REACTIONS OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES WITH BROMINE AND ALCOHOLS: MECHANISM OF THE PUMMERER REARRANGEMENT

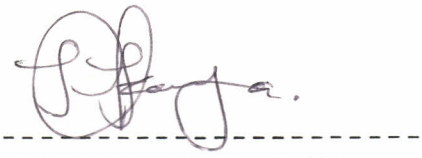
BY

JOHN FRANCIS OKONYA

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN THE UNIVERSITY OF NAIROBI.

MARCH 1988

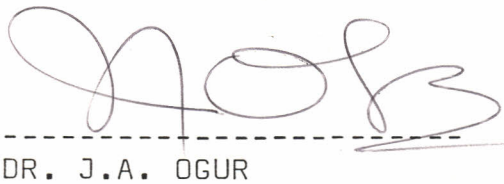
This thesis is my original work and has not been presented for a degree in any other university.



JOHN FRANCIS OKONYA

This thesis is submitted for examination with our approval as university supervisors.

PROFESSOR R.M. MUNAVU



DR. J.A. OGUR

DEDICATION

To my parents: Joseph Otigo, Mary Nakijoba and Domtila Atieno.

ACKNOWLEDGEMENTS

I would like to express my greatest appreciation to my main supervisor Prof. R.M. Munavu whose devoted and constant guidance and encouragement was of great value to me throughout this project.

I also owe my gratitude to my second supervisor Dr. J.A. Ogur for the encouragement and guidance I received from him; and Dr. F. Kaberia for his constructive comments and suggestions.

I am greatly indebted to Kenyatta University for offering me a scholarship to do my M.Sc degree; and the University of Nairobi, Chemistry Department for offering me a place to do my M.Sc degree and providing some of the necessary facilities and materials in the course of this project.

Finally, I would like to thank everyone who, directly or indirectly, contributed to the success of this work especially my parents, relatives and friends. Their patience, encouragement and moral support was very useful to me.

ABSTRACT

REACTIONS OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES WITH BROMINE AND ALCOHOLS: MECHANISM OF THE PUMMERER REARRANGEMENT

Nine mono para-substituted dibenzyl sulphides were prepared in 63.2-96.7% yield by the reaction of p-substituted benzyl bromides and p-substituted benzyl alcohols with benzyl mercaptan.

Dibenzyl sulphide reacted with bromine to yield both cleavage and Pummerer products in various proportions depending on the temperature and solvent used. In tetrachloromethane, the formation of Pummerer products was favoured while in the more polar solvents, dichloromethane and trichloromethane, formation of cleavage products was favoured. High temperature slightly favoured the yield of Pummerer products at the expense of cleavage products.

Diols reacted with dibenzyl sulphide and mono para-substituted dibenzyl sulphides to yield the corresponding benzylidene acetals. The acetals formed were isolated in 20-35% yield. Monohydric alkanols with exception of methanol resisted reaction and were not converted to acetal.

The cleavage reaction of the intermediate mono para-substituted dibenzyl bromosulphonium bromides was shown to proceed by a synchronous S_N2 mechanism when the substituent was electron withdrawing, and by mixed S_N1 and S_N2 mechanisms when the substituent was electron donating.

A Hammett correlation of the rates of the α-bromination reaction of mono para-substituted dibenzyl sulphides at room temperature in tetrachloromethane with substituent constants (σ) afforded a ρ value of 0.97 ± 0.02. A ρ value of 1.27 ± 0.02 was obtained for the α-alkoxylation reaction of mono para-substituted dibenzyl sulphides at reflux in tetrachloromethane. These results indicated that the Pummerer reaction of intermediate bromosulphonium and alkoxysulphonium salts proceeds *via* an ylide intermediate.

CONTENTS

PAGE

PAGE

CHAPTER 1

INTRODUCTION

1.1 GENERAL

The reaction of sulphides with halogens or halogenating agents in non-nucleophilic solvents is generally considered to proceed through a halosulphonium salt intermediate (e.g 1) [Wilson, 1982; Wilson and Albert, 1973]. Halosulphonium salts (e.g 1) have also been generated by the action of hydrogen halides on sulphoxides in anhydrous solvents [Gilman, 1943].

$$R_2S + X_2 \longrightarrow R_2SX_2$$

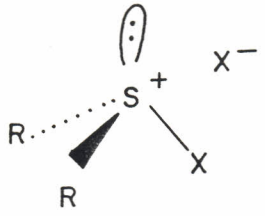
1

$$R_2SO + HX \longrightarrow R_2SX_2 + H_2O$$

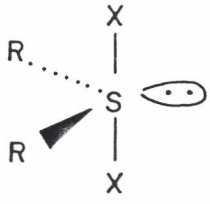
1

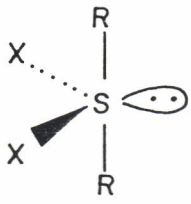
Halosulphonium salts may exist in any of the three forms shown below:

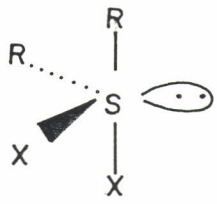
(i) cation with pyramidal tricoordinate structure



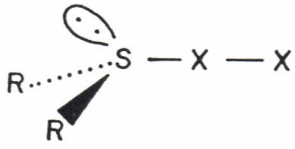
(ii) sulphurane with trigonal bipyramidal structure

(a) 

(b) 

(c) 

(iii) molecular complex



These three major forms (cation, sulphurane and molecular complex) are in theory interconvertible by simple mechanistic steps.

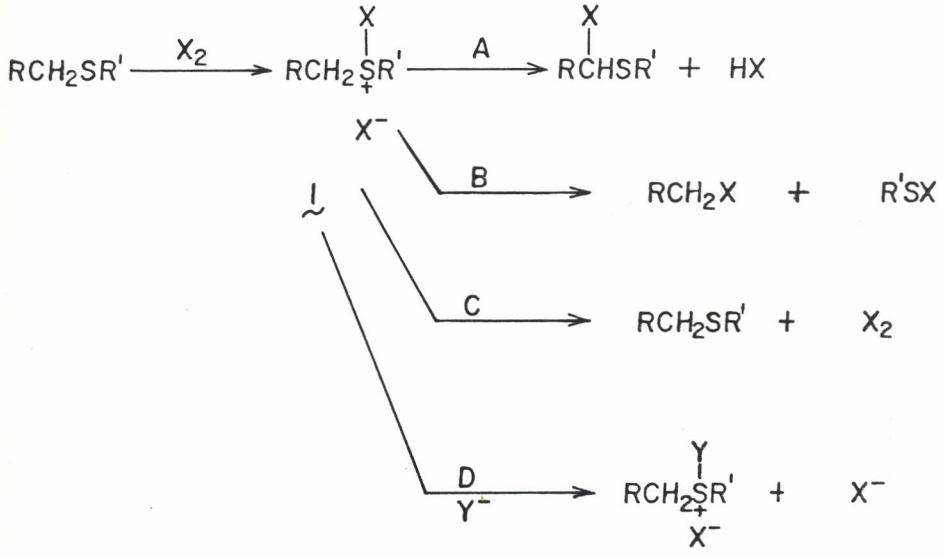
1.2 TRANSFORMATIONS OF HALOSULPHONIUM SALTS

Halosulphonium salts (1) are metastable reaction intermediates and have been isolated only at low temperatures [Wilson, 1982]. The generation of halosulphonium salt intermediates may be followed

by various transformations involving the sulphur atom and the α-carbon atom. These are summarised in Scheme 1.

Scheme 1

Reactions of Halosulphonium Salts



The pathways of the halosulphonium salt reactions often compete, and the course of the reaction is often dependent upon the effective anion present and upon the solvent and temperature [Wilson, 1982; Tuleen and Stephens, 1969]. The most widely studied reaction of the halosulphonium

salts is the Pummerer rearrangement (pathway A) [Wilson, 1982]. The cleavage reaction (pathway B) often competes quite favourably with the Pummerer reaction [Wilson, 1982; Chupp et al, 1984].

1.21 CLEAVAGE REACTION OF HALOSULPHONIUM SALTS

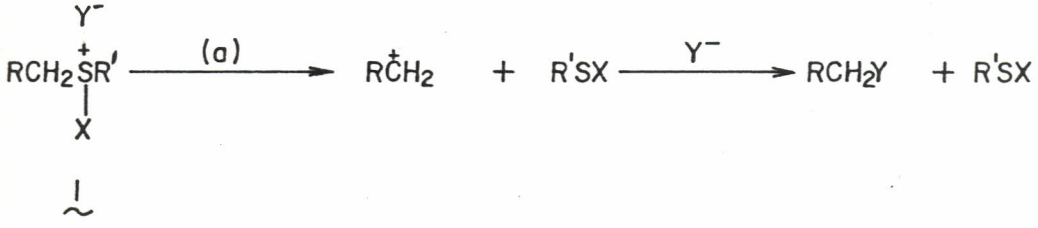
Carbon-sulphur bond cleavage (Scheme 1 pathway B) is a major pathway of halosulphonium salt reaction competitive with, and sometimes dominant over, the Pummerer rearrangement. Structural features in the sulphide that stabilize positive charge on the α-carbon have been observed to favour the cleavage of halosulphonium salts [Chupp et al, 1984]. This is considered to be so because cleavage is presumed to occur by way of stable carbenium ions. Aspects of the Pummerer rearrangement Vs cleavage of halosulphonium salts in inert solvents have been investigated using dibenzyl sulphide [Wilson and Huang, 1970]. The dibenzyl bromosulphonium bromide was found to be more susceptible to cleavage than dibenzyl chlorosulphonium chloride. This observation is reasonable since the bromide anion is more nucleophilic than the chloride anion. The per cent cleavage of halosulphonium salts was found to

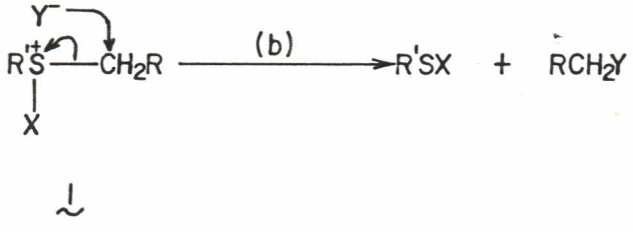
increase slightly as the polarity of the solvent increases. The predominance of cleavage reaction in polar solvents confirms the intermediacy of a stable carbenium ion.

Though cleavage of halosulphonium salts has in many cases been shown to occur by a unimolecular process *via* a stable carbenium ion [Chupp *et al*, 1984; Wilson, 1982] as indicated in Scheme 2 pathway (a), this is not always the case. Bimolecular processes for the cleavage reaction (Scheme 2 pathway b) have also been encountered [Wilson, 1982].

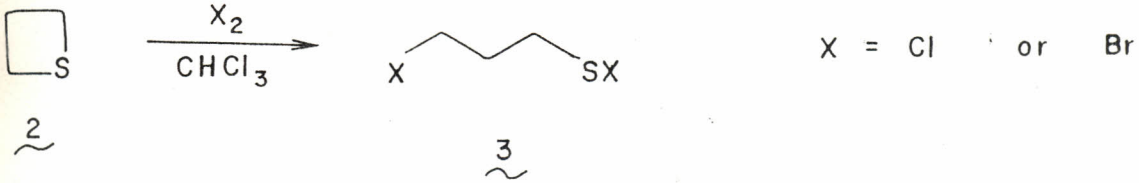
Scheme 2

Cleavage Reaction of Halosulphonium Salts





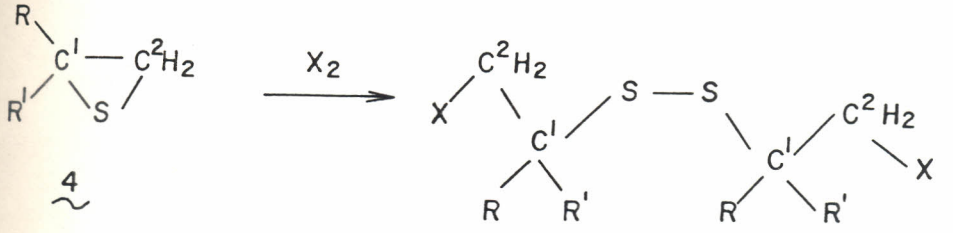
Experimental evidence in support of a bimolecular displacement of a sulphenyl halide from the halosulphonium salt intermediates (Scheme 2 pathway b) has been provided by many workers. Two examples of these observations are given below. Chlorination and bromination of thietane (2) in chloroform leads to 3 [Bordwell and Pitt, 1955].



2 3

It is unlikely that the cleavage of the halosulphonium salt arising from 2 would occur by a unimolecular process as the resulting carbenium ion intermediate would be unstable.

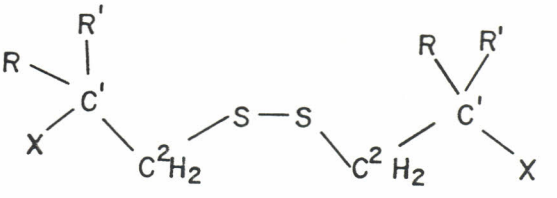
Halogenation of substituted thiiranes (4) produced mixtures of products 5 and 6 in the proportions indicated in the table below [Schwartz, 1968; Stewart and Cordts, 1952].



4

5

+



6

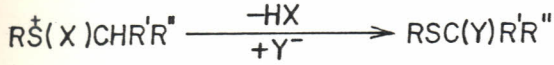
R	R'	X	5 : 6
Me	H	Cl	55 : 45
Me	H	Br	62 : 38
Me	Me	Cl	40 : 60
$ClCH_2$	H	Cl	85 : 15

It is apparent from the product distribution shown in the table above that the cleavage reaction was dictated more by steric factors than by electronic factors on C^1 and C^2.

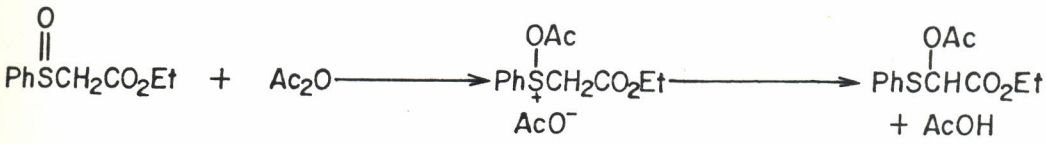
The results of these two studies on halogenation of sulphides agree with the dominant bimolecular displacement of a sulphenyl halide from the halosulphonium salt intermediate.

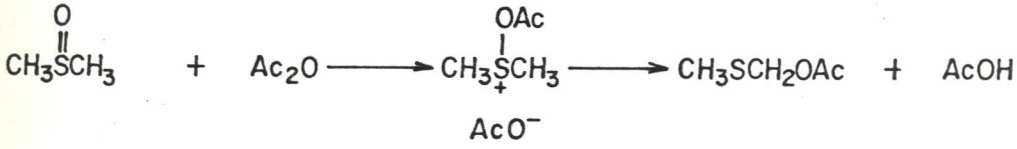
1.22 PUMMERER REARRANGEMENT OF HALOSULPHONIUM SALTS

The Pummerer rearrangement may generally be defined as a reaction involving the reduction of a sulphonium sulphur bearing at least one α-hydrogen to a sulphide with concomitant oxidation of the α-carbon.



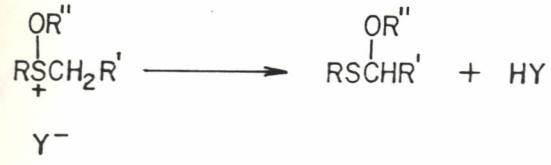
A classical example of this reaction is the reaction of sulphoxides with acetic anhydride [Pummerer, 1910]; e.g.



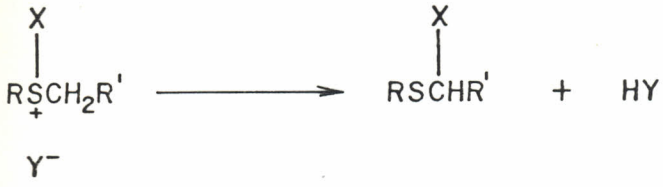


There exists a host of examples of the Pummerer reaction in the literature. A few examples of these are given below:

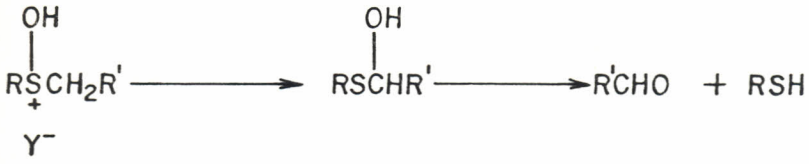
1) Alkoxysulphonium salts [Johnson and Phillips, 1969].



2) Halosulphonium salts [Tuleen and Stephens, 1969; Wilson, 1982].



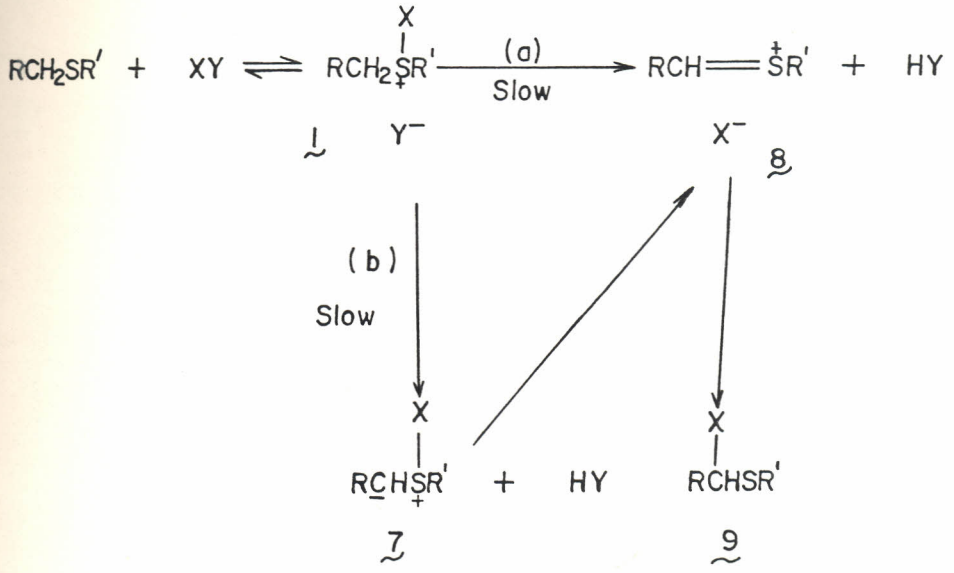
3) Hydroxysulphonium salts [Becker et al, 1963].



The Pummerer reaction of sulphonium salts has been a subject of great attention because of its mechanistic subtleties and its use in synthetic schemes. A generalised mechanism for the Pummerer reaction is indicated below in Scheme 3.

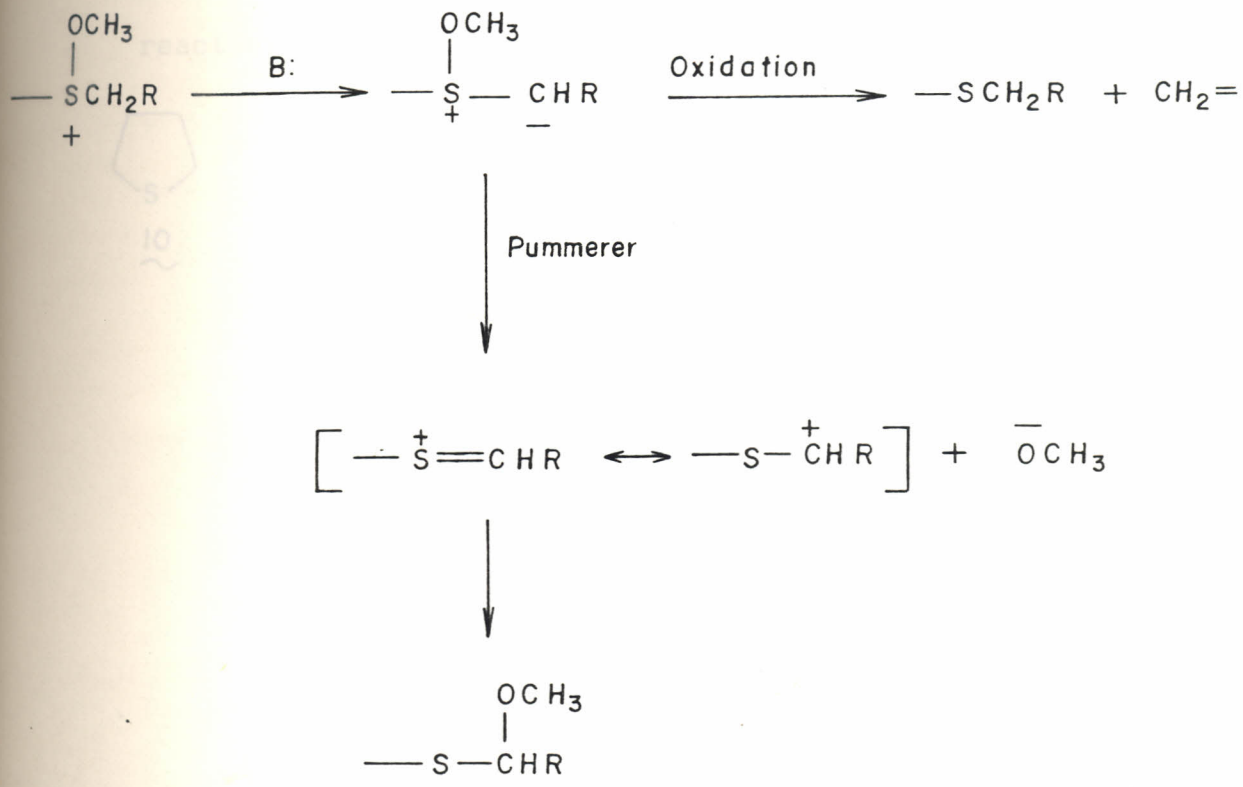
Scheme 3

Generalised Mechanism of the Pummerer Reaction



It is generally accepted that the Pummerer reaction involves, as a first step, the formation of a sulphonium salt (1). The intermediacy of a sulphocarbenium ion (8) has been established by a number of workers. Johnson and Phillips (1969) were able to show the intermediacy of a sulphocarbenium ion (8) in the Pummerer rearrangement of alkoxysulphonium salts on the basis of the following data: (i) substituents (R) (Scheme 4) which stabilise a carbenium ion were found to favour formation of Pummerer products at the expense of oxidation products.

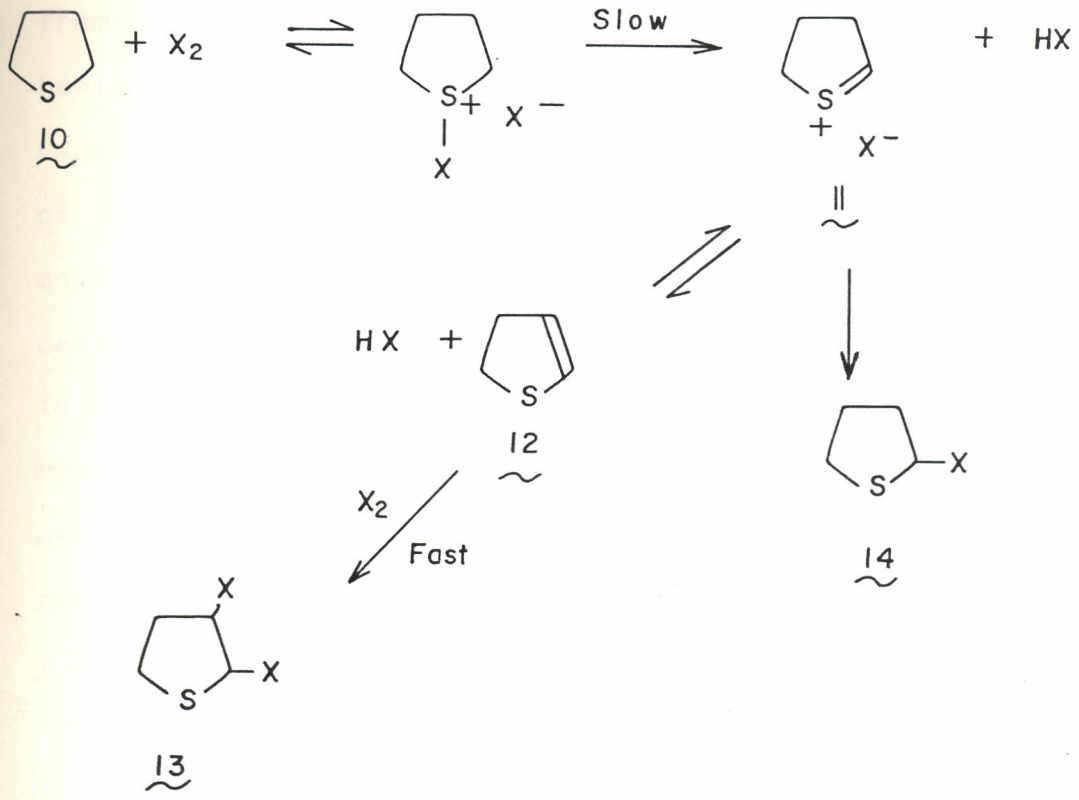
Scheme 4



(ii) highly polar solvents which are capable of stabilising carbenium ions facilitate the Pummerer reaction at the expense of the oxidation reaction. (iii) in a double-label experiment, crossover products indicated that the alkoxy group and the sulphur containing fragment become solvent separated, and hence the reaction is not necessarily intramolecular.

The existence of a sulphocarbenium ion intermediate has also been established in the halogenation reaction of tetrahydrothiophene (10) by a

careful study of the products as a function of reaction medium [Wilson and Albert, 1973].



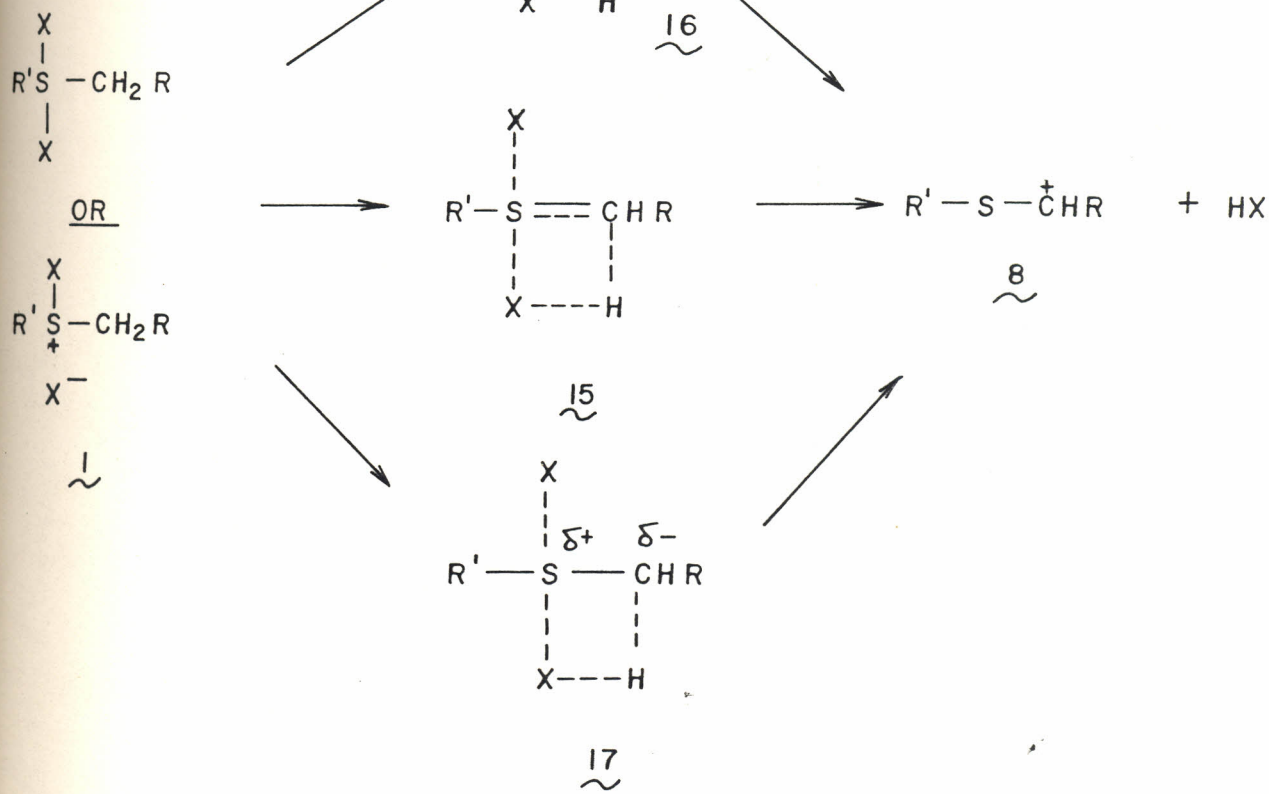
Polar solvents which stabilise the sulphocarbenium ion (11) and increase the ionisation of HX, and addition of common acid, increased ratio 14/13 by shifting the equilibrium 11 ⇌ 12 toward 11. However, reagents which reduce the nucleophilic activity of the halide ion either by complexation or protonation directed the reaction toward 13. These observations provided data in support of the existence of a sulphocarbenium ion (e.g 11) as an intermediate in the generalised Pummerer reaction

mechanism.

The nature of the elimination of the α-proton from the sulphonium salt 1 to form the sulphocarbenium ion (8) (Scheme 3 above) is not well resolved. Experimental evidence has been provided in support of both the concerted process (Scheme 3 pathway a) and the stepwise process *via* an ylide (Scheme 3 pathway b) [Block, 1968; Wilson, 1982]. Experiments to investigate the mode of the α-proton elimination have been based on studies of the regioselectivity of the Pummerer reaction and the kinetic isotope effects [Wilson, 1982]. Strong evidence for the ylide route in the formation of sulphocarbenium ion (8) has been obtained from ^{18}O tracer studies of the Pummerer reaction of acetoxysulphonium salts [Masuda *et al*, 1978], and regioselectivity studies of the Pummerer reaction of chlorosulphonium salts [Tuleen and Stephens, 1969] and alkoxysulphonium salts [Johnson and Phillips, 1969]. However, failure to trap ylides, absence of α-proton exchange expected for ylides and results of kinetic isotope effects for proton removal have presently cast doubts in the ylide route to sulphocarbenium ions from halosulphonium salts [Phillips and Ratts, 1971]. In the light of these observations, a recent

proposal that has been advanced represents the mechanism of the Pummerer rearrangement of halosulphonium salts as occuring by an E2S elimination. This mechanism of the Pummerer rearrangement is illustrated in Scheme 5.

Scheme 5

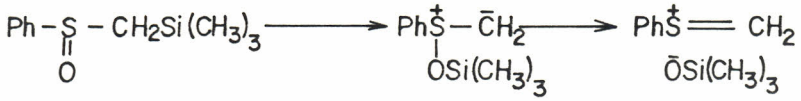


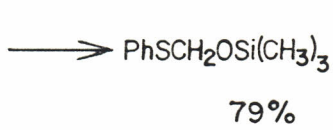
By this modified theory, the Pummerer rearrangement is viewed as occuring by a bimolecular process which embraces three types of transition states. The three transition states differ in the relative extent to which bonds are ruptured. The central transition state (15) possesses geometry of a sulphurane in which two S-X bond breaking is about the same and in which H-X is simultaneously being formed. The E1 extreme (16) resembles a carbenium ion and has cleavage of S-X bond preceding HX loss. The ElcB extreme (17) involves loss of HX proceeding ahead of S-X cleavage to provide an ylide-like transition state. The type of transition state which obtains is determined by the combined demands of substrate, base and leaving group. The competitive isotope effect should be high for the central transition state (15) and unity for the other two extremes.

The value of ρ obtained from the Hammett $\sigma\rho$ treatment for an intramolecular competitive α-halogenation is expected to be small and either positive or negative for the central mechanism through transition state 15, large and positive for an ylide mechanism through transition state 17, and

strongly negative for the E1 extreme through transition state 16.

A number of new variants of the Pummerer rearrangement have been reported in the literature. An example is the Pummerer reaction involving α-silylsulphoxides (these are referred to as Sila-Pummerer rearrangement).

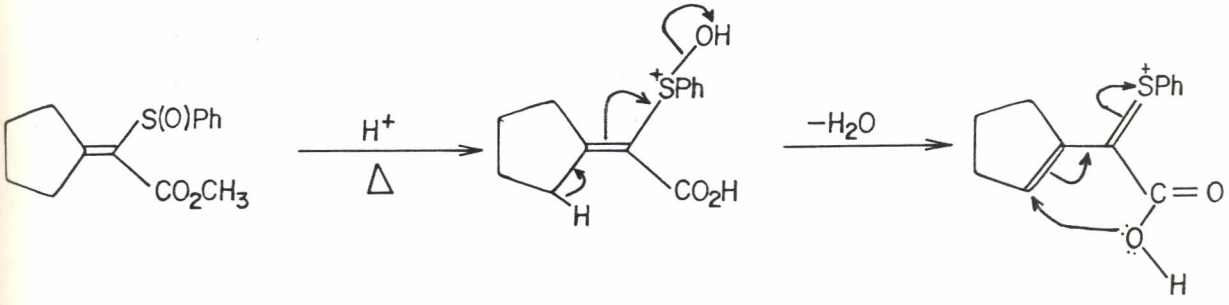


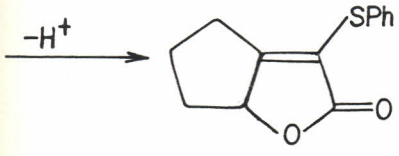


79%

[Vedejs and Mullins, 1975]

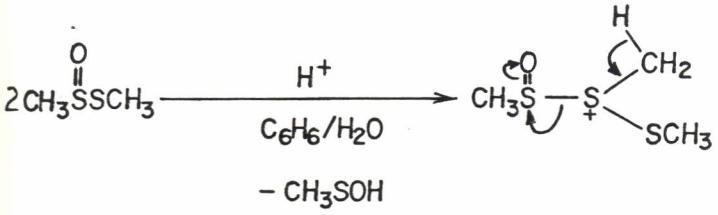
Other variants of the Pummerer rearrangement include vinylogous rearrangements and rearrangements involving disulphide S-oxides (thiosulphinates); e.g

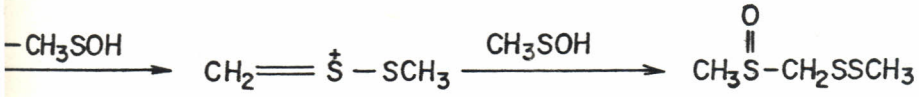


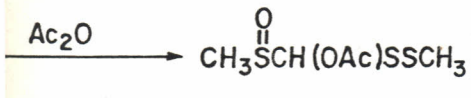


53%

[Kosugi et al, 1975]





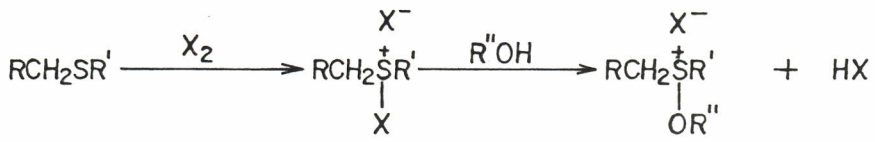


47%

[Block and O'Connor, 1974]

1.3 ALKOXYSULPHONIUM SALTS

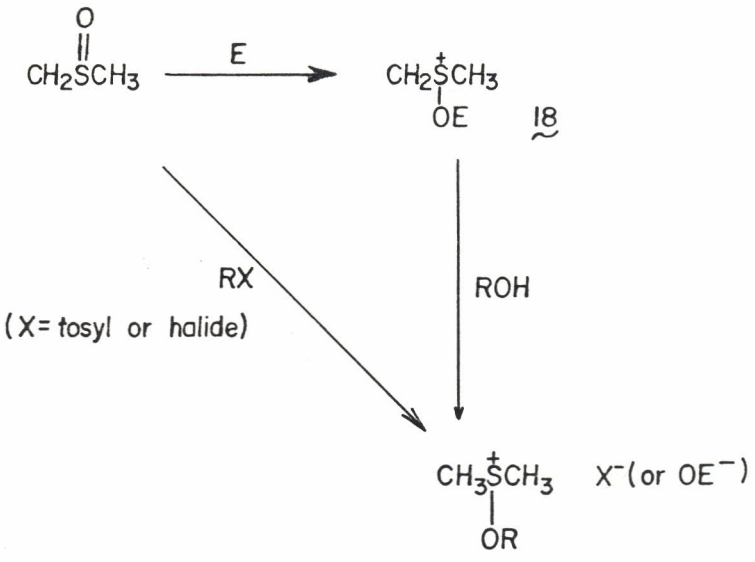
As indicated in Scheme 1 (pathway D), halosulphonium salts react with a number of substrates by displacement on sulphur to produce sulphonium salts. One such case is their reaction with alcohols to produce alkoxysulphonium salts [McCormick, 1974; Meerwein *et al*, 1965].



Alkoxysulphonium salts have also been generated by the reaction of alcohols with oxosulphonium salts of the type 18 shown in Scheme 6 which are produced by the interaction of sulphoxides with an electrophilic species E. The requirements are that the electrophilic species E react much more rapidly with sulphoxides than with alcohols, and that the group OE formed from such a reaction be a good leaving group. Alkoxysulphonium salts could also be obtained from sulphoxides by nucleophilic displacement of a tosyl or halide function by the oxygen atom of the sulphoxide (Scheme 6) [Durst, 1968].

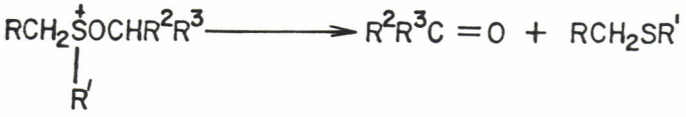
Scheme 6

Formation of Alkoxysulphonium salts from Oxosulphonium salts



Alkoxysulphonium salts, depending on their structure, undergo four basic types of reactions shown below [Johnson and Phillips, 1967; Durst, 1968]:

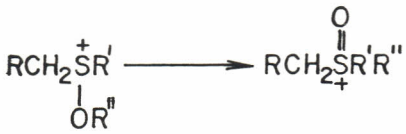
(i) Oxidation



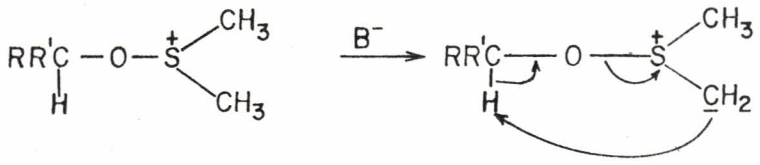
(ii) Pummerer rearrangement

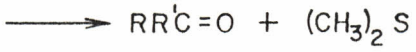
(iii) Nucleophilic displacement

(iv) Oxosulphonium salt formation

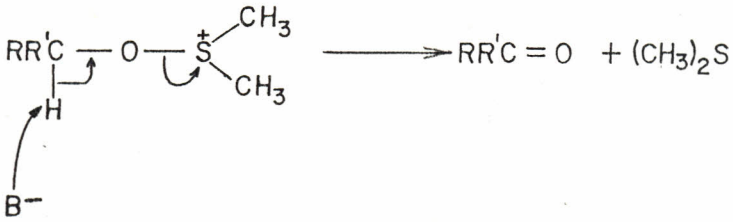


A number of highly efficient and synthetically useful oxidation procedures that depend on the intervention of alkoxysulphonium salts and especially dimethyl alkoxysulphonium salts have now been developed [Omura and Swern, 1978]. Halides, tosylates and alcohols have, for example, been converted to aldehydes and ketones by way of alkoxysulphonium salts derived from dimethyl sulphoxide or dimethyl sulphide. The decomposition of alkoxysulphonium salts to carbonyl compounds and sulphides is promoted by base and may occur by an intramolecular [Johnson and Phillips, 1965; Torsell, 1966] or an intermolecular [Torsell, 1967] mechanism. In the case of intramolecular decomposition, the α-hydrogen is abstracted by an intermediate ylide;





while in the case of intermolecular decomposition, the external base abstracts the α-hydrogen

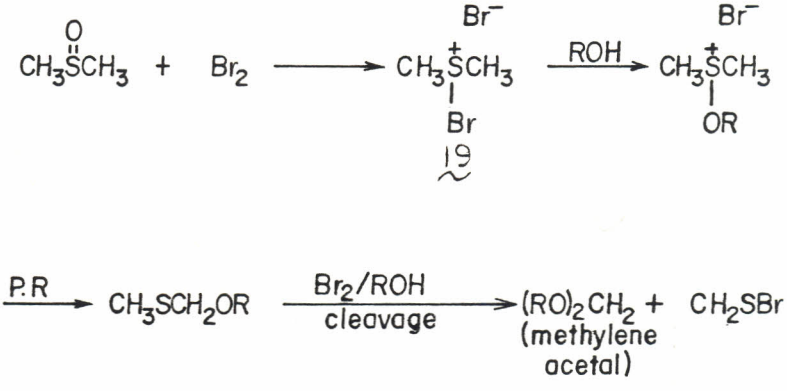


The oxidation procedures that occur by way of alkoxysulphonium salts are only efficient at low temperatures (usually below $0^{o}C$). At high temperatures (usually above $30^{o}C$), the competing Pummerer rearrangement of the alkoxysulphonium salts which gives rise to thioethers is favoured. The Pummerer rearrangement of alkoxysulphonium salts has been shown to occur via the ylide route (Scheme 3) to yield thioethers [Johnson and Phillips, 1967, 1969].

Methylene acetals have been obtained from the reaction of alcohols with DMSO in the presence of N-bromosuccinimide. The reaction has been suggested to occur via a dimethyl bromoxosulphonium salt

intermediate [Hanessian et al,1972]. An alternative suggestion has been given by Munavu (1980) that the reaction of DMSO with alcohols in the presence of bromine to yield methylene acetals proceeds via dimethyl bromosulphonium bromide (19) (Scheme 7).

Scheme 7



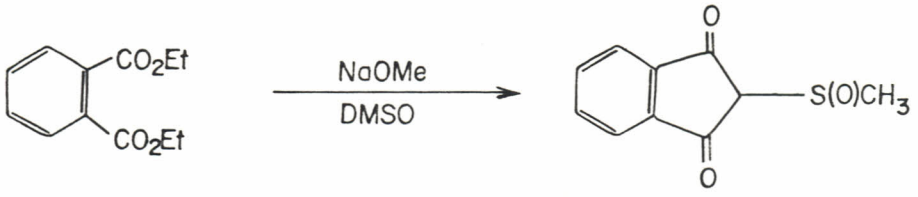
P.R ≡ Pummerer rearrangement

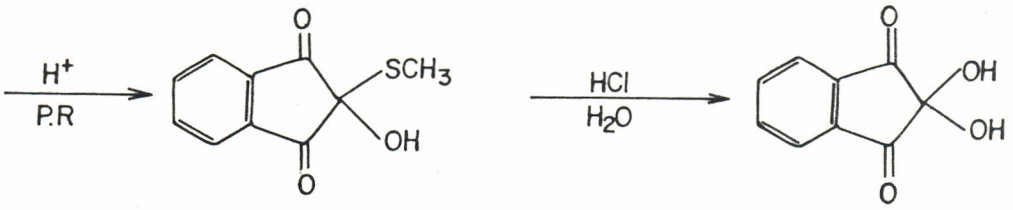
Evidence for this later proposal was provided by the formation of benzylidene and methylene acetals by treating dibenzyl sulphide and dimethyl sulphide with bromine and alcohols [Ogur, 1980].

1.4 USE OF SULPHONIUM SALTS IN SYNTHESIS

Sulphonium salt intermediates undergo numerous transformations and a number of synthetic schemes that depend on their generation as reactive

intermediates have been developed. The few examples cited below will serve to demonstrate the synthetic utility of the Pummerer reaction of sulphonium salts. The amino acid reagent, ninhydrin, has been synthesised by the acid catalysed hydrolysis of 20 which is generated by Pummerer rearrangement of the condensation product of DMSO and diethylphthalate [Russell et al, 1969].





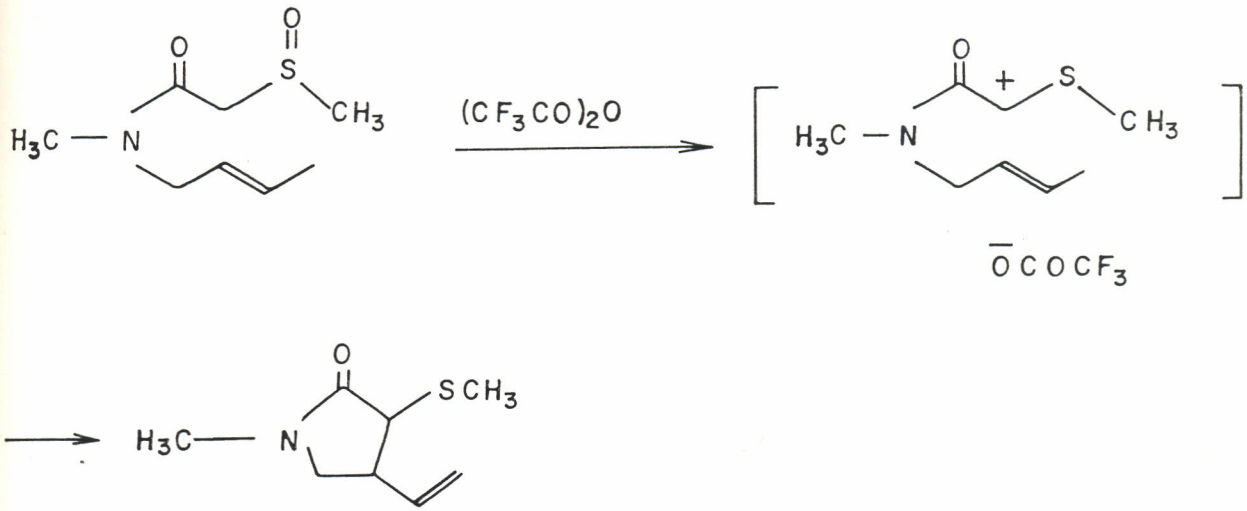
79%

20 Ninhydrin

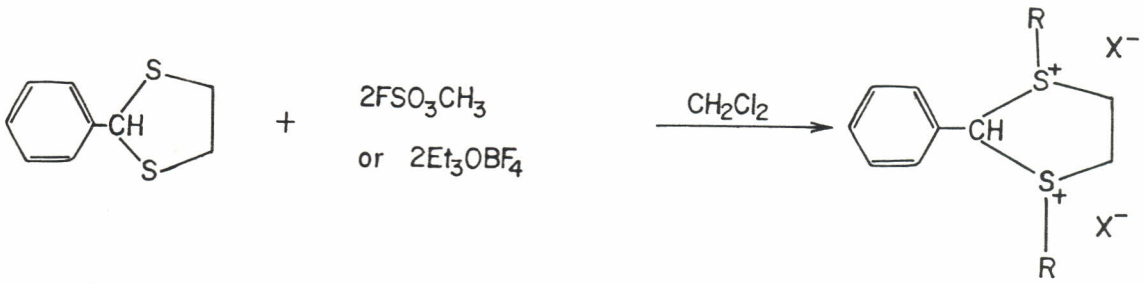
P. R ≡ Pummerer rearrangement

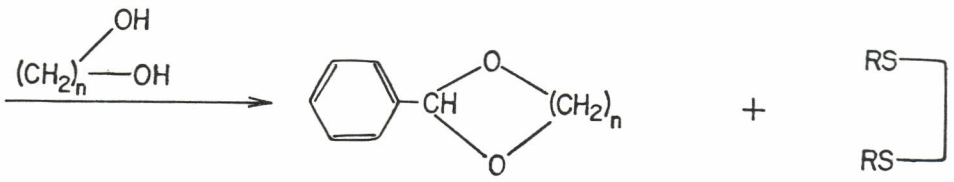
The intramolecular trapping of sulphocarbenium ions which are intermediates of the Pummerer rearrangement of sulphonium salts has found wide application in synthesis. N-(2-alkenyl)-α-sulphinyl acetamides, for example, undergo cyclisation under

the Pummerer reaction conditions to give five and six-membered lactams as shown by the reaction below [Ishibashi et al, 1986].



Methylene acetals are reported to have been prepared by the reaction of alcohols with DMSO via sulphonium salt intermediates [Munavu, 1980; Hanessian et al, 1972]. Acetals have also been formed from thioacetals and alcohols by means of an exchange reaction involving sulphonium salt intermediates an example of which is shown in the scheme below [Munavu and Szmant, 1975; Corey and Hase, 1975].





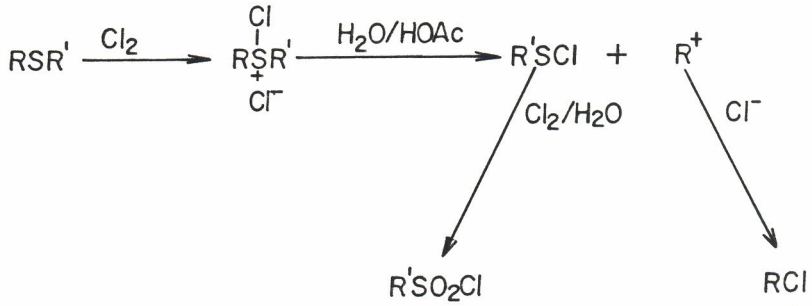
R = CH_3 or Et

X = FSO_3^- or BF_4^-

Acetals and thioacetals are stable towards a number of reagents and are extensively used as protecting groups especially in carbohydrate chemistry [Levi and Purves, 1949; Corey and Hase, 1975]. Acetals are stable towards base but are easily cleaved by acids. The conversion of alcohols to acetals via sulphonium salts offers several advantages. To begin with the protecting group can be changed without going through the free carbonyl compound, a very important consideration in dealing with β,γ-unsaturated or β-hydroxy aldehyde derivatives. Secondly, the acetals are obtained under non-acidic conditions and thus the method

offers an alternative to the usual generation of acetals under acidic conditions.

An example of the synthetic use of the cleavage reaction of sulphonium salts is the conversion of sulphides and sulphoxides to sulphonyl chlorides [Langler et al, 1979].



DMSO and DMS are widely used as oxidising agents. DMSO has been used, for example, in the oxidation of organic halides and tosylates to aldehydes [Kornblum et al, 1957, 1959]; in the oxidation of alcohols to carbonyl compounds [Omura and Swern, 1978] and in the oxidation of sulphides to sulphoxides [Searles and Hays, 1958]. Important mild and efficient synthetic procedures in which DMSO acts as an oxidant have been reported in many fields including alkaloids, carbohydrates, steroids, nucleotides and nucleosides [Durst, 1968; Martin and Hauthal, 1975]. DMSO oxidations, which occur via alkoxysulphonium salt intermediates, have the advantage of being mild and highly efficient. Primary alcohols are, for example, oxidised to the

aldehyde stage and sterically hindered alcohols have been successfully oxidised.

1.5 AIMS AND OBJECTIVES

It is generally accepted that the reaction of sulphides with halogens and alcohols involves the formation of sulphonium salts as the crucial reactive intermediates. Sulphonium salts do undergo various transformations involving the sulphur atom and the α-carbon depending on the effective anion present, the solvent polarity and the temperature. At temperatures above $0^{o}C$, the important transformations undergone by halosulphonium and alkoxysulphonium salts are the cleavage and Pummerer reactions. The foregoing literature review reveals that mechanisms of the cleavage and Pummerer reactions of sulphonium salts are still open to debate, and the synthetic potential of sulphonium salts in the synthesis of acetals yet to be explored fully. Also, data is available on the studies of the regioselectivity of the Pummerer reaction of chlorosulphonium salts by the Hammett σρ treatment [Tuleen, 1967; Tuleen and Stephens, 1969]. Similar studies have, however, not been conducted for bromosulphonium and alkoxysulphonium salts.

In view of the above, this project was initiated in order to explore the mechanistic and synthetic scope and limitations of the reactions of mono para-substituted dibenzyl sulphides with bromine and alcohols. Specifically, the aims and objectives of this work were:-

First, to study the reaction of dibenzyl sulphide with bromine in order to find the appropriate conditions for the cleavage and the Pummerer reactions of the intermediate bromosulphonium bromide.

Secondly, to study and elucidate the formation of benzylidene acetals from the reaction of dibenzyl sulphide with bromine in the presence of alcohols.

Thirdly, to explore the mechanism of the cleavage reaction of intermediate bromosulphonium bromides arising from the reaction of mono para-substituted dibenzyl sulphides with bromine.

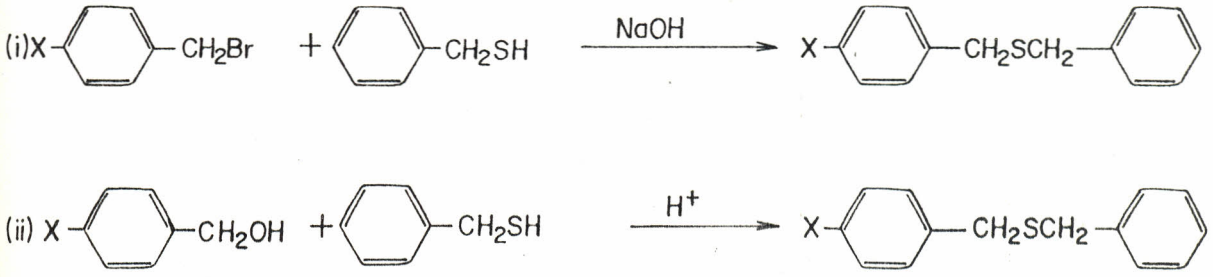
Lastly, to study the internal competitive α-bromination and α-alkoxylation of a series of mono para-substituted dibenzyl sulphides in order to elucidate the mechanistic course of the Pummerer reaction of bromosulphonium and alkoxysulphonium salt intermediates.

CHAPTER 2

RESULTS AND DISCUSSION

2.1 SYNTHESIS OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES

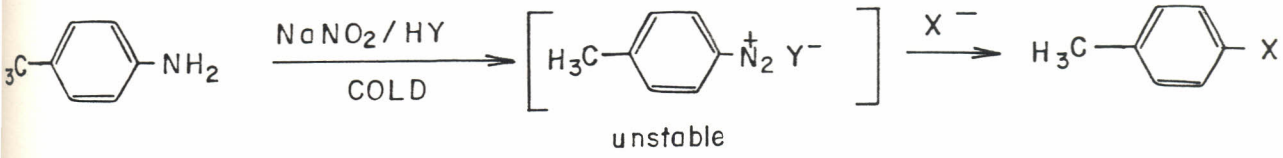
Dibenzyl sulphides with a para-substituent in one of the phenyl rings were synthesised by two methods. Both methods involved nucleophilic substitution by a mercaptan group on a carbon bearing a suitable leaving group [Tagaki, 1977; Screttas and Screttas, 1977].



The starting materials for these syntheses were not locally available and were prepared as detailed below. The compounds prepared were all characterised by melting points, and ir and ^{1}H nmr spectroscopy. Selected ir and ^{1}H nmr spectra of the starting materials are shown in the appendices.

The p-fluoro, p-bromo and p-iodotoluenes needed for the synthesis of p-halobenzyl bromides

were prepared from p-toluidine via its diazonium salt by the methods detailed in the experimental section.



(X = F, Br, I)

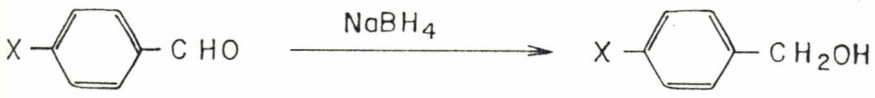
The p-substituted benzyl bromides were prepared by the direct bromination of p-substituted toluenes at 145°-150°C [Vogel, 1979].

This reaction occurs by a free radical mechanism. The yields of the benzyl bromides are shown in table 1.

TABLE 1: PREPARATION OF p-SUBSTITUTED BENZYL BROMIDES ($X-C_6H_4-CH_2Br$) FROM p-SUBSTITUTED TOLUENES

X	% YIELD	m.p. ^{o}C	COLOUR AND STATE
NO_2	57.2	98-99	pale yellow needles
F	84.6	liquid	pale orange liquid
Cl	54.2	48-51	white crystals
Br	45.1	58-60	white needle shaped crystals
I	28.4	75-76	dirty brown crystals
CN	56.7	112-114	light yellow crystals

p-Methoxy and p-methylbenzyl alcohols were prepared by the sodium borohydride reduction of the respective aldehydes [Screttas and Screttas, 1977; Vogel, 1979].



X = MeO (pale yellow liquid, 80·7%)

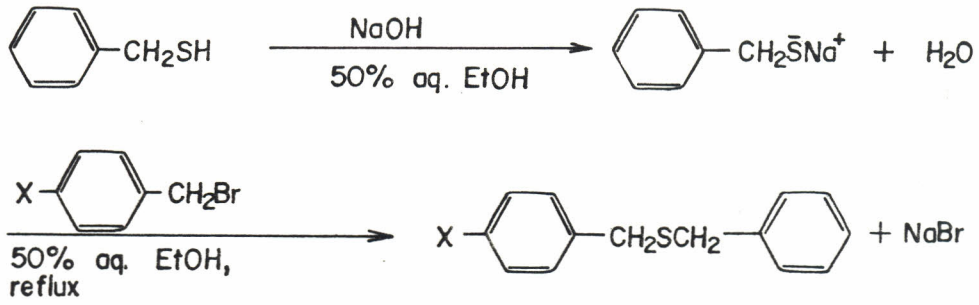
X = Me (white needle shaped crystals, m.p 56°—58°C; 94·5%)

Benzyl mercaptan was prepared by the action of sodium hydrosulphide on benzyl chloride by the method detailed in the experimental section [Ellis and Reid, 1932]

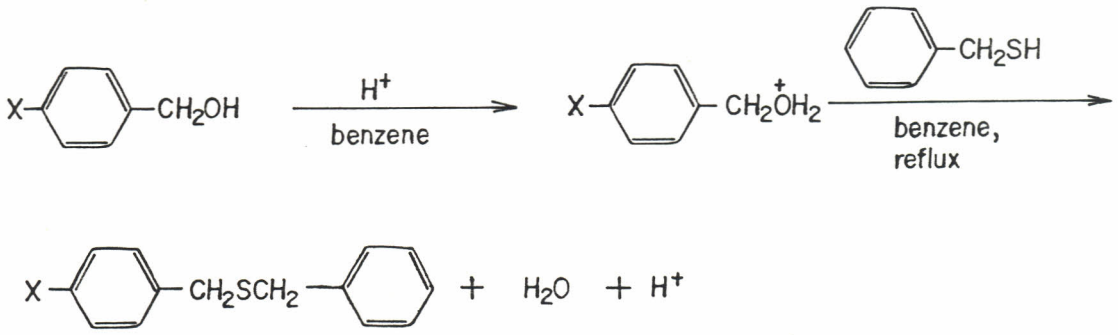
Dibenzyl sulphide was obtained as a by-product of the reaction and the benzyl mercaptan was purified by distillation.

The mono para-substituted dibenzyl sulphides were then obtained from the above starting materials by the following two methods:

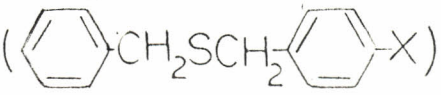
(i) Reaction of p-substituted benzyl bromides with the sodium salt of benzyl mercaptan



(ii) The displacement of water in the acid catalysed reaction between benzyl mercaptan and p-substituted benzyl alcohols



The results of these thioetherification reactions are given in table 2. The mono para-substituted dibenzyl sulphides prepared were easily characterised by ^{1}H nmr and ir spectroscopy data, and by melting points. The nmr spectra of selected sulphides are shown in the appendices.

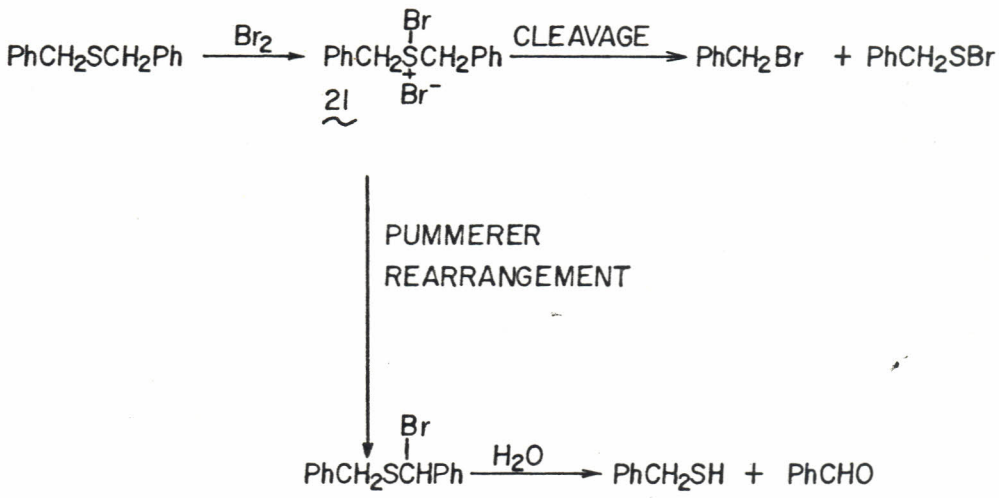
TABLE 2: PREPARATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES ()

STARTING MATERIALS	X	% YIELD	m.p ^{o}C	COLOUR AND STATE
(i) p-Substituted	F	84.6	-	Orange liquid
benzyl bromides	Cl	92.8	-	Clear yellow liquid
	Br	77.2	-	Clear yellow liquid
	I	76.8	-	Orange liquid
	CN	96.7	44-47	Yellow crystals
	NO_2	83.8	51-54	Yellow crystals
(ii) Benzyl chloride	H	63.2	46-48	White crystals
(iii)p-substituted	CH_3O	90.0	-	Orange liquid
benzyl alcohols	CH_3	88.9	-	Yellow liquid

2.2 REACTION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES WITH BROMINE

2.21 REACTION OF DIBENZYL SULPHIDE WITH BROMINE

Dibenzyl sulphide was treated with bromine under different temperature and solvent conditions. The crude products obtained from the reaction were analysed by nmr spectroscopy. Product assignments were confirmed by the enhancement of the appropriate peaks in the nmr spectra using authentic samples. At the end of the reaction, the product mixture consisted of benzyl bromide, benzaldehyde, dibenzyl disulphide, and unreacted dibenzyl sulphide. The benzyl bromide arose from the cleavage reaction of the intermediate bromosulphonium bromide (21), while benzaldehyde arose from the hydrolysis of the Pummerer product of 21.



Dibenzyl disulphide most probably arose from the disproportionation and coupling reactions of benzyl sulphenyl bromide and benzyl mercaptan which were significantly absent from the reaction products.

$$PhCH_2SX + PhCH_2SX \longrightarrow PhCH_2SSCH_2Ph \quad (X = Br, H)$$

Attempts to isolate the α-bromobenzyl benzyl sulphide were not successful because of its rapid decomposition and hydrolysis as has been noted previously [Wilson and Huang, 1970]. The results of the bromination of dibenzyl sulphide at different temperatures and in different solvents is shown in table 3.

As was observed previously by Wilson and Huang (1970), the ratio of Pummerer:cleavage products decreases only slightly with increase in solvent polarity. Cleavage reaction of bromosulphonium salts is perhaps favoured in polar solvents because of the intermediacy of carbenium ions which are stabilised in polar solvents. In our case, the cleavage reaction was observed to be greatly enhanced by increase in concentration of reactants. As is evident from table 3 above, the increase in

TABLE 3: REACTION OF DIBENZYL SULPHIDE (0.05M) WITH BROMINE

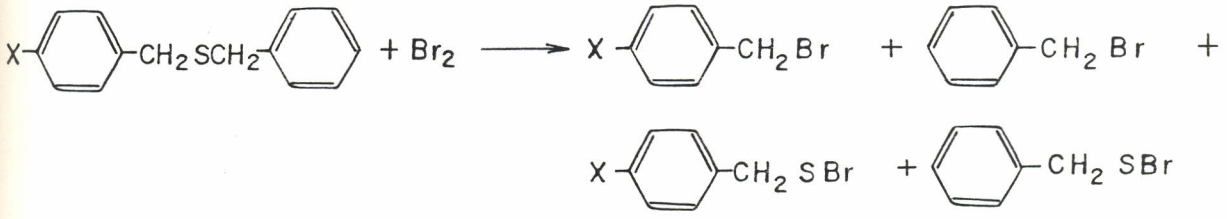
TEMP. ^{o}C	SOLVENT	RATIO OF PRODUCTS α-SUBSTITUTION (%)	CLEAVAGE (%)
0	$CHCl_3$	30.0	70.0
25	$CHCl_3$	30.0	70.0
35	$CHCl_3$	30.2	69.8
0	CH_2Cl_2	5.7	94.3
25	CH_2Cl_2	19.0	81.0
35	CH_2Cl_2	31.3	68.7
0	CCl_4	-	-
25	CCl_4	80.0	20.0
Reflux	CCl_4	83.3	16.3

the ratio of Pummerer:cleavage products with increase in temperature was only slight and the trend was not strong.

2.22 MECHANISM OF THE CLEAVAGE REACTION

Bromination of dibenzyl sulphide in dichloromethane at high concentration of reactants yielded the cleavage products almost exclusively. This offered the opportunity to study the mechanism of the cleavage

reaction of bromosulphonium salts.



The mechanism of the cleavage reaction above was studied by the Hammett σρ treatment. In the Hammett σρ treatment, the rate of the cleavage reaction and substituent constants are correlated according to the Hammett equation;

$$\text{Log } k = \rho\sigma$$

where k = rate constant for reaction of mono para-substituted dibenzyl sulphide with bromine

σ = substituent constant

and ρ = is the constant that signifies the sensitivity of the reaction to the electronic influence of the substituent and essentially, therefore, signifies susceptibility of the reaction to changes in electron density at the reaction centre.

The kinetics of the reaction was followed by use of nmr spectrometry [Ogur, 1980]. The rate constant k for the reaction of each sulphide with

bromine was determined graphically by plotting the log of concentration of the resulting benzyl and p-substituted benzyl bromides obtained from nmr spectral data against the reaction time. The rate constant k was obtained as the slope of these plots. The values of k and log k obtained for the reaction of mono para-substituted dibenzyl sulphides with bromine at $25^{o}C$ and $35^{o}C$ are listed on table 4. The ρ value for the reaction of the sulphides with bromine was evaluated by correlating log k with σ according to the Hammett equation given above. The plots obtained from these correlations are shown on figures 1 and 2.

TABLE 4: KINETIC STUDY OF REACTION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES (0.275M) WITH BROMINE IN DICHLOROMETHANE.

X	σ [JAFFE,1953]	TEMP.=25°C k(s^{-1})	TEMP.=25°C log k(s^{-1})	TEMP.=35°C k(s^{-1})	TEMP.=35°C log k(s^{-1})
OCH_3	-0.27	0.089	-1.051	0.259	-0.587
*F	-0.07	0.049	-1.310	0.106	-0.975
H	0.00	0.038	-1.420	0.099	-1.004
Cl	0.23	0.036	-1.439	0.099	-1.004
Br	0.23	0.039	-1.409	0.097	-1.013
CN	0.66	0.033	-1.477	-	-
NO_2	0.78	0.035	-1.456	-	-

* σ^+ was used.

FIG. 1. LOG k Vs σ FOR BROMINATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES AT 25°C IN DICHLOROMETHANE

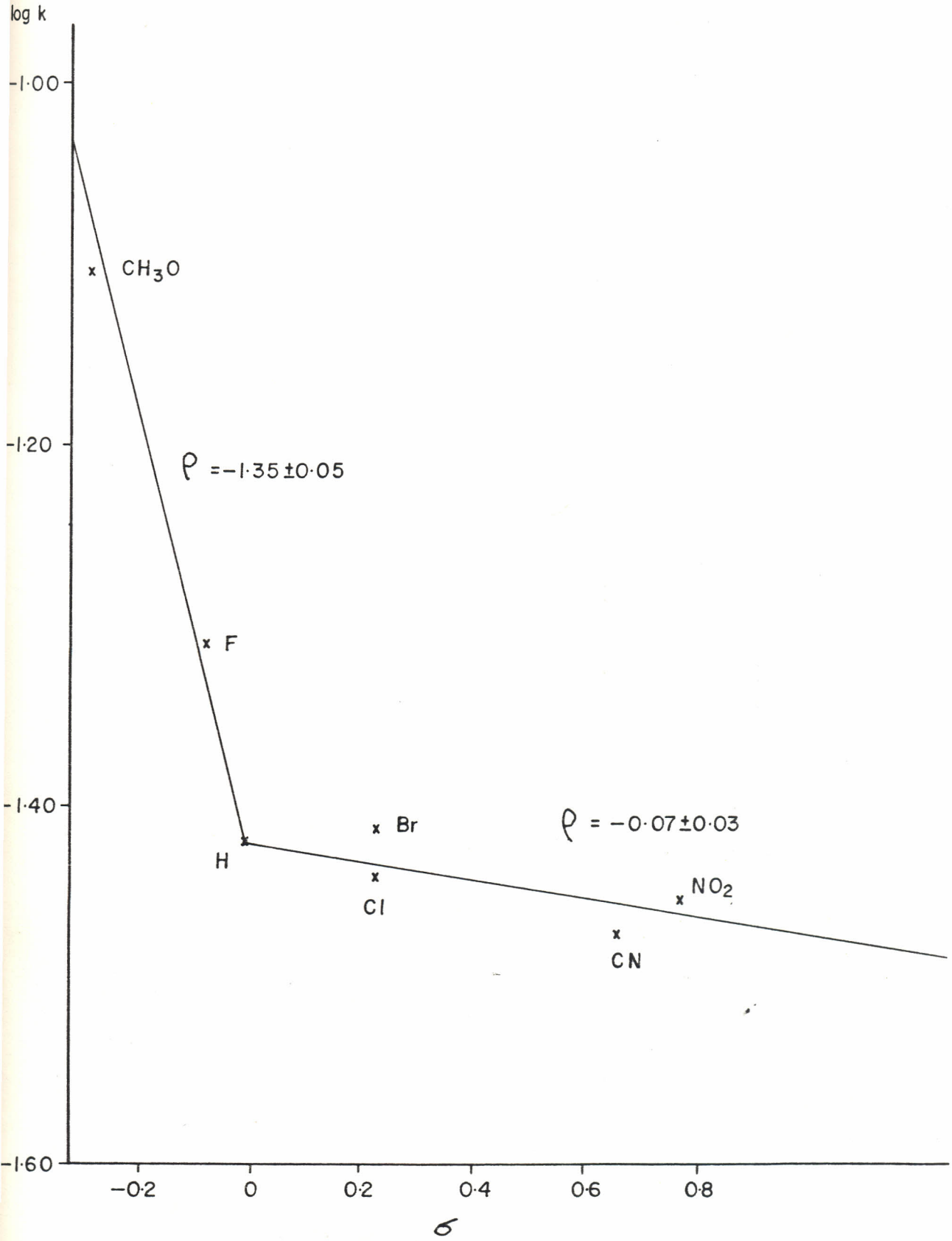
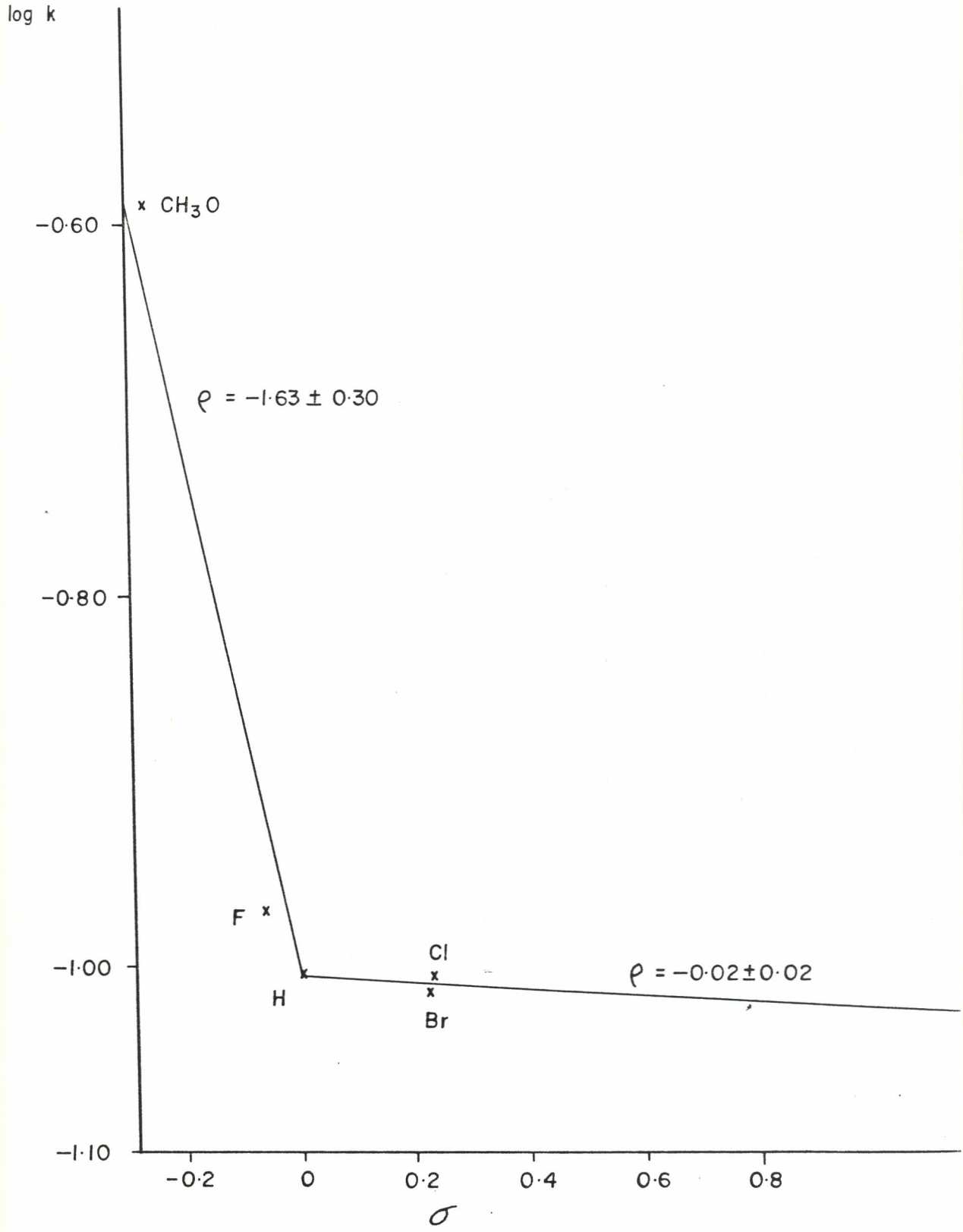
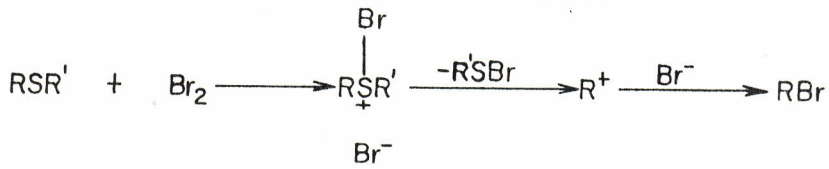


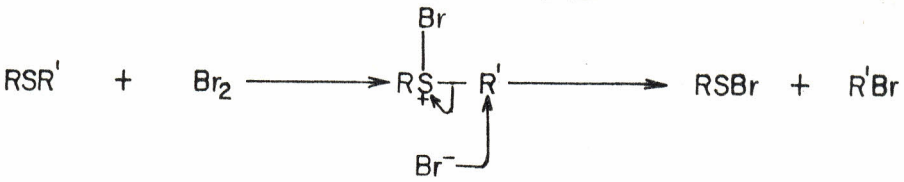
FIG. 2: LOG k Vs σ FOR BROMINATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES AT 35°C IN DICHLOROMETHANE



The Hammett correlation of the rates of the bromination reaction of the sulphides with the substituent constants (σ) may be represented by two straight lines which intersect at $\sigma = 0$ (see Figs. 1 and 2). This means that the cleavage reaction of mono para-substituted dibenzyl sulphides occurs by two different mechanisms depending on the nature of the substituent. The two extremes by which the cleavage reaction may occur are a unimolecular S_N1 mechanism;



and a bimolecular S_N2 mechanism;



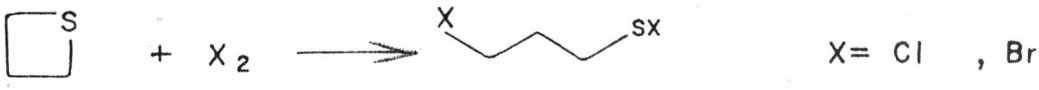
When the substituents were electron donating ($\sigma<0$) the ρ value was found to be -1.35 ± 0.05 at $25^{o}C$ and -1.63 ± 0.30 at $35^{o}C$, and when the substituents were electron withdrawing ($\sigma>0$) the ρ value was found to be -0.007 ± 0.03 at $25^{o}C$ and -0.02 ± 0.02 at $35^{o}C$.

In the case of electron withdrawing substituents ($\sigma>0$), the results are best explained by considering the cleavage reaction as occuring by a synchronous S_N2 mechanism in which there is little or no charge separation at the reaction centre in the transition state. Reaction by S_N1 mechanism in this case would be unfavourable as the intermediate carbenium ions would be unstable.

For electron donating substituents ($\sigma<0$) reaction by S_N1 mechanism is favourable as the intermediate carbenium ions involved would be stable. The ρ value of -1.35 or -1.63 is however much lower than expected for the limiting S_N1 mechanism. We suggest that the results are best explained by considering the cleavage reaction of intermediate bromosulphonium salts in this case as occuring by mixed S_N1 and S_N2 mechanisms. It is important to note that the Hammett plots given above in Figs. 1 and 2 may also be very well represented by smooth curves in the region of $\sigma<0.2$, indicating that in the mixed S_N1 and S_N2 mechanisms, the relative proportion of the two competitive mechanisms depends on the electronic nature of the substituents, the S_N1 mechanism being favoured as the substituent becomes increasingly electron donating.

The S_N2 mechanism for the cleavage reaction involving transition states of varying "looseness" and "tightness" depending on the electronic properties of the substituents is unlikely as U-shaped Hammett plots is to be expected for this mechanism [Jorge et al, 1981].

From these results, it may be concluded that where cleavage of sulphonium salts by a unimolecular mechanism would give rise to unstable carbenium ions, a synchronous S_N2 mechanism is preferred. This conclusion supports previously reported proposals that cleavage of sulphonium salts which, by a unimolecular process, are likely to give rise to unstable carbenium ions, do occur by a bimolecular process; e.g.



[Bordwell and Pitt, 1955]

In cases where stabilised carbenium ions can be generated, our results show that cleavage of benzylic bromosulphonium bromides occurs by mixed S_N1 and S_N2 mechanisms.

2.3 REACTION OF DIBENZYL SULPHIDE WITH BROMINE IN THE PRESENCE OF ALCOHOLS.

In the presence of alcohols, the treatment of dibenzyl sulphide with bromine in dichloromethane

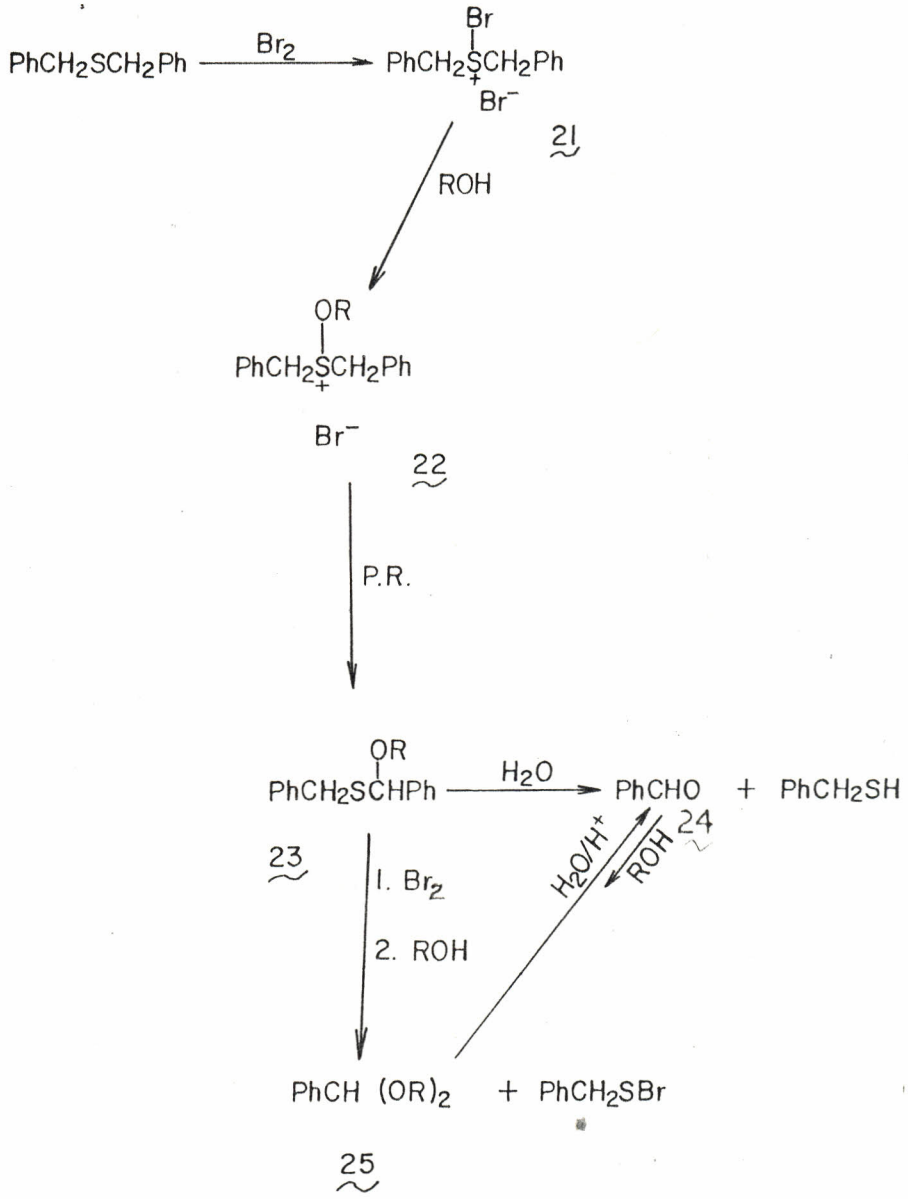
gave the cleavage products exclusively. In this case, the addition of alcohol probably makes the "mixed" solvent more polar and hence greatly enhancing the cleavage reaction. In tetrachloromethane, however, the formation of Pummerer products was favoured over the formation of cleavage products. The yield of the Pummerer products relative to the cleavage products increased slightly with increase in temperature. Table 5 gives the relative ratios of the Pummerer products formed when dibenzyl sulphide was treated with 1,3-propanediol in the presence of bromine in tetrachloromethane under different conditions.

TABLE 5: REACTION OF DIBENZYL SULPHIDE WITH BROMINE AND 1,3-PROPANEDIOL IN TETRACHLOROMETHANE

CONDITIONS	RATIO OF PUMMERER PRODUCTS PhCHO (%)	PhCH<O>O> (%)
0°C	67	33
25°C	60	40
Reflux	30	70
Reflux + K_2CO_3	0	100
Reflux + trace H_2SO_4	100	0

Monohydric alkanols were not converted to acetals, except methanol which gave benzaldehyde and acetal in 1:2 ratio. For most of the other monohydric alkanols tried, benzaldehyde was the only Pummerer product. The reaction mechanism is postulated to be as shown in scheme 8.

Scheme 8



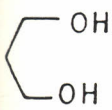
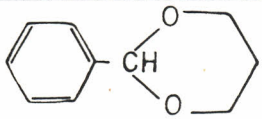
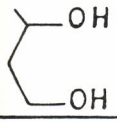
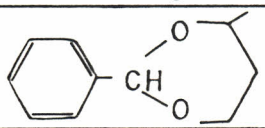
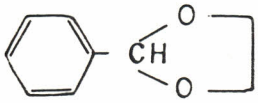
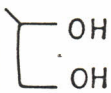
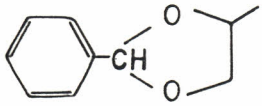
P. R ≡ Pummerer rearrangement

As shown in the scheme, dibenzyl alkoxysulphonium bromide (22) is formed by the reaction of alcohol with initially formed dibenzyl bromosulphonium bromide [McCormick, 1974; Meerwein et al, 1965]. The alkoxysulphonium salt (22) then undergoes a Pummerer rearrangement [Johnson and Phillips, 1969] to give an α-alkoxysulphide (23) which reacts with more bromine and alcohol to form the acetal (25). The formation of benzaldehyde (24) appears to arise from the hydrolysis of either the benzyl α-alkoxy-benzyl sulphide (23) or the benzylidene acetal (25). It appears that the formation of aldehyde (24) is favoured at the expense of acetal (25) when monohydric alkanols are used in the reaction because nucleophilic attack of 23 by water is less sterically hindered relative to attack of brominated salt of 23 by alcohol. The fact that diols yield the acetal (25) while monohydric alkanols, except methanol, do not may be explained because conversion of 23 to 25 is an intramolecular process and thus favoured over the hydrolysis of 23 which is an intermolecular process. Potassium carbonate serves as an acid scavenger and thus prevents the acid catalysed hydrolysis of the preformed cyclic acetal to benzaldehyde. Some acetal could have arisen from the equilibration of the diol with benzaldehyde [Traynelis and

Hergenrother, 1964]. Water in the above reaction arises from the reaction of K_2CO_3 with HBr and from ambient moisture.

The utility of the above reaction in the synthesis of cyclic acetals was tested with other diols. Diols were found to be converted to cyclic acetals in high yields (85-96% by nmr). This method was, however, of limited scope because the product mixture contained several by-products such as dibenzyl disulphide, benzaldehyde and benzyl bromide. The separation of these by-products by column chromatography gave pure benzylidene acetal in only very low yields as shown in table 6. Dibenzyl disulphide was also isolated from the column chromatography in about 50% yield in all the cases. The acetals and disulphides obtained were characterised by ir and nmr spectroscopy, and by melting points.

TABLE 6: REACTION OF DIBENZYL SULPHIDE WITH BROMINE AND SELECTED DIOLS AT REFLUX IN CCl_4 IN THE PRESENCE OF K_2CO_3.

DIOL	ACETAL	YIELD (%)
		26
		35
		20
		27

The absence of benzyl mercaptan and benzyl sulphenyl bromide from the products of the reaction of dibenzyl sulphide with bromine and alcohols was significant. The explanation for this is that the mercaptan and sulphenyl bromide reacted further to form dibenzyl disulphide. The disulphide could arise from any of the following processes [Wilson and Strong, 1972].

(i) $PhCH_2\overset{Y}{\underset{}{S}}CH_2Ph\ Br^-$ $\xrightarrow[-YX]{PhCH_2SX}$ $PhCH_2\overset{PhCH_2S}{\underset{}{S}}CH_2Ph\ Br^-$ $\xrightarrow{PhCH_2SX}$

$PhCH_2SSCH_2Ph + PhCH_2SCH_2Ph + XBr$

Y = OR or Br; X = Br or H.

(ii) $PhCH_2SH + PhCH_2SBr \longrightarrow PhCH_2SSCH_2Ph + HBr$

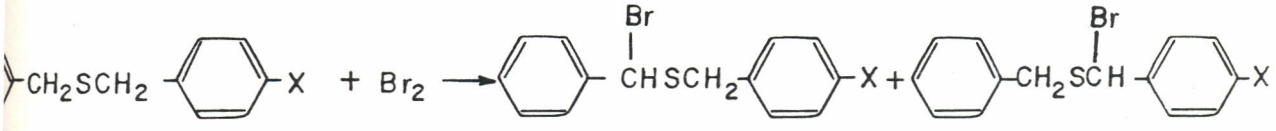
The conversion of diols to acetals by way of bromosulphonium salt intermediates (scheme 8) provides evidence to the suggestion that DMS-Br_2 salt is an intermediate in the formation of methylene acetals from reaction of alcohols with DMSO in the presence of bromine [Munavu, 1980].

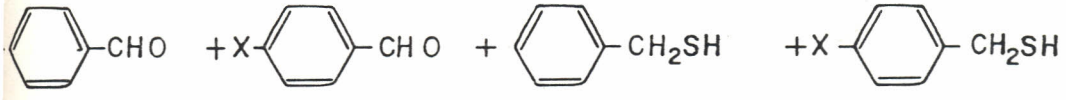
2.4 MECHANISM OF THE PUMMERER REARRANGEMENT

It is clear from the foregoing results and discussion that both acetal and benzaldehyde derived from the bromination and acetalation reaction of dibenzyl sulphide are Pummerer reaction products. In order to establish the mechanistic course of the Pummerer rearrangement, a study of the internal

competitive α-bromination and α-alkoxylation of a series of mono para-substituted dibenzyl sulphides in tetrachloromethane was conducted.

In the case of α-bromination, the initially formed α-bromosulphides were hydrolysed into the corresponding aldehydes and their relative yields (27/26) determined by nmr analysis [Tuleen and Stephens, 1969; Tuleen, 1967];





26 27

The relative ratios of the aldehydes (27/26) were generally assessed from the nmr spectra of the crude products by evaluation of the relative areas of the aldehydic protons. The nmr peaks for the aldehydic protons of the substituted and unsubstituted benzaldehyde are separate and appear in the region δ9.5ppm-δ10.0ppm. The products were identified by nmr peak enhancement on addition of authentic aldehyde samples. The relative reactivities (k_{rel}) of the internally competitive α-bromination were then expressed as the ratios of the aldehydes

^{1}H NMR (CCl_4) δ2.25(S,3H,CH_3); δ6.95(d of d, 4H, ). IR(neat) ν960-1280 cm^{-1} (C-F str.).

3.12 SYNTHESIS OF p-IODOTOLUENE

p-Toluidine (27g, 0.25mol) was diazotized by the procedure above. A solution of potassium iodide (44g, 0.265mol) in an equal weight of water was gradually added to the diazonium salt solution with stirring. The mixture was left to stand for 1hr at room temperature and then cautiously heated on a water bath until evolution of nitrogen had ceased. It was cooled. A dark coloured oil settled to the bottom and soon solidified. The aqueous layer was poured off, and 2g of sodium metabisulphite was added and then the mixture gently warmed to remove the dark colour. The mixture was then rendered alkaline with 10% sodium hydroxide solution in order to retain any cresol which may have formed. The mixture was steam distilled and each time the p-iodotoluene solidified in the condenser, the condenser was turned off until the solid melted and ran down into the receiver. The solid was then recrystallised from ethanol to yield colourless plates, 48g (88.3%), m.p 33^o-35^{o}C(lit. value 36^o-37^{o}C; CRC, 1976-7). ^{1}H NMR (CCl_4) δ2.3(S,3H,CH_3); δ7.1 (d of d,4H, ). IR (KBr) ν470 cm^{-1} (C-I).

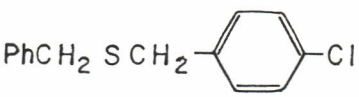
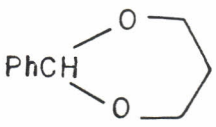
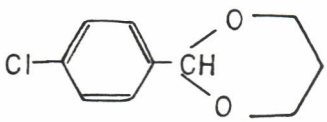
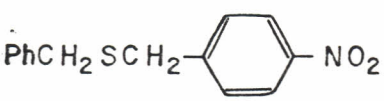
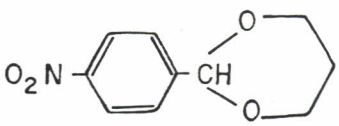
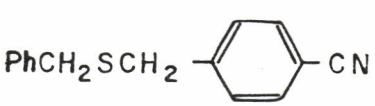
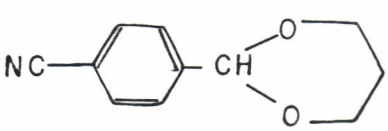
TABLE 7: INTERNAL COMPETITIVE BROMINATION AND ACETALATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES IN CCl_4

X	σ [Jaffe, 1953]	BROMINATION 25°C 27/26	Log 27/26	ACETALATION (REFLUX) 29/28	Log 29/28
OCH_3	-0.27	-	-	0.50	-0.301
CH_3	-0.17	0.60	-0.222	0.63	-0.201
*F	-0.02	1.00	0.000	1.00	0.000
H	0.00	1.00	0.000	1.00	0.000
Cl	0.23	1.67	0.223	2.00	0.301
Br	0.23	1.67	0.223	2.00	0.301
I	0.28	2.00	0.301	2.10	0.322
*CN	0.90	6.70	0.824	15.00	1.176
*NO_2	1.24	16.00	1.204	40.00	1.602

*σ^- was used.

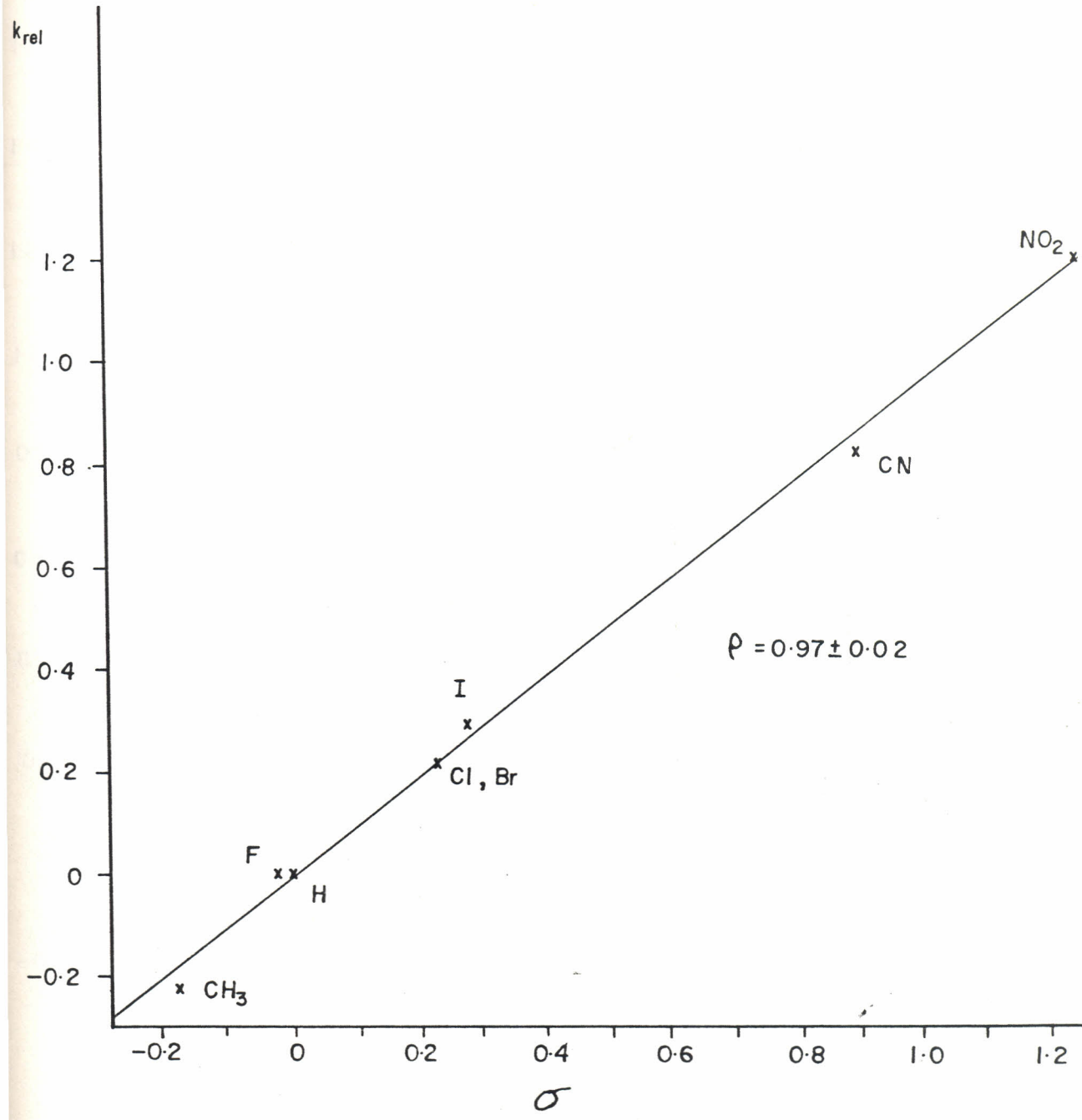
In a few selected cases shown on table 8, the acetals derived from the acetalation reaction were isolated pure by column chromatographic separation and characterised by nmr and ir spectroscopy.

TABLE 8: REACTION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES WITH BROMINE AND 1,3-PROPANEDIOL IN PRESENCE OF K_2CO_3 AT REFLUX IN CCl_4

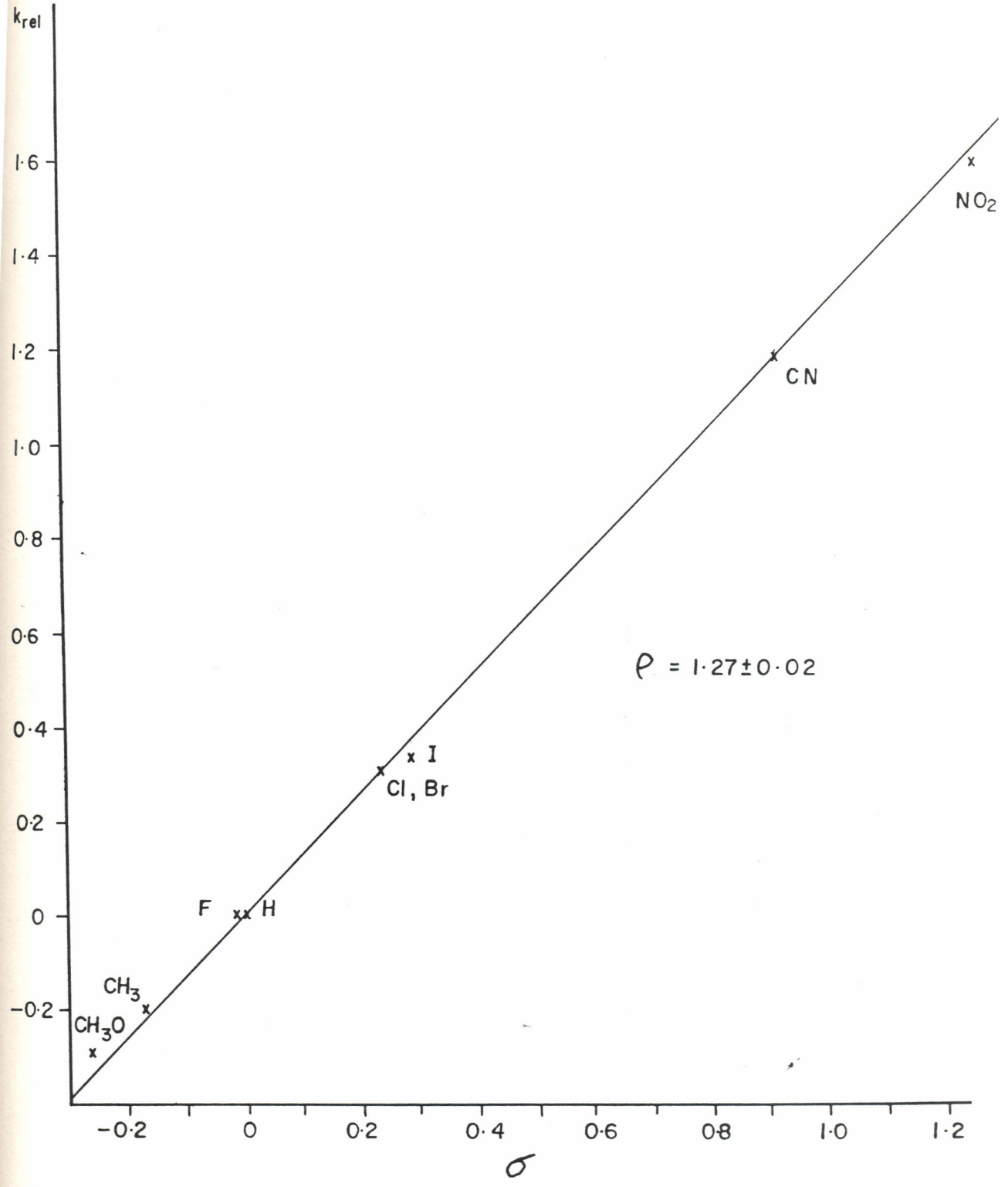
SULPHIDE	ACETALS (%)
	 (15%)  (m.p 49–52°C, 18%)
	 (m.p 109–110°C, 25%) + Trace 2–Phenyl –1, 3–dioxane
	 (m.p 105–106° C, 30%) + Trace 2–Phenyl –1, 3– dioxane

The relative reactivities of the internal competitive α-bromination and α-alkoxylation (table 7) were correlated with substituent constants (σ) according to the Hammett σρ treatment as shown in the Hammett plots below.

G. 3: CORRELATION OF LOG k_{rel} FOR BROMINATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES Vs σ



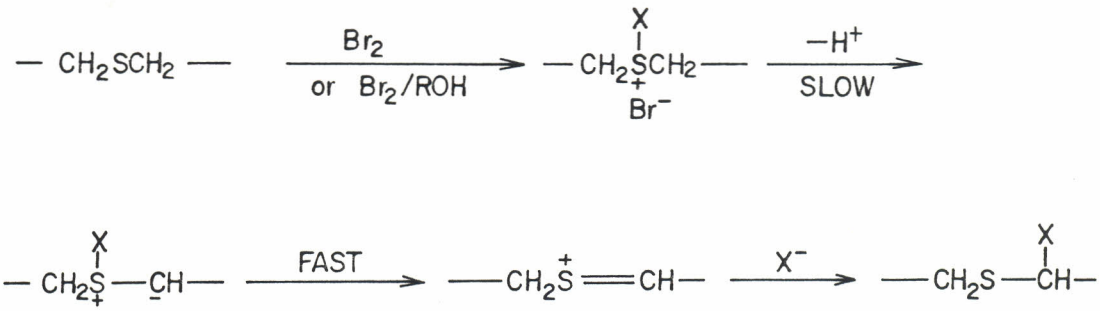
G. 4: CORRELATION OF LOG k_{rel} FOR ACETALATION OF SULPHIDES Vs σ



The correlation of log k_{rel} Vs σ by the Hammett $\sigma\rho$ treatment affords a ρ value of 0.97 ± 0.02 for the bromination reaction at room temperature and a value of 1.27 ± 0.02 for the acetalation reaction at reflux, in tetrachloromethane.

The conversion of a sulphonium salt (1) to the corresponding sulphocarbenium ion (8) has been suggested to occur either by a stepwise mechanism via an ylide intermediate or by a concerted E2S mechanism [Wilson, 1982] (see schemes 3 and 5). In this study the relatively high positive ρ value obtained from the Hammett $\sigma\rho$ study of the Pummerer reaction of bromosulphonium and alkoxysulphonium salts suggested that the reaction proceeded through an intermediate which is sensitive to the electronic effects of the aromatic system. These high ρ values also rule out an E2S mechanism, for which a relatively low ρ-value would be expected. The directive effects observed for both α-bromination and α-alkoxylation of mono para-substituted dibenzyl sulphides can best be explained in terms of the preferential abstraction of the more acidic proton from an intermediate bromosulphonium or alkoxysulphonium salt by an anionic species (Br^-) to generate an ylide intermediate (scheme 9). The generation of the ylide, which is stabilised by electron withdrawing substituents on the phenyl ring, is the rate determining step.

Scheme 9



X = Br or RO

The results of this study indicate that in the Pummerer rearrangement of bromosulphonium and alkoxysulphonium salt intermediates, the formation of the corresponding sulphocarbenium ions occurs by a stepwise mechanism via an ylide intermediate. The data obtained from this study is consistent with mechanisms proposed for α-chlorination of unsymmetrical sulphides [Tuleen, 1967], and for the Pummerer reaction of Alkoxysulphonium salts [Johnson and Phillips, 1969]

CHAPTER 3

EXPERIMENTAL

GENERAL

The reagents and solvents used were analytical laboratory grade and where required were purified further by standard procedures. Merck silica gel (60,0.040-0.063 mm/230-400 mesh) was used for column chromatography. IR spectra were recorded on a Pye-Unicam SP3-300 spectrometer. NMR spectra were obtained with Perkin Elmer R-12 spectrometer using CCl_4 as solvent and Me_4Si as internal standard. The m.p were determined using an oil bath and are uncorrected. A Buchi rotary vacuum film evaporator was used for solvent evaporation.

3.1 SYNTHESIS OF p-SUBSTITUTED TOLUENES

3.11 SYNTHESIS OF p-FLUOROTOLUENE

53.5g (0.5mol) of p-toluidine was dissolved in a mixture of 126 cm^3 of conc. hydrochloric acid (d= 1.18) and 126 cm^3 of water in a 500 cm^3 conical flask. The mixture was warmed until all the amine dissolved. The solution was cooled with vigorous mechanical stirring to 0^o-5^oC by immersion in an ice bath. A chilled solution of sodium nitrite (37g,

0.54mol) in 40 cm^3 of water was added slowly to the mixture with frequent shaking until a slight excess of sodium nitrite was present when tested with KI-starch paper indicator. The temperature was always maintained between 0^o-5^oC by addition of crushed ice if necessary. A chilled solution of sodium fluoroborate (76g, 0.69mol) in 150 cm^3 of water was slowly added with good stirring to the cold diazonium salt solution. Stirring was continued for 15 min. The toluene p-diazonium tetrafluoroborate salt was filtered on a buchner funnel and washed with about 30 cm^3 of ice water, 15 cm^3 methanol and 50 cm^3 ether. The salt was then dried overnight upon absorbent paper in a vacuum dessicator. The yield of the toluene p-diazonium tetrafluoroborate was 70g (68.2%). The toluene p-diazonium tetrafluoroborate was then carefully decomposed [Vogel, 1979]. The liquid obtained was washed three times with equal volumes of 10% sodium hydroxide solution to remove any cresol present. The last sodium hydroxide washing was removed as completely as possible and then shaken with an equal volume of almost saturated sodium chloride solution. The product was dried over magnesium sulphate, and then distilled at 114^o-116^oC/ 730 mmHg to give a colourless liquid 25g(44.6%).

^{1}H NMR (CCl_4) δ2.25(S,3H,CH_3); δ6.95(d of d, 4H, ). IR(neat) ν960-1280 cm^{-1} (C-F str.).

3.12 SYNTHESIS OF p-IODOTOLUENE

p-Toluidine (27g, 0.25mol) was diazotized by the procedure above. A solution of potassium iodide (44g, 0.265mol) in an equal weight of water was gradually added to the diazonium salt solution with stirring. The mixture was left to stand for 1hr at room temperature and then cautiously heated on a water bath until evolution of nitrogen had ceased. It was cooled. A dark coloured oil settled to the bottom and soon solidified. The aqueous layer was poured off, and 2g of sodium metabisulphite was added and then the mixture gently warmed to remove the dark colour. The mixture was then rendered alkaline with 10% sodium hydroxide solution in order to retain any cresol which may have formed. The mixture was steam distilled and each time the p-iodotoluene solidified in the condenser, the condenser was turned off until the solid melted and ran down into the receiver. The solid was then recrystallised from ethanol to yield colourless plates, 48g (88.3%), m.p 33°-35°C(lit. value 36°-37°C). ^{1}H NMR (CCl_4) δ2.3(S,3H,CH_3); δ7.1(d of d, 4H, ). IR (KBr) ν470 cm^{-1} (C-I).

3.13 SYNTHESIS OF p-BROMOTOLUENE

A solution of copper (I) bromide was prepared in a 2 litre two necked round bottom flask by heating under reflux a mixture of 25.2g (0.099mol) of copper (II) sulphate pentahydrate, 8g(0.126mol) of copper turnings, 61.6g(0.44mol) of crystallised sodium bromide, 12g(8.2 cm^3) of conc. sulphuric acid and 400 cm^3 of water for 4 hrs. A few grammes of sodium sulphite was then added to complete the reduction, colour of the solution became yellow. In a 1l flask 42.8g(0.4mol) of p-toluidine and 320 cm^3 of water were mixed, and then 78.4g(42.8 cm^3) of conc. sulphuric acid was cautiously added. The mixture was warmed until all the p-toluidine dissolved. The flask was cooled to 0^o-5^oC by placing it in an ice bath and 100g of crushed ice was added to the contents to accelerate the cooling. A solution of 28g(0.4mol) of sodium nitrite in 48 cm^3 of water was added slowly with frequent shaking until a slight excess of sodium nitrite was present when tested with KI-starch paper indicator. The temperature of the mixture was always maintained between 0^o-5^oC. The 2l two necked flask containing the copper (I) bromide solution was equipped for steam distillation. Into the side neck a tube (7-8mm in diameter)

leading to almost the bottom of the flask *via* a screw capped adaptor was inserted. A separatory funnel supported by a ring clamp retort stand was attached to this tube *via* a short length rubber tubing. The copper (I) bromide solution was heated to boiling. The toluene p-diazonium sulphate solution was then added from the separatory funnel whilst steam was rapidly passed through the mixture. In order to reduce the decomposition of the diazonium salt solution only little of it at a time was transferred to the funnel without interrupting the addition until all the diazonium salt solution was added. The steam distillation was continued until no more organic matter distilled. The distillate was rendered alkaline with 20% sodium hydroxide solution (to remove any cresol by-product), shaken well and the crude p-bromotoluene separated. The crude product was then washed with 40 cm^3 of warm (30^oC) conc. sulphuric acid, then with warm water, sodium hydroxide solution and finally with water. The product was dried over magnesium sulphate, warmed and filtered through a pre-heated buchner funnel. It was then distilled at 170^o-174^oC/730mmHg through an air cooled condenser. The colourless liquid obtained formed colourless crystals on

standing, 42g(61.4%), m.p 28^{o}-30^{o}C (lit. value 28.5^{o}C; CRC,1976-77). ^{1}H NMR(CCl_4) δ2.3(S,3H,CH_3), δ7.2 (d of d, 4H, ). IR (KBr) ν530 cm^{-1} (C-Br)

3.2 SYNTHESIS OF p-SUBSTITUTED BENZYL BROMIDES

The p-substituted benzyl bromides were prepared by the direct bromination of p-substituted toluenes at 145^{o}-150^{o}C.

p-NITROBENZYL BROMIDE

p-Nitrotoluene (50g, 0.37mol) was placed in a 250 cm^3 three necked round bottom flask equipped with a magnetic stirrer, a reflux condenser, a gas trap and a separatory funnel with stem reaching nearly to the bottom of the flask. The flask was heated in an oil bath at 145^{o}-150^{o}C and bromine (19.7 cm^3, 0.38mol) was slowly added from the separatory funnel during 2 hrs, the reaction mixture being magnetically stirred in the process. After all the bromine had been added stirring was continued for a further 10min. The whole content was then poured into a 1l round bottom flask containing 700 cm^3 of hot light petroleum spirit (b.p 80^{o}-100^{o}C) and decolourising carbon (3g). The mixture was refluxed for 10min. and then rapidly filtered through a

pre-heated buchner funnel. The filtrate was cooled and the crystals which formed were filtered with sunction and washed twice with 5 cm^3 portions of light petroleum spirit (b.p 80^o-100^oC). The crude p-nitrobenzyl bromide was purified further by dissolving it in 600 cm^3 of petroleum spirit (b.p. 80^o-100^oC), refluxing with decolourising carbon (3g) and then filtering through a pre-heated buchner funnel. The filtrate was cooled, filtered with sunction and washed twice with 5 cm^3 portions of light petroleum spirit (b.p 80^o-100^oC) to obtain pale yellow needle shaped crystals, 45.3g (57.2%), m.p 98^o-99^oC (lit. value 99-100^oC;CRC, 1976-7). ^1H NMR(CCl_4) δ4.5 (S,2H, $-CH_2-$); δ7.9 (d of d, 4H, ). IR(KBr) ν599cm^{-1} (C-Br, alkyl); ν1335-1365 cm^{-1}, 1540 cm^{-1} (N---O).

Other p-substituted benzyl bromides listed in table 1 were prepared by the same method described above.

3.3 PREPARATION OF p-SUBSTITUTED BENZYL ALCOHOLS

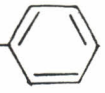
p-Methoxybenzyl alcohol and p-methylbenzyl alcohol were obtained by the sodium borohydride reduction of p-anisaldehyde and p-tolualdehyde respectively.

p-METHOXYBENZYL ALCOHOL

A 500 cm^3 beaker equipped with a mechanical stirrer, a thermometer and a burrette was set with an ice bath below it for the purpose of cooling. To a stirred solution of p-anisaldehyde (27.23g, 0.2mol) in 100 cm^3 of methanol a solution of sodium borohydride (2.8g, 0.074mol $NaBH_4$ in 4 cm^3 of 2M sodium hydroxide diluted with 36 cm^3 of water) was added at the rate of 0.5 cm^3/min. (approx.) with occasional cooling to keep the reaction at 18^o-25^oC. When about three-quarters of the solution had been added and there was no tendency for temperature to rise, addition was stopped. Most of the methanol was removed by distillation on a water bath and the residue was diluted with 200 cm^3 of water. The mixture was extracted with two 50 cm^3 portions of diethyl ether. The upper layer was washed with water and then dried rapidly with a little anhydrous magnesium sulphate. The ether was removed by evaporation in vacuo to yield a pale yellow liquid, 22.3g (80.7%). ^1H NMR (CCl_4) δ3.4(br, 1H, OH); δ3.7 (S,3H, OCH_3); δ7.0 (d of d, 4H, ). IR(neat) ν1030 cm^{-1}, 1300 cm^{-1} (C-O); ν3300 cm^{-1}, broad (OH).

p-Methylbenzyl alcohol was prepared by the reduction of p-tolualdehyde under the same procedure described above.

3.4 PREPARATION OF BENZYL MERCAPTAN

A solution of sodium hydrosulphide (1.67mol in 200 cm^3 of water) was prepared by bubbling hydrogen sulphide generated by the reaction of ferrous sulphide and dilute hydrochloric acid through a solution of sodium hydroxide (67g, 1.67mol) in 200 cm^3 of water. A pale green solution was obtained. A solution of benzyl chloride (110g, 0.87mol) in 95% ethanol (200 cm^3) was added to the solution in a 1l flask. The mixture was carefully refluxed over a small flame for 3 hrs. The reaction mixture was then cooled to ambient temperature. The upper oily layer was separated and distilled at reduced pressure. The distillate was collected at 91^oC/20 mmHg to give a colourless liquid, 95.2g (88.5%). ^1H NMR (CCl_4) δ1.5(t, 1H, SH); δ3.5 (d, 2H, $-CH_2S-$); δ7.15 (s, 5H, ). IR (neat) ν2550 cm^{-1} (S-H).

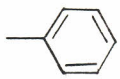
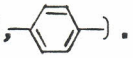
3.5 PREPARATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES.

3.51 DIBENZYL SULPHIDE

Benzyl mercaptan (20g, 0.161 mol) was added to a solution of sodium hydroxide (6g, 0.17 mol) in 100 cm^3 of 50% ethanol in a 500 cm^3 three necked round bottom flask fitted with a reflux condenser and a magnetic stirrer. The mixture was heated to reflux on a boiling water bath. A solution of benzyl chloride (20.83g, 0.17 mol) was slowly added to the mixture and refluxing continued for 2½ hrs. Most of the ethanol was then distilled off. The mixture was cooled to ambient temperature and then the whole content poured into 100g of crushed ice. The precipitate formed was recrystallised from 70% ethanol to give white crystals 21.8g (63.2%), m.p 46^o-48^oC (lit. value 49^o-50^oC; CRC, 1976-7). ^{1}H NMR(CCl_4) δ3.55 (s, 4H, $-CH_2SCH_2-$); δ7.25(s, 10H, Aromatic protons). IR (KBr) ν670 cm^{-1}, 700 cm^{-1} (C-S).

3.52 BENZYL p-NITROBENZYL SULPHIDE

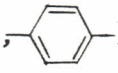
A mixture of sodium hydroxide pellets (0.96g, 0.024 mol) in 10 cm^3 of water and benzyl mercaptan (2.98g, 0.024 mol) in 10 cm^3 of 95% ethanol in 500 cm^3 three necked round bottom flask was heated to reflux on a water bath. A solution of p-nitrobenzyl bromide (5g, 0.023 mol) in 150 cm^3 of

95% ethanol was slowly added. After addition was complete, the mixture was refluxed for a further 2½ hrs and then most of the ethanol was distilled off. The reaction mixture was cooled to ambient temperature and then the whole content poured into 20g of crushed ice. The mixture was cooled further if necessary. The precipitate formed was filtered and recrystallised from 70% ethanol to yield yellow crystals 5g (83.8%), m.p 52^{o}-54^{o}C. ^{1}H NMR (CCl_4) δ3.5 (s, 4H, $-CH_2SCH_2-$); δ7.25 (s,5H, ); δ7.75 (d of d, 4H, ). IR (KBr) ν700 cm^{-1} (C-S); ν1350 cm^{-1}, 1520 cm^{-1} (N---O).

The results of other mono para-substituted dibenzyl sulphides prepared under the same procedure given above are listed in table 2.

3.53 BENZYL p-METHOXYBENZYL SULPHIDE

A three necked 500 cm^3 round bottom flask was equipped with a magnetic stirrer, a Dean-Stark water separator and a reflux condenser. A stirred mixture of benzyl mercaptan (12.42g, 0.1 mol); p-methoxybenzyl alcohol (13.82g, 0.1 mol); and 60% perchloric acid (1.17 cm^3)in 100 cm^3 of benzene was heated to reflux. After 30 min. about 2 cm^3 of water had been collected in the Dean-Stark water

separator. 10% sodium hydroxide solution (50 cm^3) was added to the mixture and stirred for a few minutes. The benzene layer was separated, washed with water and dried over magnesium sulphate. The solvent was removed using a rotary evaporator to give an orange liquid 22g(90%). ^1H NMR (CCl_4) δ3.4(s,2H,$ArCH_2S$); δ3.45(s,2H,$PhCH_2S$); δ3.7(s,3H,CH_3O); δ7.0(d of d, 4H, ); δ7.25(s, 5H, ). IR(neat) ν700 cm^{-1} (C-S); ν1030 cm^{-1}, 1240 cm^{-1} (C-O).

Benzyl p-methylbenzyl sulphide was prepared by the same procedure described above.

3.6 BROMINATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES

3.61 REACTION OF DIBENZYL SULPHIDE WITH BROMINE

A stock solution containing bromine (0.44g, 0.0028mol) in 14 cm^3 of dichloromethane was added to dibenzyl sulphide (0.59g, 0.0028mol) in 40 cm^3 of dichloromethane in a 250 cm^3 round bottom flask fitted with a reflux condenser, a magnetic stirrer and a dropping funnel. The mixture was stirred at room temperature for 3 hrs. The reaction mixture was then poured to a 10% solution of sodium metabisulphite (40 cm^3) and the organic layer was separated, washed with water, dried ($MgSO_4$) and the

solvent evaporated in vacuo to leave a yellow liquid. The crude product was then analysed by nmr spectroscopy. The products were identified by nmr peak enhancement on addition of authentic samples.

The experiment above was repeated under different solvent and temperature conditions. The results of the analyses are given in table 3.

3.62 KINETIC STUDY OF THE BROMINATION OF DIBENZYL SULPHIDE AT ROOM TEMPERATURE IN DICHLOROMETHANE

A stock solution containing bromine (0.88g, 0.0055mol) in 14 cm^3 of dichloromethane was added to a solution of dibenzyl sulphide (1.19g, 0.0055mol) in 40 cm^3 of dichloromethane in a 250 cm^3 three necked round bottom flask fitted with a reflux condenser and a magnetic stirrer. The mixture was magnetically stirred at room temperature. 5 cm^3 aliquots were drawn from the reaction mixture at the following time intervals:- 5 min., 10 min., 15 min., 20 min., 25 min., 30 min. Each aliquot drawn was immediately quenched by washing with 10% sodium metabisulphite solution, then with water and dried over magnesium sulphate. Each aliquot was evaporated to dryness and the nmr run in 1 cm^3 tetrachloromethane. Concentration of benzyl bromide produced from the

reaction was expressed as area under the corresponding methylene nmr peak. The log of concentration of benzyl bromide Vs time was plotted to determine rate constant k.

Several mono para-substituted dibenzyl sulphides were treated under the procedure described above at room temperature and at 35°C. The results of the analyses are listed on table 4.

3.7 REACTION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES WITH BROMINE AND ALCOHOLS

3.71 REACTION OF DIBENZYL SULPHIDE WITH BROMINE AND 1,3-PROPANEDIOL

Bromine (0.44g, 0.0028mol) in 10 cm^3 of tetrachloromethane was added to a solution of dibenzyl sulphide in 80 cm^3 of tetrachloromethane in 250 cm^3 three necked round bottom flask fitted with a reflux condenser, a magnetic stirrer and a dropping funnel. 1,3-Propanediol (0.19g, 0.0028mol) was immediately added. The mixture was stirred at room temperature for 18 hrs. The mixture was then poured to a 10% solution of sodium bicarbonate (40 cm^3) and the organic layer was extracted, washed with water, dried ($MgSO_4$) and the solvent evaporated in vacuo from a rotary evaporator to leave a yellow liquid. The

crude product was analysed by nmr spectroscopy and products identified by nmr peak augmentations on addition of authentic samples. The crude product consisted of benzaldehyde, benzylidene acetal and benzyl bromide in the ratio 6:1:1 respectively.

Dibenzyl sulphide was treated under the same procedure in dichloromethane, and in tetrachloromethane at $0^{o}C$ and at reflux for 3 hrs. The results of these reactions are shown in table 5. Treatment of dibenzyl sulphide with monohydric alkanols, for example, methanol, 1-propanol, 2-propanol, 1-butanol and 3-pentanol, under similar reaction conditions, with exception of methanol, yielded no benzylidene acetals. Benzaldehyde was the only Pummerer product obtained when these monohydric alkanols were used.

3.72 REACTION OF DIBENZYL SULPHIDE WITH BROMINE AND 1,3-PROPANEDIOL IN THE PRESENCE OF K_2CO_3

A stock solution containing bromine (0.44g, 0.0028mol) in 10 cm^3 of tetrachloromethane was added with stirring to a solution of dibenzyl sulphide (0.59g, 0.0028mol) in 80 cm^3 of tetrachloromethane in a 250 cm^3 round bottom flask

fitted with a reflux condenser and a magnetic stirrer. 1,3-Propanediol (0.19g, 0.0028mol) was immediately added followed by finely ground anhydrous potassium carbonate (2g). The mixture was stirred at reflux for 3 hrs. The reaction mixture was then washed two times with water (40 cm^3), dried ($MgSO_4$) and the solvent evaporated in vacuo from a rotary evaporator. The crude product was analysed by nmr spectroscopy and found to consist of benzyl bromide and benzylidene acetal in the ratio 1:9.5 respectively. Only trace benzaldehyde was formed (table 5).

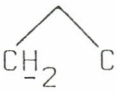
Monohydric alkanols, for example methanol, 1-propanol, and 3-pentanol, were treated under the same procedure above but, with the exception of methanol, yielded only benzaldehyde as the Pummerer product. No benzylidene acetal was formed.

3.73 CONVERSION OF DIOLS TO ACETALS

A stock solution containing bromine (0.22g, 0.0014mol) in 5 cm^3 of tetrachloromethane was added with stirring to a solution of dibenzyl sulphide (0.3g, 0.0014mol) in 40 cm^3 of tetrachloromethane in a 250 cm^3 round bottom flask fitted with a reflux condenser and a magnetic

stirrer. 1,3-Butanediol (0.11g, 0.0014mol) was immediately added followed by finely ground anhydrous potassium carbonate (1g). The mixture was thoroughly stirred for 3 hrs at reflux. The reaction mixture was then washed two times with water (40 cm^3), dried ($MgSO_4$) and the solvent evaporated in vacuo from a rotary evaporator to give a yellow liquid. The crude product was passed through a column of silica gel eluted with dichloromethane then tetrachloromethane to give the following compounds:-

(i) White crystals of dibenzyl disulphide (0.09g, 50%) m.p 65°-69°C (lit. value 66°-69°C;CRC,1976-7). ^1H NMR (CCl_4) δ3.5(s,4H,CH_2SSCH_2); δ7.2(s,10H, Aromatic protons). IR (KBr) ν460 cm^{-1} (-S-S-, str); ν660 cm^{-1} (C-S str).

(ii) 4-Methyl-2-phenyl-1,3-dioxane, pale yellow liquid, 0.09g (35%). ^1H NMR (CCl_4) δ1.2(d,3H,CH_3); δ1.3-2(br,2H,CH_2); δ3.5-4.3(br,3H, ); δ5.3(s,1H,OCHO); δ7.25(br,5H, Aromatic protons). IR (neat) ν1100 cm^{-1} (C-O str, cyclic ethers).

The acetals obtained from the chromatographic separation of the products of the reaction of mono para-substituted dibenzyl sulphides with bromine

and various diols are listed in tables 6 and 8.

3.8 INTERNAL COMPETITIVE BROMINATION AND ACETALATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES

3.81 INVESTIGATION OF RELATIVE RATIOS OF ALDEHYDES FORMED ON BROMINATION OF MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES

A stock solution containing bromine (0.22g, 0.0014mol) in 5 cm^3 of tetrachloromethane was added with stirring to a solution of benzyl p-chlorobenzyl sulphide (0.35g, 0.0014mol) in 40 cm^3 of tetrachloromethane in a 250 cm^3 round bottom flask fitted with a reflux condenser and a magnetic stirrer. The mixture was stirred for 14 hrs. The reaction mixture was then washed with a 10% solution of sodium bicarbonate (40 cm^3) then with water (40 cm^3). The organic layer was separated, dried ($MgSO_4$) and the solvent removed in vacuo from a rotary evaporator. The crude product was analysed by nmr spectroscopy. The aldehydes produced were identified by nmr peak augmentation on addition of authentic samples. NMR spectral analysis showed p-chlorobenzaldehyde and benzaldehyde were formed

in the ratio 1.67:1 respectively.

The results of other mono para-substituted dibenzyl sulphides treated under the same procedure are given in table 7.

3.82 INVESTIGATION OF RELATIVE RATIOS OF CYCLIC ACETALS FORMED ON TREATING MONO PARA-SUBSTITUTED DIBENZYL SULPHIDES WITH BROMINE AND 1,3-PROPANEDIOL

Bromine (0.22g, 0.0014mol) in 5 cm^3 of tetrachloromethane was added with stirring to a solution of benzyl p-chlorobenzyl sulphide (0.35g, 0.0014mol) in 40 cm^3 of tetrachloromethane in a 250 cm^3 round bottom flask fitted with a reflux condenser and a magnetic stirrer. 1,3-Propanediol (0.1g, 0.0014mol) was immediately added followed by finely ground anhydrous potassium carbonate (1g). The mixture was stirred for 3 hrs at reflux. The mixture was then washed two times with water (40 cm^3), dried ($MgSO_4$) and the solvent evaporated in vacuo from a rotary evaporator. The crude product was analysed by nmr spectroscopy. NMR spectral analysis of the crude product showed 2-p-chlorophenyl-1,3-dioxane and 2-phenyl-1,3-dioxane were formed in the ratio 2:1 respectively.

The results of other mono para-substituted dibenzyl sulphides treated under the same procedure are listed in table 7.

REFERENCES

1. Becker, H.D., Mikol, G.J., and Russell, G.A. (1963), J.Am.Chem.Soc., 85, 3410.

2. Block, E. (1968) Reactions of Organosulphur Cpds, Academic Press, New York, p154-162.

3. Block, E. and O'Conner, J. (1974), J.Am.Chem. Soc., 96, 3929.

4. Bordwell, F.G. and Pitt, B.M. (1955), J. Am. Chem. Soc., 77, 572.

5. Chupp, J.P., Balthazor, T.M., Miller, M.J., Pozzo, M.J. (1984), J.Org.Chem., 49, 4711.

6. Corey, E.J. and Hase, T. (1975) Tetrahedron Lett., 3267.

7. CRC (1976-7) Handbook of Chemistry and Physics 57th edn., CRC Press Inc., Ohio.

8. Durst, T. (1968) "Dimethyl Sulphoxide In Organic Synthesis" in Taylor, E.C. and

Wynberg, H. (eds), Advances In Org. Chem. Vol. 6, John Willey and Sons, N.Y., p257.

9. Ellis, L.M., Jr. and Reid, E.E. (1932) J.Am.Chem.Soc., 54, 1674

10. Gilman, H. (1943) Org. Chem., John Willey and Sons, N.Y.

11. Hanessian, G., Yang-Chung, G., Lavalee, P., and Pernel, A.G. (1972) J.Am.Chem.Soc., 94, 8929.

12. Ishibashi, H., Ishiyama, K., Yamashita, H., and Tamura, Y. (1986), Synthesis, 848.

13. Jaffe, H.H. (1953) Chem. Review, 53, 191.

14. Jorge, A.L.J., Nilo, Z.K., Yukino,M. and Miller, J., (1981) J.C.S. Perkin 2 100.

15. (a) Johnson, C.R. and Phillips, W.G. (1965) Tetrahedron Lett.,2101.
(b) J.Org.Chem.,32, 1926 (1967).
(c) J.Am.Chem.Soc., 91, 682 (1969).

16. Kornblum, N., Jones, W.J., Powers, J.W., Anderson, G.J., Larson, H.O., Levand,O., and Weaver, W.M. (1957) J.Am.Chem.Soc., 79, 6562.

17 Kornblum, N., Jones, W.J., and Anderson, G.J. (1959) J.Am.Chem.Soc., 81, 4113.

18. Kosugi, H., Uda, H., and Yamagiwa, S. (1975) Chem. Commun., 192

19. Langler, F.R., Marini, Z.A., and Spalding, E.S. (1979) Can.J.Chem., 57, 3194.

20. Levi, I. and Purves, C.B. (1949) Adv. Carbohyd. Chem., 4, 1.

21. Martin, O. and Hauthal, H.G. (1975) Dimethyl Sulphoxide, Van Nostrand Reinhold Co. Ltd.

22. Masuda, T., Numata, T., Furukawa, N., and Oae, S. (1978) J.Chem.Soc., Perkin II, 1302.

23. McCormick, J.P. (1974) Tetrahedron Lett., 1701.

24. Meerwein, H., Zenner, K. F., and Gipp, R. (1965) Justus Liebigs Ann. Chem., 687, 67.

25. Munavu, R.M. (1980) J.Org.Chem., 45, 3341.

26. Munavu, R.M. and Szmant, H.H. (1975) Tetrahedron Lett., 4543.

27. Ogur, J.A. (1980) Ph.D. Thesis, Univ. of Nairobi.

28. Omura, K. and Swern, D. (1978) Tetrahedron, 34, 1651.

29. Phillips, W.G. and Ratts, K.W. (1971) J.Org.Chem., 36, 3145.

30. Pummerer, R. (1910) Ber dtsch. Chem. Ges., 43, 1401.

31. Russell, G.A., Sabourin, E.T., and Hamprecht, G. (1969) J.Org.Chem. 34, 2339.

32. Schwartz, N.V. (1968) J.Org.Chem., 33, 2895.

42. Vogel, A.I. (1979) A Text Book of Practical Org. Chem. 4th edn., Longman Group Ltd., London.

43. Waldron, W.R. and Reid, E.E. (1923) J.Am.Chem.Soc., 45, 2399.

44. Wilson, G.E., Jr. (1982) Tetrahedron, 38, 2597.

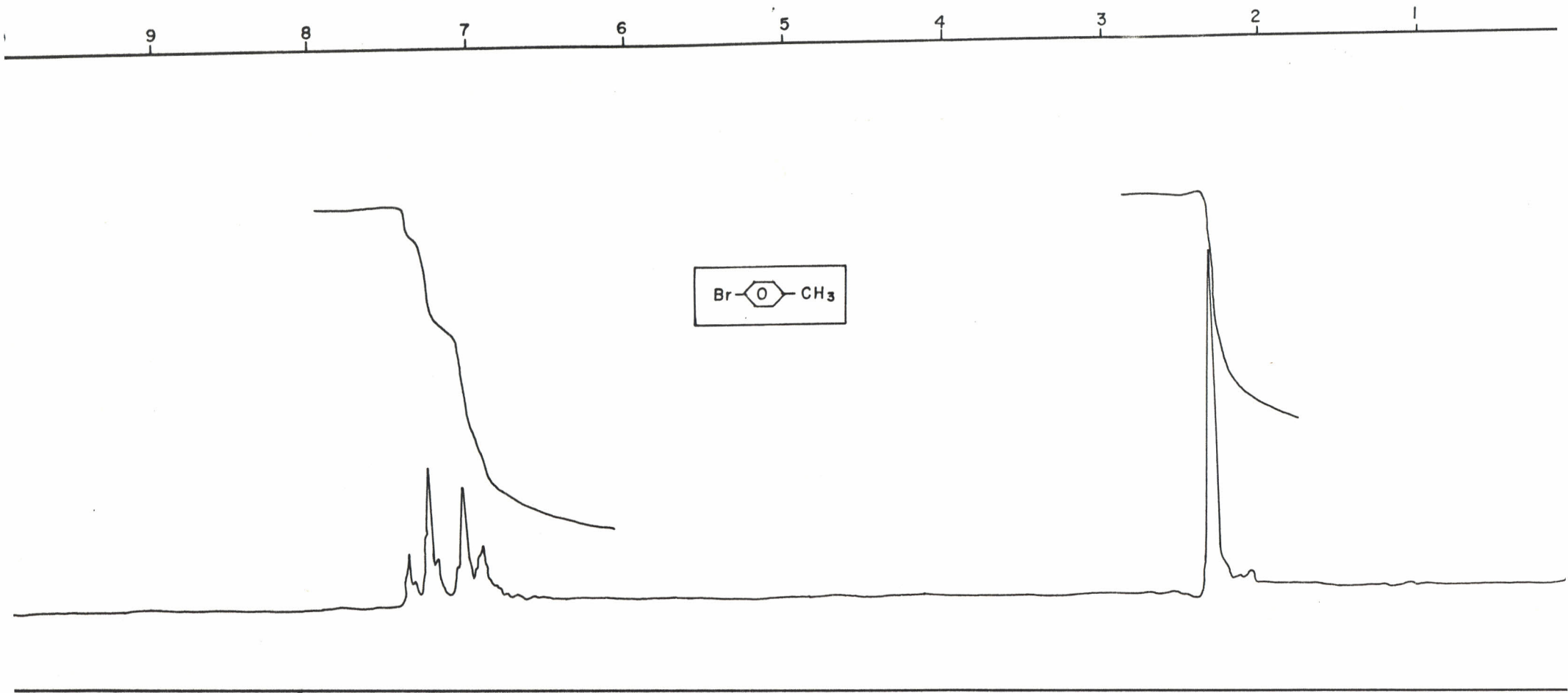
45. Wilson, G.E., Jr. and Albert, R. (1973), J. Org. Chem., 38, 2160.

46. Wilson, G.E., Jr. and Chang, M.M.Y. (1971) Tetrahedron Lett., 875

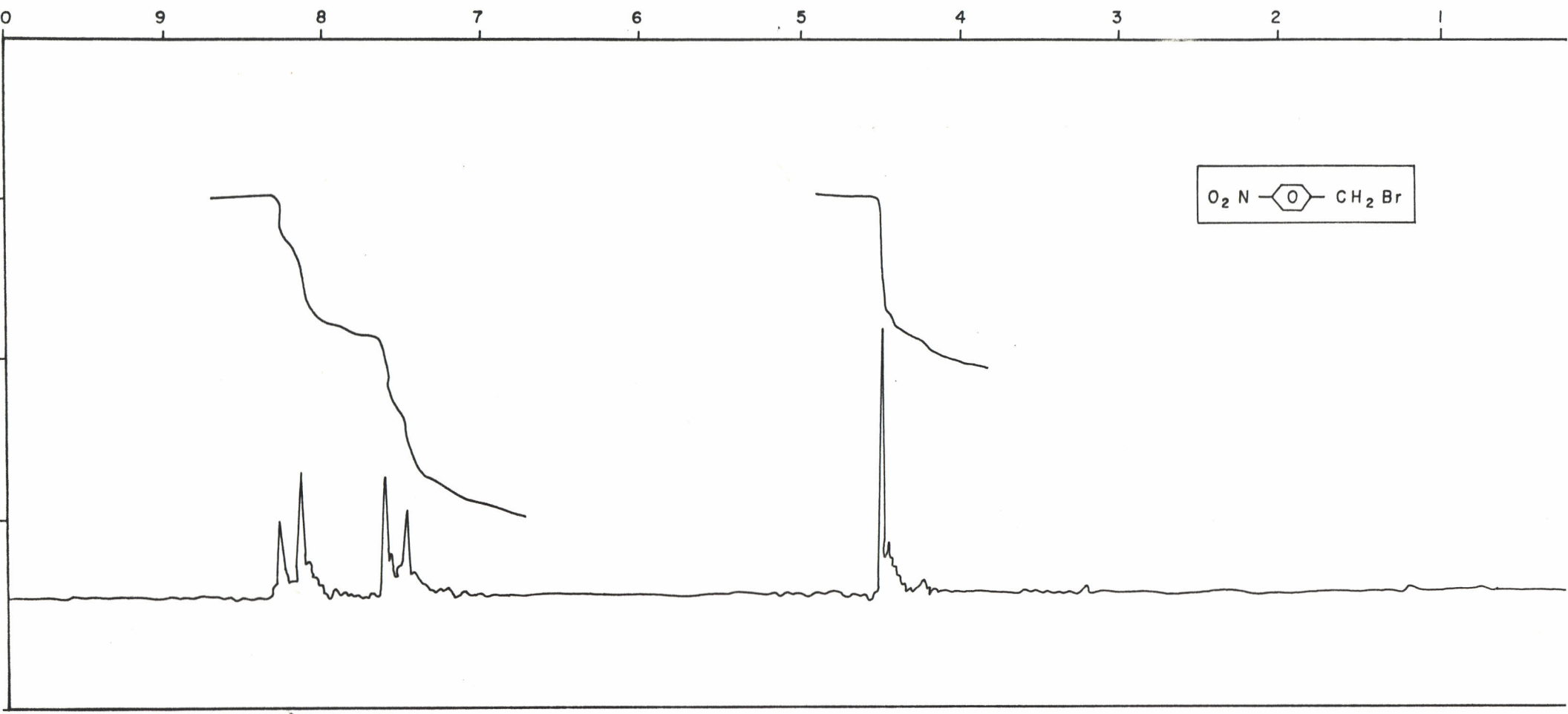
47. Wilson, G.E., Jr. and Huang, M.G. (1970) J.Org.Chem., 35, 3002.

48. Wilson, G.E., Jr. and Strong, C.J. (1972) J.Org.Chem., 37, 2376.

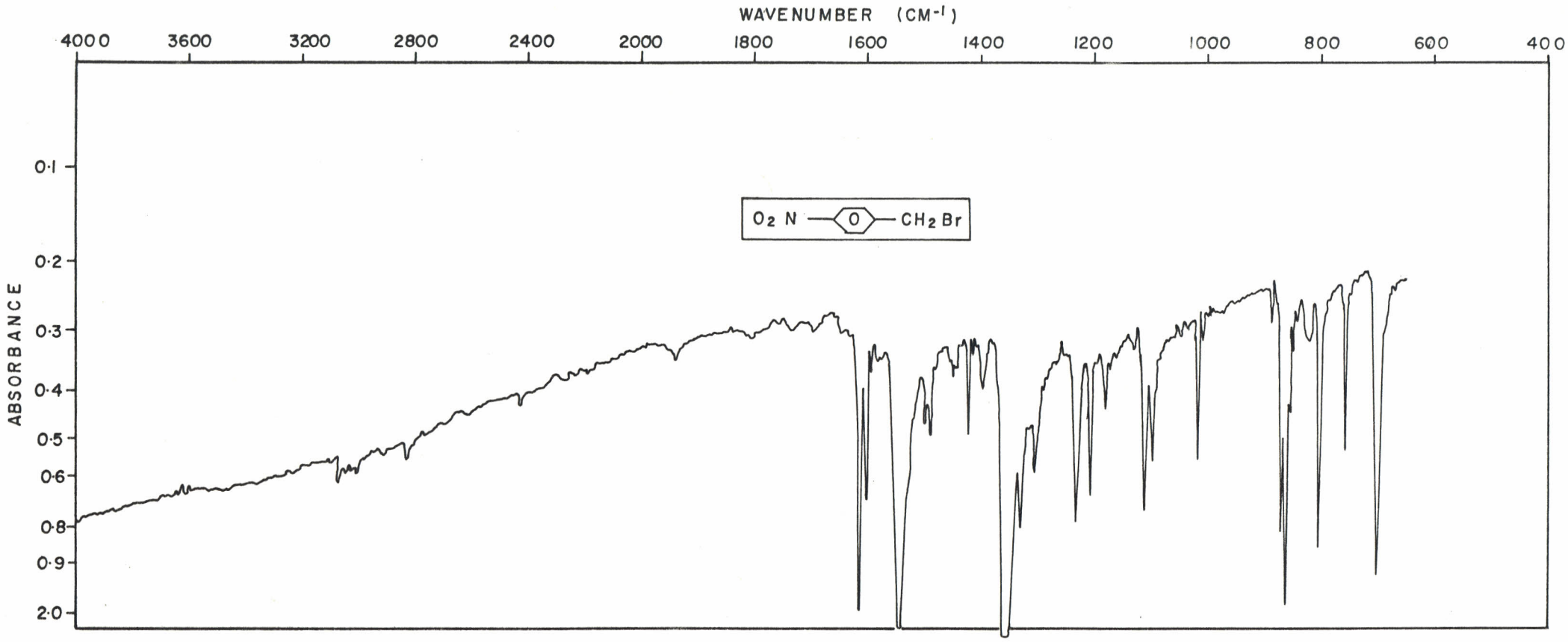
APPENDIX 1: NMR SPECTRUM OF p-BROMOTOLUENE



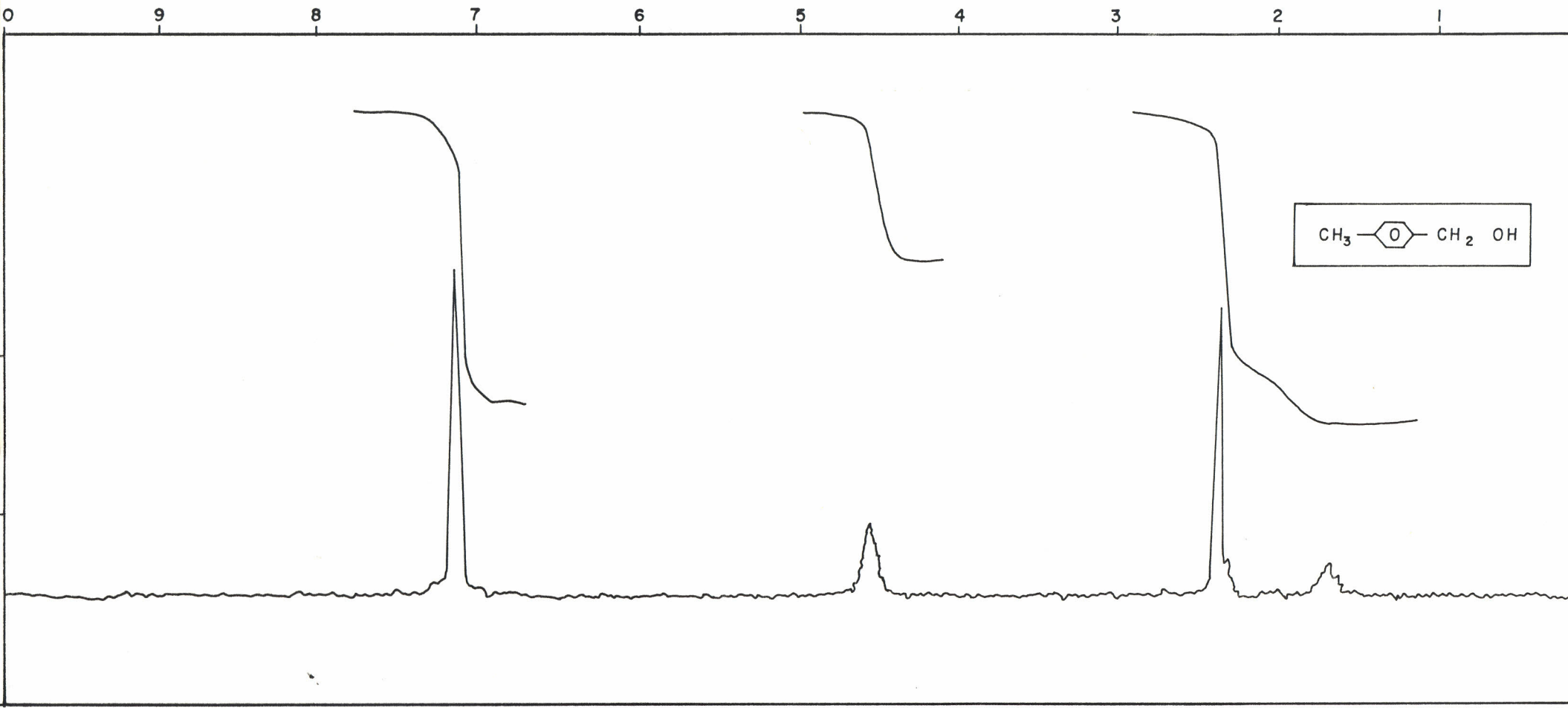
APPENDIX 2: NMR SPECTRUM OF p-NITROBENZYL BROMIDE



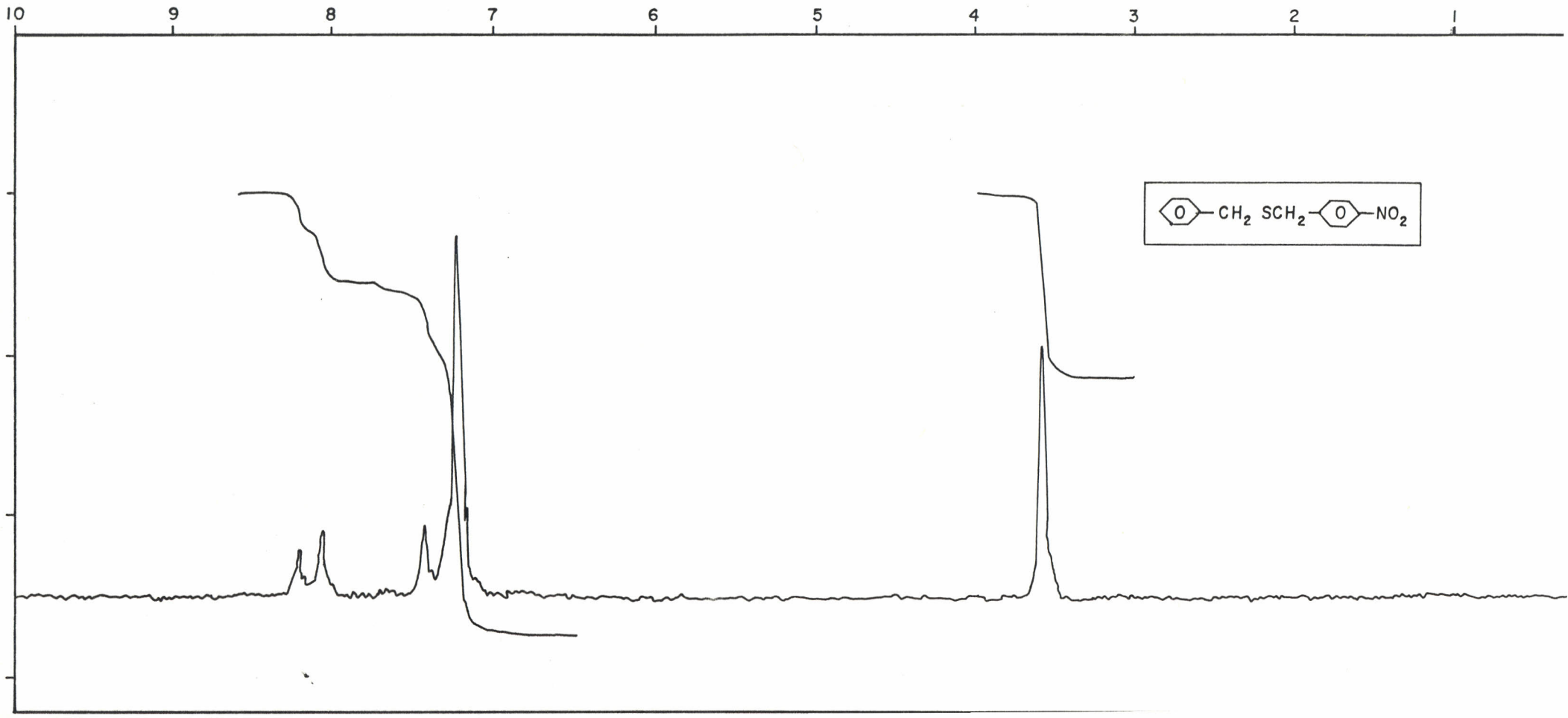
APPENDIX 3: IR SPECTRUM OF p-NITROBENZYL BROMIDE



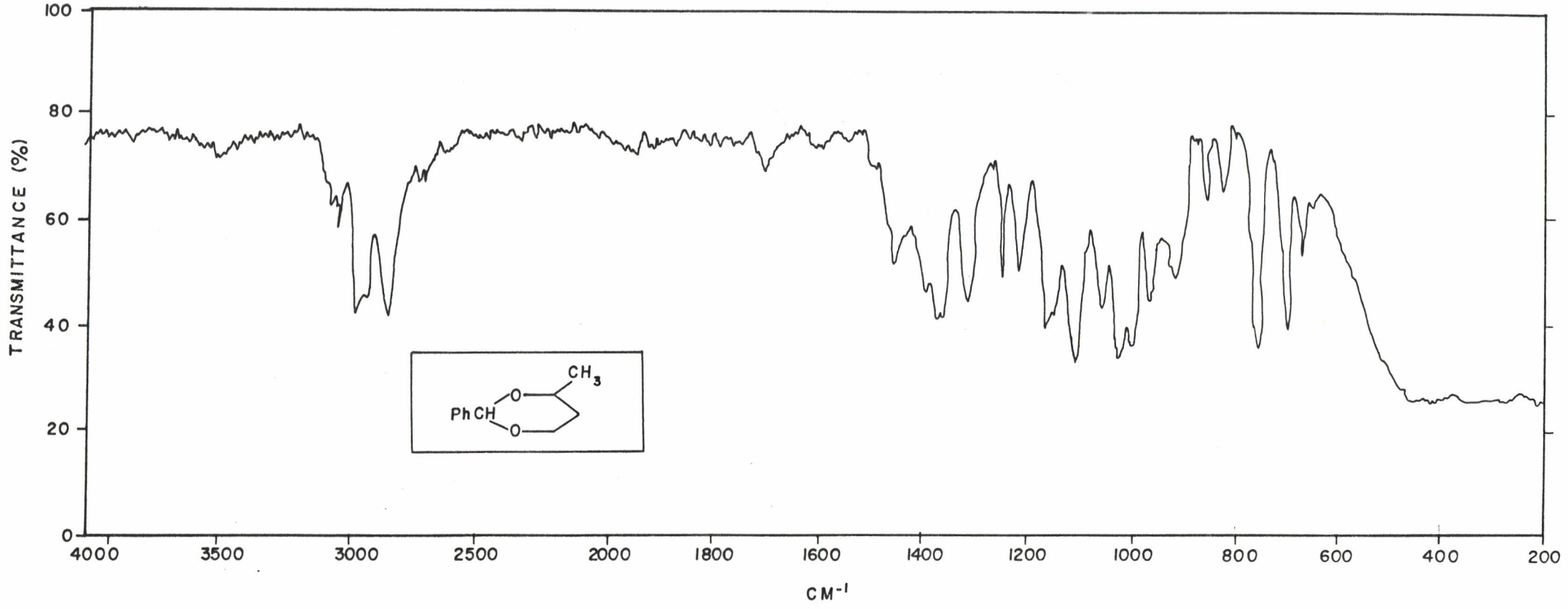
APPENDIX 4: NMR SPECTRUM OF p-METHYLBENZYL ALCOHOL



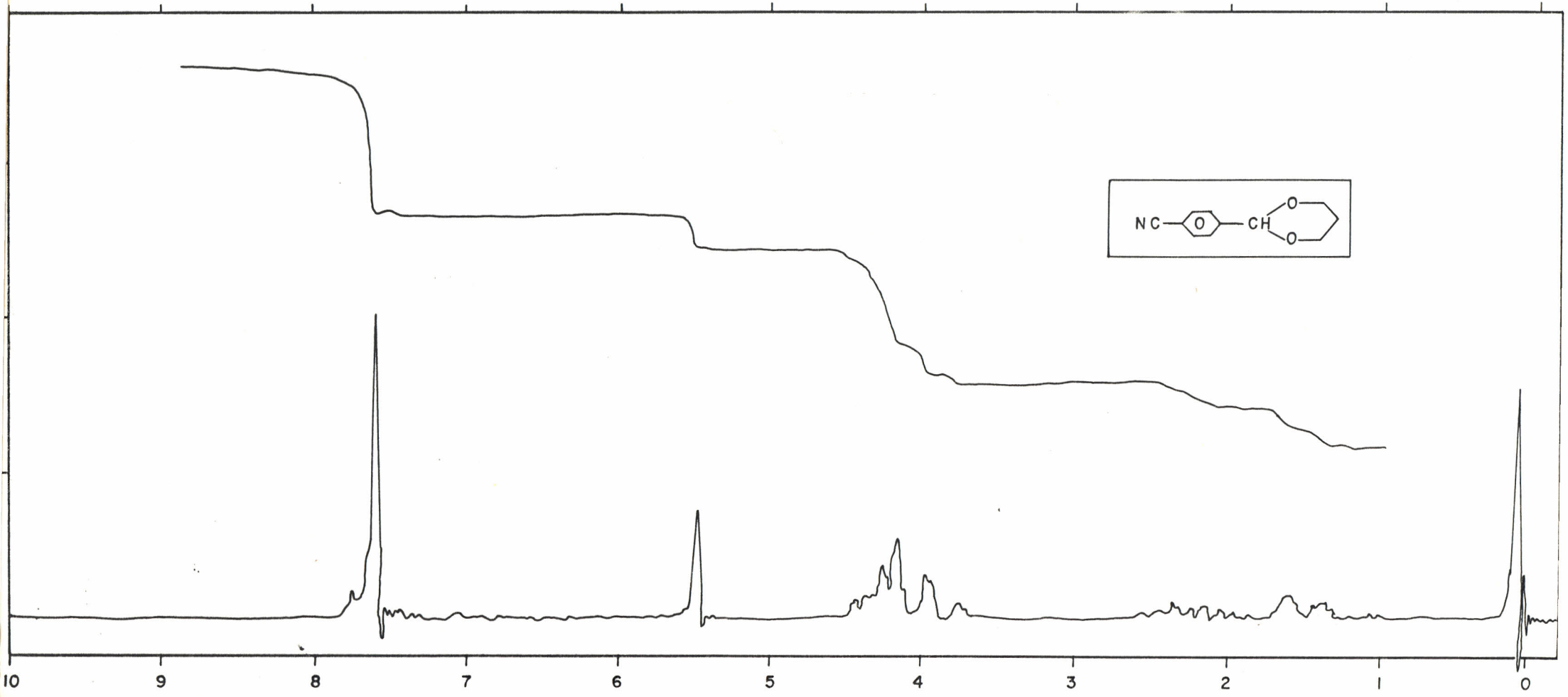
APPENDIX 7: NMR SPECTRUM OF BENZYL p-NITROBENZYL SULPHIDE



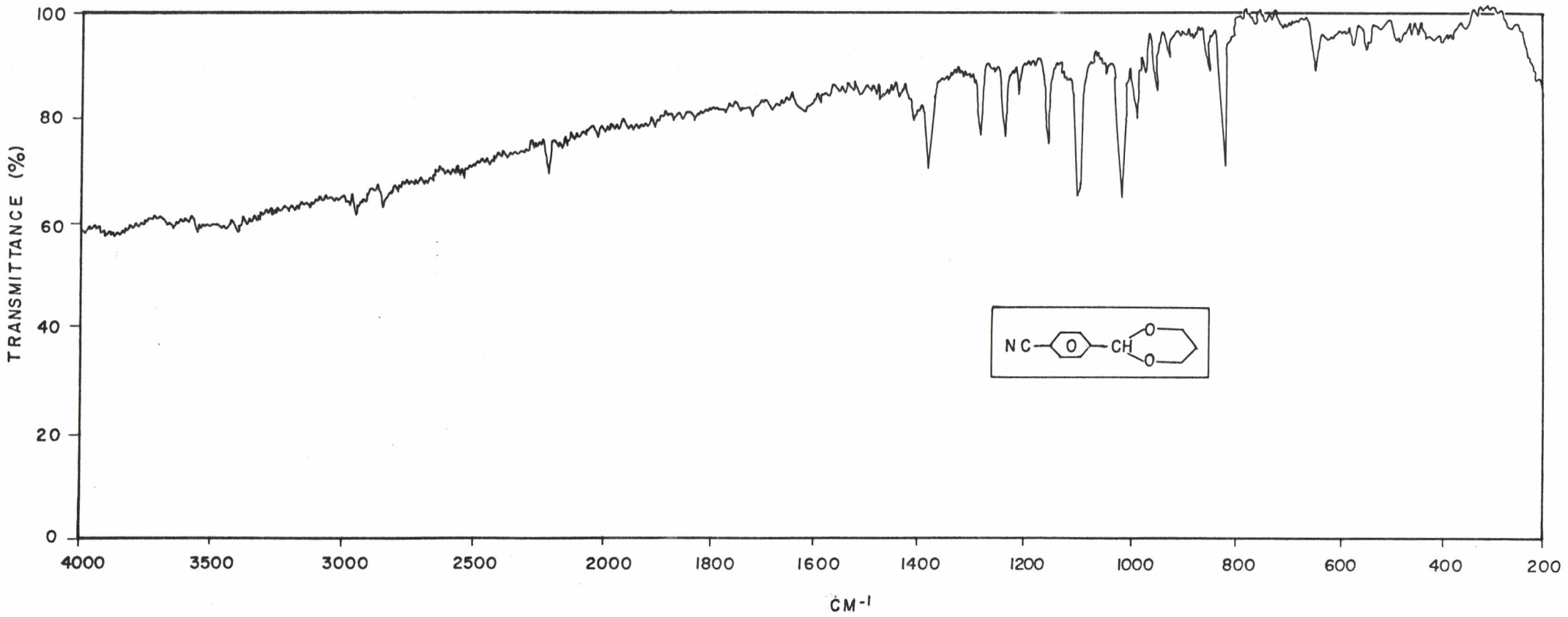
APPENDIX 9: IR SPECTRUM OF 4-METHYL-2-PHENYL-1,3-DIOXANE



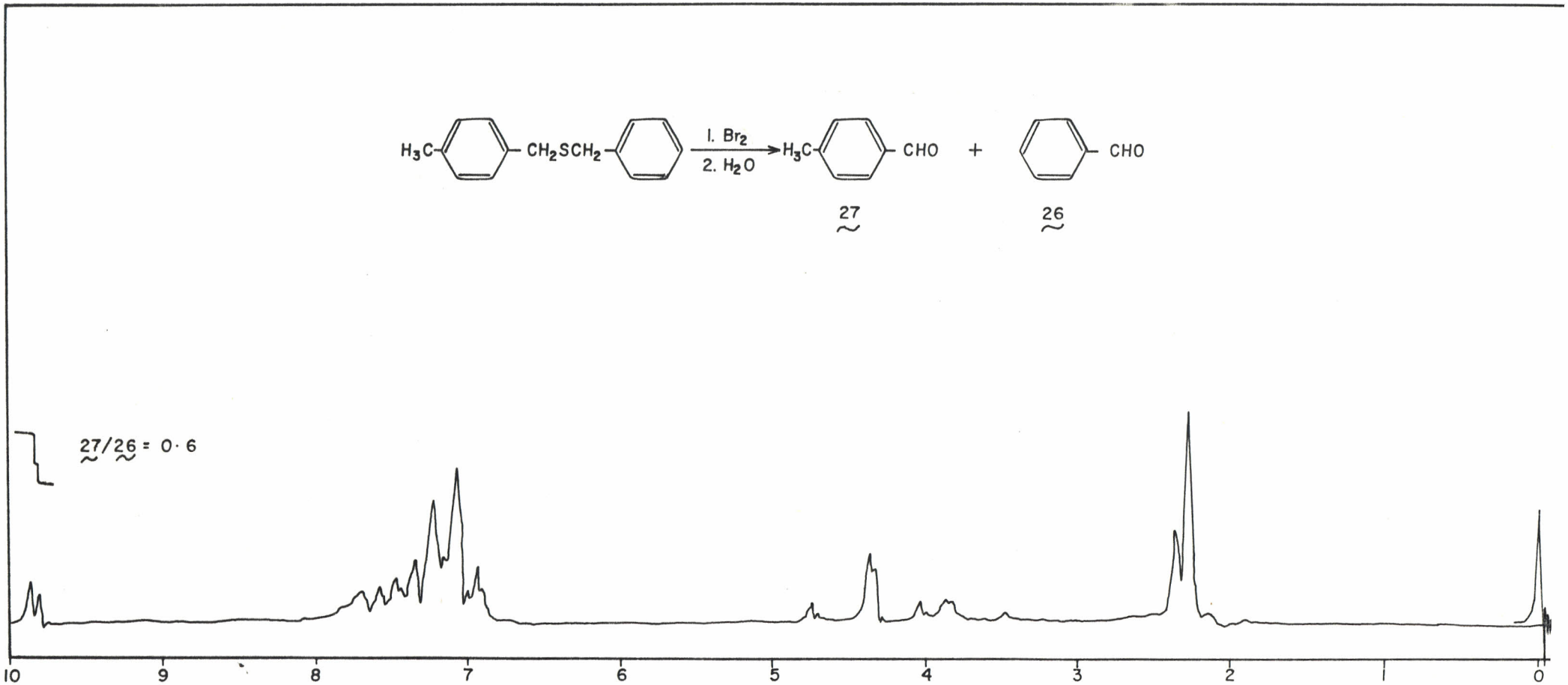
APPENDIX 10: NMR SPECTRUM OF 2-p-CYANOPHENYL-1,3-DIOXANE



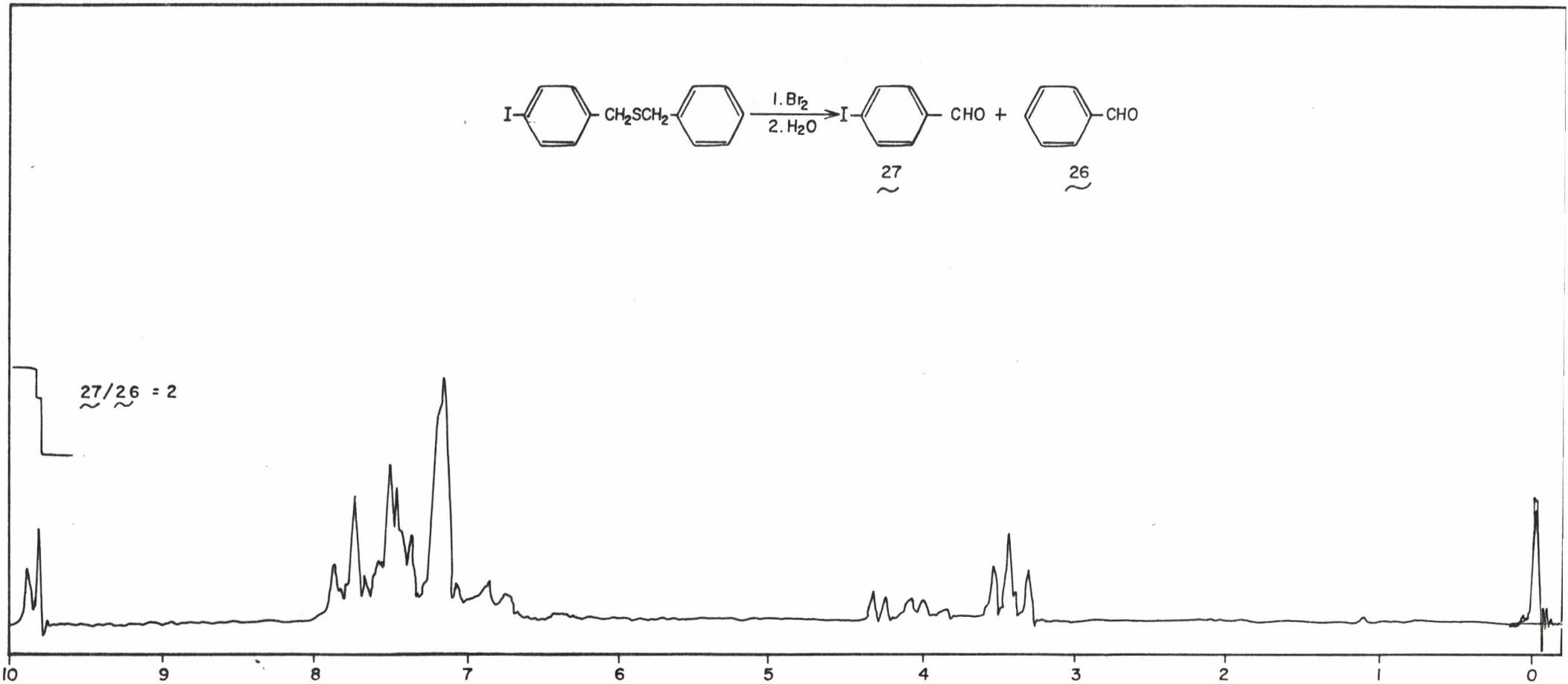
APPENDIX 11: IR SPECTRUM OF 2-p-CYANOPHENYL-1,3-DIOXANE



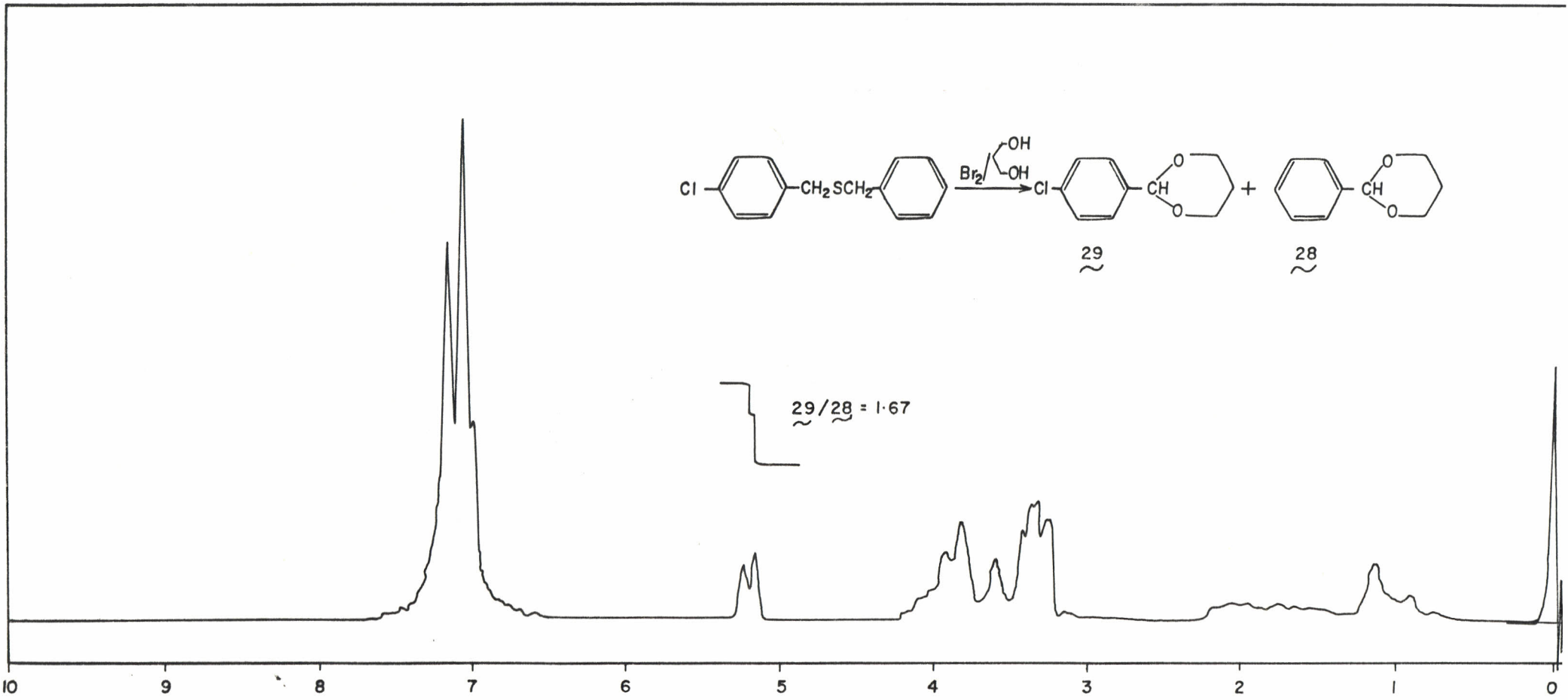
APPENDIX 12:



APPENDIX 13:



APPENDIX 14:



APPENDIX 15: