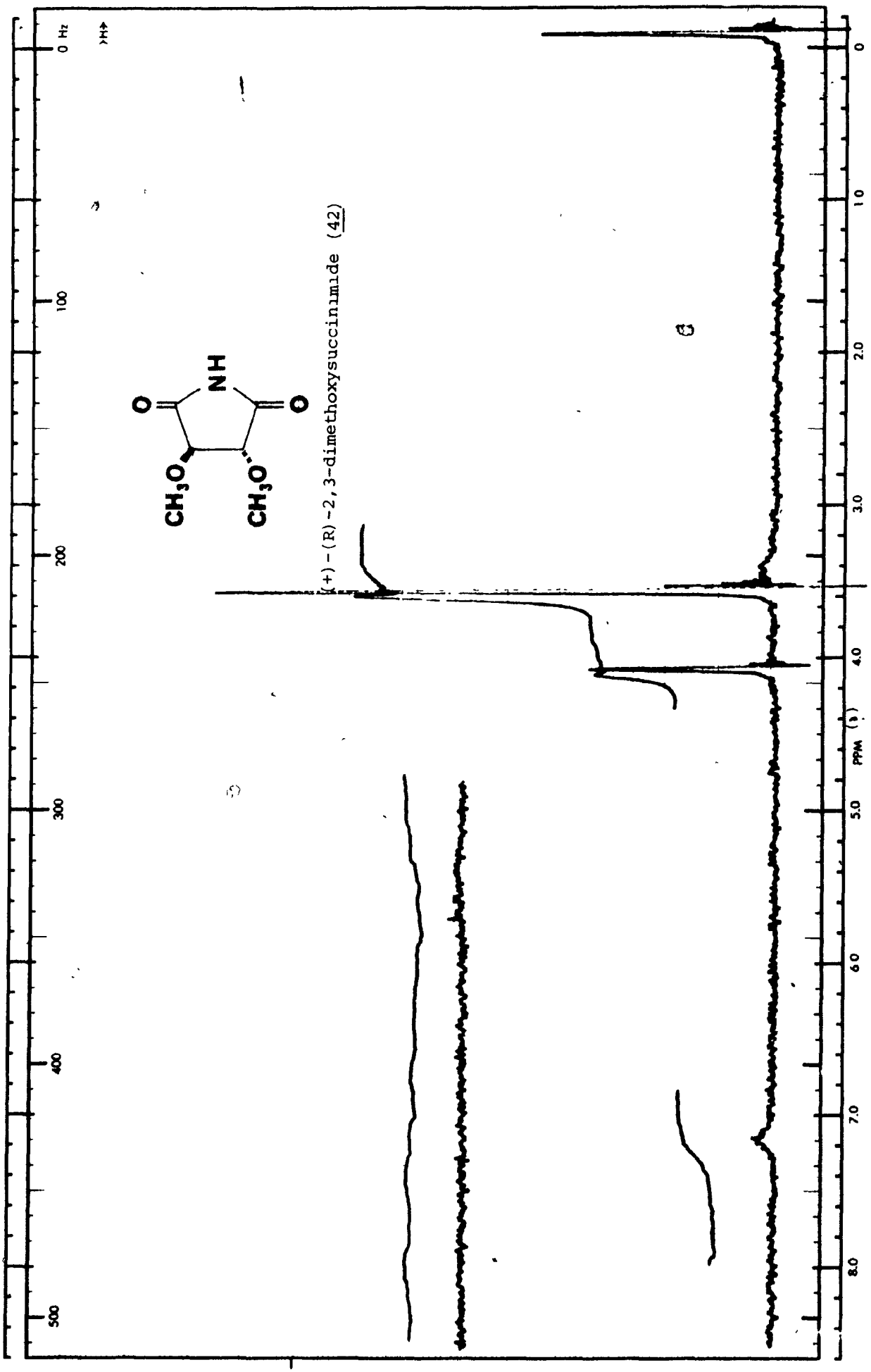


Diemthyl (+)-(R)-2,3-dimethoxysuccinate

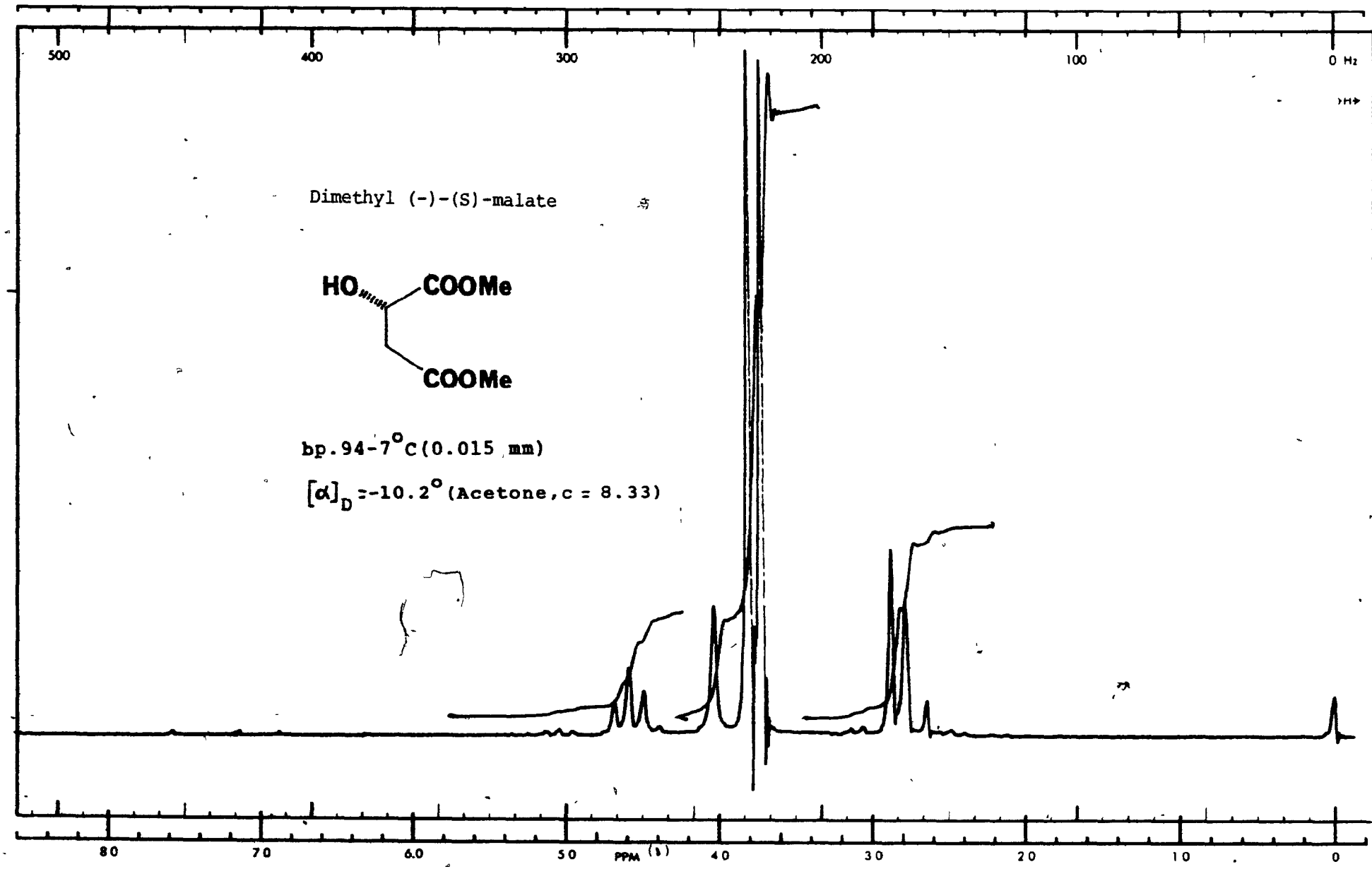
(41)

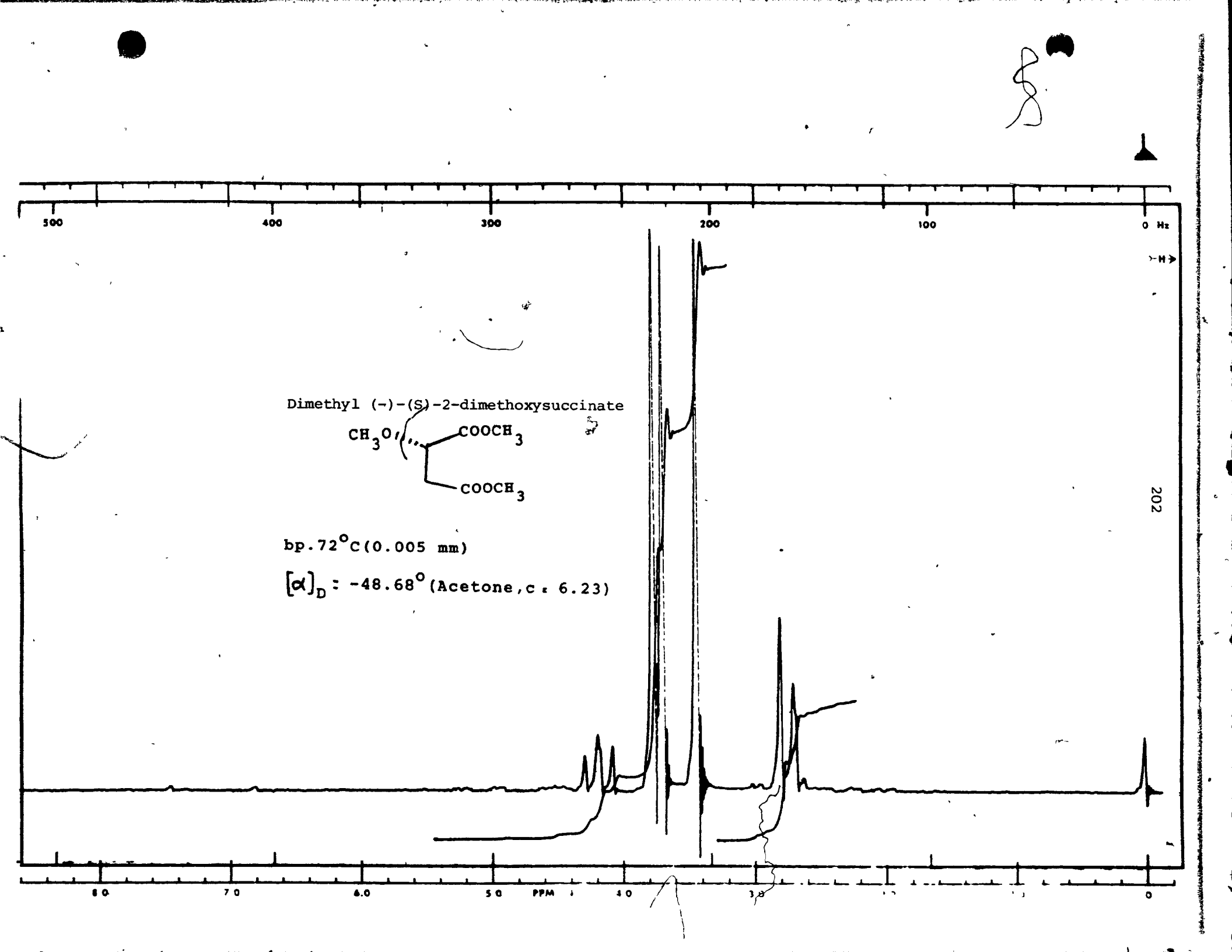


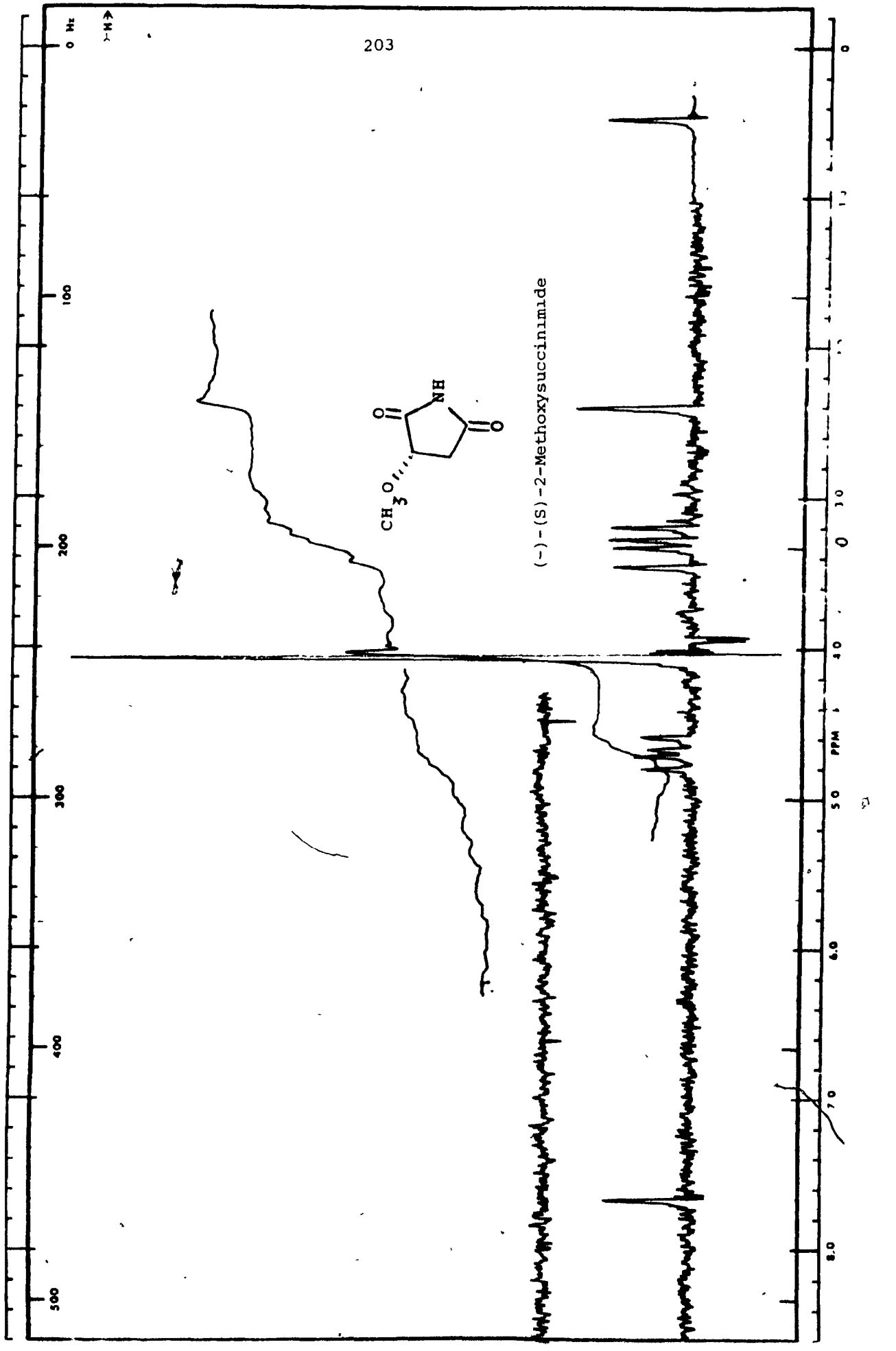
(+)-(R)-2,3-dimethoxysuccinimide (42)



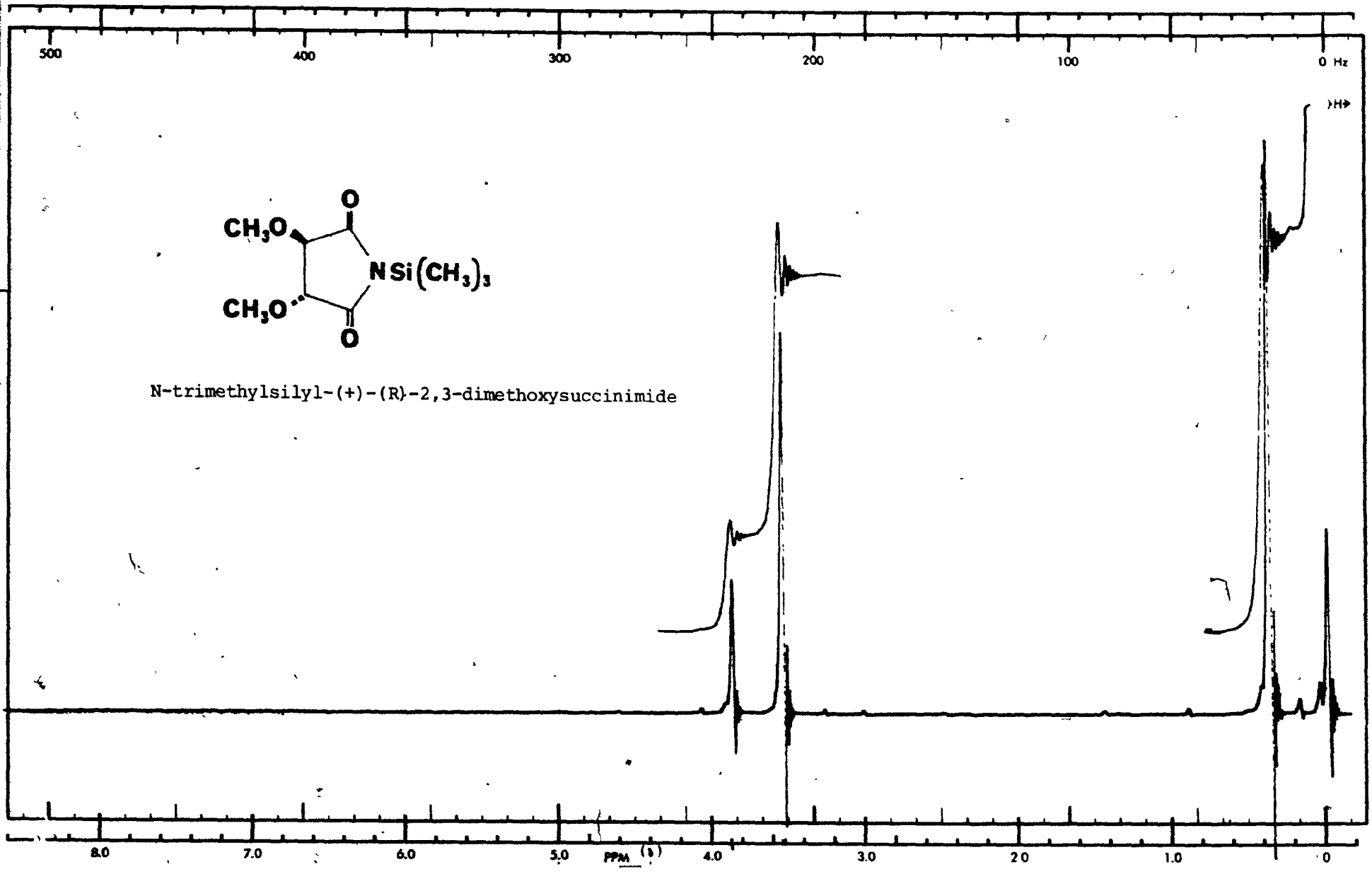
(+)-(R)-2,3-dimethoxysuccinimide (42)


500
400
300
200
100
0 Hz
Dimethyl (-)-(S)-malate
HO
COOMe
COOMe
bp.94-7°C(0.015 mm)
[α]D=-10.2°(Acetone,c = 8.33)
201
80
70
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0

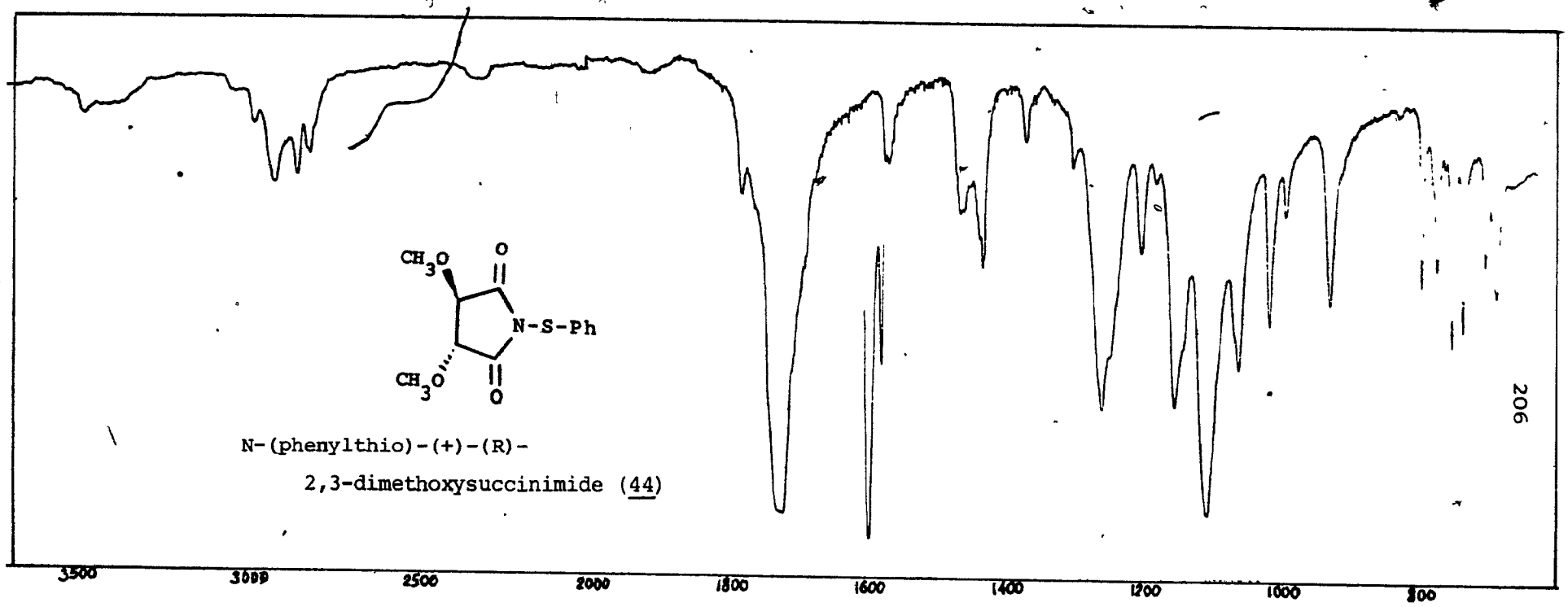

500
400
300
200
100
0 Hz
H
Dimethyl (-)-(S)-2-dimethoxysuccinate
CH3O
COOCH3
COOCH3
bp.72°C(0.005 mm)
[α]D : -48.68° (Acetone, c = 6.23)
202
8.0
7.0
6.0
5.0
PPM
4.0
3.0
0


0 Hz
100
200
300
400
500
PPM
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
NH
O
O
CH_3O
(-)-(S)-2-Methoxysuccinimide

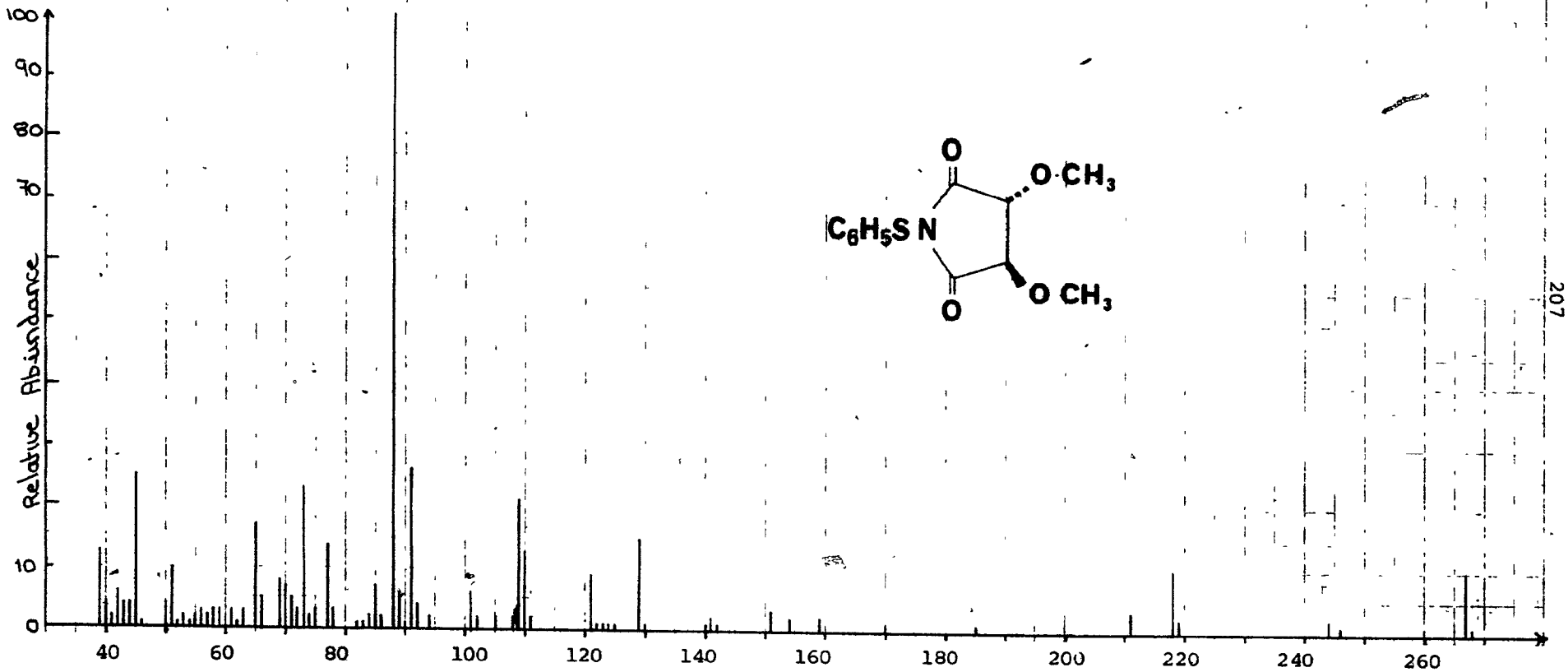
CHIRAL SULFINIMIDE DERIVATIVES



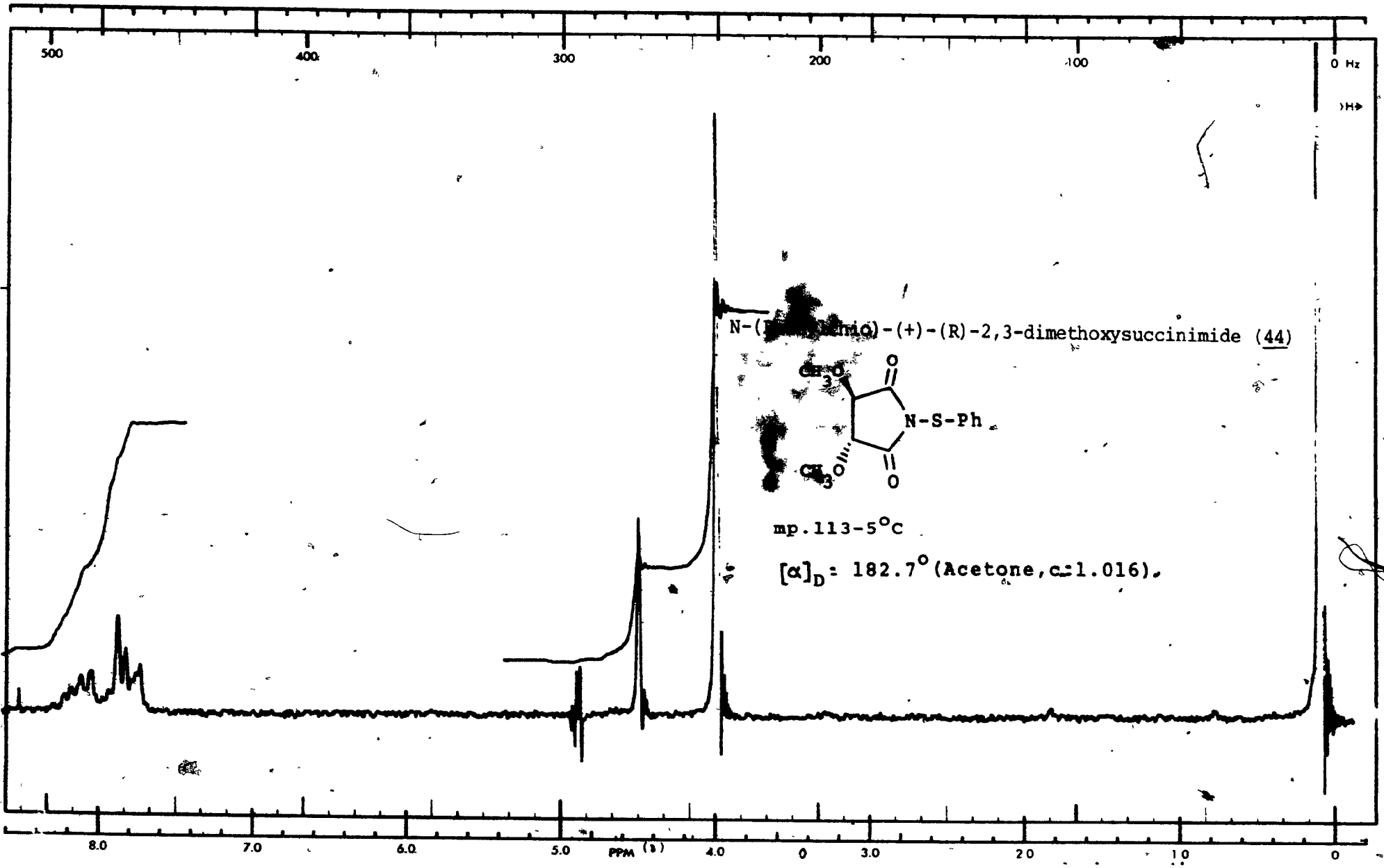
N-trimethylsilyl-(+)-(R)-2,3-dimethoxysuccinimide

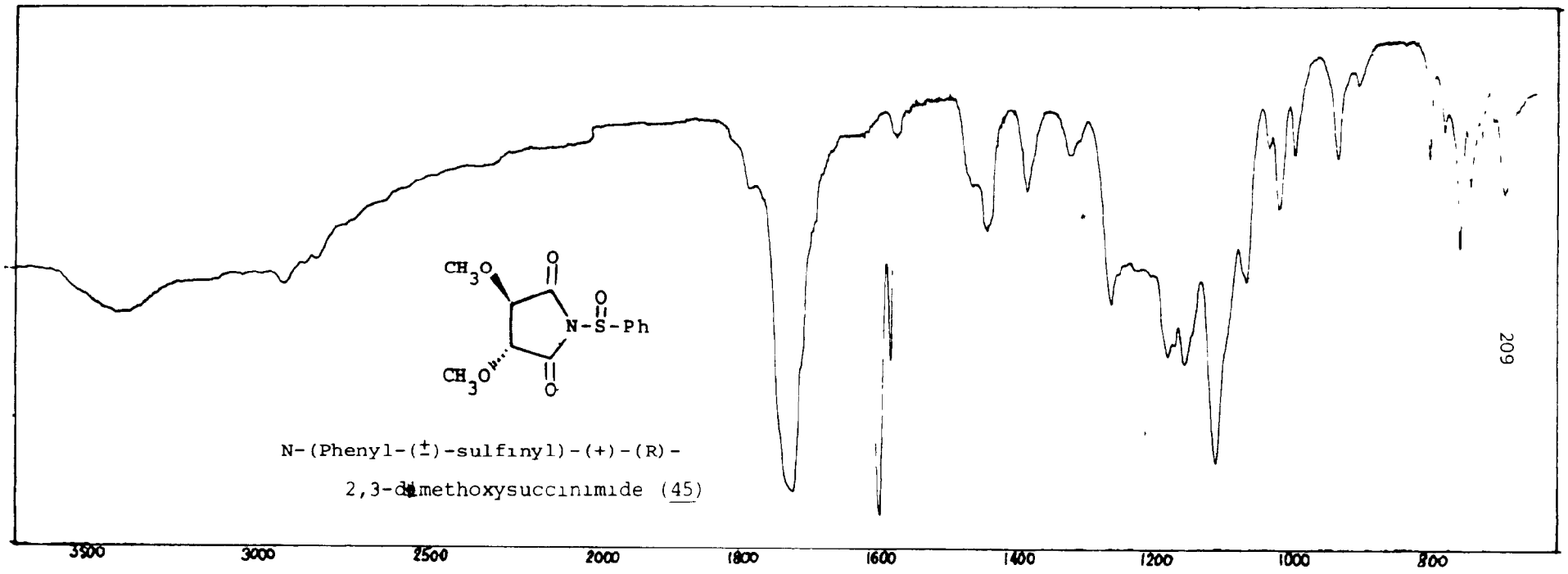


N-(phenylthio)-(+)-(R)-
2,3-dimethoxysuccinimide (44)

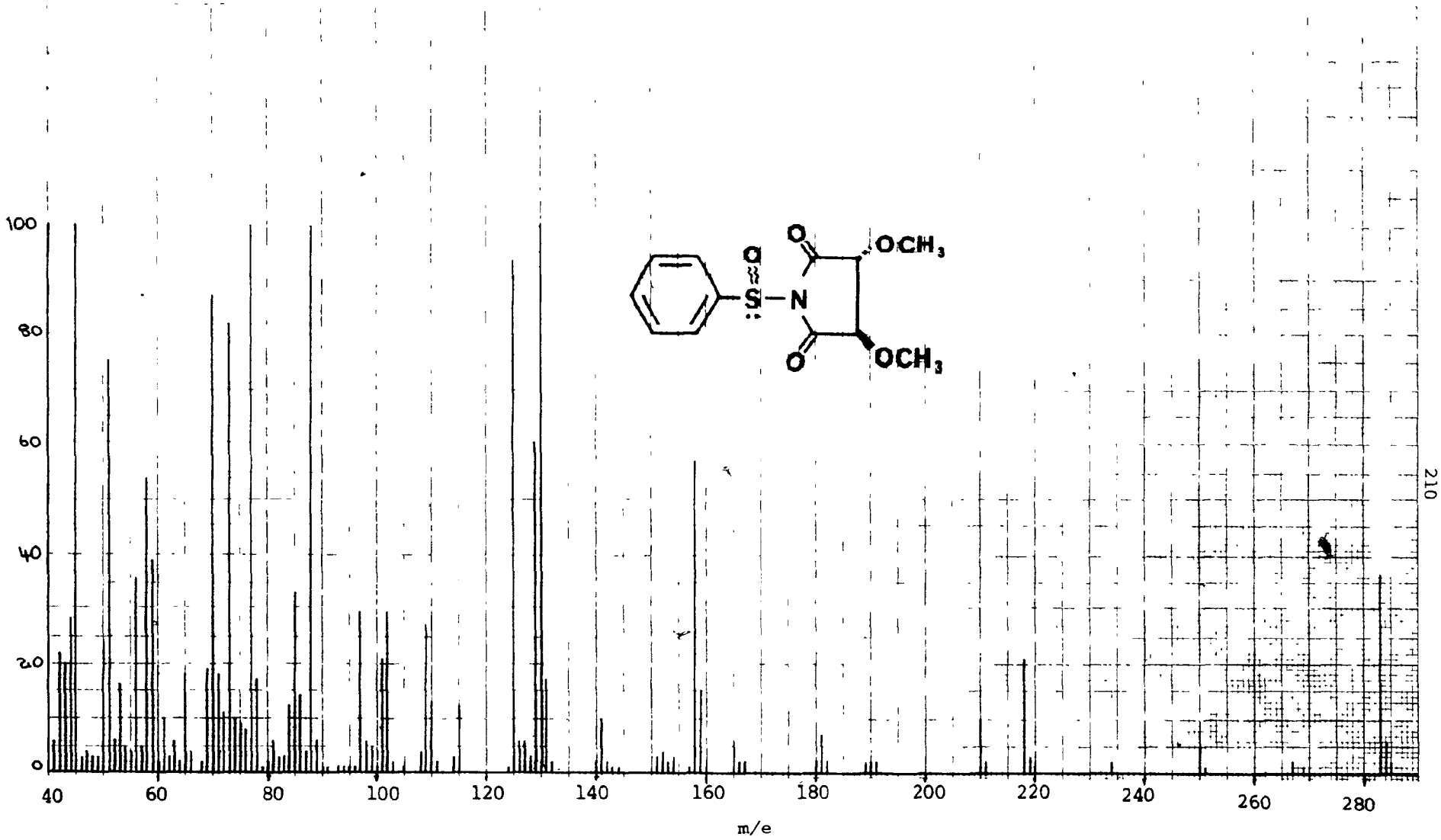


N-(Phenylthio)-(+)-(R)-2,3-dimethoxysuccinimide (44)

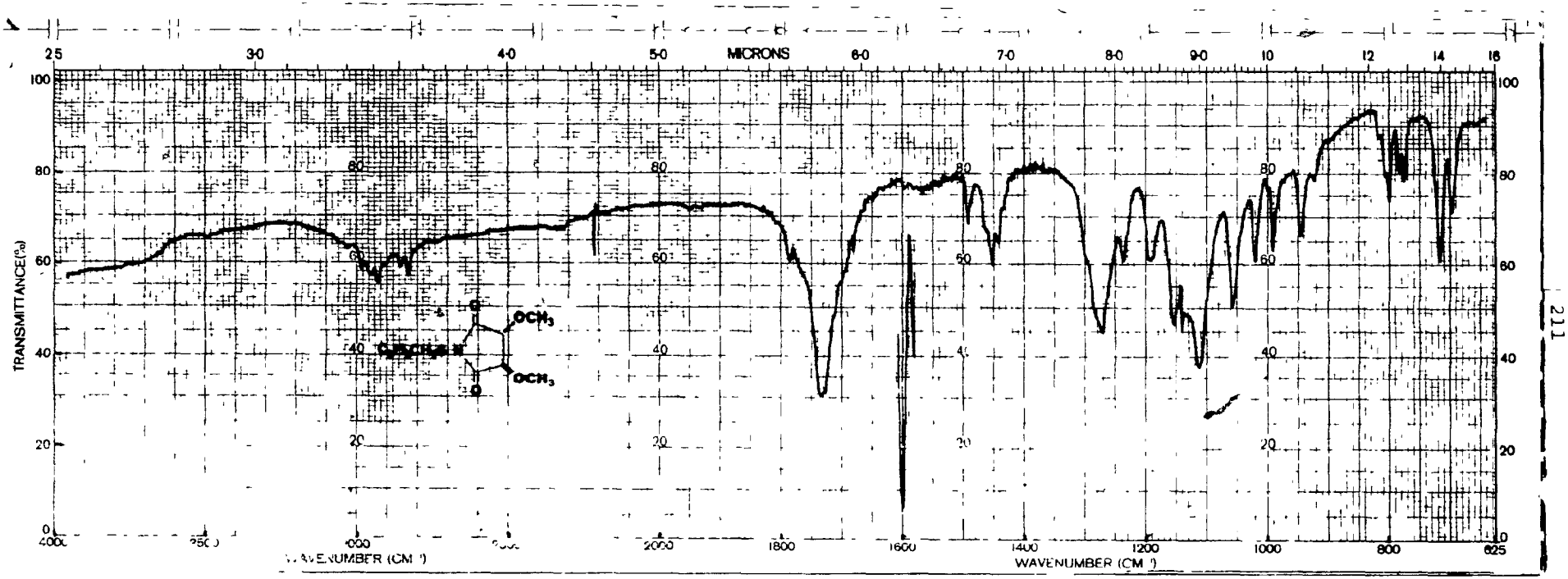

500
400
300
200
100
0 Hz
N-(Phenylthio)-(+)-(R)-2,3-dimethoxysuccinimide (44)
N-S-Ph
mp.113-5°C
[α]D = 182.7° (Acetone, c=1.016).
8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0



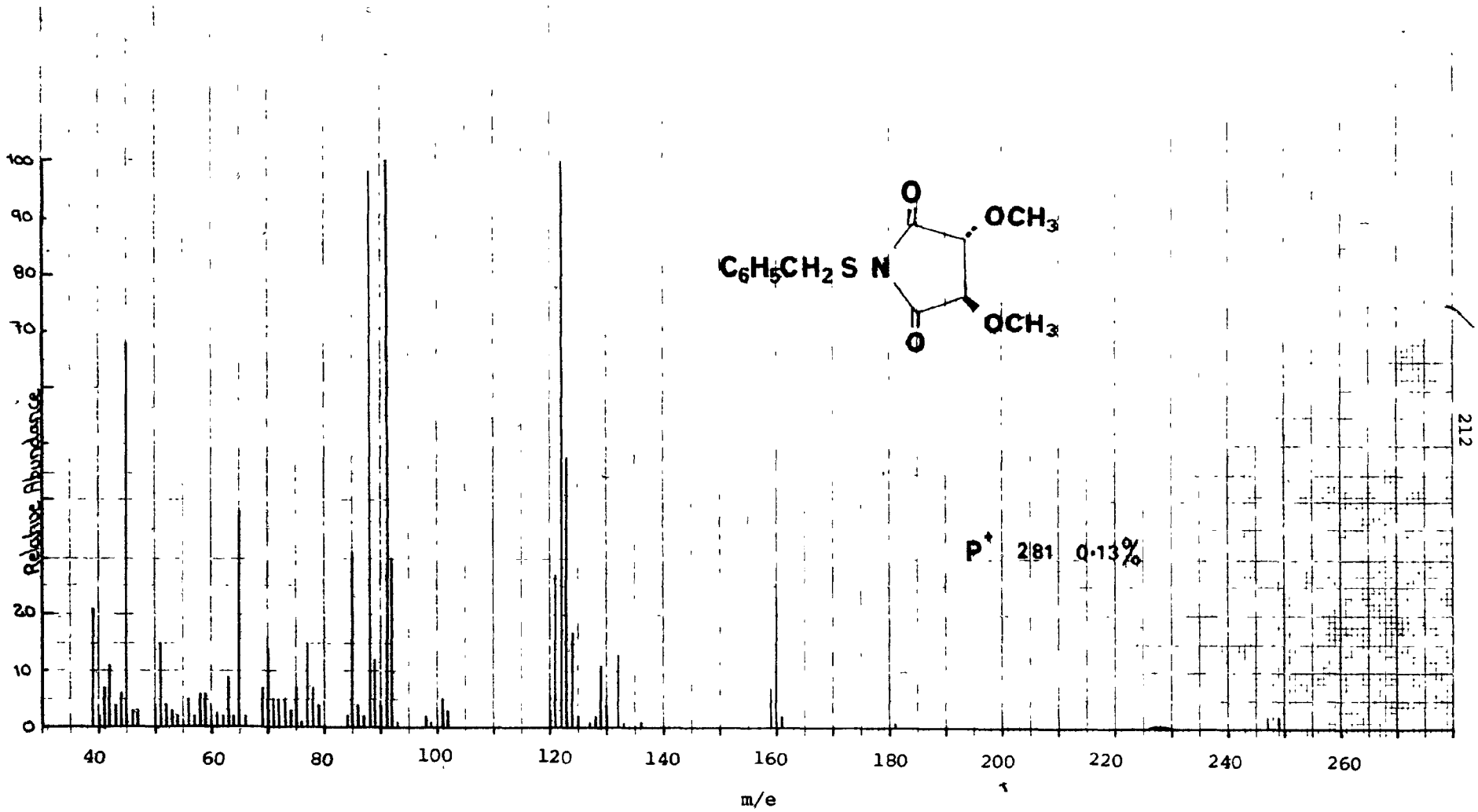
N-(Phenyl-(±)-sulfinyl)-(+)-(R)-
2,3-dimethoxysuccinimide (45)



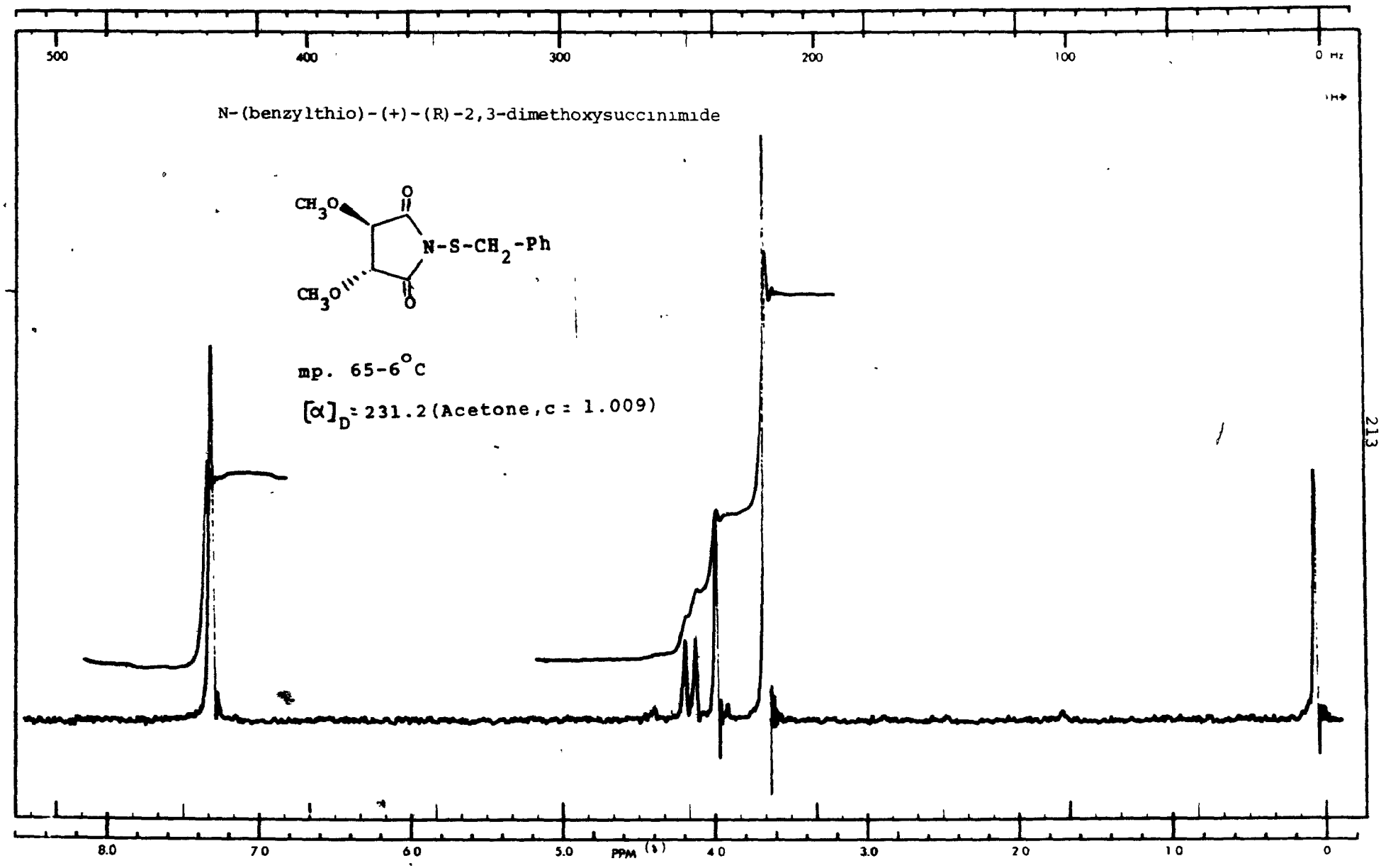
N-(Phenyl-($\pm$)-sulfinyl-(+)-(R)-2,3-dimethoxysuccinimide (45)

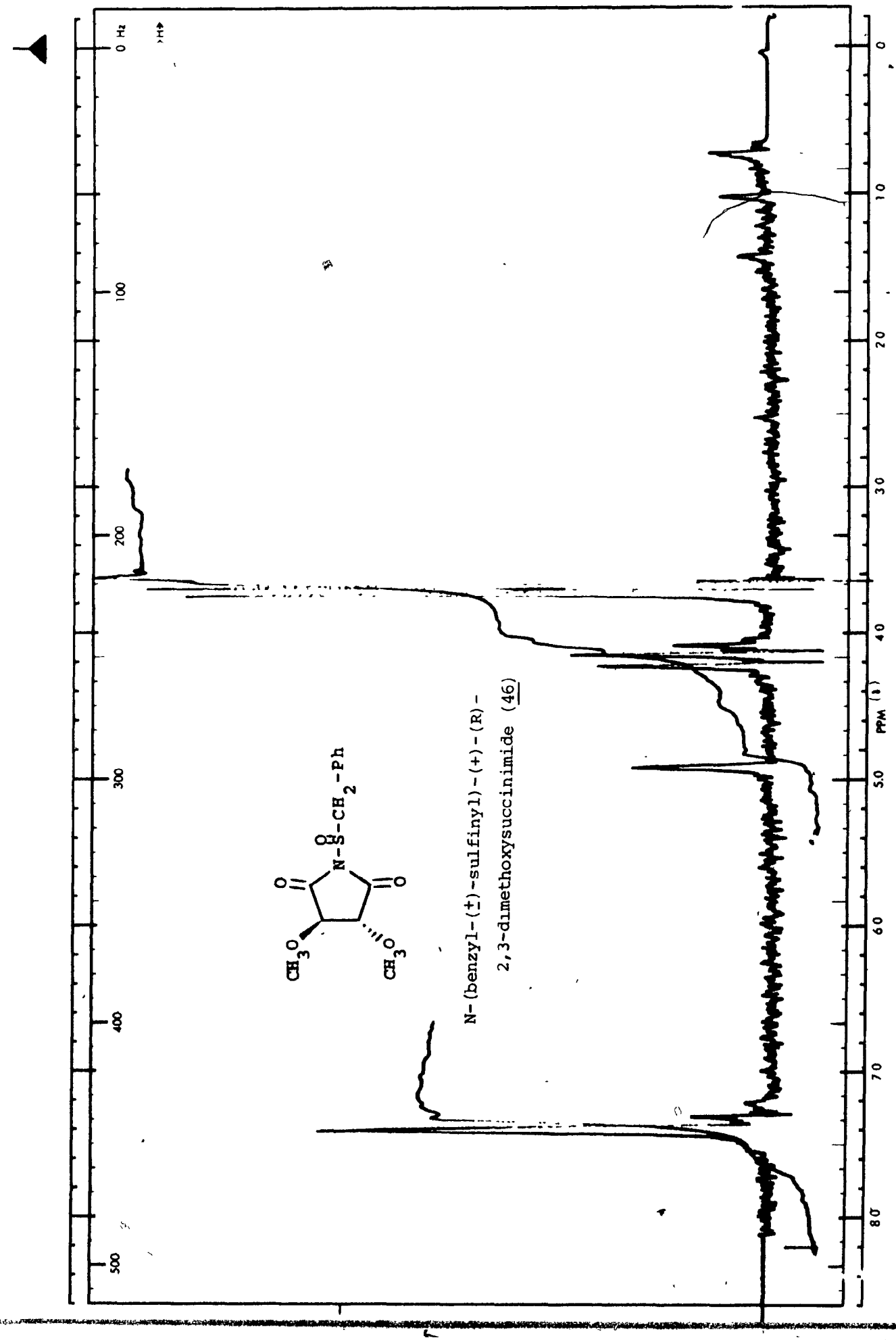


N-(benzylthio)-(+)-(R)-2,3-dimethoxysuccinimide



N-(benzylthio)-(+)-(R)-2,3-dimethoxysuccinimide


500
400
300
200
100
0 Hz
N-(benzylthio)-(+)-(R)-2,3-dimethoxysuccinimide
CH3O
O
N-S-CH2-Ph
CH3O
O
mp. 65-6°C
[α]D = 231.2 (Acetone, c = 1.009)
8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0



N-(benzyl-(±)-sulfinyl)-(+)-(R)-2,3-dimethoxysuccinimide (46)

5. SUMMARY AND CLAIMS TO ORIGINAL RESEARCH

1. It has been demonstrated that sulfinate esters react with lithium organocuprates to give sulfoxides in higher yields than those obtained in the corresponding Grignard reactions.

2. The major by-product in these reactions is a sulfide corresponding in structure to the sulfoxide; in contrast to the Grignard reactions these reactions give no products resulting from addition of two moles of the organometallic reagent.

3. Formation of sulfoxide occurs with complete inversion at sulfur.

4. A high efficiency liquid chromatographic technique for sulfoxide purification has been developed.

5. Sulfinimides have been shown to give higher yields of sulfoxide in a reaction that is more rapid than that of the corresponding sulfinate ester.

6. A versatile route that gives high yields of chiral imides has been developed.

7. The feasibility of synthesizing diastereomeric sulfinimides has been demonstrated.

8. A new synthesis of thioimides (*via* organosilicon reagents) has been identified.