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# SYNTHESIS OF SULPHONES: INTERACTIONS OF SULPHURIC ACID AND SULPHONIC ACIDS WITH TRIFLUOROACETIC ACID ANHYDRIDE.

A thesis submitted by Themba E. Tyobeka
in candidature for the degree of Doctor of Philosophy
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Dedicated to my wife and parents.

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## ABSTRACT

Some diaryl sulphones have been prepared by the reaction of p-toluene sulphonic acid with aromatic hydrocarbons in the presence of trifluoroacetic anhydride. The various isomeric products were separated by g.l.c., the major isomers isolated by fractional recrystallisation and their structures confirmed using various spectroscopic techniques.

The kinetics of the interactions between trifluoroacetic anhydride and the sulphonic acids (methane sulphonic and mesitylene sulphonic acid) have been studied and these results used to propose a mechanism for the trifluoroacetic anhydride 'catalysed' formation of sulphones in the reaction of p-toluene sulphonic acid with aromatic hydrocarbons in nitromethane. This mechanism involves the formation of an intermediate (p-toluene sulphonyl trifluoroacetate) which ionises into p-toluene sulphonylium and trifluoroacetate ions. Electrophilic attack by the sulphonylium ions on the aromatic hydrocarbon results in the formation of sulphones.

Symmetrical diaryl sulphones have been prepared from the reaction of sulphuric acid with aromatic hydrocarbons using trifluoroacetic anhydride. The major isomers were isolated and identified. Unsymmetrical diaryl sulphones have also been prepared by a similar method by the sequential addition of two different aromatic hydrocarbons to solutions of trifluoroacetic anhydride and sulphuric acid in nitromethane. The isomeric products formed in both these reactions were separated by g.l.c. The interactions of trifluoroacetic anhydride and sulphuric acid in various mixtures of dichloromethane and nitromethane were studied and the results again utilised to propose the mechanisms for the reactions of

sulphuric acid with aromatic hydrocarbons in the presence of trifluoroacetic anhydride. This mechanism involves the formation of first a monoanhydride (trifluoroacetyl sulphuric acid) which reacts further to give the dianhydride [di-(trifluoroacetyl) sulphate]. The dianhydride gives rise to an initial regiospecific electrophilic attack upon the aromatic hydrocarbon to form the aryl sulphonyl trifluoroacetate. The aryl sulphonyl trifluoroacetate then reacts with the second aromatic hydrocarbon to give sulphones with the normal pattern of electrophilic substitution.

Symmetrical diaryl sulphones have also been prepared from the reaction of aromatic hydrocarbons with hydroxylamine-O-sulphonic and trifluoroacetic anhydride and the mechanism of this reaction proposed on the basis of the above reactions.

# CONTENTS

# 1. GENERAL INTRODUCTION

Trifluoroacetic anhydride has in recent years been widely used as a reagent in organic synthesis. It first found application in the esterification of carboxylic acids. Unlike other carboxylic anhydrides, its use results in the formation exclusively of esters other than trifluoroacetates and furthermore, the reactions can be carried under milder conditions than those necessary with other carboxylic anhydrides[1].

$$R'COOH + R''OH + (CF_3CO)_2O \longrightarrow RCOOR'' + 2CF_3COOH \quad (1)$$

The applicability of this reaction is not limited to carboxylic acids but acids such as sulphonic, nitric and derivatives of phosphoric acid have been esterified by this method. J.M. Tedder[7] in his review of the reactions of trifluoroacetic anhydride lists all such acids that may be so esterified.

Trifluoroacetic anhydride has been used to bring about the condensation of carboxylic acids and aromatic hydrocarbons to form ketones. Most carboxylic anhydrides require extremely vigorous conditions to 'catalyse' condensation of these reactions, but in the case of trifluoroacetic anhydride the reactions are in many cases spontaneous. However in practice, it is often necessary to accelerate the reaction by gentle warming[2].

$$ArH + RCOOH + (CF_3CO)_2O \longrightarrow ArCOR + 2CF_3COOH \quad (2)$$

As with the esterification reaction the application of trifluoroacetic anhydride is not limited to carboxylic acids only but may be utilised when other acids are condensed with aromatic hydrocarbons to form related aromatic compounds.

The use of trifluoroacetic anhydride as a solvent and reagent has been found to be very useful for the nitration of aromatic hydrocarbons[3].

The

$$ArH + HNO_3 + (CF_3CO)_2O \rightarrow ArNO_2 + 2CF_3COOH \qquad (3)$$

nitronium trifluoroacetate ($CF_3COONO_2$) can be regarded as the reagent.

The synthesis of diazonium salts was achieved by dissolving an alkyl nitrite in trifluoroacetic anhydride and a subsequent addition of an aromatic hydrocarbon

$$ArH + 5RONO + 3\,(CF_3CO)_2O \rightarrow Ar\overset{+}{N} = N\,NO_3^-$$

$$+\ 5RO{\cdot}COCF_3 + CF_3COOH + 2NO_2 \qquad (4)$$

Sulphonic acids can be condensed with aromatic hydrocarbons under mild conditions in the presence of trifluoroacetic anhydride[2]...

$$A'rH + A''rSO_3H + (CF_3CO)_2O \rightarrow A'rSO_2A''r + 2CF_3COOH \qquad (5)$$

Trifluoroacetyl hypohalites have been used as halogenating reagents. Although this reaction is not a condensation reaction of trifluoroacetic anhydride, the trifluoroacetyl hypohalites resemble products of the reaction of trifluoroacetic anhydride and hypohalous acids and therefore deserve to be mentioned here[4].

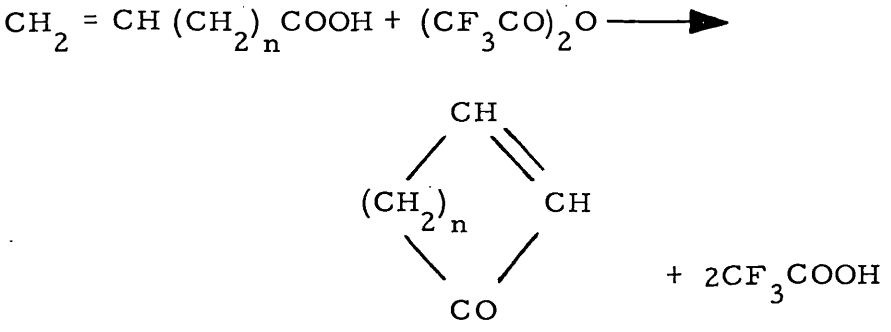
$$CF_3COOX + ArH \rightarrow ArX + CF_3\ COOH \qquad (6)$$

The addition of carboxylic acids to alkenes has been known to result in esters in an acid catalysed reaction[131]. However in the presence of trifluoroacetic anhydride acyl trifluoroacetates are formed. These are unstable and eliminate trifluoroacetic acid to form unsaturated $\beta$-ketones[5].

$$RCOOH + (CF_3CO)_2O + R'CH{:}CHR'' \rightarrow CF_3COOH +$$

$$RCOCHR'CHR''OCOCF_3 \rightarrow RCOCR'{:}CHR'' + 2CF_3COOH \qquad (7)$$

This reaction can be adapted for the synthesis of cyclic ketones. Here a suitable unsaturated acid undergoes an intramolecular condensation.



(8)

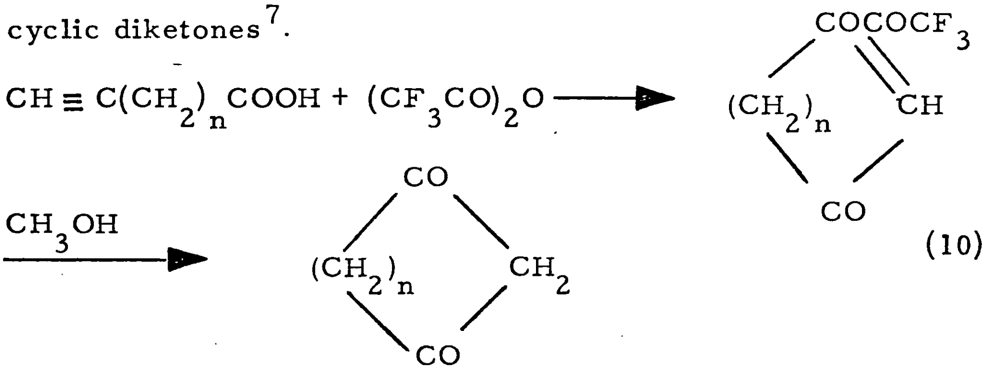
For (n = 3) good yields of ketone are obtained but considerable polymerisation takes place for n = 2[7].

Acyl addition to acetylenes with trifluoroacetic anhydride results in an enol trifluoroacetate of a α, β-diketone. This addition product is fairly stable but can be easily converted to the β-diketone by transesterification with an alcohol[48].

$$\mathrm{RCOOH + R'C \equiv CH + (CF_3CO)_2O \longrightarrow}$$

$$\mathrm{CF_3COOCR' : CHCOR + CF_3COOH \xrightarrow{CH_3OH} R'COCH_2COR' + 2CF_3COOH} \qquad (9)$$

Similarly, alkynoic acids can be cyclised to yield cyclic diketones[7].



(10)

As with the aromatic substitution reactions, the addition of carboxylic acids can be extended to other oxy-acids. One such reaction has been reported by J.M. Tedder[7] and involves the addition of nitrous acid to an alkene in the presence of trifluoroacetic anhydride.

$$\mathrm{RONO + R'CH = CHR'' + (CF_3CO)_2O \longrightarrow}$$

$$\mathrm{CF_3COOCHR'CH(NO)R'' + CF_3COOR \xrightarrow{CH_3OH} CF_3COOCH_3 +}$$

$$\mathrm{R'(OH)CH\ CH(NO)R'' \rightleftharpoons R'(OH)CH\ CR'':NOH} \qquad (11)$$

Mixtures of trifluoroacetic anhydride and hydrogen peroxide have been used to oxidise amines to nitrocompounds[6]

$$\mathrm{ArNH_2 + (CF_3CO)_2O + H_2O_2 \longrightarrow ArNO_2 + 2CF_3COOH + H_2O} \qquad (12)$$

The oxidizing species is a peroxy trifluoroacetic acid and this is found to be the most effective with aromatic amines and give yields between 85 and 100%.

This reagent has also been used effectively for the hydroxylation of alkenes.

$$\mathrm{R'CH = CHR'' + (CF_3CO)_2O + H_2O_2 \longrightarrow CF_3COOH +}$$

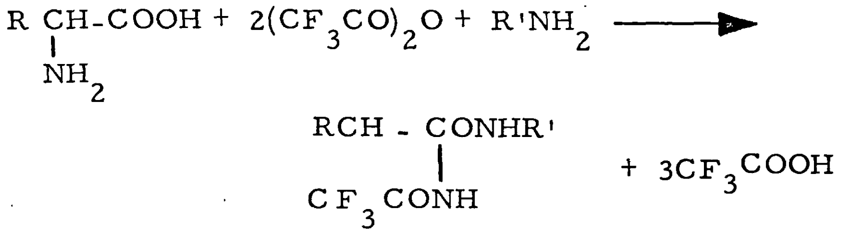
$$\mathrm{R'(OH)CH\ CH(CF_3COO)R'' \xrightarrow{CH_3OH} R'(OH)CH\ CH(OH)R''} \qquad (13)$$

When this reagent is used alone in the hydroxylation, the products are contaminated by higher boiling materials but these can be prevented by addition of triethylammonium trifluoroacetate which acts by increasing trifluoroacetate concentration[49]

The conversion of amines to amides using trifluoroacetic anhydride differs from the corresponding conversion of alcohols to esters in that a mixture of amides is produced with the trifluoroacetamide predominating[50, 51].

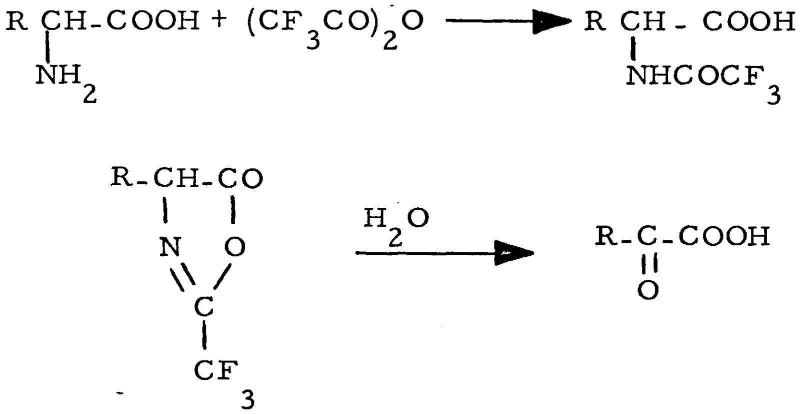
$$\mathrm{RCOOH + (CF_3CO)_2O + R''NH_2 \longrightarrow R'CONHR'' + CF_3CONHR''} \qquad (14)$$

This difference is attributed to the basic properties of amines due to the lone pair of electrons which is always available for protonation. Of interest in this field has been the reaction of trifluoroacetic anhydride with amino acids. The N-trifluoroacetyl derivative may be prepared in good yield. However when a mixture of an amino acid and a primary amine is reacted with 2 molar proportions of trifluoroacetic anhydride, a N-trifluoroacetyl amino acid amide is formed[52].



$$\underset{\displaystyle NH_2}{R\,CH}\text{-}COOH + 2(CF_3CO)_2O + R'NH_2 \longrightarrow \underset{\displaystyle CF_3CONH}{RCH}\text{-}CONHR' + 3CF_3COOH \qquad (15)$$

However, when an α-amino acid is treated with trifluoroacetic anhydride, the initial amide rapidly cylices and on hydrolyses gives an α-keto-acid[132].



$$\underset{\displaystyle NH_2}{R\,CH}\text{-}COOH + (CF_3CO)_2O \longrightarrow \underset{\displaystyle NHCOCF_3}{R\,CH}\text{-}COOH$$

$$\xrightarrow{H_2O} R\text{-}\underset{\displaystyle \overset{\|}{O}}{C}\text{-}COOH \qquad (16)$$

In this project, the interest of the author is mainly on the reaction of aromatic hydrocarbons with sulphonic acid in the presence of trifluoroacetic anhydride. This project therefore involves the synthesis of sulphones by this method and subsequent separation and analysis of all theproducts formed in this reaction. Secondly, the use of reagents other than sulphonic acids for the synthesis of sulphones in the presence of trifluoroacetic anhydride will be investigated. The emphasis in these reactions will be laid on those that either improve the yield of sulphones or simplify the above method of synthesis. Also of great importance is the extension of the reaction of carboxylic acids with alkene in the presence of trifluoroacetic anhydride to sulphonic acids (reaction 7) which has so far not been attempted.

Lastly, a study of the mechanisms and kinetics of these reactions is envisaged with special reference to the interaction of sulphonic acids and other reagents with trifluoroacetic anhydride. With this information the author hopes to give a better insight into the mechanisms of sulphonylation reactions.

# 2. SYNTHESIS OF AROMATIC SULPHONES

## 2.1. INTRODUCTION

Sulphones are compounds in which a sulphur atom is bonded to two carbon atoms and two terminal oxygens. Thus diphenyl sulphone is represented as shown in Fig. 2.1 - 2.

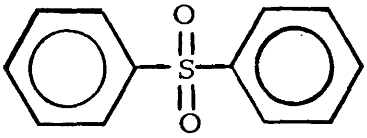


Fig. 2.1 - 1

The sulphur-oxygen bonds are polar and this results in sulphones having large dipole moments i.e. comparable to those of ketones. They are generally stable compounds and those that are liquids can usually be distilled without decomposition. Generally they are soluble in most organic solvents and insoluble in water. Their infrared spectra are characterised by two absorption bands. The absorption due to the $SO_2$ symmetric stretching vibration occur in the range 1300-1350 $cm^{-1}$ and those due to the assymmetric stretching vibrations between 1120-1160 $cm^{-1}$ [53]. In contrast to the carbonyl group, the sulphone group exhibits no absorption chromophore in the ultraviolet. There are now a variety of methods of preparation of sulphones, most of which will be dealt with in some detail in this chapter.

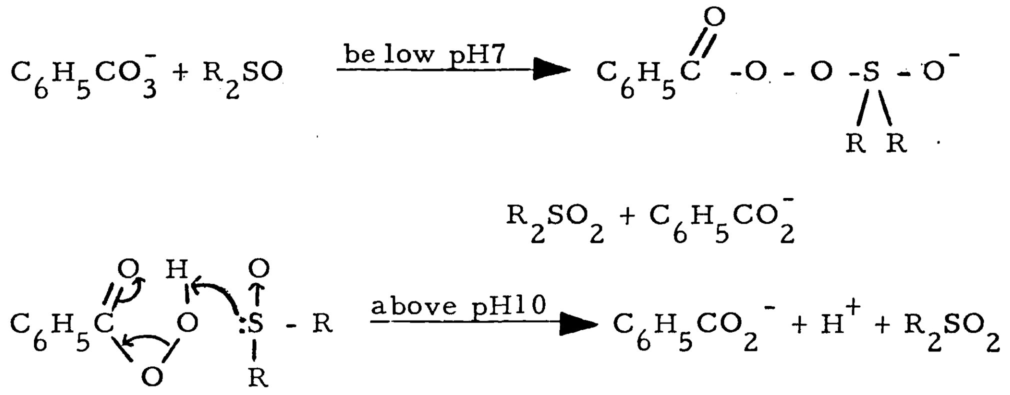
### 2.1.1. Oxidation of sulphides and sulphoxides.

The most widely used method for the synthesis of sulphones involves the direct oxidation of sulphides or sulphoxides. A variety of oxidising agents can be used to effect these transformations such as hydrogen peroxides, peracids, chlorine, nitric acid, oxides of nitrogen, oxygen, ozone and metal oxides.

$$C_6H_5SC_2H_5 \xrightarrow[HOAC]{H_2O_2} C_6H_5SO_2C_2H_5 \qquad (1)$$

The most commonly used reagent is a mixture of hydrogen peroxide in acetic acid since it can be carried in the presence of other potentially oxidisable functional groups such as the hydroxyl groups [10].

Oxidation of sulphides and sulphoxides in the presence of peracids has been found to proceed by two mechanisms both of which are controlled by the pH of the reaction mixture [11,12]. e.g. with perbenzoic acid.



$$C_6H_5CO_3^- + R_2SO \xrightarrow{\text{below pH7}} C_6H_5C(=O)\text{-O-O-}SR_2\text{-O}^-$$

$$R_2SO_2 + C_6H_5CO_2^-$$

$$\xrightarrow{\text{above pH10}} C_6H_5CO_2^- + H^+ + R_2SO_2$$

(2)

Chlorine in aqueous methanol oxidises sulphoxides to sulphones. This method however becomes inconvenient owing to the accompanying cleavage reaction that results in the formation of sulphonyl chlorides [13].

$$(C_6H_5CH_2)_2SO \xrightarrow[\text{Aq}\,CH_3OH]{Cl_2} (C_6H_5CH_2)_2SO_2 + C_6H_5CH_2SO_2Cl$$

40% 19%

(3)

Electrochemical chemical oxidation of sulphides proceeds in good yields, but the yields can be improved by addition of salts of tungsten, selenium, molybdenum and vanadium [14].

## 2.1.2 Friedel-Crafts Method.

Another common method for the preparation of sulphones is the Friedel-Crafts method in which a sulphonyl chloride reacts with a hydrocarbon in the presence of a Lewis'acid such as aluminium chloride, ferric chloride or zinc chloride[8, 9].

$$ArH + RSO_2Cl \xrightarrow{AlCl_3} ArSO_2R + HCl \qquad (4)$$

Sulphonyl bromides and sulphonyl fluorides can also be used in this reaction. The first stage involves the formation of a complex between the catalyst and the sulphonyl chloride.

$$RSO_2Cl + AlCl_3 \longrightarrow RSO_2Cl.\ AlCl_3 \qquad (5)$$

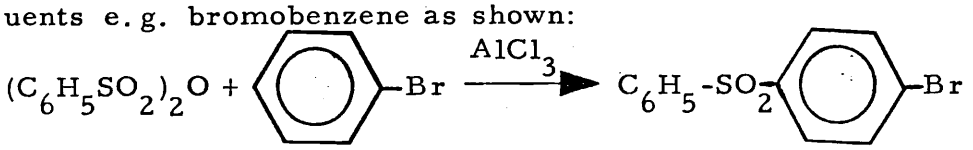
This is followed by the ionisation of the complex releasing the sulphonylium ion which then undergoes electrophilic attack on the aromatic hydrocarbon[53, 54]. The product is

$$RSO_2Cl.AlCl_3 \rightleftarrows RSO_2^{+} + AlCl_4^{-} \qquad (6)$$

$$RSO_2^{+} + AlCl_4^{-} + ArH \longrightarrow ArSO_2R.AlCl_3 + HCl$$

a complex similar to the arene sulphonyl-aluminium chloride between the sulphone and the aluminium chloride. It is therefore necessary that a full equivalent of the Lewis acid is employed in these preparations if a high rate of formation of the product is required.

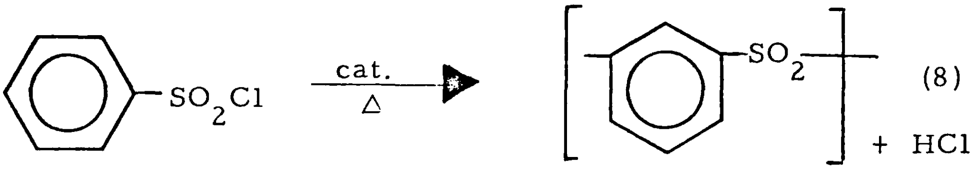
Apart from sulphonyl halides, sulphonic anhydrides have been found to react with aromatic hydrocarbons in the presence of a Lewis acid to give sulphones. The yields here are superior to those above and furthermore they react with aromatic hydrocarbons having electron withdrawing substituents e.g. bromobenzene as shown:



$+ C_6H_5SO_3H$ (7)

This substitution reaction is not possible with benzene sulphonyl chloride[56].

Polyarylsulphones have been synthesised by the heating of a sulphonyl chloride in the presence of a Friedel-Craft type catalyst. Inert solvents such as dimethyl sulphone or nitrobenzene are necessary in which to conduct these polymerisations. These sulphone polymers have high thermal stabilities, high



(8)

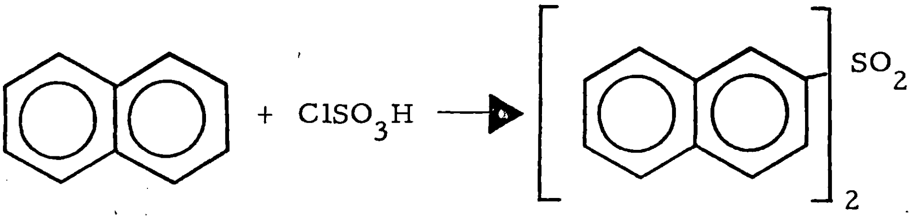
electrical resistivities, good mechanical properties and chemical inertness including resistance to hydrolysis. These properties allow these polymers to find application over a wide temperature range and in severe corrosive environments [57].

## 2.1.3 Dehydration Processes.

Sulphones are often produced as by-products in aromatic sulphonation reactions using sulphuric acid. By deliberately removing the water formed in the sulphonation reaction, the sulphone can be formed as a major product. In the case of benzene, water was removed by azeotropic distillation [16] whilst with catechol - a direct distillation of water from the mixture results in the sulphone.

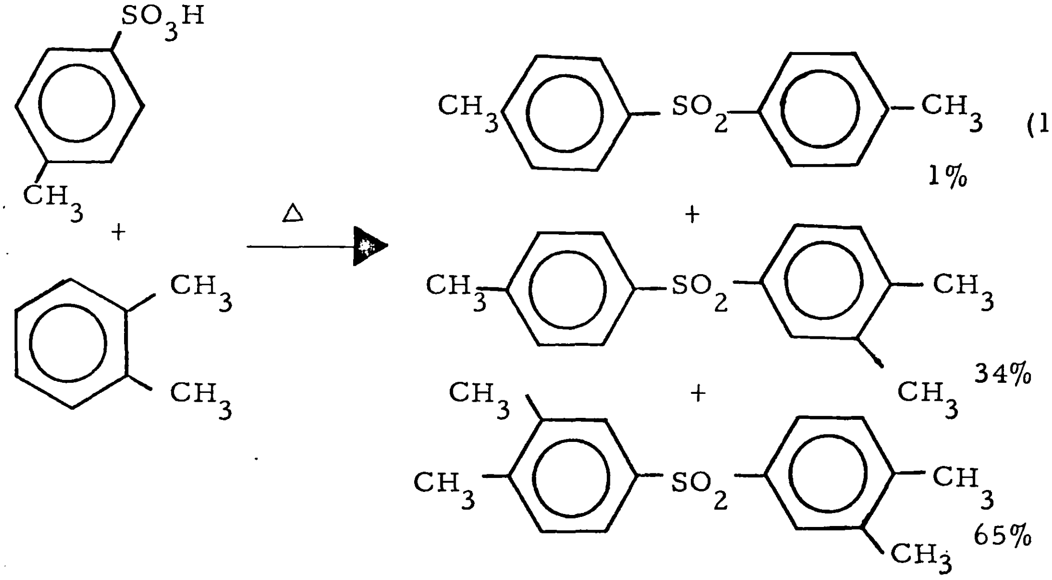
$$2ArH + H_2SO_4 \xrightarrow[\Delta]{-2H_2O} Ar_2SO_2 \qquad (9)$$

Chloro-sulphonic acid can be used in the place of sulphuric acid[21]



(10)

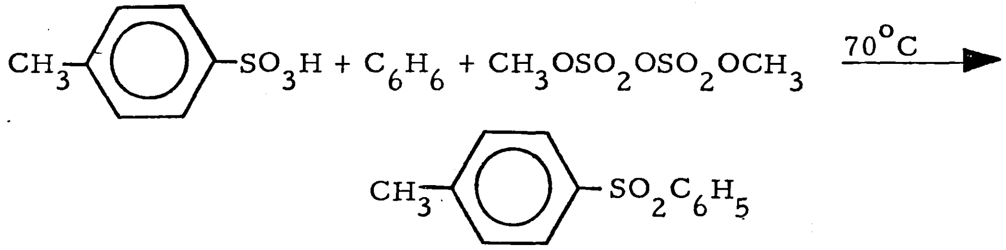
Similarly, assymetrical sulphones can be prepared by dehydration reactions between sulphonic acids and aromatic hydrocarbons[18]



(11)

This reaction may be improved by addition of dehydrating agents such as phosphorus pentoxide. When polyphosphoric acid is used, as a dehydrating agent, the product distribution suggests that the reaction proceeds via a sulphonylium cation. The formation of products conforms to the same orientation rules as observed in the corresponding Friedel-Crafts reaction[19]

Addition of dimethylpyrosulphate effects sulphone formation at a lower temperature[20]. In this case the reaction is believed to go via a $ArSO_2OSO_2OCH_3$ intermediate.



61% (12)

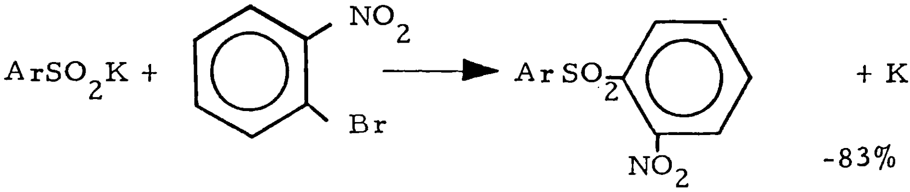
2.1.4 <u>Use of Sulphinates</u>.

Salts of sulphuric acids readily displace the halide ions from an alkyl halide to form sulphones. This reaction is generally carried in alcohols[22] but other solvents that facilitate nucleophilic attack such as D.M.F. can also be used.[23]

$$p\ CH_3C_6H_4SO_2Na + CH_3I \longrightarrow CH_3C_6H_4SO_2CH_3 + NaI$$

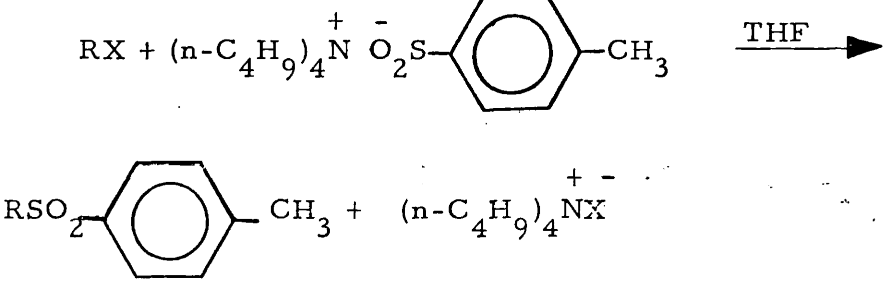
85% (13)

Sulphinate displacements also occur at appropriate aromatic centres activated towards nucleophilic attack.[126-128]



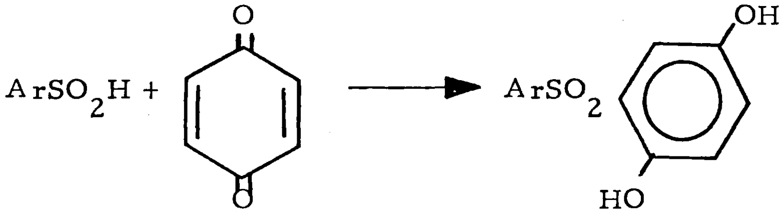
(14)

Tetrabutyl-ammonium salts react with halides giving high yields of sulphones[58]



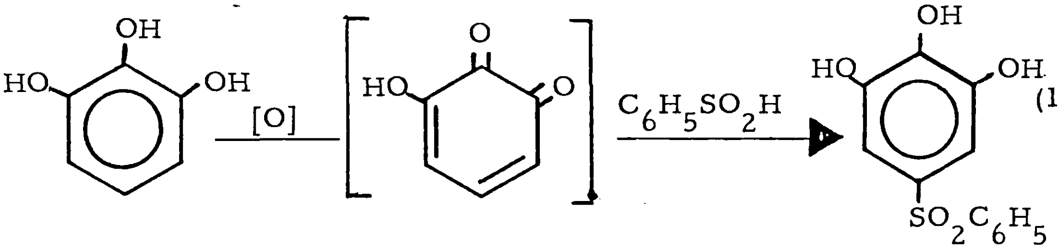
(15)

Aromatic sulphinic acids themselves undergo reactions with benzoquinones to give dihydroxy diaryl sulphones.[24]



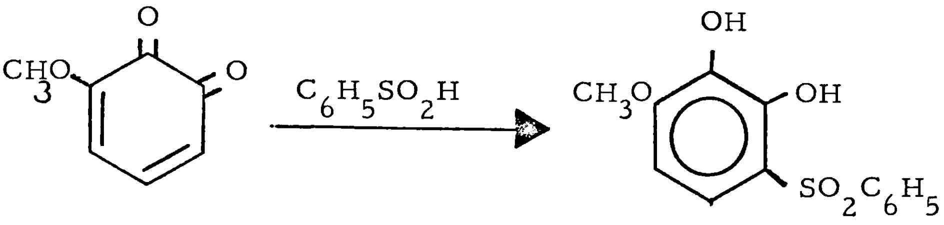
(16)

When benzoquinone is replaced by a mixture of pyrogallol and chromic acid, addition of benzene sulphinic acid results in the formation of trihydroxydiphenyl sulphones[25]



(17)

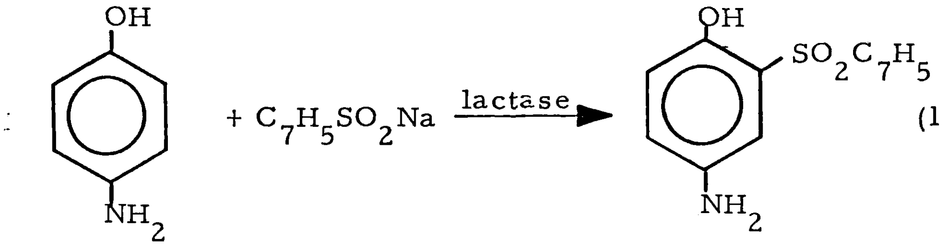
However when 3 methoxy 1,2 benzoquinone reacts with benzene sulphinic acid, substitution occurs at position 6[26]



(18)

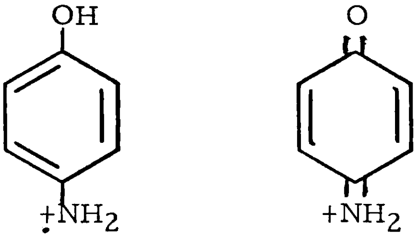
The difference in the behaviour of 3-hydroxyand 3 methoxy 1,2 benzoquinone towards benzene sulphinic acid is not yet understood.

An oxidative sulphonylation catalysed by enzymes occurs with 4-aminophenol and sodium sulphinate.[27]



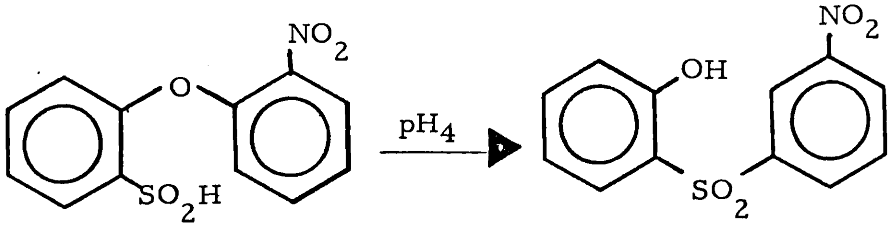
(19)

The oxidation is carried out with ferric chloride and the oxidation intermediate believed to be either a protonated aryl amino radical or a protonated aminoquinone.



(20)

Substituted diphenyl ethers with an ortho sulphinic acid group in one ring and an electron withdrawing group in the other ring rearrange in buffered solutions such that the sulphinic acid ionises but not the phenolic product[28]

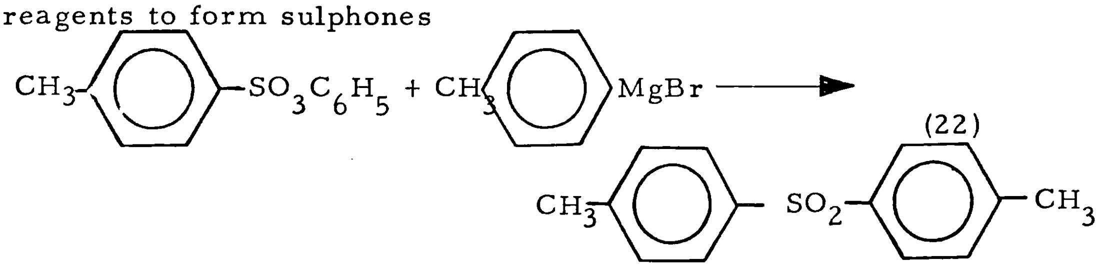


(21)

42%

### 2.1.5 Grignard Reagents.

Interactions between sulphonic acid derivatives and organometallic reagents results in the formation of sulphones. In particular sulphonate esters have been found to react with Grignard reagents to form sulphones



(22)

This method can be used for both alkyl and aryl sulphones as long as the other substituents are inert towards the Grignard reagent. However this method is preferrably used for the synthesis of diaryl and aryl alkyl sulphones since aryl Grignard compounds give better yields than corresponding alkyl reagents.[29]

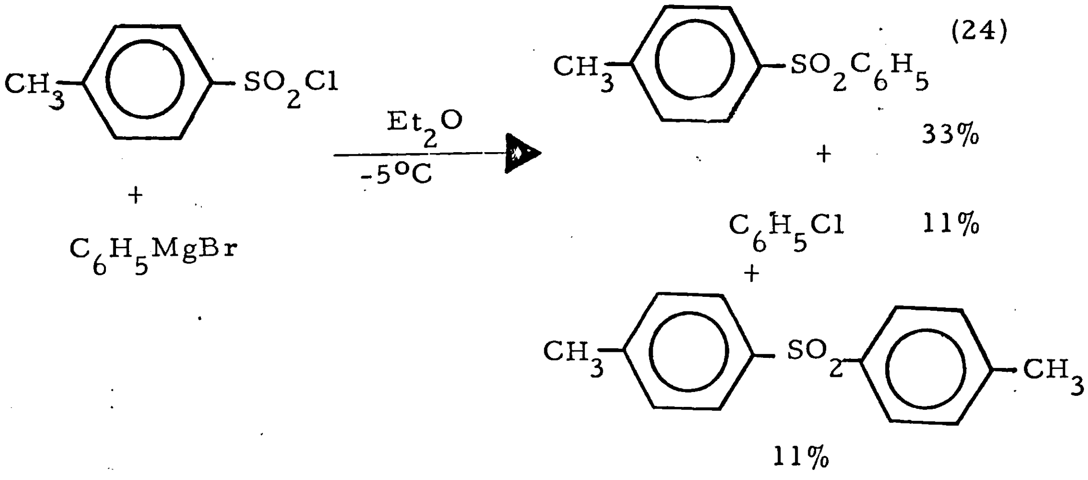
Arene sulphonyl chlorides also react with Grignard reagents to form sulphones, but this method is limited by accompanying side reactions even at low temperatures.

$$ArSO_2Cl + PhMgBr \longrightarrow ArSO_2Ph + MgBr$$

$$ArSO_2Cl + PhMgBr \longrightarrow ArSO_2MgBr + PhCl$$

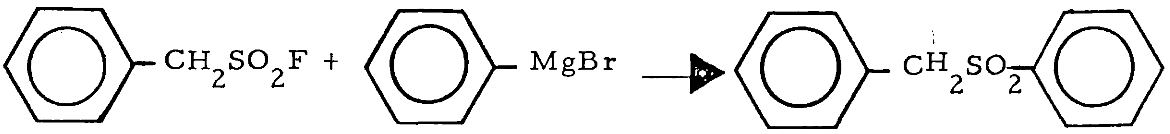
(23)

H. Burton and W.A. Davy showed that apart from the formation of compounds such as sulphides and sulphoxides a mixture of sulphones is always obtained.[31]



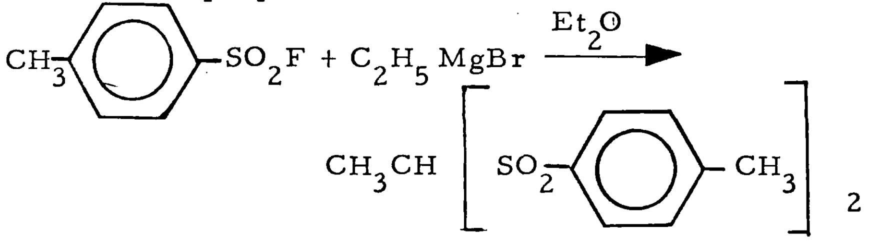
(24)

Sulphonyl fluorides have been found to give better yields of sulphones than sulphonyl chlorides[32]



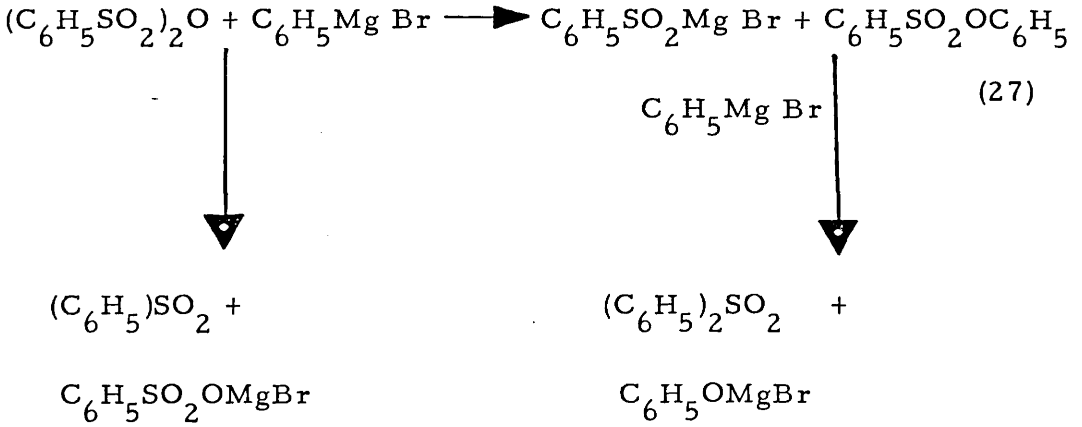
(25)

With excess organometallic reagent and sulphonyl fluoride, β-disulphones can be prepared[33]



(26)

Sulphonic anhydrides react with Grignard reagents to give sulphones. Just as in the case of arene sulphonyl chlorides a mixture of products is obtained. In the reaction of benzene sulphonic anhydride with phenyl magnesium bromide only 20% is the diphenyl sulphone together with 8% benzene sulphonic acid salt, 35%, benzenesulphinic acid salt and 2% phenol. The course of the reaction can be represented at least in part as follows:-[56]

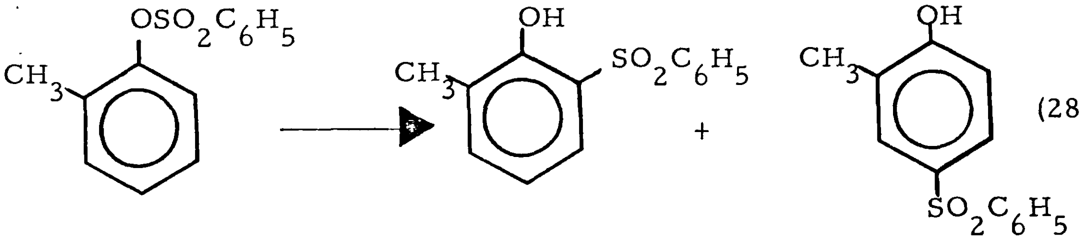


$$\begin{tikzcd}
(C_6H_5SO_2)_2O + C_6H_5MgBr \arrow[r] \arrow[d] & C_6H_5SO_2MgBr + C_6H_5SO_2OC_6H_5 \arrow[d, "C_6H_5MgBr"'] \\
(C_6H_5)SO_2 + C_6H_5SO_2OMgBr & (C_6H_5)_2SO_2 + C_6H_5OMgBr
\end{tikzcd}$$

(27)

### 2.1.6. Fries and related rearrangements.

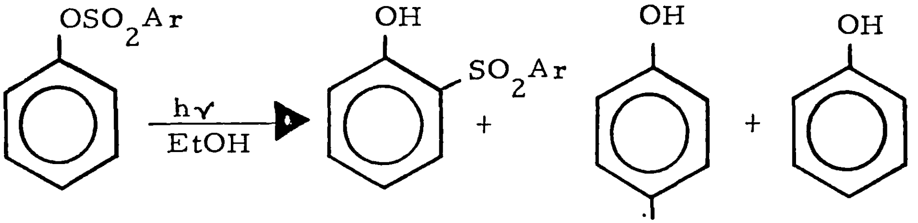
Aryl sulphonates rearrange in the presence of Lewis acids to give hydroxyl aryl sulphones. This is an extension of the Fries rearrangement of carboxylic acid esters.



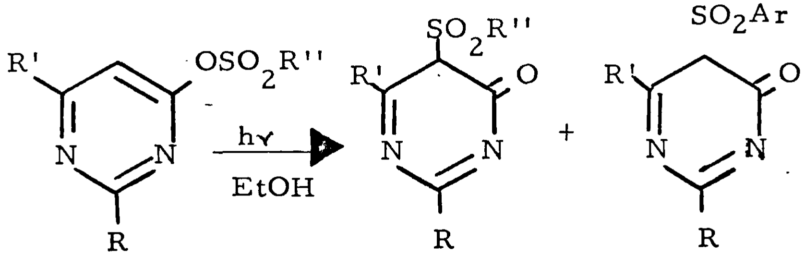
(28)

The position of the substitution by the sulphonyl group is predominantly the <u>ortho</u> position, although the <u>para</u> isomer is also present. Solvents such as nitrobenzene having dielectric constants which favour separation of charges, increase the proportion of the <u>para</u> isomer.[34]

In the absence of a Lewis acid catalyst, the rearrangement can also take place but under photolytic conditions[35].

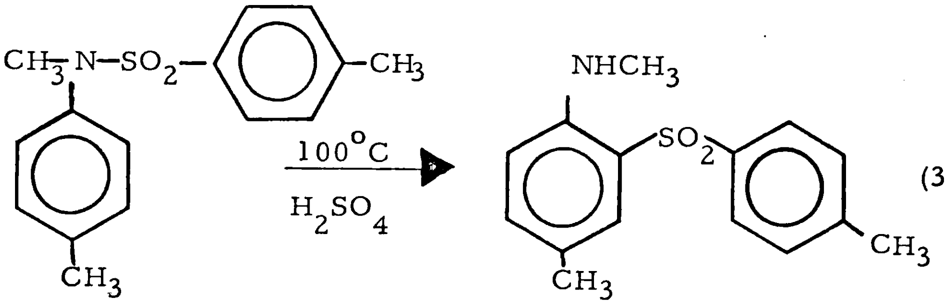


(29)

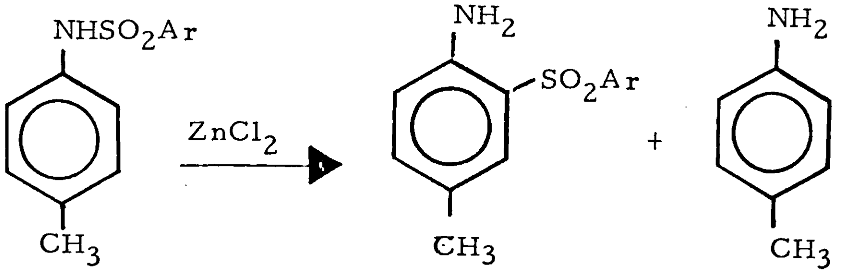


(30)

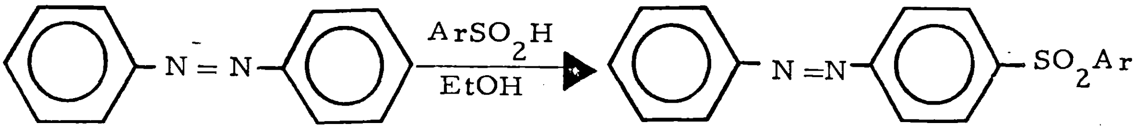
N. N. Diaryl-and N-alkyl-N-aryl-arylsulphonamides rearrange in a reaction similar to the Fries arrangement to form amino diaryl sulphones. This reaction takes place in the presence of hot concentrated sulphuric acid and is enhanced by the presence of electron donating substituents and retarded by electron withdrawing substituents. This reaction does not occur with primary anilides and alkyl sulphonamides since under these conditions they are readily hydrolysed.[129]


(31)

However in the presence of $ZnCl_2$ an HCl derivative of primary anilides rearrange to give predominantly the <u>para</u> isomer. <u>Ortho</u> substitution occurs if the <u>para</u> position is blocked. The presence of an N-alkyl group results in <u>ortho</u> substitution even in the absence of a <u>para</u>-blocking group. No explanation has yet been found for such a change in orientation.[36]


(32)

The formation of sulphones from arene sulphinic acids and diazobenzene or phenazine is thought to be related to the above rearrangement.


(33)

The intermediate is believed to be an <u>N</u>-aryl sulphonamide which rearranges to give the sulphone.[37]

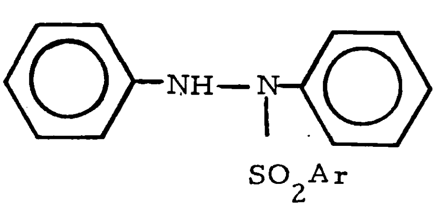
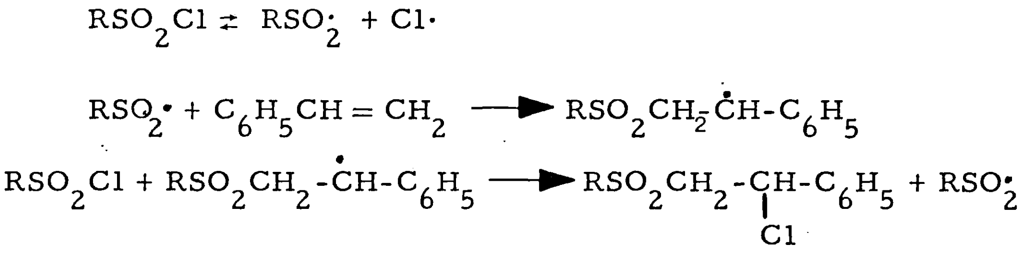


Fig.2.1.6 - 1

### 2.1.7. Addition of sulphonyl halides to alkenes and alkynes.

In the presence of light or benzoyl peroxides, sulphonyl halides add to alkenes to form β-halogenosulphones. The accompanying polymerisation that takes place with some alkenes is minimised by the addition of copper(II) chloride and ethylamine hydrochloride[38]



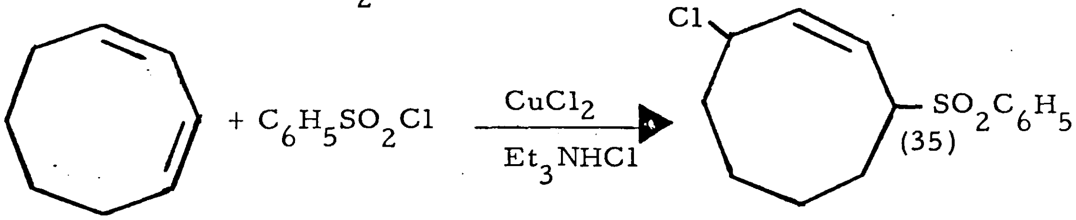
$$RSO_2Cl \rightleftarrows RSO_2^{\cdot} + Cl^{\cdot}$$

$$RSO_2^{\cdot} + C_6H_5CH=CH_2 \longrightarrow RSO_2CH_2\dot{C}H\text{-}C_6H_5$$

$$RSO_2Cl + RSO_2CH_2\text{-}\dot{C}H\text{-}C_6H_5 \longrightarrow RSO_2CH_2\text{-}\underset{Cl}{CH}\text{-}C_6H_5 + RSO_2^{\cdot}$$

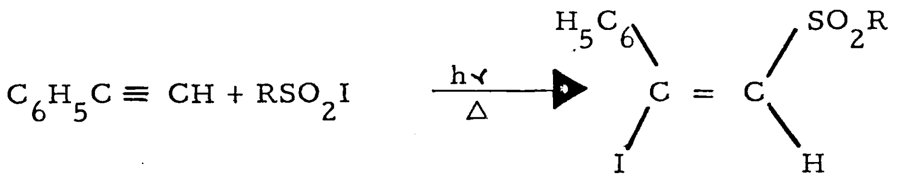
(34)

Conjugated dienes undergo 1,4-addition of sulphonyl chlorides in the presence of $CuCl_2$ to give unsaturated chloro sulphones.[39]



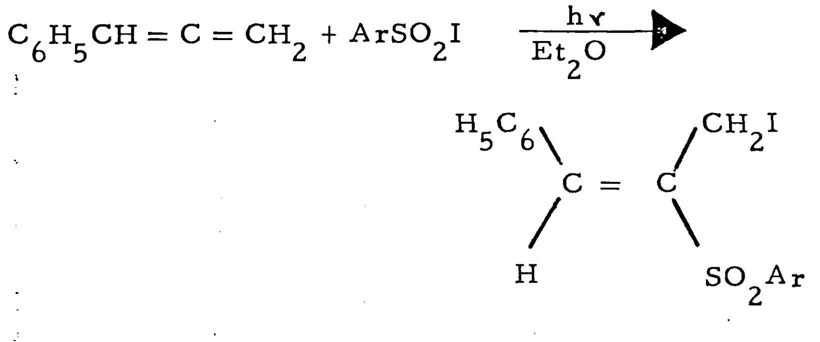
(35)

Sulphonyl iodides react with acetylenes to give good yields of β-halogenovinyl sulphones[40,41] in a reaction catalysed by light and induced by heat.



(36)

The addition of sulphonyl iodides to allenes is identical to the above reaction



(37)

### 2.1.8. Miscellaneous Preparations.

H. Burton and H. B. Hopkins found that a mixture of benzene sulphonyl chloride and silver perchlorate readily sulphonylates aromatic hydrocarbons. They assumed that the reactive species in this process was the benzene sulphonyl perchlorate[42].

$$PhSO_2Cl + AgOClO_3 \rightleftarrows PhSO_2OClO_3 + AgCl \qquad (38)$$

F. Klages and I. E. Malecki later confirmed this result using equimolar amounts of silver perchlorate at -10°C. The precipitate of silver bromide formed was quantitative and the species in solution found to be appreciably dissociated. This solution reacted readily with aromatic compounds including those with electron withdrawing groups like chlorobenzene and bromobenzene to give very high yields of sulphones. This observation suggested the presence of a highly reactive arene sulphonylium ion formed from the dissociation of the sulphonyl perchlorate[43].

$$\begin{aligned} &ArSO_2OClO_3 \rightleftarrows ArSO_2^{+} + ClO_4^{-} \\ &ArSO_2^{+} + Ar'H \longrightarrow ArSO_2Ar' \end{aligned} \qquad (39)$$

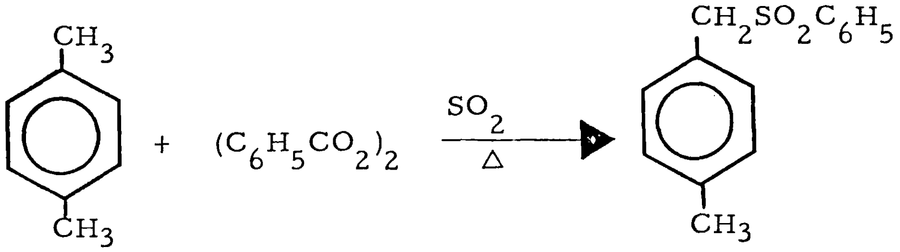
Alkane sulphonyl bromides react with silver trifluoromethane sulphonate to form alkyl sulphonic trifluoromethane sulphonic anhydrides. These unsymmetrical anhydrides react readily with aromatic hydrocarbons to form alkyl aryl sulphones (45).

$$\begin{aligned} &RSO_2Br + CF_3SO_3Ag \longrightarrow RSO_2OSO_2CF_3 + AgBr \\ &RSO_2OSO_2CF_3 + ArH \longrightarrow RSO_2Ar + CF_3SO_3H \end{aligned} \qquad (40)$$

The isomeric distribution of the sulphone products corresponds to that of the Friedel-Crafts catalysed reaction suggesting that it is the sulphonylium ions rather than the sulphonyl halide catalyst complexes that are the reactive species for the catalysed reactions.

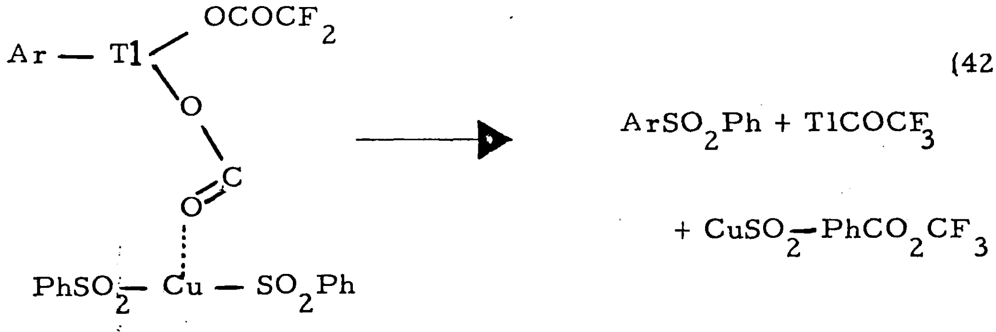
Aryl sulphonyl bromides react in a similar way to give diaryl sulphones. This reaction takes place under milder conditions than the Friedel-Crafts reaction and the positional selectivities of the mixed anhydrides are comparable to those of other sulphonylating agents.[46]

Thermal decomposition of benzoyl peroxides in the presence of sulphur dioxide and aromatic hydrocarbons results in the formation of sulphones. The yields are very low and it is suggested that phenyl radicals play an important part in the mechanism of this reaction.[44]



(41)

Copper(II) salts of benzene sulphinic acid react readily with aryl thallium bistrifluoroacetate to give diaryl sulphones.[47] This displacement is believed to proceed by a synchronous nucleophilic substitution following the coordination of copper by a ligand. The method seems to be improved by the presence of an electron withdrawing group such as a chlorine on the aryl group attached to the thallium. The yields range from 41-63%.



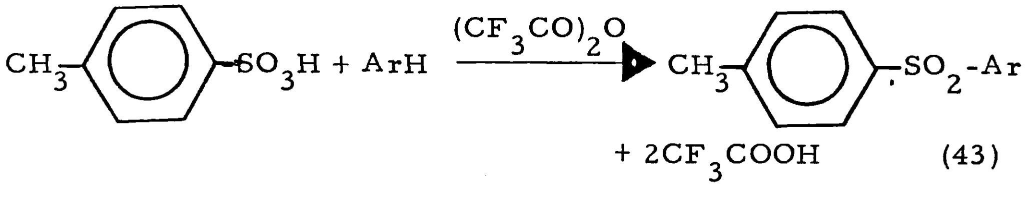
(42)

## 2.2. RESULTS AND DISCUSSION.

### 2.2.1. The synthesis of unsymmetrical diaryl sulphones

### 2.2.1.1 The reaction between *p*-toluene sulphonic acid and an aromatic hydrocarbon in the presence of trifluoroacetic anhydride.

Some unsymmetrical sulphones have been prepared by dissolving *p*-toluene sulphonic acid in trifluoroacetic anhydride and subsequent addition of an aromatic hydrocarbon by a procedure similar to that described by E.J.Bourne et al.[2] The yields obtained by this method were low since the sulphones were precipitated from aqueous alcohol in the presence of trifluoroacetic acid of unreacted *p*-toluene sulphonic acid. Consequently, most of the product remained in solution. However the reaction conditions were fairly mild requiring only gentle warming and the reaction was fast. The results obtained by this method are given on table 2.2.1-1. The overall reaction may simply be written as:-



(43)

In order to improve the yield anhydrous *p*-toluene sulphonic acid was used (prepared by heating the monohydrate at 140°C for 30 minutes) and the reactants were all dissolved in dry nitromethane. The removal of the free acids from the reaction mixture was facilitated by the addition of aqueous sodium carbonate. These improvements to the method of synthesis resulted in increased yields. Table 2.2.1-2 gives the yields obtained under these new conditions.

The percentages in this table are yields obtained simply after drying the crude sulphone overnight. The purification of some of these products was difficult. Sulphones of mesitylene, biphenyl, xylene and chlorobenzene were easy to purify giving sharp melting points after only one recrystallisation while others required several

Table 2.2.1 - 1

Crude yields and melting points of major isomers of sulphones prepared by a procedure similar to that of E. J. Bourne et al.[2]

| Aromatic hydrocarbon | % Yield of crude sulphone | Major isomer substituted diphenyl sulphone | m.p. of sulphone | Literature m.p. |
|---|---|---|---|---|
| Toluene | 32.0 | 4,4'-dimethyl- | 157°C | 158 (8) |
| Ethylbenzene | 34.0 | 4-ethyl, 4'methyl- | 108°C | 109-110(43) |
| Cumene | 36.2 | 4-isopropyl, 4'-methyl- | 100°C | 98 (140) |
| Mesitylene | 56.0 | 2,4,4'6-tetramethyl- | 117°C | 118 (46) |
| Anisole | 42.0 | 4-methoxy, -4' methyl- | 103°C | 103 (2) |
| Phenetole | 40.0 | 4-ethoxy, 4' methyl- | 160°C | 159-160(43) |
| Biphenyl | 42.5 | 4 methyl-4'phenyl- | 201°C | |
| Nitrobenzene | - | - | | |
| Chlorobenzene | - | - | | |

Table 2.2.1 - 2

Crude yields and melting points of major isomers of sulphone products prepared from p toluene sulphonic acid with the improved method.

| Aromatic hydrocarbon | % Yield of crude sulphone | Major isomer substituted diphenyl sulphone | m.p. of sulphone | Literature m.p. |
|---|---|---|---|---|
| Toluene | 47.8 | 4,4'-dimethyl | | |
| Ethylbenzene | 69.4 | 4 ethyl, 4'-methyl- | | |
| m-Xylene | 57.3 | 2,4,4'-trimethyl- | 50°C | 49 (19) |
| Mesitylene | 70.7 | 2,4,4,'6-tetramethyl- | 118°C | 118 (46) |
| Cumene | 55.7 | 4-isopropyl, 4'-methyl- | | |
| Anisole | 72.7 | 4-methoxy, 4'-methyl- | | |
| Phenetole | 69.4 | 4-ethoxy, 4'-methyl- | | |
| Biphenyl | 66.7 | 4-methyl 4'-phenyl- | 201°C | |
| Chlorobenzene | 18.9 | 4-chloro, 4' methyl- | 124°C | 124 (46) |
| Nitrobenzene | | | | |

recrystallisations before sharp melting could be obtained. It therefore became evident that rather than one product, a number of isomers were formed in these reactions. The analysis of the crude product was therefore an obvious necessity.

The effects of substituents on the aromatic hydrocarbon is clearly demonstrated here by the percentage yields of these products. Aromatic hydrocarbons containing electron donating groups such as anisole, phenetole and mesitylene give very high yields while those with electron-withdrawing groups such as chlorobenzene give poor yields. Nitrobenzene having the strongest electron-withdrawing group in this series does not react at all.

### 2.2.1.2. The g.l.c. of the unsymmetrical diaryl sulphones.

The crude products of the reaction of p-toluene sulphonic anhydride with aromatic hydrocarbons in the presence of trifluoroacetic anhydride were analysed by gas-liquid chromatography (g.l.c.) The conditions for the separation of these isomeric sulphones are given in detail in Chapter 5. The isomer distribution, $R_t$ values, and the relative abundance of each isomer are shown in Table 2.2.1-3. All the retention times ($R_t$) were calculated with respect to diphenyl sulphone.

Since the major products (i.e. in most cases the para-para disubstituted diphenyl sulphones) had already been isolated, purified by recrystallisation and characterised by their m.p.s N.M.R., infra-red spectra and mass spectra, it was therefore easy to identify these in a mixture by their $R_t$ values. In the case of the minor isomers, the task of identifying their structure was relatively difficult. The column (5% Silicone S.E.30 on Chromosorb W) used for the separation of these isomers relies on relative polarity for its separations. The more polar the compound the smaller the retention time. Para-ortho disubstituted diphenyl sulphones are relatively more polar than para-meta disubstituted diphenyl sulphones and hence have smaller $R_t$ values. It was therefore on this basis

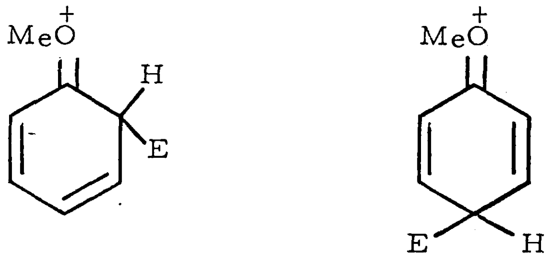
Table 2.2.1 - 3

Isomers, $R_t$ values and percentages of each isomer in the reaction mixture of p toluene sulphonic acid with aromatic hydrocarbon.

| Aromatic hydrocarbon | Substituted diphenyl sulphone | $R_t$ values obtained | Standard $R_t$ values | % of isomer |
|---|---|---|---|---|
| Toluene | 4,4'-dimethyl- | 0.67 | 0.66 | 67.3 |
| | 4,2'-dimethyl- | 0.57 | | 20.8 |
| | 4,3'-dimethyl- | 0.60 | | 12.8 |
| Ethylbenzene | 4 - ethyl 4'-methyl- | 0.92 | 0.92 | 80.7 |
| | 2 - ethyl 4'-methyl- | 0.66 | | 9.7 |
| | 3 - ethyl 4'-methyl- | 0.76 | | 9.6 |
| Cumene | 4-isopropyl 4'-methyl- | 1.07 | 1.06 | 84.6 |
| | 2-isopropyl 4'-methyl- | 0.84 | | 12.8 |
| m-Xylene | 2,4,4'-trimethyl- | 0.89 | 0.89 | 100 |
| Mesitylene | 2,4,6,4'-tetramethyl- | 1.00 | 1.00 | 100 |
| Anisole | 4-methoxy 4'-methyl- | 1.10 | 1.11 | 53.2 |
| | 2-methoxy 4'-methyl- | 0.84 | | 46.8 |
| Phenetole | 4-ethoxy 4'-methyl- | 1.41 | 1.41 | 51.1 |
| | 2-ethoxy 4'-methyl- | 1.00 | | 48.9 |
| Biphenyl | 4-methyl 4'phenyl- | not analysed | | - |
| Chlorobenzene | 4-chloro 4'-methyl | 0.70 | 0.70 | 100 |
| Nitrobenzene | no reaction | — | — | — |

that the structure of the minor isomers was assigned.

Those products that had been found difficult to purify by recrystallisation contained more than one isomer, in some cases three isomers. The product distributions from the reactions of p-toluene sulphonic acid with anisole and phenetole showed percentages of para substitution comparable to the yield of the ortho products. The methoxy and ethoxy group have a strong +M effect and a -I effect. Although the -I effect decreases the reactivity of the ortho position more than that of the para position, this effect is only significant with highly reactive electrophiles and should therefore be insignificant with the para toluene sulphonylium cation, a weak electrophile. More important here are the stabilities of the cationic $\sigma$-complexes that are intermediates in electrophilic substitution (Fig. 2.2.1-4). Quantum mechanical calculations suggest that the para-quinonoid complex has a significantly lower energy than the ortho-quinonoid complex. It can therefore be expected that the route to the para-product will be favoured thereby reducing the ortho/para ratio from a statistical 2:1 irrespective of the steric effects of the methoxy group.[133, 134]



where E is the electrophile

Fig. 2.2.1 - 4

The steric effect is also important in explaining the ortho/para ratio in electrophilic substitution reactions of substituted aromatic hydrocarbons. The following ortho/para ratios were obtained in the reaction of these aromatic hydrocarbons with toluene sulphonic acid and trifluoroacetic anhydride:-

| $PhCH_3$ | $PhCH_2CH_3$ | $PhCH(CH_3)_2$ |
|---|---|---|
| 0.30 | 0,12 | 0,03 |

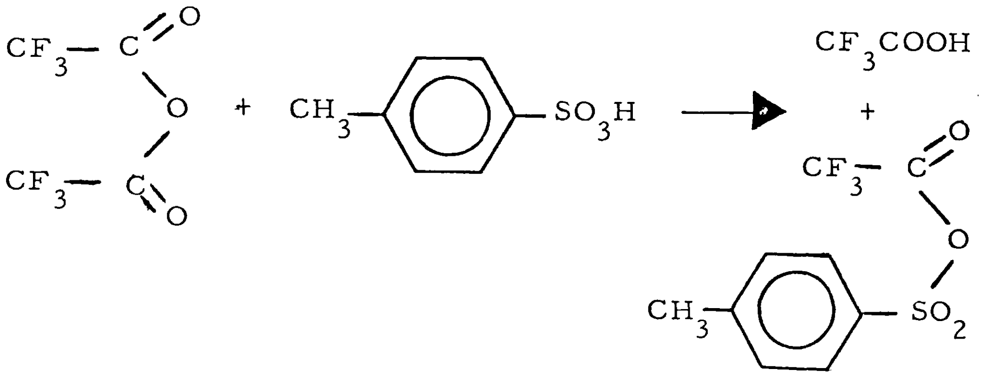
There is no doubt that the substituent on the aromatic ring interferes with the reaction at the ortho position. The bulkier the group, the more significant is the inhibition of the reaction at that position.

Isomer distribution has often been used to provide evidence about the nature of the sulphonylating agent in electrophilic substitution. A table comparing the distribution of the isomers of ditolylsulphone, obtained with various sulphonylating reagents and Lewis acid catalysts, is given by F. Effenberger and K. Huthmacher[46]. Table 2.2.1-5 compares the present results (first column) with those obtained by F. Effenberger and K. Huthmacher. The orientation is similar to that observed for the Friedel-Crafts catalysed reactions. The Friedel-Crafts reactions have been studied in detail and sulphonylium ions found to be responsible for the electrophilic attack on the aromatic ring. Therefore it is suggested that sulphonylation of aromatic hydrocarbons with p-toluene sulphonic acid in the presence of trifluoroacetic anhydride proceeds by way of intermediacy of sulphonylium ions. It is interesting to note that 4,3'-dimethyl-diphenyl-sulphone is not formed in the Lewis acid catalysed sulphonylation reactions while p-toluene sulphonyl trifluoromethane sulphonate gives 5% of the isomer. This observation reinforces earlier suggestions that a mixed anhydride is formed between trifluoroacetic anhydride and p-toluene sulphonic acid analogous to the toluene sulphonyl trifluoromethane sulphonate reagent (Column 2).

Table 2.2.1 - 5

A table comprising the isomer abundance of ditolyl sulphones in this reaction with other sulphylating reagents.

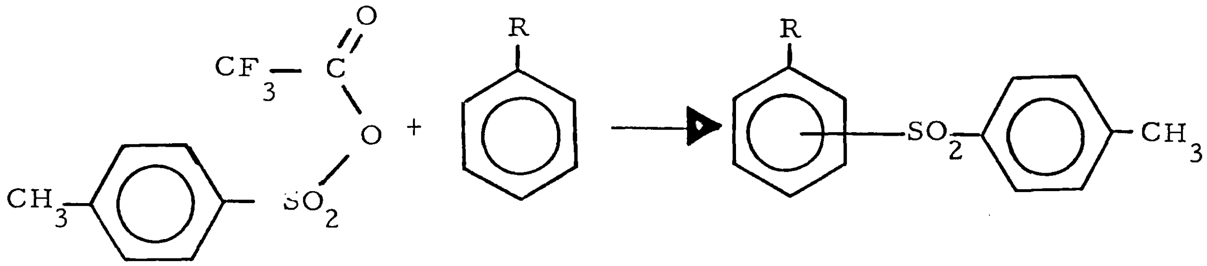
| This result | K.Huthmacher and F. Effenberger | | | | | |
|---|---|---|---|---|---|---|
| $(CF_3CO)_2O$ + | p.$CH_3C_6H_4SO_2$ | p.$CH_3C_6H_4SO_2Cl$ + | | | | ditolyl sulphone |
| p.$CH_3C_6H_4SO_3H$ | $SO_3CF_3$ | $AlCl_3$ | $SbCl_5$ | $TlCl_4$ | $FeCl_3$ | isomer % |
| 67 3 | 53 | 55.4 | 58 | 54 | 67.2 | p, p-ditoly- |
| 12 8 | 5 | - | - | - | - | p tolyl <u>m</u> tolyl- |
| 20 8 | 42 | 44.6 | 42 | 45 | 32.8 | p tolyl <u>O</u> tolyl- |



(44)

The mechanism of this reaction will be discussed in detail in Chapter 3. Now considering the formation of three isomeric products a representation of the reaction of a sulphonic acid and an aromatic hydrocarbon can be given thus:-

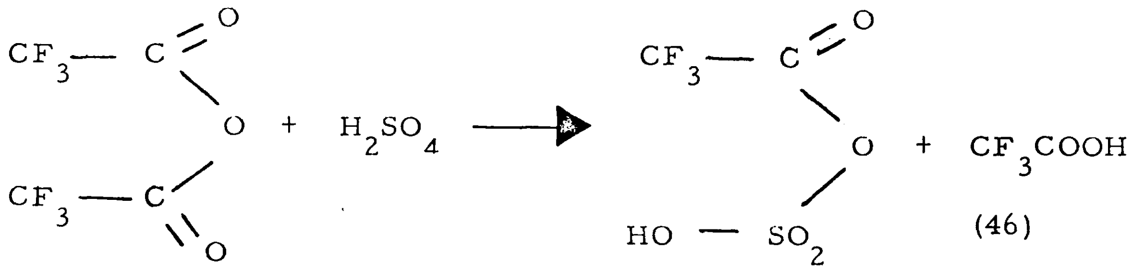
(45)



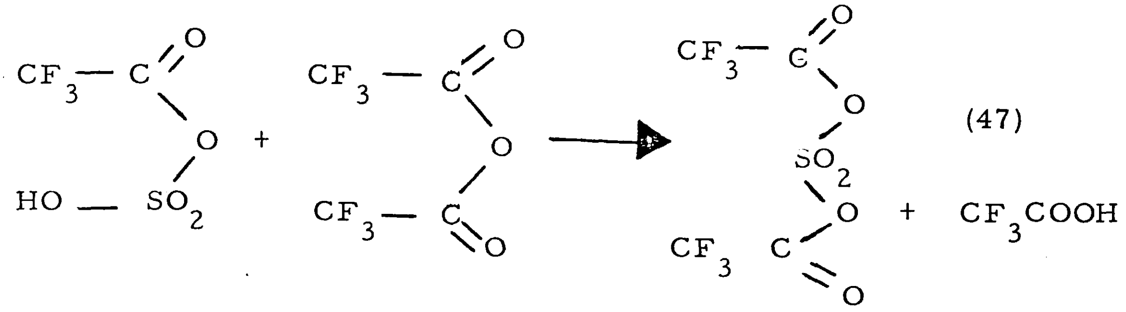
## 2.2.2. The synthesis of symmetrical diaryl sulphones.

### 2.2.2.1. The reaction between sulphuric acid and an aromatic hydrocarbon in the presence of trifluoroacetic anhydride.

An attempt was made to find reagents other than sulphonic acids that would undergo a sulphonylation reaction and perhaps produce sulphones more effectively. Sulphuric acid is one such reagent investigated for this purpose. It was anticipated that sulphuric would react with trifluoroacetic anhydride to form mixed anhydrides thus:-

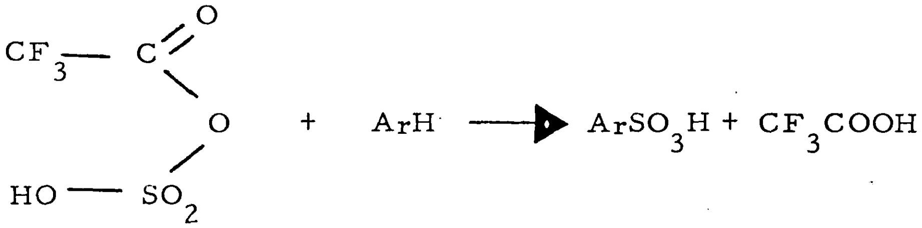


(46)

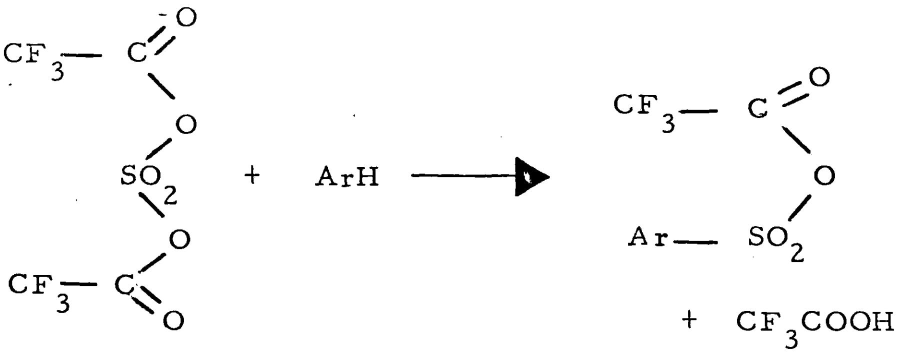


(47)

This reaction is known to occur with acetic anhydride[102]. These anhydrides can therefore interact with aromatic hydrocarbons as follows:-



(48)

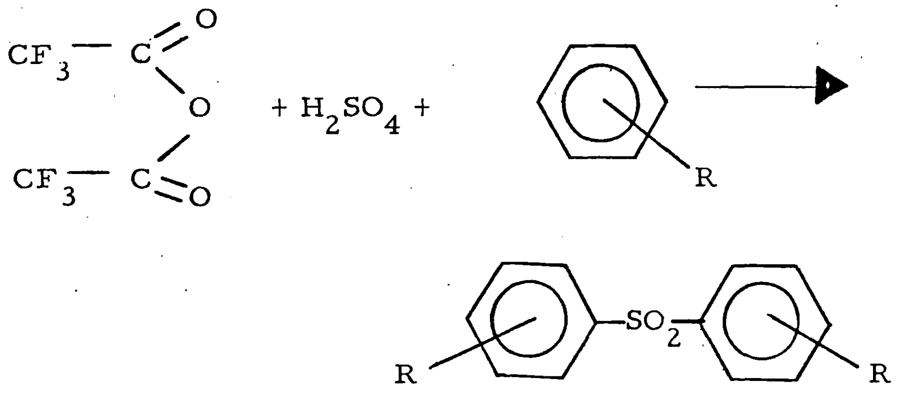


(49)

The sulphonic acid produced in reaction 48 could also react further in excess trifluoacetic anhydride with an aromatic hydrocarbon by reaction 44 and 45 to give sulphones. It was on this basis therefore that sulphuric acid was chosen.

Sulphuric acid was found to react with aromatic hydrocarbons in the ratio of 1:2 in the presence of trifluoroacetic anhydride. The reaction was observed to take place in the absence of a solvent but this sometimes resulted in charring of the hydrocarbon and thereby reducing the yield of the final product. In many instances the reaction was retarded by the insolubility of sulphuric acid in trifluoroacetic anhydride. Nitromethane was found to be the only solvent inert to the interaction between trifluoroacetic anhydride and sulphuric acid and in which both compounds have a high solubility.

The reaction conditions for the sulphonylation in nitromethane are fairly mild. Sulphuric acid and trifluoroacetic anhydride are dissolved in nitromethane and the reaction mixture allowed to equilibriate for 15 minutes. The aromatic hydrocarbon is then added and the resulting solution warmed gently for another 30 minutes. In the case of activated aromatic hydrocarbons such as mesitylene, anisole and phenetole, warming is not necessary since the reaction proceeds spontaneously to completion at room temperature. For the best results this reaction should be carried under anhydrous conditions. The reaction can be represented thus:-



(50)

Table 2.2.2-1 gives the total yields of the crude products and m.p.s. of the major isomers. The yields in this reaction are very high; they are in fact higher than those obtained in Lewis acid catalysed reactions and comparable with those obtained using arenesulphonyl trifluoromethane sulphonates[46] and arenesulphonyl perchlorates.[43]

The effect of substituents is also very evident here. Activated aromatic hydrocarbons give almost 100% yields in this reaction while those aromatic hydrocarbons with electron-withdrawing substituents such as chlorobenzene give very poor yields. Nitrobenzene appears to undergo a different type of reaction probably associated with the nitrogroup; the originally yellow solution darkens to give a dark brown colour and no sulphone can be isolated.

### 2.2.2.2. The g.l.c. of symmetrical sulphones.

The isomer distribution of the products obtained in section 2.2.1.2 in which the reaction was carried out with p-toluene sulphonic acid often gave three isomers, resulted in sceptism as to whether the reaction of sulphuric acid with aromatic hydrocarbons and trifluoroacetic anhydride would be of any synthetic value. Here the number of isomer products possible from a mono-substituted aromatic hydrocarbon should be six. This would present the difficulty of quantitatively separating isomers, the retention times during g.l.c. of which are very close. However this was not found in practice. The maximum number of isomers found was three. Their distribution paralleled those of the products when p-toluene sulphonic acid was used. The results for the separation of the isomers by g.l.c. obtained under exactly identical conditions as in the previous synthesis are given in Table 2.2.2-2.

The most significant finding about these results is that a new method for the synthesis of sulphones has been discovered which has isomeric products comparable to other sulphonylation reaction. Table 2.2.2-3 gives a comparison of

Table 2.2.2 - 1

A table of crude yields and melting points of major isomers of sulphone products prepared from the reaction of sulphuric acid with aromatic hydrocarbons and trifluoroacetic anhydride.

| Aromatic hydrocarbon | % Yield of sulphone | Major isomer substituted diphenyl sulphone | m.p. of sulphone | Literature m.p. |
|---|---|---|---|---|
| Benzene | 61.3 | unsubstituted - | 126°C | 128 (8) |
| Toluene | 87.6 | 4, 4'-dimethyl- | 158°C | 158 (8) |
| Ethylbenzene | 83.2 | 4'4'-dimethyl- | 99-100°C | 102 (143) |
| Cumene | 80.1 | 4, 4'-di-isopropyl- | 95°C | 96 (140) |
| Mesitylene | 99.1 | 2, 2,'4, 4', 6, 6'-hexamethyl- | 201-2°C | 201 (19) |
| m-Xylene | 73.2 | 2, 2', 4, 4'-tetramethyl- | 122-3°C | 122 (140) |
| Anisole | 98.5 | 4, 4'-dimethoxy | 129-30°C | 129 (14) |
| Phenetole | 95.9 | 4, 4'-diethoxy- | 160-1°C | 159 (141) |
| Diphenylmethane | 75.1 | 4, 4'-dibenzyl- | 171°C | |
| Chlorobenzene | 36.1 | 4', 4-dichloro- | 148-9°C | 148 (8) |
| Nitrobenzene | no sulphone | - | - | - |

Table 2.2.2 - 2

Isomers, $R_t$ values and percentages of each isomer formed in the reaction of sulphuric acid with an aromatic hydrocarbon and trifluoroacetic anhydride.

| Aromatic hydrocarbon | substituted diphenyl sulphone | $R_t$ value obtained | Standard $R_t$ values | % of isomer |
|---|---|---|---|---|
| Benzene | unsubstituted | 1.00 | 1.00 | 100 |
| Toluene | 4, 4'-dimethyl- | 0.65 | 0.66 | 62.2 |
| | 4, 2'-dimethyl- | 0.56 | | 36.2 |
| | 4, 3'-dimethyl- | 0.58 | | 1.6 |
| Ethylbenzene | 4, 4'-diethyl- | 1.19 | 1.20 | 71.9 |
| | 4, 2'-diethyl- | 0.85 | | 12.2 |
| | 4, 3'-diethyl- | 0.97 | | 15.9 |
| Cumene | 4, 4'-di-isopropyl- | 1.51 | 1.50 | 79.8 |
| | 4,2'-di-isopropyl- | 1.00 | | 5.1 |
| | 4, 3'-di-isopropyl- | 1.22 | | 15.0 |
| Mesitylene | 2, 2'-4, 4'-6, 6'-hexamethyl- | not analysed | | 100 |
| m-Xylene | 2, 2', 4, 4' tetramethyl- | 0.96 | 1.00 | 100 |
| Anisole | 4, 4' dimethoxy- | 1.76 | 1.75 | 61.9 |
| | 4, 2' dimethoxy- | 1.34 | | 31.1 |
| Penetole | 4, 4' diethoxy- | 2.60 | 2.60 | 62.3 |
| | 4, 2' diethoxy- | 1.80 | | 37.1 |
| Diphenylmethane | 4, 4' dibenzyl- | not analysed | | 100 |
| Chlorobenzene | 4, 4' dichlorobenzene | " " | | |
| Nitrobenzene | - | - | - | - |

Table 2.2.2. - 3

A table comparing the isomer abundance of ditolyl sulphone in this reaction with the previous results and those of F. Effenberger and K. Huthmacher.

| F. Effenberger and K. Huthmacher | Previous results | This work | |
|---|---|---|---|
| p-$CH_3C_6H_4SO_2$-$SO_3CF_3$. | p-$CH_3C_6H_4SO_3H$ + $(CF_3CO)_2O$ | $CH_3C_6H_5$ + $H_2SO_4$ + $(CF_3CO)_2O$ | ditolyl sulphone isomer % |
| 0°C | 60 - 80°C | 60 - 80°C | |
| 53 | 67.3 | 62.2 | p, p ditolyl |
| 5 | 12.8 | 1.6 | p, m ditolyl |
| 42 | 20.8 | 36.2 | p, o ditolyl |

the isomeric products obtained in this work and that of F. Effenberger and K. Huthmacher[46] in the synthesis ditolylsulphone.

Secondly, trifluoroacetic anhydride and sulphuric acid react in the same way with aromatic hydrocarbons as other sulphonylating reagents. The evidence for this is provided by the mole fraction of the isomeric products which is similar to those of other sulphonylating reactions which proceed via sulphonium ions. One of the intermediates responsible for the attack on one of the aromatic hydrocarbons is probably similar to toluene sulphonyl trifluoromethane sulphonate as shown below:-

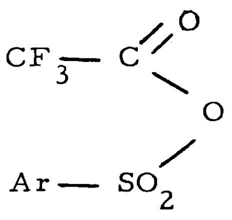


Fig. 2.2.2 - 4.

Finally, two electrophilic aromatic substitution reactions occur in this reaction. The first involves an attack by a reagent formed between trifluoroacetic anhydride and sulphuric acid on the first aromatic hydrocarbon to form an intermediate product. This is followed by an attack by the intermediate product on the second aromatic hydrocarbon to form sulphones. The number of isomers formed in this reaction suggests that one of these two substitution reactions is regiospecific. It is difficult at the moment to say whether it is the first or the second step since it is not yet known whether trifluoroacetyl or di(trifluoroacetyl) sulphate is responsible for the initial attack. One can only speculate that if the di(trifluoroacetyl) sulphate was the only intermediate responsible for the initial attack, it is likely that it would be sterically hindered in the <u>ortho</u> position since it is such a large molecule. This controversy will be dealt with in the next section.

### 2.2.3. The synthesis of unsymmetrical diaryl sulphones.

### 2.2.3.1. The reaction between sulphuric acid and two aromatic hydrocarbons in the presence of trifluoroacetic anhydride.

The previous reaction of sulphuric acid with an aromatic hydrocarbon and trifluoroacetic anhydride has left one problem unresolved. Which of the two electrophilic substitution reaction is regiospecific?

$$\text{sulphonylating reagent} \xrightarrow[\text{I}]{\text{Ar'H}} \begin{array}{c}\text{intermediate}\\\text{product}\end{array} \xrightarrow[\text{II}]{\text{Ar''H}} \text{Ar'SO}_2\text{Ar''} \qquad (51)$$

An attempt to solve this problem was made by the synthesis of unsymmetrical diaryl sulphones. This experiment involved a dropwise addition of an aromatic hydrocarbon (Ar'H)(1 mole) to a solution of trifluoroacetic anhydride (2 moles) and sulphuric acid (1 mole) in nitromethane. This was followed by the addition of a different aromatic hydrocarbon (1 mole) and the reaction mixture subjected to the same reaction conditions as those in the synthesis of the symmetrical diaryl sulphones.

The first aromatic hydrocarbons was added dropwise in order to avoid symmetrical diaryl sulphone contamination. This was done so that the rate of addition of the aromatic hydrocarbon did not exceed the rate of formation of the intermediate product. In this way, it was hoped that from the distribution of the isomeric products, an answer would be found as to which of the two electrophilic substitution reaction was regiospecific. Table 2.2.3 - 1 lists a series of such reactions and their corresponding yields where Ar'H is the hydrocarbon added first and Ar''H second. The overall yields were fairly high.

Table 2.2.3 - 1

Crude yields of unsymmetrical sulphones prepared by the reaction of sulphuric acid with two different aromatic hydrocarbons and trifluoroacetic anhydride.

| First aromatic hydrocarbon Ar'H | Second aromatic hydrocarbon Ar''H | $Ar'SO_2Ar''$ % yield |
|---|---|---|
| Toluene | Benzene | 52.2 |
| Toluene | Mesitylene | 74.5 |
| Toluene | Anisole | 70.0 |
| Toluene | m-Xylene | 66.1 |
| Toluene | Cumene | 60.1 |
| Benzene | Toluene | 50.0 |
| m-Xylene | Mesitylene | 70.0 |
| m-Xylene | Anisole | 72.4 |

The reactivity of both the reacting hydrocarbons seemed to be the main yield determining factor. The order in which the aromatic hydrocarbons were added did not seem to affect the yield. An example of this is given by the reaction of benzene and toluene. When the order of addition was reversed, there was no substantial change in total yield of the products.

### 2.2.3.2. The g.l.c. of unsymmetrical diaryl sulphones.

If the synthesis of symmetrical diaryl sulphones using sulphuric acid and trifluoroacetic anhydride had resulted in all the thermodynamically possible isomers, this experiment would never have been contemplated at all. There could be nine possible products (excluding the symmetrical diaryl sulphone by-products). However it was anticipated that only a few would be formed and so the experiment would be a practical synthetic method. Even when the possibility of so many products had been allayed, the presence of symmetrical diaryl sulphone contamination still remained. The reaction products obtained from the above described reaction were analysed by g.l.c. and a table of the various isomers, their $R_t$ values and abundance is given below (Table 2.2.3-2).

The results were simpler than had been expected. Symmetrical diaryl sulphone contamination was minimal (e.g. ca. 3% in the reaction of xylene and anisole). The only case in which symmetrical diaryl sulphone percentage was large, was the reaction of anisole and toluene where 24% of the total yield was due to the two dianisyl sulphone isomers shown in table 2.2.3 - 2.

It seems that the reaction between the sulphonylating reagent and the aromatic hydrocarbon added in the first stage is regiospecific and substitution occurs at the <u>para</u> position, but the substitution on the hydrocarbon of the next stage follows the usual pattern of isomer distribution. An illustrative example is the synthesis of methyl diphenyl sulphone. When

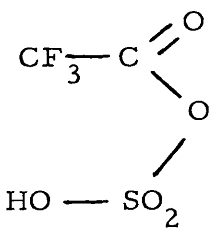
Table 2.2.3. - 2

$R_t$ values and isomer abundance of sulphones obtained from the reaction of sulphuric acid with two different aromatic hydrocarbons and trifluoroacetic anhydride.

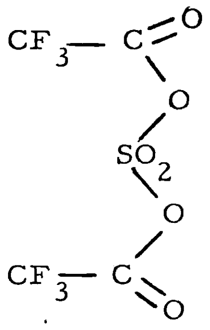
| Ar'H Aromatic hydrocarbon I | Ar''H Aromatic hydrocarbon II | Substituted diphenyl sulphone | $R_t$ values obtained | Standard $R_t$ values | % of isomer |
|---|---|---|---|---|---|
| Toluene | Benzene | 4-methyl- | 0.48 | 0.48 | 100 |
| Benzene | Toluene | 4-methyl- | 0.46 | | 49.9 |
| | | 2-methyl- | 0.41 | | 42.2 |
| | | 3-methyl- | 0.32 | | 7.9 |
| Toluene | Mesitylene | 2, 4, 4'6 tetramethyl- | 1.00 | 1.00 | 100 |
| Toluene | Cumene | 4-isopropyl 4'-methyl- | 1.06 | 1.06 | 84.2 |
| | | 2-isopropyl 4'-methyl- | 0.69 | | 4.2 |
| | | 3-isopropyl 4'-methyl- | 0.86 | | 11.6 |
| Toluene | Anisole | 4-methoxy 4'-methyl | 1.11 | 1.11 | 43.5 |
| | | 2-methoxy 4'-methyl | 0.86 | | 32.0 |
| | | 4, 4' dimethoxy- | 1.75 | | 14.0 |
| | | 2, 4' dimethoxy- | 1.35 | | 10.5 |
| m-Xylene | Mesitylene | 2, 2', 4, 4'6 pentamethyl | 1.15 | | 100 |
| m-Xylene | Anisole | 4-methoxy 2', 4',dimethyl- | 1.38 | | 59.7 |
| | | 2-methoxy 2, 4' dimethyl | 1.00 | | 37.2 |
| | | 4, 4'-dimethoxy- | 1.75 | 1.75 | 3.1 |
| Toluene | m-Xylene | | 0.85 | 0.89 | 100 |

toluene is Ar'H and benzene is Ar''H only one isomer is produced, 4-methyl-diphenyl sulphone, i.e. only the para position in toluene has reacted. Reversal of the addition, i.e. benzene is A'rH and toluene is Ar"H gives three isomers, showing that the toluene added during the second stage is substituted in the usual regio selective manner. Reaction 52 illustrates this selectivity.

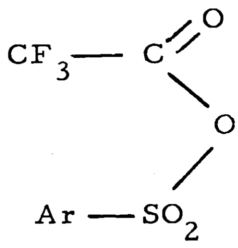
Another significant finding about this regiospecificity of the first stage of this electrophilic substitution is that it helps to identify the nature of the sulphonylating reagent.



and

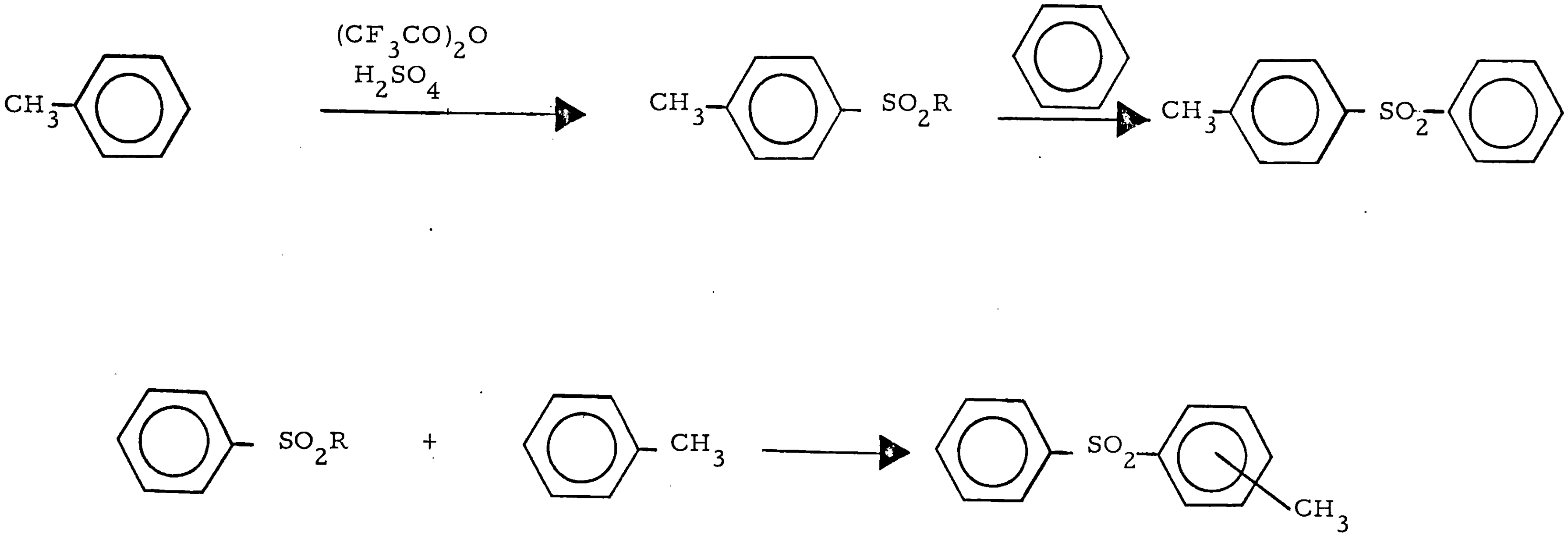


There is no reason why the mono trifluoroacetyl sulphuric acid should be regiospecific since it is similar to the intermediate involved in the second step of this reaction.



The di(trifluoroacetyl) sulphate is therefore the most likely sulphonylating reagent since it is large and is likely to be sterically hindered at the ortho position. However this evidence alone is not enough to exclude the monotrifluoroacetyl sulphuric acid as a sulphonylating reagent.

Finally, this reaction is a great success as a synthetic method. It provides a simple and inexpensive method for the



where $R = [\ CF_3\overset{\overset{O}{||}}{C} - O - \ ]$

(three isomers)

(52)

synthesis of a variety of diaryl sulphones in good yields, especially since aromatic hydrocarbons are readily accessible and the conditions under which the reaction occurs are fairly mild.

## 2.2.4 Structural analysis by spectroscopic methods.

### 2.2.4.1 Infra-red Spectroscopy.

The infra-red spectra of sulphonyl compounds have been extensively studied [110, 112]. The $SO_2$ group is tetrahedral and gives characteristic bands corresponding to the assymetric and symmetric stretching modes about the sulphur atom. These modes are given respectively below.

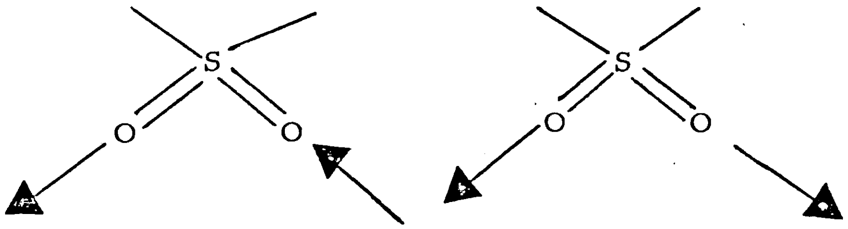


Fig. 2.2.4 - 1.

E.A.Robinson[110] suggested that infrared absorptions in the ranges between 1358 - 1336 $cm^{-1}$ correspond to the assymmetric vibration ( $\nu_{as}$ ) and those between 1169 - 1159 $cm^{-1}$ to the symmetric vibrations ( $\nu_s$ ). However Momose et al[111] have reported values as low as 1282 $cm^{-1}$ for the assymmetric and 1143 $cm^{-1}$ for the symmetric vibrations. Table 2.2.4.2 gives the frequencies obtained for the symmetric and assymmetric vibrations of symmetrical diaryl sulphones studied here.

Table 2.2.4 - 2.

Infra-red of symmetrical diaryl sulphones prepared in Sect. 2.2.2.

| Substituted diphenyl sulphone | $\nu_{as}$ cm$^{-1}$ | $\nu_{s}$ cm$^{-1}$ |
|---|---|---|
| 4,4'-dimethyl- | 1320 | 1160 |
| 2,2,'4,4',6,6'-hexamethyl- | 1300 | 1140 |
| 4,4'-diethoxy- | 1300 | 1150 |
| 4,4'-dimethoxy- | 1305 | 1145 |
| 4,4' dibenzyl- | 1310 | 1160 |

The dominant influence of the S = O stretching vibrations are the inductive effects of the substituent groups. The sulphur-oxygen bond can be considered as a hybrid between the structures S = O and $\overset{+}{S} - \overset{-}{O}$. In the S = O situation, the electrons are equally shared in a covalent bond between the sulphur and the oxygen atoms. This situation is favoured by an electronegative group attached to the sulphur atom. Decreasing the electronegativity of the substituent results in the double bond becoming polar and thus approaching the $\overset{+}{S} - \overset{-}{O}$ situation. An increase in the double bond character due to the increase in the electronegativity of the substituent, will increase the force constant of the bond and thus the $\nu_{as}$ and $\nu_{s}$ vibrations will occur at higher frequencies. Conversely an increase in electron density will shift the absorption to lower frequencies.

### 2.2.4.2 Nuclear Magnetic Resonance (N.M.R.)

Proton N.M.R. has been used extensively in organic chemistry for the determination of structure of organic compounds. This topic will not be discussed here since standard monographs (118 - 120) give a detailed account on this subject.

The details of the N.M.R. spectra of some symmetrical diarly sulphones prepared by the reaction of sulphuric acid with aromatic hydrocarbons and trifluoroacetic anhydride in section 2.2.2, are given below.

### Table 2.2.4 - 3

### 4,4'-dimethyl diphenyl sulphone

| | | | |
|---|---|---|---|
| doublet | 8,00 δ | J = 80 Hz | H(2,2'6,6') |
| doublet | 7,43 δ | J = 80 Hz | H(3,3',5,5') |
| singlet | 2,43 δ | - $CH_3$ (4,4') | |

### 2,2,'4,4'6,6' - hexamethyldiphenyl sulphone

| | | |
|---|---|---|
| singlet | 7,03 δ | H (3,3,'5,5') |
| singlet | 2,50 δ | -$CH_3$(2,2',6,6') |
| singlet | 2,33 δ | -$CH_3$ (4,4') |

### 4,4' diethoxydiphenyl sulphone

| | | | |
|---|---|---|---|
| doublet | 8,03 δ | J = 90 Hz | H(2,2,'6,6') |
| doublet | 7,10 δ | J = 90 Hz | H(3,3',5,5') |
| singlet | 3,90 δ | -$OCH_3$ (4,4') | |

### 4,4' diethoxy diphenyl sulphone

| | | | |
|---|---|---|---|
| doublet | 8,03 δ | J = 90 Hz | H(2,2',6,6') |
| doublet | 7,06 δ | J = 90 Hz | H(3,3',5,5') |
| Quartet | 4,13 δ | J = 70 Hz | -$CH_2$- (4,4') |
| Triplet | 1,40 δ | J = 70 Hz | -$CH_3$ (4,4') |

### 4,4' dibenzyl diphenyl sulphone

| | | |
|---|---|---|
| doublet | 8,00 δ | J = 80 Hz |
| doublet | 7,43 δ | J = 80 Hz |
| singlet | 7,36 δ | -$C_6H_5$ (4,4') |
| singlet | 4,10 δ | -$CH_2$ (4,4') |

The assignment of the protons is based on the fact that the protons ortho to the sulphonyl group are more deshielded than those ortho to other substituent groups on the aromatic ring. These results confirm the structures of the symmetrical diaryl sulphone prepared in this work.

2.2.4.3. Mass Spectrometry.

The molecular weights of the symmetrical diaryl sulphones prepared in this work were determined by chemical ionisation mass spectroscopy.[113-115] This technique is based on ion molecule reactions. Highly reactive ions are produced by introduction of a reactant gas isobutane into the ion-source.

$$(CH_3)_3CH + e \longrightarrow [\ (CH_3)_3CH\ ]^{+\cdot} + 2e \qquad (53)$$

These ions formed from the initial electron impact and fragmentation further react with the gas to produce secondary ions.

$$[(CH_3)_3CH\ ]^{+\cdot} \longrightarrow CH_3\cdot + (CH_3)_2CH^+ \quad m/e = 43 \qquad (54)$$

$$(CH_3)_2CH^+ + (CH_3)_3\ CH \longrightarrow (CH_3)_2CH_2 + (CH_3)_3C^+ \quad m/e = 57 \qquad (55)$$

These ions react further with the compounds under observation (AH) to give $AH_2^+$ ions.

$$(CH_3)_3C^+ + AH \longrightarrow AH_2^+ + (CH_3)_2C = CH_2 \qquad m/e\ [M + 1]^+ \qquad (56)$$

Since the ionisation of organic molecules is due to the reaction of $(CH_3)_3C^+$ ions, very little energy is transferred to the $AH_2^+$ ion and therefore the fragmentation of it is considerably reduced. This method therefore is very convenient especially for the determination of the molecular weights of those compounds, whose molecular ions produced by direct electron impact, are particularly unstable. Accordingly, spectra produced by this method are much simpler than those produced by the electron impact method and therefore aid relative molecular mass determinations especially in complex organic molecules e.g. carbohydrates, peptides, antibiotics etc. Table 2.2. 4-4. gives the results obtained by this method.

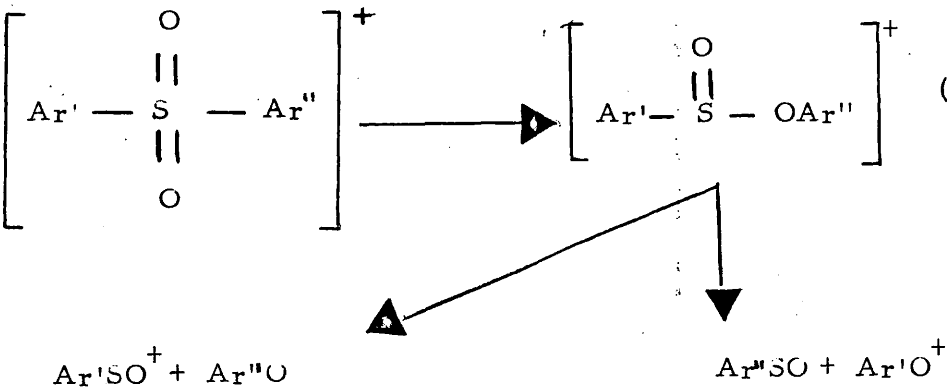
However chemical ionisation spectrometry is not very useful for the determination of the detailed structure of aromatic diaryl sulphones because the molecular ions of the sulphones are very stable hence no fragmentation of the ion molecule takes place.

Table 2.2.4 - 4.

Molecular ions and relative molecular mass of symmetrical diaryl sulphones prepared from the reaction of sulphuric acid with aromatic hydrocarbons and trifluoroacetic anhydride.

| Substituted diphenyl sulphone | M/z | Relative molecular mass |
|---|---|---|
| 4,4'-dimethyl- | 247 | 246 |
| 2,2'4,4'6,6'-hexamethyl- | 305 | 304 |
| 4,4'dimethoxy- | 279 | 278 |
| 4,4'-diethoxy- | 307 | 306 |
| 4,4'-dibenzyl- | 399 | 398 |

The electron impact mass spectrometry of diaryl sulphones has been studied in detail by H.Drews and E.K. Fields[125]. The decomposition takes place via two pathways. The first involves the rearrangement of the parent ion into an aryl arenesulphinate followed by a rupture of the S-OAr bond. The migration of the aryl group suggests that the electrons in the non-bonding oxygen are localised, as a result, the oxygen is electron deficient. Therefore in an unsymmetrical diaryl sulphone the aryl group which is more electron donating Ar'' should preferentially migrate to the oxygen.



(57)

The second path is characteristic to ortho methylated sulphones. This involves the loss of OH and $H_2O$ followed by the loss of SO. Although the metastable ions corresponding to the loss of SO are not found strong ions corresponding to the loss of $SO_2H$ are observed in these spectra and thus strongly suggesting such a sequence. The loss of $-CH_3$ and-SO occurs in all ortho methylated diaryl sulphones except 2-methyl diphenylsulphones since this sequence requires a second methyl group in the molecule. Although in some cases no peaks corresponding to the loss of $-CH_3$ are observed, peaks corresponding to the loss of $SO_2CH_3$ $SO_2CH_2$ and $SO_2CH_5$ are found. Examples of the electron impact spectra of diphenyl sulphone and 2,4,4'6 tetramethyl diphenyl sulphone are given on Fig.2.2.4-5, Fig.2.2.4-6, and Table 2.2.4.-7.

There is no doubt that evidence obtained from the various spectroscopic methods fully confirms the structure of the sulphones. In addition melting points have been found to agree with those observed by other workers.

### 2.2.5. The preparative separation of sulphone isomers.

The presence of many isomeric sulphones in reaction mixtures requires a method for their preparative separation if these reactions are to be of any use in synthesis. The isomers can easily be separated by thin layer chromatograph on silica with 5% ethyl acetate in toluene (v/v) as a solvent and therefore T.L.C. can be used to detect these isomers and for their quantitative separations.

Medium pressure chromatography was found to be very useful for this purpose. Although this technique has been extensively used at Colorado University and Sheffield University, no publications have been made so far. However related techniques such as rapid chromatography[116] and short column chromatography[117] are described.

This technique is basically an air pressure driven

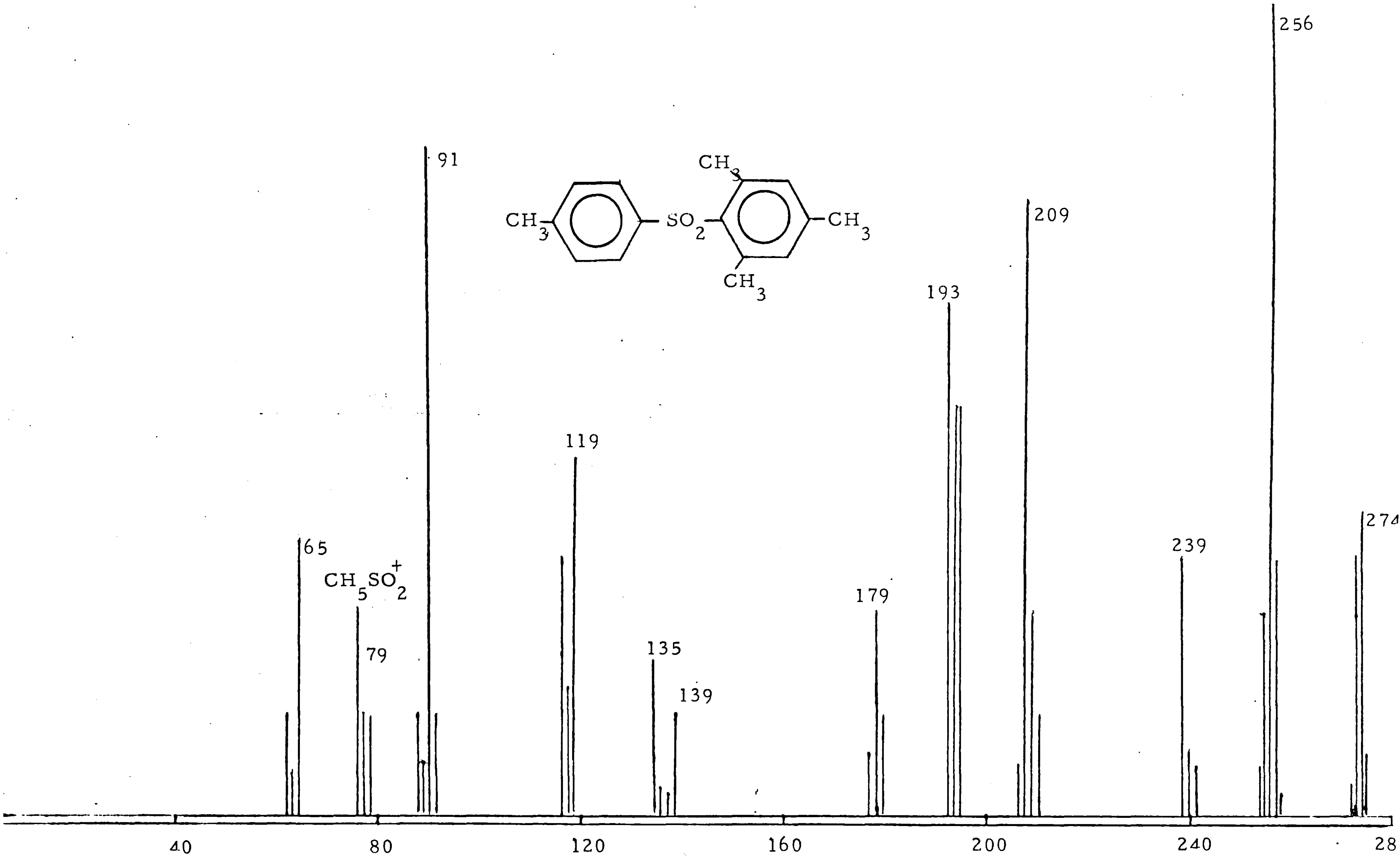


Fig. 2.2.4.-5. The electron impact mass spectrum of 2, 2'-4, 4'-6 pentamethyl diphenyl sulphone.

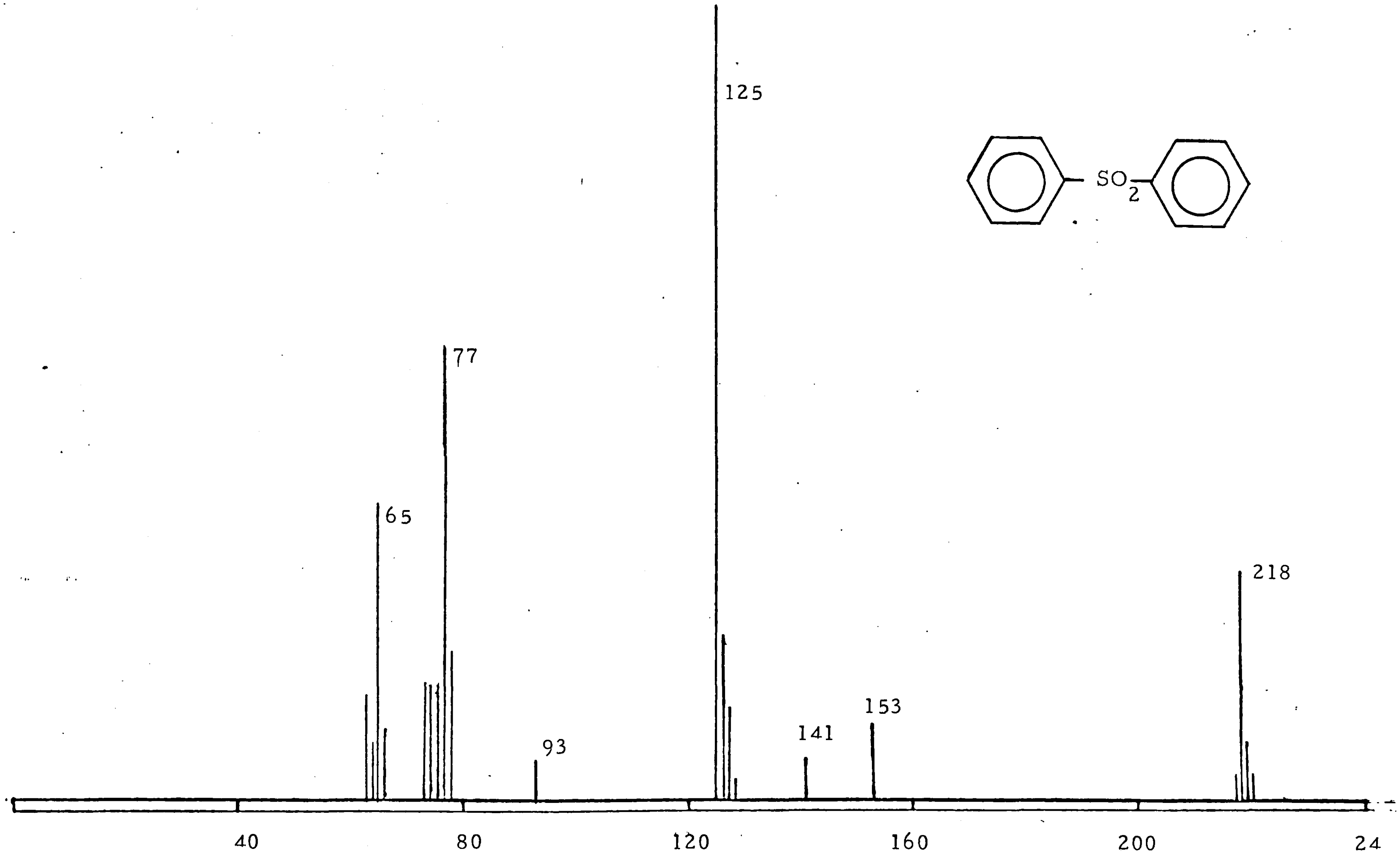


Fig.2.2.4 - 6. The electron impact mass spectrum of diphenyl sulphone

Table 2.2.4 -7

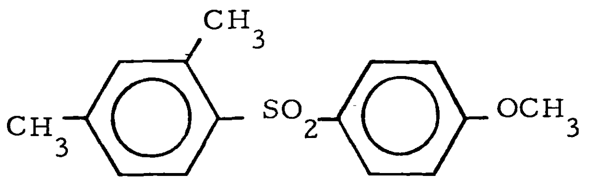
A table of ions found in the mass spectra of diphenyl sulphone 2,4,4'6-tetramethyl diphenyl sulphone.

| Diphenyl sulphone Parent ion (P) = 218 | | 2,4,4'6-tetramethyl diphenyl sulphone. Parent ion (P) = 274 | |
|---|---|---|---|
| m/e | Ion | m/e | Ion |
| 65 | $SO_2H^+$ | 65 | $SO_2H^+$ |
| 77 | $Ph^+$ | 79 | $CH_3SO_2^+$ |
| 93 | $PhO^+$ | 80 | $CH_4SO_2^+$ |
| 125 | $PhSO^+$ | 81 | $CH_5SO_2^+$ |
| 141 | $PhSO_2^+$ | 91 | $CH_3C_6H_5^+$ |
| 154 | $P^+ - (SO_2H)_2$ | 119 | $(CH_3)_3C_6H_2^+$ |
| 153 | $P^+ - (SO_2H)$ | 135 | $(CH_3)_3C_6H_2O^+$ |
| 218 | $P^+$ | 139 | $CH_3C_6H_5SO^+$ |
| | | 193 | $P^+ - (SO_2CH_5)$ |
| | | 194 | $P^+ - (SO_2CH_4)$ |
| | | 195 | $P^+ - (SO_2CH_3)$ |
| | | 208 | $P^+ - (SO_2H_2)$ |
| | | 209 | $P^+ - (SO_2H)$ |
| | | 210 | $P^+ - (SO_2)$ |
| | | 256 | $P^+ - (H_2O)$ |
| | | 257 | $P^+ - (HO)$ |
| | | 274 | $P^+$ |

type of column chromatography in which T.L.C. grade silica gel is used as stationary phase. The pressure may be generated by either an air pump or simply a cylinder of compressed nitrogen. Between the pressure generator and the column is a mercury manometer for measuring the applied pressure. The solvent used for the elution of the isomers is that used for achieving good separations in T.L.C. A diagram showing the assembled apparatus is shown in Fig. 2.2.5 - 1.

The conditions for a good separation require that there be a flat surface on the packing material. This can be achieved by use of a sinter at the bottom of the packing material and a filter paper between the packing material and the solvent. To ensure a good separation the solvent height should be at least twice the height of the silica gel at the beginning of each separation. The effect of increased pressure does not appear to affect the efficiency of the separation but merely decreases the time needed for the separation. However care must be exercised when increasing the pressure in case the apparatus bursts.

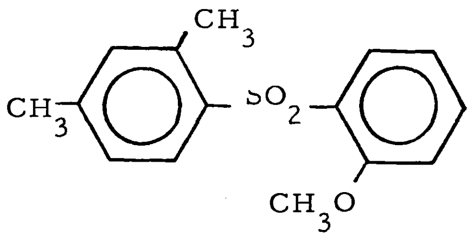
The following isomers were separated by this method with 5% ethylacetate as solvent.



m.p. = 59°C

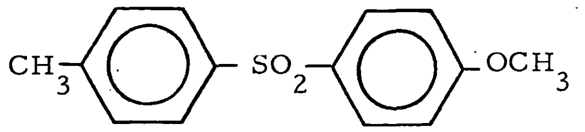
$R_t$ = 1.38

and



m.p. = 159°C

$R_t$ = 1.00

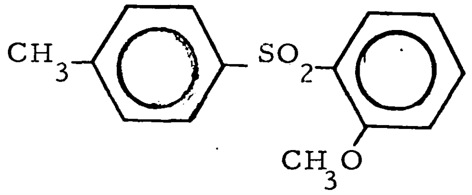


m.p. = 105°C

Litt. m.p. = 104-105°C

$R_t$ = 1.11

and



m.p. = 70°C

$R_t$ = 0.86

Fig. 2.2.5. - 2

These compounds were prepared by the reaction of sulphuric acid with two aromatic hydrocarbons and trifluoroacetic anhydride. After the separation the isomers were analysed by g.l.c. and their $R_t$ values recorded. N.M.R. spectroscopy was used to identify the isomers. Fig. 2.2. 5-3-5.

The separation is quick requiring only 30-45 minutes. Its resolution is good hence this technique has sometimes been referred to as 3-dimensional thin layer chromatography.

A diagrammatic representation of the apparatus used for medium pressure chromatography.

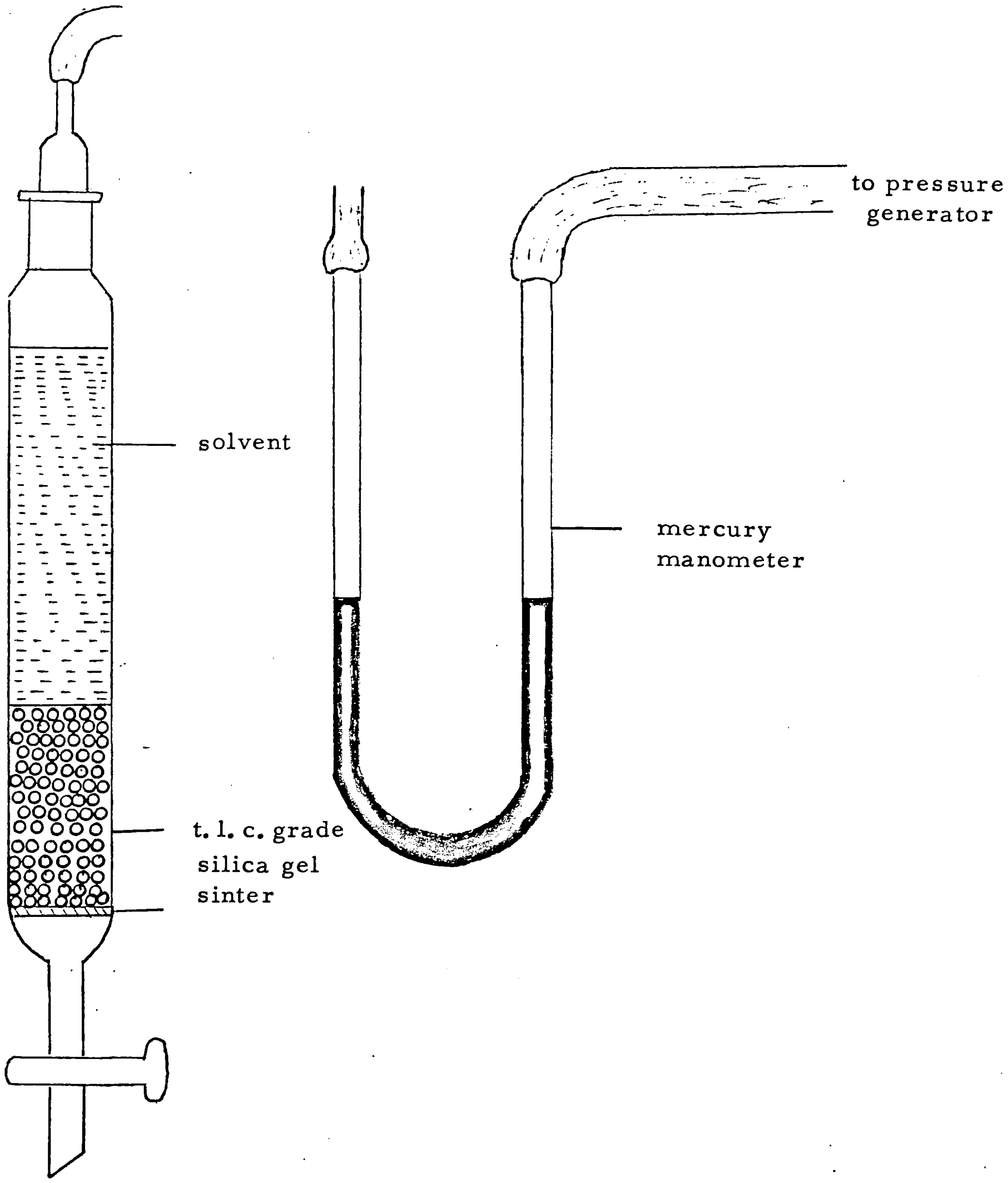


Fig. 2. 2. 5 - 1.

Fig. 2.2.5 - 3.

$^{1}$H n.m.r. spectrum of 4-methoxy 2, '4'-dimethyl diphenyl sulphone.

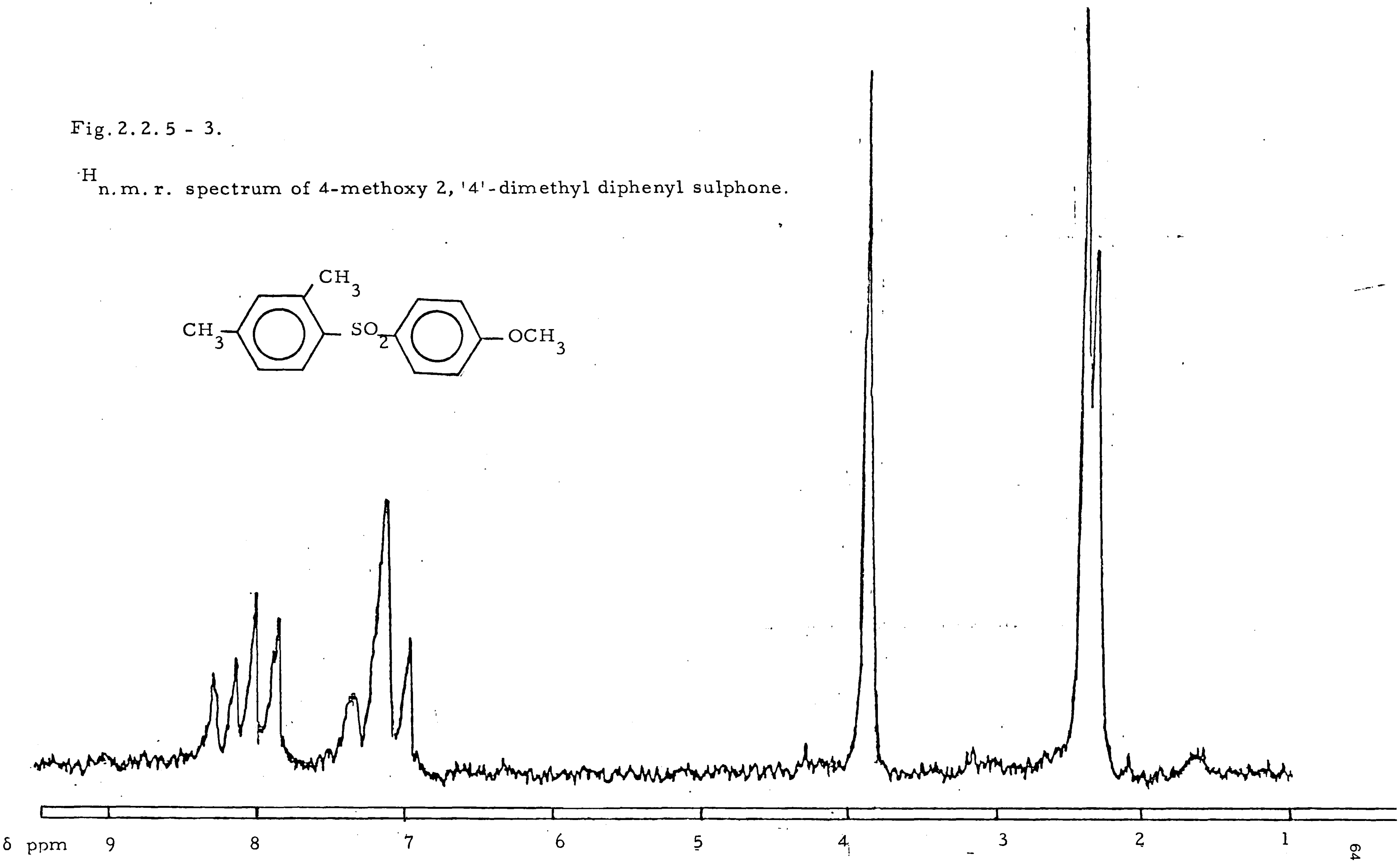


Fig.2.2 5 - 4.

H
n.m.r. spectrum of 2-methoxy 2,'4'-dimethyl diphenyl sulphone

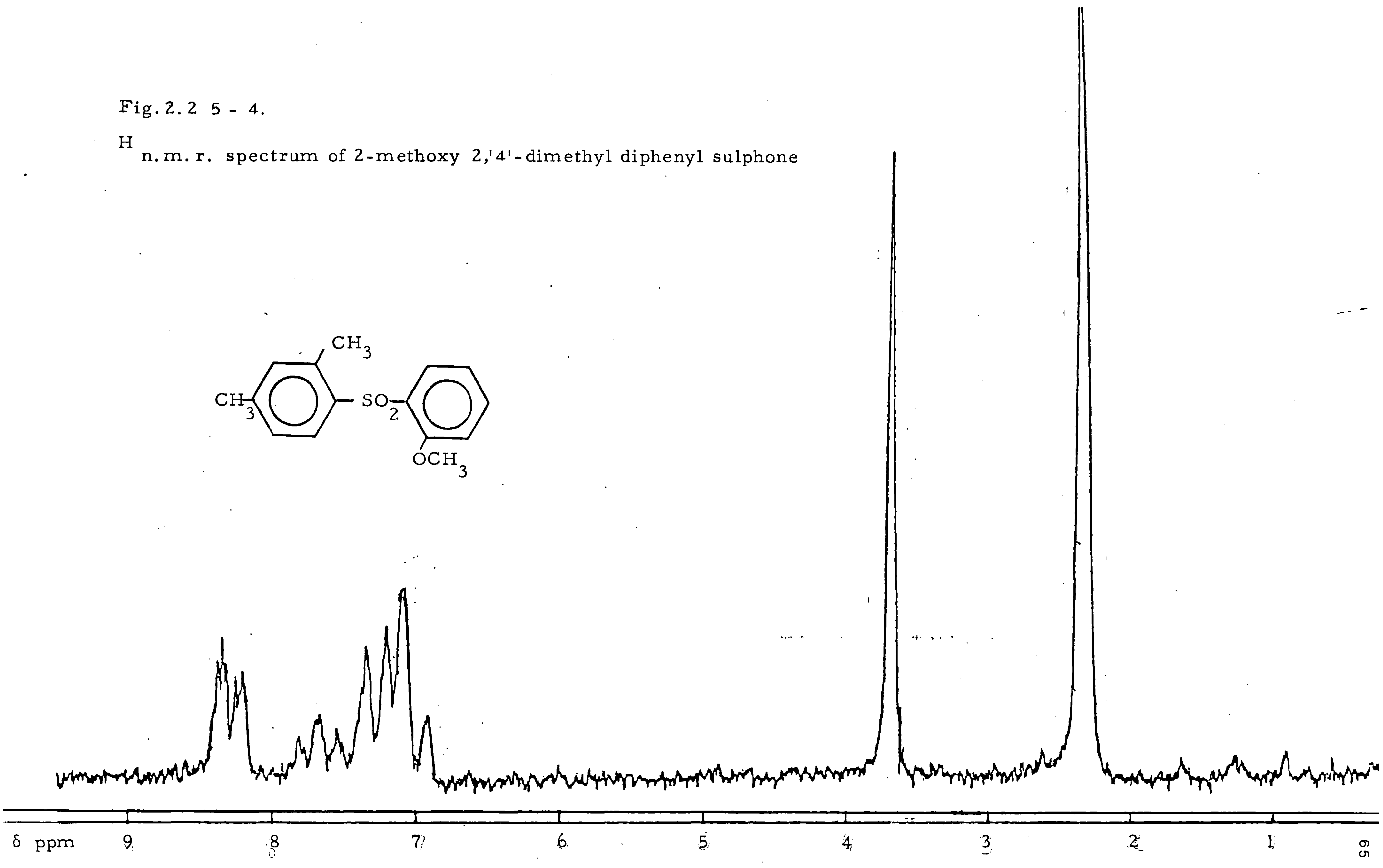
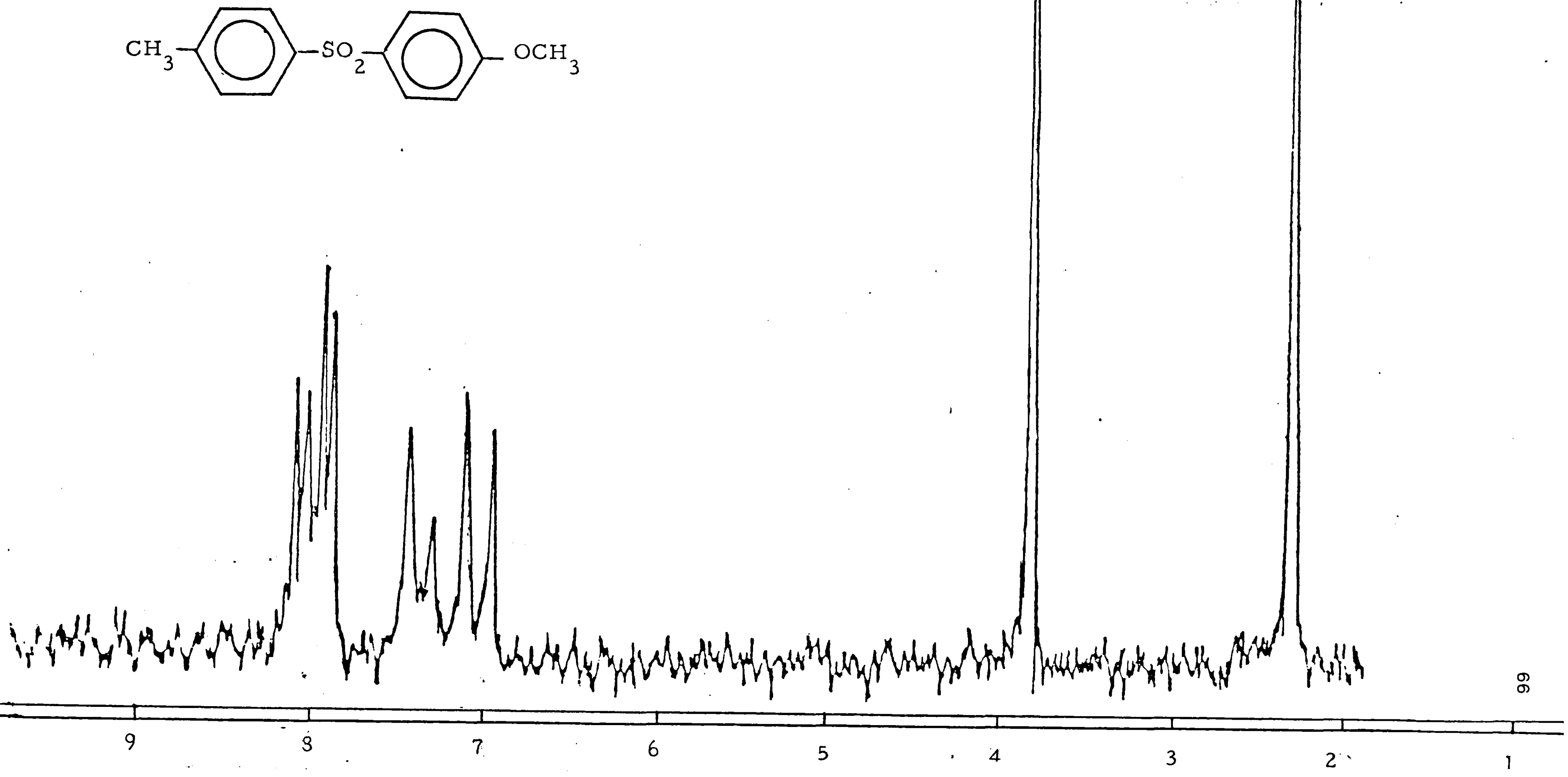


Fig. 2.2.5 - 5

H n.m.r. spectrum of 4-methoxy-4-methyl diphenyl sulphone

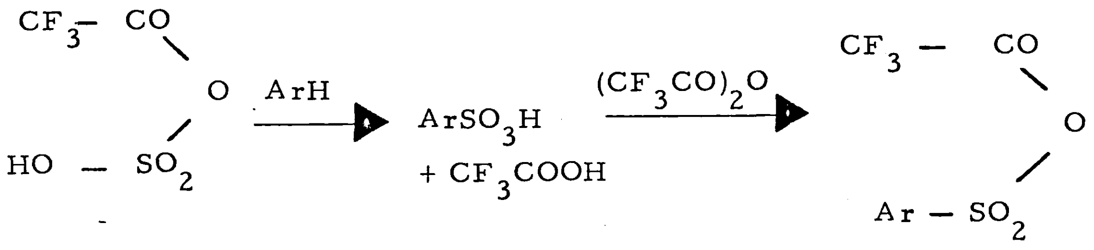


## 3. MISCELLANEOUS SYNTHESIS OF SULPHONES WITH TRIFLUOROACETIC ANHYDRIDE.

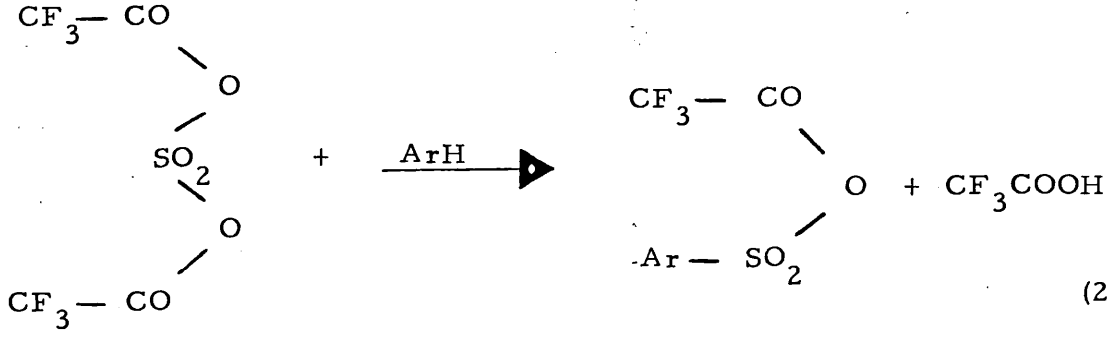
### 3.1. Polymerisation of diphenylmethane.

This reaction is an extension of the reaction of sulphuric acid with aromatic hydrocarbon in the presence of trifluoroacetic anhydride. For the synthesis of sulphones the ratio of sulphuric acid: aromatic hydrocarbon used was 1:2. However when the ratio of 1:1 sulphuric acid:diphenyl methane and excess trifluoroacetic anhydride was used, it was anticipated that polymerisation would take place.

It has already been mentioned in Chapter 2 that trifluoroacetic anhydride and sulphuric acid are expected to react to form a mono trifluoroacetyl sulphuric acid and a di(trifluoroacetyl) sulphate (Chapter 2 reaction 46 and 47). These intermediates can react further with an aromatic hydrocarbon to form mixed trifluoroacetyl-aryl sulphonic anhydride.

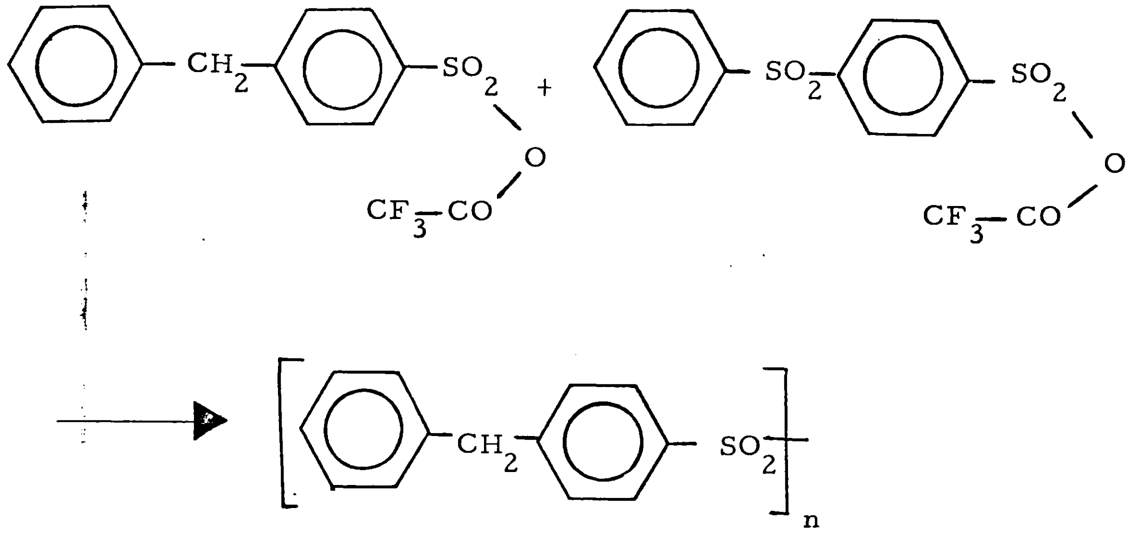


(1)



(2)

When ArH is diphenyl methane, it was anticipated in the second electrophilic substitution step that this mixed anhydride would react with itself instead of another hydrocarbon to give polymers of diphenylmethane.



(3)

Sulphuric acid and an excess trifluoroacetic anhydride were dissolved in nitromethane and the diphenylmethane added to this solution. After refluxing the reaction mixture at $100^{\circ}C$, for 2 hours, the nitromethane and the acids were removed by evaporation under reduced pressure. A solid light green polymeric compound was left in the flask. It was found to be insoluble in organic solvents like ether alcohols acetone and chloroform. However with water it formed a soapy colloidal solution. The structure of the polymer was unfortunately not studied.

Similar polymers have been prepared by H. A. Vogel[57] and were found to have high thermal stabilities, high electrical resistivities and good mechanical properties. No attempt was made to study such properties in this work. However this reaction can be easily extended to other diphenyl alkanes and the

the effect of an increased length of chain between the phenyl rings on the properties studied. Further how the introduction of alkyl and alkoxy groups, substitutents that activate both rings towards electrophilic attack would affect the properties of the polymers, could prove very interesting.

## 3.2. The reaction of hydroxylamine-O-sulphonic acid with aromatic hydrocarbons in the presence of trifluoroacetic anhydride.

Hydroxylamine-O-sulphonic acid has been used with Lewis acids for the amination of aromatic compounds. The yields were in most cases low ( 1 - 21%)[121, 123, 125]. G. P. Dhareshwar and B. D. Hosangadi[122] were the first to investigate why the yields were so low. They found that hydroxylamine-O-sulphonic acid reacted with aromatic ethers in the presence of polyphospheric acid to form predominantly diaryl sulphones. When they used sulphuric acid instead of hydroxylamine-O-sulphonic acid the yields were increased. They concluded that hydroxylamine-O-sulphonic acid released sulphuric acid in the presence of polyphosphoric acid which then reacted further to form diaryl sulphones.

In this project the use of this reagent as a substitute for sulphuric acid to form diaryl sulphones was more important than amination. Nitromethane could not be used as a solvent for this reaction owing to the insolubility of hydroxylamine-O-sulphonic acid. However, 1,1,1,trichloroethane was found to be more useful, since hydroxylamine-O-sulphonic-acid dissolved on warming slightly. Trifluoroacetic anhydride, hydroxylamine-O-sulphonic acid and an aromatic hydrocarbon were mixed in the ratio of 3:1:3 respectively and the sulphones isolated in the usual way. Table 3-1 gives yields and melting points of symmetrical diaryl sulphones obtained by this method. The reaction is given in a simplified manner below.

$$3\,ArH + NH_2OSO_2OH + 3(CF_3CO)_2O \longrightarrow ArSO_2Ar + ArNHCOCF_3 + 5\,CF_3COOH \qquad (4)$$

Partial crystallisation of the crude sulphone product in the reaction of anisole with hydroxylamine-O-sulphonic acid and trifluoroacetic anhydride showed that apart from the diaryl sulphone another by product was formed. The melting point was 110°C and was shown by mass spectrometry to have a relative molecular mass of 220. These properties correspond to para N-trifluoroanisidine (Literature m.p. 112°C [144]) and molecular weight 220). This aspect of the project was not thoroughly investigated. However it seems possible that direct amination of aromatic hydrocarbons might be achieved if some improvements could be made to this reaction.

Table 3 - 1

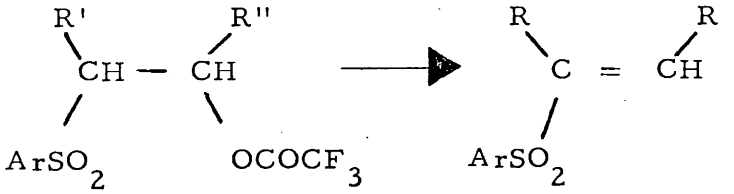
A table of yields and melting points of symmetrical diaryl sulphones prepared from hydroxylamine-O-sulphonic acid.

| Aromatic hydrocarbon | % Yield | m.p. °C |
|---|---|---|
| Anisole | 78 | 129 - 130 |
| Phenetole | 70 | 159 - 160 |
| Ethylbenzene | 54 | 99 - 100 |
| Toluene | 26 | 157 - 158 |
| Mesitylene | 64 | 200 - 1 |
| Cumene | 42 | 96 |

## 3. 3. The synthesis of unsaturated sulphones.

Since carboxylic acids are know to react with alkenes in the presence of trifluoroacetic anhydride to form 1, -keto-olefins (Chapter 1 reaction 7), it was anticipated that sulphonic acids would react with cyclohexene to form 1-sulphonyl cyclohexene. The intermediate here, a sulphonyl trifluoroacetyl cyclohexane, would most likely be unstable as with the trifluoroacetic anhydride/carboxylic acid additions and undergoes a similar 1,2 elimination reaction to restore the double bond.

$$ArSO_3H \quad + \quad R'CH = CHR'' + (CF_3CO)_2O$$



(5)

However it was observed when the reaction was carried under the same condition as those of carboxylic acids, that considerable polymerisation took place (tarry products observed). Repeating the reaction with the temperature lowered to $0^\circ C$, a product of simple addition of a sulphonic acid to a double bond was formed viz. a sulphonate ester.

$$R'CH = CH R'' + ArSO_3H \longrightarrow R'CH_2\text{-}CHR''(OSO_2Ar) \qquad (6)$$

This reaction observed occurs in alkenes except acetylene and does not require the participation of trifluoroacetic anhydride. However for reaction (5) to occur, the formation of an unsymmetrical anhydride between trifluoroacetic anhydride and the sulphonic acid is a prerequisite.

$$(CF_3CO)_2O + ArSO_3H \rightleftarrows CF_3COOSO_2Ar + CF_3COOH \qquad (7)$$

The removal of the aryl sulphonic acid by the alkene disturbs this equilibrium and as a result the product is chiefly a sulphonate ester. It was therefore important that the unsymmetrical anhydride be prepared in the absence of a sulphonic acid if reaction (5) is to occur. First attempt to prepare this unsymmetrical anhydride was by the reaction of the arene sulphonyl bromide with silver trifluoroacetate in nitromethane. This reaction could be observed by the amount of silver bromide precipitated. However with Ar = toluene, an insignificant amount of silver bromide could be precipitated thus making the reaction below unsuitable for the preparation of unsymmetrical anhydrides.

$$AgO\ COCF_3 + ArSO_2Br \longrightarrow ArSO_2OCOCF_3 + AgBr \qquad (8)$$

However similar unsymmetrical sulphonic anhydrides have been prepared by the action of silver trifluoromethane sulphonate on arene sulphonyl bromides (46). The unsymmetrical anhydrides are formed almost quantitatively.

$$AgSO_3CF_3 + ArSO_2Br \longrightarrow ArSO_2OSO_2CF_3 + AgBr \qquad (9)$$

However when this unsymmetrical anhydride (with $Ar = p\text{-}CH_3C_6H_4$) was reacted with various alkenes (cyclohexene, pentene, 2 methylbutene, styrene and stilbene), considerable polymerisation took place and only in the case of cyclohexene could a product be isolated.

The relative molecular mass was found to 234 (expected relative molecular mass = 236) and the N. M. R. showed the presence of an unsaturated proton ($\delta = 7, 55$Hz) as is expected in tosylcyclopentene. The structure of this product has not been fully investigated.

An attempt was made to react sulphonyl perchlorates by reaction 2 - 39 with alkenes. Here the addition products from this reaction decomposed and became charred probably due to the release of perchloric acid. This reaction also needs to be investigate further.

# 4. INTERACTIONS OF SULPHONIC AND SULPHURIC ACIDS WITH TRIFLUOROACETIC ANHYDRIDE.

## 4.1. Introduction.

When a carboxylic acid is dissolved in a carboxylic anhydride of a different acid, an equilibrium is established between the above components and the unsymmetrical anhydride product formed from both the acid and the anhydride. Unsymmetrical carboxylic anhydrides have been studied in detail but only those of trifluoroacetic acid have found application in organic synthesis. Although this chapter deals mainly with the unsymmetrical trifluoroacetic - sulphonic and trifluoroacetic-sulphuric anhydrides, a discussion on unsymmetrical anhydrides in general seems justified since their properties are closely related to those of mixed anhydrides of trifluoroacetic acid.

### 4.1.1. Unsymmetrical carboxylic anhydrides.

These compounds were originally prepared by the reaction of an acid chloride with the sodium salt of a different acid.[59, 60]

$$\mathrm{RCOCl + R'COONa \longrightarrow RCOOCOR' + NaCl} \qquad (1)$$

They were also prepared from a carboxylic acid and a carboxylic anhydride of a different acid.[61, 62]

$$\mathrm{RCOOH + (R'CO)_2O \longrightarrow RCOOCOR' + R'COOH} \qquad (2)$$

Two symmetrical anhydrides have also been used.[64]

$$\mathrm{(RCO)_2O + (R'CO)_2O \longrightarrow 2RCOOCOR'} \qquad (3)$$

Although these reactions were widely investigated difficulties were experienced in the isolation of the products. M. L. Rousset[65] found that both acetic-butryic and acetic-valeric anhydrides yielded symmetrical anhydrides on distillation. It was on this basis that he proposed that unsymmetrical anhydrides do not exist. Béhal attempted to purify isovaleric-acetic anhydride by solvent extraction but even under these mild conditions symmetrical anhydrides were formed. He therefore suggested that although the unsymmetrical anhydrides could be formed in the above reaction, there exists a disproportionation equilibrium with the symmetrical anhydrides.[63,64]

$$2RCOOCOR' \rightleftarrows (RCO)_2O + (R'CO)_2O \qquad (4)$$

As a result of this equilibrium, all attempts to purify the unsymmetrical anhydride by removal of the symmetrical anhydrides resulted in a complete breakdown of the unsymmetrical anhydride.

Hydrolysis of the unsymmetrical anhydride confirmed the existence of the unsymmetrical anhydride. This was found to be first order for acetic propionic and butyric-isopropyl anhydrides.[66] This result would be different in the case of a mixture of anhydride because the differences in the rate of hydrolysis would result in a decreasing rate constant, as the symmetrical anhydride which hydrolyses most rapidly becomes consumed.

Further evidence for the existence of the unsymmetrical anhydride was provided by infra-red spectroscopic measurements in which bands attributed to the ether oxygen characteristic of different anhydrides were observed and compared.[9]

A far superior method for the preparation of unsymmetrical anhydrides was subsequently discovered. This involved the reaction of a ketene with a carboxylic acid[108,109]

$$RCOOH + CH_2 = C = O \longrightarrow CH_3COOCOR \qquad (5)$$

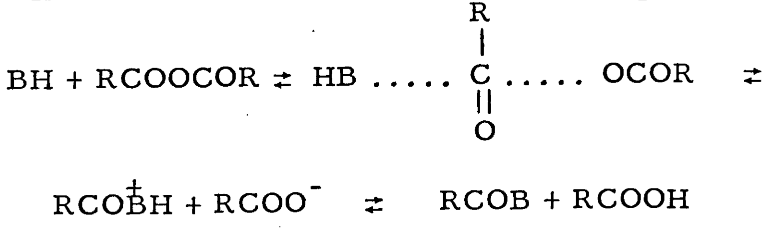
In this method disproportionation according to equation (4) can be minimal since ketene is highly volatile and may be removed by distillation under reduced pressure at low temperature.

Early workers on the reactions of these unsymmetrical anhydrides with alcohols and amines reported conflicting results as to which acyl derivative of the unsymmetrical anhydride was formed. W. Autenrieth reported that the acyl derivative of the carboxylic with the greatest number of carbon atoms is exclusively formed in the reactions with amines.[61,62] A. Be'hal performing the same experiments reported the opposite and later extending his work to alcohols found that both esters were formed.[63,64]

R. Kahn was the first to consider arguments based on relative acid strength[68]. Working on aromatic unsymmetrical anhydrides, he found that the derivative of the stronger acid is formed either exclusively or as a major product in a mixture, but there were exceptions to the rule such as in the case of benzoic-mesitoic anhydride in which the derivative of the weaker acid is exclusively formed. A. Baroni[69] found that both in esterification and aminolysis unsymmetrical anhydrides from acetic, chloro-substituted acetic and butryic acids yielded chiefly the derivative of the stronger acid.

The relative strength of the acids is however not the most important factor in determining the nature of the product in these reactions. The most important factor is the equilibrium between the unsymmetrical and the two symmetrical anhydrides. The position of this equilibrium varies from one system to the other. In the case of similar acids such as butryric and acetic acid, the equilibrium favours the symmetrical anhydrides[70] whereas in unsymmetrical anhydrides of trifluoroacetic acid and other carboxylic acids, the equilibrium favours the formation of the unsymmetrical anhydrides[71]. The rates of establishment of these equilibria are very slow but they can be accelerated by both acid and base catalysts.

The mechanism by which any nucleophilic reaction takes place is also important. Uncatalysed reactions of carboxylic anhydrides can basically be divided into two categories. First there is the Sn2 bimolecular substitution represented as follows:[72]



$$BH + RCOOCOR \rightleftharpoons HB \;.....\; \underset{\underset{O}{\|}}{\overset{\overset{R}{|}}{C}} \;.....\; OCOR \rightleftharpoons$$

$$RCO\overset{+}{B}H + RCOO^{-} \rightleftharpoons RCOB + RCOOH \qquad (6)$$

In the case of an unsymmetrical anhydride, this mechanism would favour the formation of the acyl derivative of the stronger acid since nucleophilic attack is better facilitated at the carbon atom which is more deficient of electrons. It is evident from the experimental findings that most unsymmetrical anhydride reactions take place via this mechanism.

Secondly there is the heterolytic fission of the Snl type which may be written thus:-

$$RCOOCOR \overset{slow}{\rightleftarrows} RCO^{+} + RCOO^{-} \qquad (a)$$

$$RCO^{+} + BH \overset{fast}{\rightleftarrows} RCO\overset{+}{B}H \qquad (b)$$

$$RCO\overset{+}{B}H + RCOO^{-} \overset{fast}{\rightleftarrows} RCOB + RCOOH \qquad (c)$$

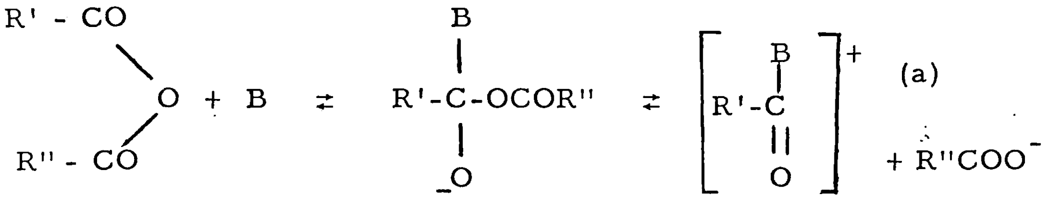
(7)

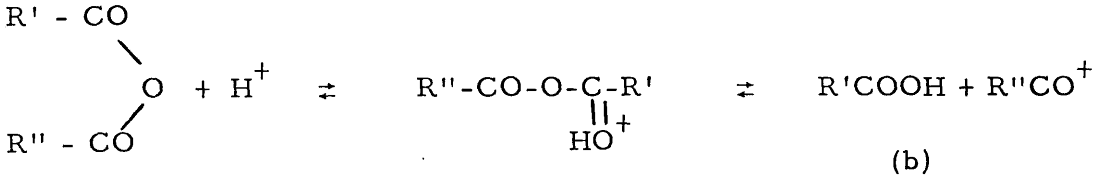
In an unsymmetrical anhydride, this mechanism would favour formation of the acyl derivative of the weaker acid since ionisation always results in the formation of the more stable anion, i.e. the anion of the stronger acid. A good example of this mechanism is the benzoic-mesitoic anhydride in which the 2,4,6 trimethylbenzoylium cation is known to be particularly stable and thus the pre-ionisation route is favoured.

A.R. Emery and V. Gold[74] investigating the reactions of unsymmetrical anhydrides of acetic acid and the three chloroacetic acid with 2,4 dichloroaniline, showed how both increasing steric and electronic effects working in opposition to one another can affect the mode of acetylation.

In this case the monochloroacetic-acetic anhydride yields principally the chloroacetyl derivative while the dichloroacetyl acetate gives both the acetyl and the dichloroacetyl derivative in almost equimolar amounts. However the trichloroacetyl acetate yields exclusively the acetyl derivative. In their discussion they concluded that the reaction of trichloroacetic-acetic anhydride is not necessarily proceeding by a $S_n1$ mechanism but a bimolecular mechanism is operational and that the steric hindrance overwhelms the electronic effects. This results in the derivative of the weaker acid being formed via the bimolecular mechanism.

Catalysts affect the course of these reactions. Their influence is very complicated since they also accelerate disproportionation of the unsymmetrical anhydride. However ignoring the latter effects, base catalysts favour acylation by the acyl group of the stronger acid while acid catalysts promote acylation by the weaker acyl group.[7, 75]


(a)


(b)

$$K_{R'COOH} > K_{R''COOH} \qquad (8)$$

This analysis of unsymmetrical anhydride reactions should not be regarded as complete as there are more complex situations which the author has not included in this review, e.g. solvent effects which makes the division into SnI and Sn2 mechanisms an oversimplified view.

### 4.1.2 Unsymmetrical trifluoroacetic-carboxylic acid anhydrides.

Unsymmetrical trifluoroacetic carboxylic anhydrides deserve a special treatment in this review not only because their reactions are rarely reflected amongst unsymmetrical carboxylic anhydrides but also because of the significant role they play in organic synthesis especially in the reaction which will be examined later.

In 1945 M.S. Newman[76] observed that the reaction between anisole and acetic anhydride was catalysed by trifluoroacetic acid. This was suspected to be due to the reaction of the acid with the anhydride giving first the unsymmetrical anhydride which then reacted faster to give p-methoxy acetophenone.

P. W. Morgan[77] measured the depression of the freezing point of acetic acid by addition of either trifluoroacetic acid or trifluoroacetic anhydride. He observed that trifluoroacetic acid had a van't Hoff factor of one whilst for trifluoroacetic anhydride it was two. He therefore concluded in the first case that the reaction occurring was:

$$(CF_3CO)_2O + CH_3COOH \longrightarrow CF_3COOCOCH_3 + CF_3COOH \qquad (9)$$

since a factor of 3 would have to have been observed for the alternative reaction below producing acetic anhydride.

$$(CF_3CO)_2O + 2CH_3COOH \longrightarrow (CH_3CO)_2O + 2CF_3COOH \qquad (10)$$

Extensive research on interactions of trifluoroacetic acid anhydride with carboxylic acids was carried out in the University of Birmingham in the 1950's. Upon mixing equimolar amounts of trifluoroacetic anhydride and carboxylic acids, these workers observed the changes in the infrared absorption in the carbonyl region and found that new carbonyl peaks appeared at the expense of the carbonyl peaks of the components. These new peaks were attributed to the unsymmetrical anhydride carbonyl stretching modes.

Conductivity studies were also carried out on mixtures of trifluoroacetic anhydride and carboxylic acids.[79] As the solutions were mixed, heat was evolved showing that the initial reaction was fast, the conductivity rose to a maximum and then slowly fell until it reached a constant value. This was attributed to the fast formation of the unsymmetrical anhydride, which would be expected to be highly conductive and then followed disproportionation to the less conducting symmetrical anhydrides.

Attempts to isolate the unsymmetrical anhydrides by reacting acid chlorides with silver trifluoroacetate in ether, followed by flash distillation under reduced pressure usually resulted in much disproportionation, thought to be due to the presence of unreacted silver trifluoroacetate.[80]

$$RCOCl + CF_3COOAg \longrightarrow RCOOCOCF_3 + AgCl \qquad (11)$$

E. J. Bourne, M. Stacey, J. C. Tatlow and R. Worral[81] nevertheless reported a method for the isolation of the unsymmetrical anhydride using the reaction of a carboxylic acid and trifluoroacetic anhydride.

$$RCOOH + (CF_3CO)_2O \longrightarrow RCOOCOCF_3 + CF_3COOH \qquad (12)$$

The trifluoroacetic acid was removed by addition of an ethereal solution of pyridine and the unsymmetrical anhydride distilled. However these results are disputed by E. G. Gabb and T. G. Bonner[82] who found that the distillation of the products of the above reaction always resulted in a distillate containing both symmetrical and unsymmetrical anhydrides.

Studies on the kinetics of the formation of acetyl-trifluoroacetate have been made[82] by observing the infrared absorption in the region 1000 - 1250 $cm.^{-1}$ Equimolar solution of acetic anhydride and trifluoroacetic anhydride in carbon tetrachloride reacted slowly and showed a conversion eventually to 98% acetyl trifluoroacetate. The reaction of trifluoroacetic anhydride with acetic acid was found to be considerably faster than the above yielding 95% of the acetyl trifluoroacetate. However when equimolar solutions of trifluoroacetic acid and acetic anhydride in carbon tetrachloride were reacted, although the equilibrium was established rapidly, only 40% of the unsymmetrical anhydride was formed.

The effects of addition of equimolar quantities of either acetic or trifluoroacetic acids upon the reaction between trifluoroacetic anhydride and acetic acid were investigated. Whilst trifluoroacetic acid was found to have no effect upon this reaction described above, acetic acid was found to result in its conversion into acetic anhydride in a yield of 60%. These results suggest that in excess acetic acid the acetyl trifluoroacetate first formed becomes converted into acetic anhydride.

$$(CF_3CO)_2O + CH_3COOH \longrightarrow CH_3COOCOCF_3 + CF_3COOH \quad (a)$$

$$CH_3COOCOCF_3 + CH_3COOH \longrightarrow (CH_3CO)_2O + CF_3COOH \quad (b)$$

The overall reaction is:-

$$(CH_3CO)_2O + 2CH_3COOH \longrightarrow (CH_3CO)_2O + 2CF_3COOH \quad (c)$$

(13)

T.G. Bonner and E.G. Gabb found that the reaction between acetic and trifluoroacetic anhydrides took between one and seven days to reach equilibrium. T.G. Bonner, P. Macnamara and B. Smethurst[83] reported that this reaction was catalysed by small quantities of both acetic and trifluoroacetic acids and also that in both cases the zeroth order kinetic law was observed. They concluded that the reaction between trifluoroacetic and acetic anhydrides does not proceed at any measurable rate under anhydrous conditions and that the slow reaction presumably observed by T.G. Bonner and E.G. Gabb[82] might have been caused by an ingress of adventitious moisture. The observed rate of the reaction between trifluoroacetic anhydride and acetic acid was fast but the reaction between acetic anhydride and trifluoroacetic acid was slower.

$$(CF_3CO)_2O + CH_3COOH \rightleftarrows CH_3COOCOCF_3 + CF_3COOH \quad (a)$$

$$(CH_3CO)_2O + CF_3COOH \rightleftarrows CH_3COOCOCF_3 + CH_3COOH \quad (b)$$

(14)

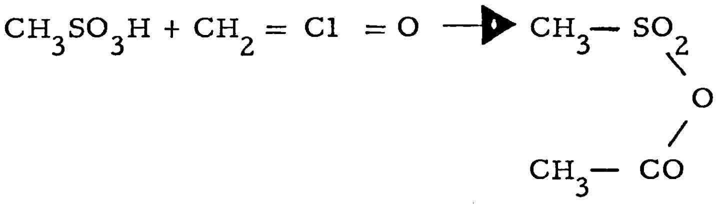
In the overall interaction of the two anhydrides, the presence of one of the acids results in small amounts of the other acid. Therefore the amount of anhydride undergoing a change per unit time will be the same with reaction 14 (b) being the rate limiting step irrespective of whether the reaction is catalysed by trifluoroacetic acid or acetic acid.

### 4.1.3. Sulphonic-carboxylic anhydrides.

Work on sulphonic carboxylic anhydrides started in 1889 when O-sulphobenzoic anhydride was prepared by A. Fahlberg.[84] However it was not until 1933 that sulphonic aliphatic carboxylic anhydrides were prepared. A. Baroni[85] prepared acetyl sulphonates from silver or sodium acetates and a sulphonyl-chloride.

$$AgOAc + C_6H_5SO_2Cl \longrightarrow AcOSO_2C_6H_5 + AgCl \qquad (15)$$

Ketene was later used in a method analogous to the synthesis of unsymmetrical carboxylic anhydrides.



$$CH_3SO_3H + CH_2 = Cl = O \longrightarrow CH_3-SO_2-O-CO-CH_3$$

(16)

However the yields were low compared with those of unsymmetrical carboxylic anhydrides and in most less than 10%.

G. G. Overberger and E. Sarlo[93] using A. Baroni's method isolated these anhydrides and studied their chemical properties. They were found to have reasonable melting points and analysed satisfactorily. These compounds were demonstrated to be active acylating agents and gave good yields under mild conditions.

Most of the work on sulphonic carboxylic anhydrides was carried out by M. H. Karger and Y. Mazur,[88, 89, 90, 91, 92]. They used basically two methods of synthesis. The first involved treatment of an acid chloride with a sulphonic acid resulting in the evolution of hydrogen chloride gas.

$$RCOCl + R'SO_3H \longrightarrow RCOOSO_2R' + HCl \qquad (17)$$

This method was found to give good yields. However, the anhydrides were contaminated by traces of both free acids either due to incomplete reaction, or hydrolysis to which all unsymmetrical anhydrides are susceptible, and also sulphonic anhydride, probably because of disproportionation of the unsymmetrical anhydride at elevated temperatures. Purification by distillation accordingly, was found to be applicable only to acetyl methane sulphonate whilst similar compounds decomposed on attempted distillation.

The second method of synthesis consisted of heating an excess of carboxylic anhydride with a sulphonic acid at 120°C followed by removal of the anhydride and the free acid by distillation under reduced pressure.

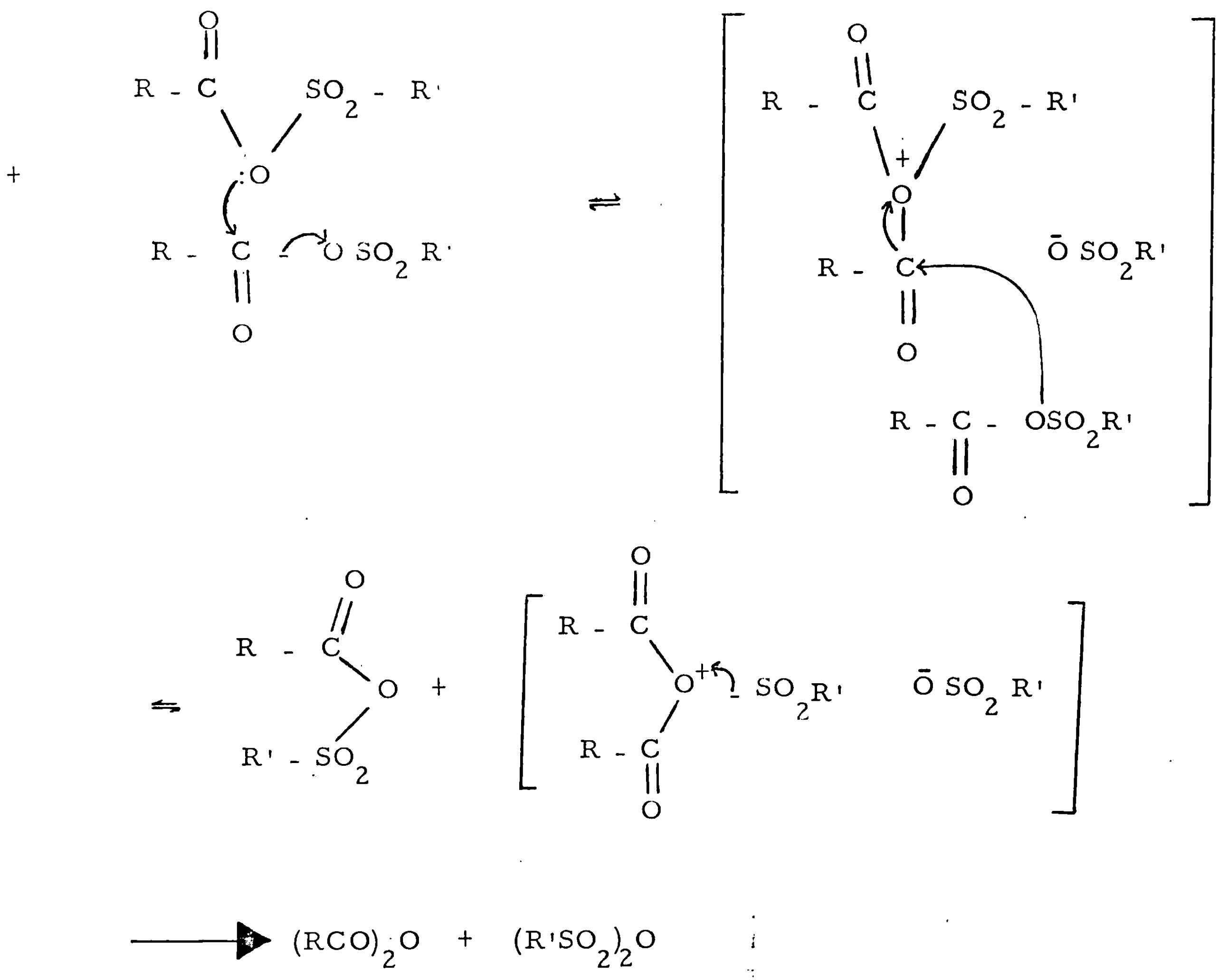
$$(CH_3CO)_2O + CH_3C_6H_4SO_3H \longrightarrow CH_3COOSO_2C_6H_4CH_3 + CH_3COOH \qquad (18)$$

This method also had disadvantages in the case of high molecular weight anhydrides because their involatibility necessitates high temperatures for removal and consequently resulted in the decomposition of the unsymmetrical anhydride.

Sulphonic carboxylic anhydrides were found to undergo basically two types of thermal decomposition. At temperatures below 30°C only a simple disproportionation took place.

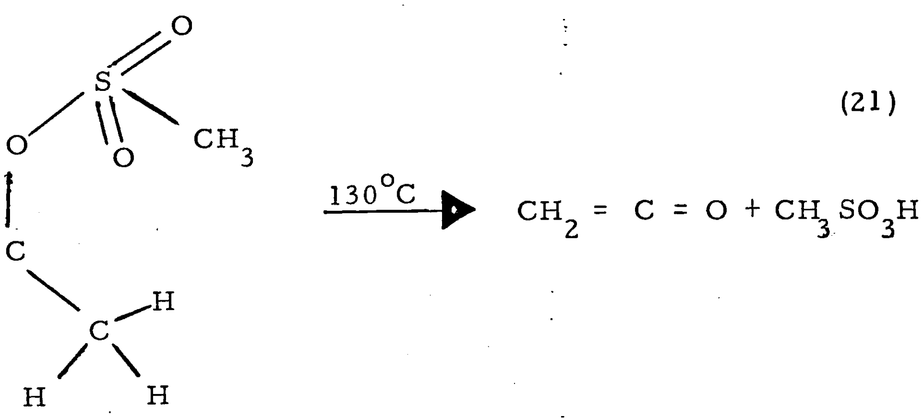
$$2CH_3COOSO_2CH_3 \longrightarrow (CH_3CO)_2O + (CH_3SO_2)_2O \qquad (19)$$

The mechanism of this reaction was postulated as follows:-



(20)

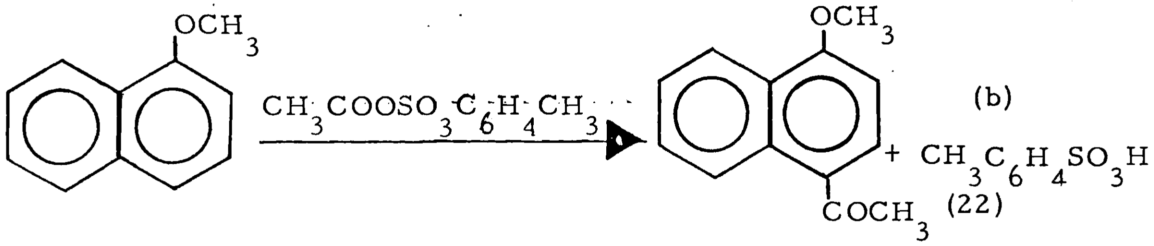
At temperatures above 130°C a second reaction was found to predominate in which the sulphonic acid is regenerated with a simultaneous evolution of ketene this reaction is only possible with those anhydrides having transferrable β-hydrogen atoms.



(21)

An interesting reaction of these sulphonic-carboxylic anhydrides occurs with aliphatic and aromatic ethers. Aliphatic ethers are cleaved to give a mixture of carboxylate and sulphonate ester, whilst aromatic ethers are acylated with no apparent accompanying sulphonation.

$$RCOOSO_2R' + R''OR''' \longrightarrow \begin{cases} RCOOR'' + R'''OSO_2R' \\ RCOOR''' + R''OSO_2R' \end{cases} \qquad (a)$$



(b)

(22)

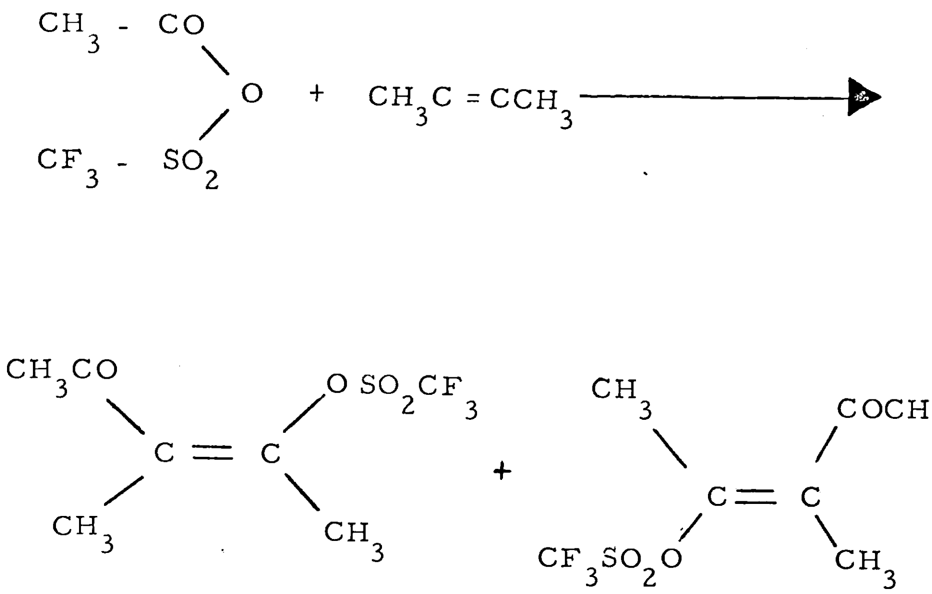
H.Boehme and K. H. Meyer-Dulheuer[87] studied the cleavage reactions of bis-dialkyl amino ethers ($R_2N - CH_2 - OR$) with sulphonic carboxylic anhydrides.

$$R''SO_2OCOR' + R_2N\text{-}CH_2NR_2 \longrightarrow R'CONR_2 + R_2N{=}CH_2 \;\; {}^{+}RSO_3^{-} \qquad (a)$$

$$R''SO_2OCOR' + R_2N - CH_2OR''' \longrightarrow R'CO_2R''' + R_2N{=}CH_2 \;\; {}^{+}RSO_3^{-} \qquad (b)$$

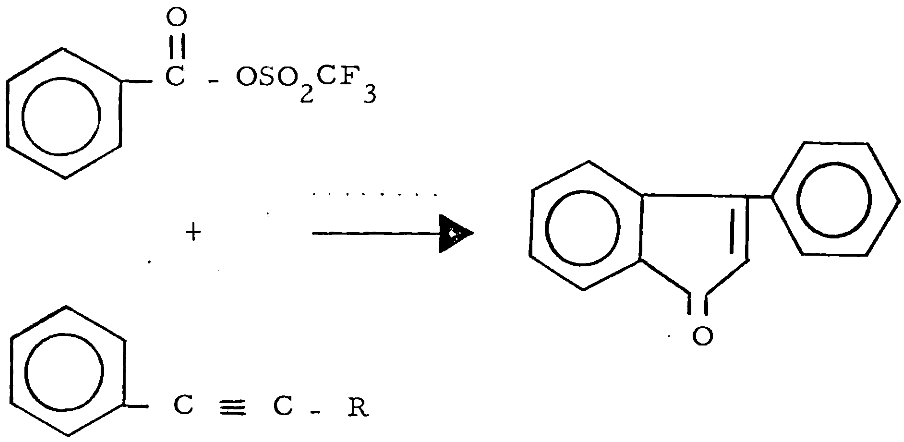
(23)

Acyl trifluoromethane sulphonates are also very excellent acylating agents[135-137] but their most interesting reaction is with acetylenes[138].



(24)

When aroyl trifluoromethane sulphonates are used indinones may be formed.



(25)

### 4.1.4. Unsymmetrical sulphonic anhydrides.

Very little has been reported on unsymmetrical sulphonic anhydrides probably because they resemble unsymmetrical carboxylic anhydride in their behaviour. Most of the study of these anhydrides was carried out by F. Effenberger and K. Huthmacher[46, 94]. They successfully prepared them by treating silver trifluoromethane sulphonate with a sulphonyl bromide.

$$RSO_2Br + AgSO_3CF_3 \longrightarrow RSO_2OSO_2CF_3 + AgBr \qquad (26)$$

They were able to purify the methyl and the ethyl analogues by careful distillation under reduced pressure. However the isopropyl compound decomposed on attempted distillation.

These anhydrides are thermolabile and decompose in various ways depending on the nature of R. In the case of R being an alkyl group, heterolytic dissociation and subsequent loss of $SO_2$ results in a sulphonate. With various R groups decomposition temperature falls as the stabilization of the associated carbonium ions increases.

$$RSO_2OSO_2CF_3 \rightleftarrows RSO_2^+ + OSO_2CF_3 \xrightarrow{-SO_2} R^+ + OSO_2CF_3 \qquad (27)$$

In the case where R is a polyalkyl or a polyalkoxy aromatic group, decomposition proceeds by homolysis into radicals followed by loss of $SO_2$.

$$RSO_2OSO_2CF_3 \rightleftarrows RSO_2\cdot + \cdot OSOCF_3 \xrightarrow{SO_2} R\cdot + \cdot OSO_2CF_3 \qquad (28)$$

However unsymmetrical anhydrides with aryl and monosubstituted aryl sulphonic components (R = ArH X-ArH) suffer disproportionation into symmetrical anhydrides upon warming to 50°C.

$$2ArSO_2OSO_2CF_3 \longrightarrow (ArSO_2)_2O + (CF_3SO_2)_2O \qquad (29)$$

The reactions of these anhydrides have already been discussed in Chapter 2.

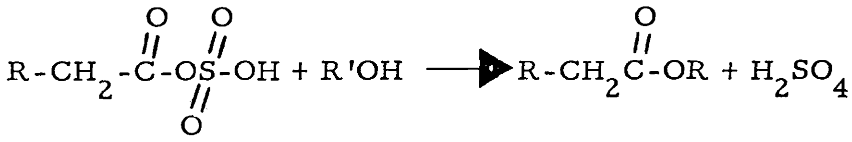
### 4.1.5. Interactions between sulphuric acid and carboxylic anhydrides.

As early as 1881 Franchmont showed that sulphoacetic formed when acetic anhydride and sulphuric acid react[96,97].

$$(CH_3CO)_2O + H_2SO_4 \longrightarrow HOSO_2CH_2COOH \qquad (30)$$

He suggested that the reaction mechanism involved the formation of a mixed anhydride of sulphuric and acetic acid sometimes called acetyl sulphuric acid and which subsequently rearranges to sulphoacetic acid. J. Russell and A. E. Cameron[98] studying the acidity of mixtures of sulphuric acid and acetic anhydride concluded that anultra-acidic mixed anhydride is first formed which then rearranges to sulphoacetic acid and which does not show this ulta-acidic behaviour.

These results were later confirmed by T. F. Murray and W. O. Kenyon[99] who studied the kinetics of reactions between sulphuric acid and carboxylic anhydrides. They further suggested that this intermediate was formed even when sulphuric acid was present in catalytic quantities. On this basis they provided the mechanism for the acylation of alcohols with acetic anhydride in the presence of sulphuric acid.



$$\text{R-CH}_2\text{-}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{-O}\underset{\underset{\text{O}}{\|}}{\overset{\text{O}}{\overset{\|}{\text{S}}}}\text{-OH} + \text{R'OH} \longrightarrow \text{R-CH}_2\overset{\text{O}}{\overset{\|}{\text{C}}}\text{-OR} + \text{H}_2\text{SO}_4 \qquad (31)$$

Since sulphuric acid is regenerated, the acylation cycle may either be repeated several times or else rearrangement of the unsymmetrical anhydride to sulphoacetic acid occurs.

E. A. Jeffrey and D. P. N. Satchell[100, 101], have to date made the most detailed study of both acylation in the presence of sulphuric acid and sulphoacetic acid and also the mechanism of formation of sulphoacetic acid. In the acylation of phenols with acetic anhydride, they found that sulphoacetic acid behaved as a sulphonic acid while sulphuric acid was unique owing to its dibasic nature. They first proposed that sulphoacetic acid behaves as a monobasic acid thus:-

$$\text{Ac}_2\text{O} + \text{HOSO}_2\text{CH}_2\text{COOH} \rightleftarrows \text{Ac OSO}_2\text{CH}_2\text{CO}_2\text{H} + \text{AcOH} \qquad \text{(a)}$$

$$\text{AcOSO}_2\text{CH}_2\text{CO}_2\text{H} + \text{ArOH} \longrightarrow \text{ArOCOCH}_3 + \text{HOSO}_2\text{CH}_2\text{CO}_2\text{H} \qquad \text{(b)}$$

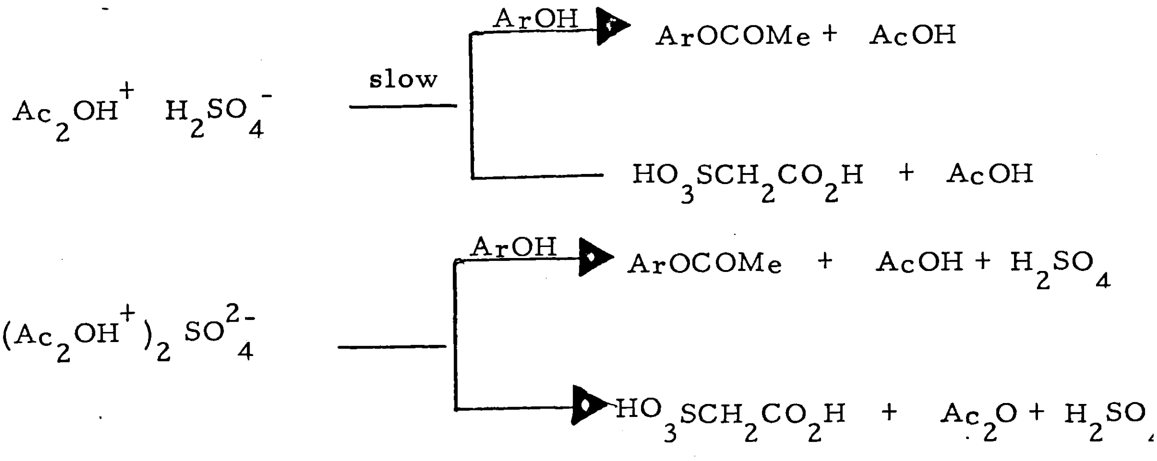
(32)

However they were very critical of the findings of T. F. Murray and W. O. Kenyon[99] on the formation of sulphoacetic acid. The criticism resulted from the observation that there were certain restrictions for the concentration of sulphuric acid in the formation of sulphoacetic acid. The concentration of sulphuric acid had to be small compared to the anhydride, so small that it should not constitute a large medium effect. Secondly, the concentration dependancy of acetic anhydride on both the rate of formation of sulphoacetic and the rate of acetylation of phenol was identical. This implied that the reactions followed identical reaction pathways. This contrasts with the need for rearrangement only in the case of sulphoacetic acid formation as had been suggested by T. F. Murray and W. O. Kenyon.

They were therefore faced with the problem of suggesting a mechanism in which the intermediate would be playing similar kinetic roles in both the formation of sulphoacetic acid and acetylation of phenol. The first mechanism they suggested was thus:-

$$Ac_2O + H_2SO_4 \overset{\text{fast}}{\rightleftharpoons} Ac_2OH^+ + H_2SO^-_4 \qquad \text{(a)}$$

$$2Ac_2O + H_2SO_4 \rightleftharpoons (Ac_2OH^+)_2\,SO_4^{2-} \qquad \text{(b)}$$



(33)

This mechanism was discarded however since it requires that the rearrangement of the protonated species proceed via a simpler species. The following scheme was thus preferred:-

$$\mathrm{Ac_2O + H_2SO_4 \rightleftharpoons AcOSO_3H + AcOH} \qquad \text{(a)}$$

$$\mathrm{2Ac_2O + H_2SO_4 \rightleftharpoons (AcO)_2SO_2 + 2AcOH} \qquad \text{(b)}$$

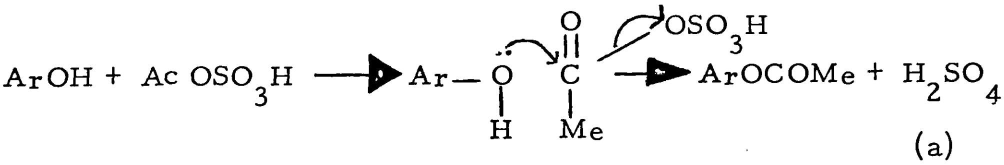
$$\mathrm{AcOSO_3H \longrightarrow HOSO_2CH_2CO_2H} \qquad \text{(c)}$$

$$\mathrm{(AcO)_2SO_2 \longrightarrow AcOSO_2CH_2CO_2H} \qquad \text{(d)}$$

$$\mathrm{AcOSO_2CH_2CO_2H \xrightleftharpoons{AcOH} Ac_2O + HO_3SCH_2CO_2H} \qquad \text{(e)}$$

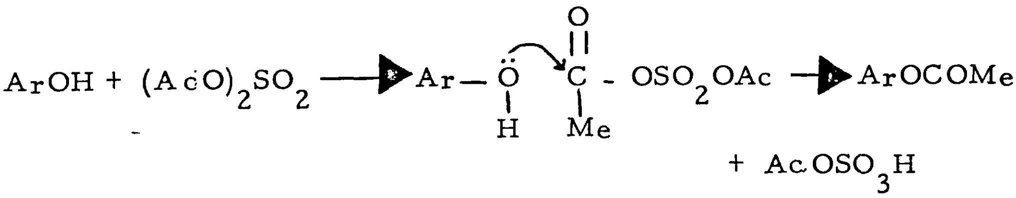
(34)

The acetylation of phenol would therefore take place thus:-



$$\mathrm{ArOH + AcOSO_3H \longrightarrow Ar-}\underset{\displaystyle \mathrm{H}}{\ddot{\mathrm{O}}}\;\underset{\displaystyle \mathrm{Me}}{\overset{\displaystyle \mathrm{O}}{\overset{\|}{\mathrm{C}}}}\mathrm{-OSO_3H \longrightarrow ArOCOMe + H_2SO_4}$$

(a)

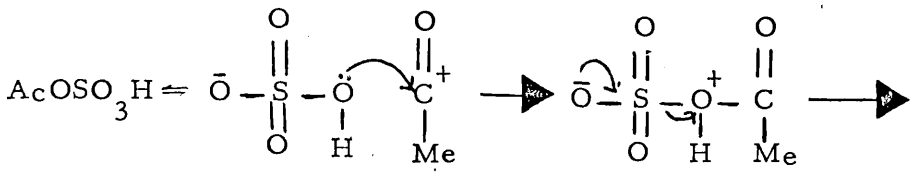


$$\mathrm{ArOH + (AcO)_2SO_2 \longrightarrow Ar-}\underset{\displaystyle \mathrm{H}}{\ddot{\mathrm{O}}}\;\underset{\displaystyle \mathrm{Me}}{\overset{\displaystyle \mathrm{O}}{\overset{\|}{\mathrm{C}}}}\mathrm{-OSO_2OAc \longrightarrow ArOCOMe + AcOSO_3H}$$

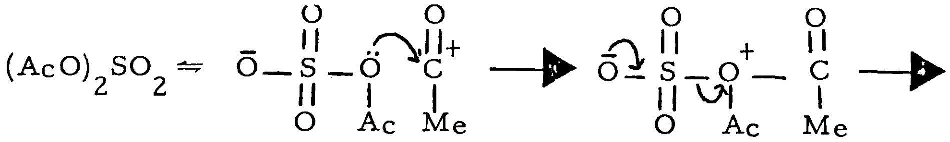
(b)

(35)

In the case of the formation of sulphoacetic acid a similar reaction would take place involving disproportionation of the unsymmetrical anhydride into sulphurtrioxide.



$$SO_3 + AcOH \xrightarrow{fast} HOSO_2CH_2COOH \qquad (a)$$



$$Ac_2O + SO_3 \xrightarrow[fast]{AcOH} HOSO_2CH_2CO_2H \qquad (b)$$

(36)

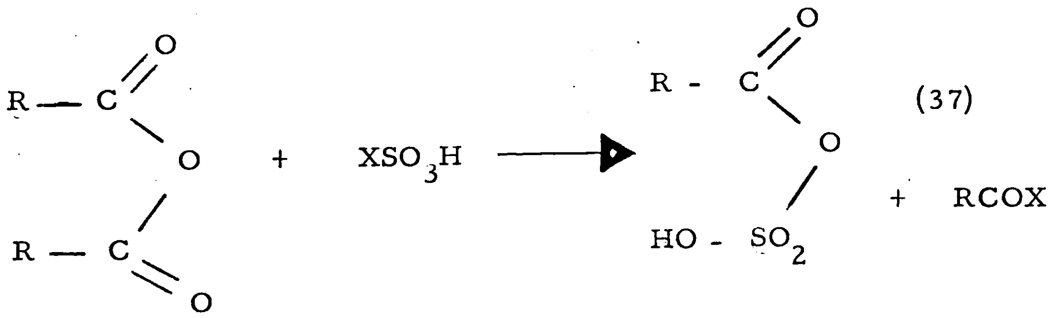
Sulphur trioxide is known to produce sulphoacetic acid rapidly with acetic acid even at low temperature.

H. Sihtola and L. Laumanen[102] carried out conductivity studies on mixtures of acetic anhydride and sulphuric acid. Their findings confirm D. P. N. Satchell and E. A. Jeffery's results especially with regard to the formation of diacetylsulphuric acid. They found that in a 1:1 mixture of acetic anhydride: sulphuric acid there is a considerable rise in the conductivity of the solution with time. They attributed this to the formation of acetyl sulphuric acid, which being an unsymmetrical molecule, dissociates considerably into acetylium ions. In a 2:1 acetic anhydride sulphuric acid mixture, they recorded an initial increase in conductivity with time to a maximum, which was followed by a decrease in conductivity due to conversion of the monoacetyl sulphuric into diacetyl sulphate and not sulphoacetic acid, as T. F. Murray and W. O. Kenyon had suggested. They argued that diacetyl sulphate does not dissociate to any appreciable extent and its formation accords with the decrease in conductivity. Addition of acetic acid to the diacetyl sulphate resulted in the restoration of the conductivity, i.e. a reconversion of diacetyl to monacetyl sulphuric acid which shows that these reactions are equilibrium reactions. They also used N.M.R. spectroscopy to demonstrate the existence of acetylium ions the protons of which were found to have a lower chemical shift than those of the anhydride and the acid.

However their experiments on the acetylation of cellulose appear to show that diacetyl sulphate has no acetylation activity since it does not dissociate into ions and that only monoacetyl sulphuric acid was an acetylating intermediate. This is hard to believe since it would make it difficult to explain the catalytic role since in that situation only the dianhydride is present. This is contrary to the mechanism suggested by E.A. Jeffery and D.P.N. Satchell in which both the monoacetyl and the diacetyl sulphate play an active role in the acetylation of phenol. This controversy so far remains unresolved.

### 4.1.6. Interactions of carboxylic anhydrides with other strong acids.

Carboxylic anhydrides have been found to acetylate in the presence of acids other than sulphuric acid. Halosulphonic acids react directly with carboxylic anhydrides in a reaction that provides a suitable preparation for acid halides[103]. This reaction has been successfully used for the synthesis of acid halides where (X = F or Cl)



(37)

Perchloric acid forms very powerful acetylating reagent when added to excess acetic anhydride.

$$Ac_2O + HClO_4 \longrightarrow Ac^+ + ClO_4^- + AcOH \qquad (38)$$

This reagent can also be prepared from silver perchlorate and acetyl chloride.[104]

Carboxylic anhydrides and nitric acid readily react to form acylnitrates amongst other species.[105]

$$HNO_3 + (RCO)_2O \rightleftharpoons RCO_2NO_2 + RCO_2H \qquad (39)$$

This equilibrium lies more to the right and acyl nitrates known to ionise preferentially into carboxylate and nitronium ions.

$$RCO_2NO_2 \rightleftharpoons RCO_2^- + NO_2^+ \qquad (40)$$

Acyl phosphates are usually prepared from a sodium or a silver salt and an acylchloride. Like other acyl derivatives they are difficult to isolate but can be purified as their barium or sodium salt.[30]

$$AgOP(O)(OH)_2 + RCOCl \longrightarrow RCOP(O)(OH)_2 + AgCl \qquad (41).$$

## 4.2. RESULTS AND DISCUSSION

### 4.2.1. Kinetics of the reaction of methane sulphonic acid with trifluoroacetic anhydride.

Unsymmetrical sulphonic-carboxylic anhydrides have been prepared by the reaction of sulphonic acids and carboxylic anhydrides[90]. However, all attempts to isolate the unsymmetrical anhydride ($CH_3SO_2OCOCF_3$) by reacting methane sulphonic acid with trifluoroacetic anhydride in nitromethane failed. Removal of nitromethane, trifluoroacetic acid and excess trifluoroacetic anhydride under reduced pressure resulted in a white crystalline product with a sharp melting point (71°C) and which was identified as methane sulphonic anhydride. This however does not preclude the initial formation of the unsymmetrical anhydride. If it is unstable, the removal of the symmetrical anhydrides could result in its complete disproportionation:

$$CH_3SO_3H + (CF_3CO)_2O \rightleftharpoons CH_3SO_2OCOCF_3 + CF_3COOH \quad (a)$$

$$2\,CH_3SO_2OCOCF_3 \rightleftharpoons (CH_3SO_2)_2O + (CF_3CO)_2O \quad (b)$$

(42)

Since this unsymmetrical anhydride could not be isolated, it was therefore impossible to study the kinetics of the formation of methyl aryl sulphones. However, by studying the reaction of trifluoroacetic anhydride and methane sulphonic acid, information regarding the role of the unsymmetrical anhydride in the sulphonylation of aromatic hydrocarbons could be gathered.

Infra-red spectroscopy was used for the determination of the concentration of trifluoroacetic anhydride in reacting systems. This was achieved by monitoring the absorption due to the C = O stretching vibrations at $1910^{-1}\,cm^{-1}$. All reactions were carried out under anhydrous conditions using thermostatted cells fitted with silver chloride windows.

When solutions of methane sulphonic acid in nitromethane (0. 03 mol. $dm^{-3}$) were reacted with trifluoroacetic anhydride (o. o3 mol. $dm^{-3}$) at 24°C, the reaction was very fast. The trifluoroacetic anhydride had completely reacted in less than two minutes and thus making it impossible to obtain good kinetic data. However in dichloromethane, in which both the sulphonic acid and the anhydride dissolved, the reaction rate was considerably slower.

In dichloromethane the rate of decrease in the concentration of trifluoroacetic anhydride was observed to be completely independent of the concentration of methane sulphonic acid. The reaction was found to show a first-order dependence upon the trifluoroacetic anhydride concentration. Accordingly the rate law may be written thus:-

$$\frac{-d[A]}{dt} = k\,[A] \qquad (43)$$

where [A] is the concentration of trifluoroacetic anhydride. Rearrangement and integration of this expression

$$-\int_{O}^{t}\frac{d[A]}{[A]} = \int_{O}^{t} k\,dt$$

$$\ln[A_o] - \ln[A_t] = k\,t \qquad (44)$$

where $[A_o]$ is the concentration of trifluoroacetic anhydride at t = O. Therefore plotting ln $[A_t]$ against t, a straight line is obtained with a slope equal to the rate constant and an intercept equal to ln $[A_o]$. The rate constant for this reaction was calculated for different initial concentrations of methane sulphonic acid, the initial concentration of trifluoroacetic anhydride in each case being 0. 03 mol. $dm^{-3}$. The reaction temperature was 24°C ± 0.05°C. Table 4.2.1.-1 gives rate constants obtained at different concentrations of methane sulphonic acid and Figs. 4.2.1 - 3, -4, and -5 are the kinetic plots obtained in these reactions.

Table 4.2.1. - 1

Rate constants obtained at various concentrations of methane sulphonic acid.

Average $k = 5.25 \times 10^{-5} \pm 0.08\ s^{-1}$

| Concentration of methane sulphonic acid ($mol.\ dm^{-3}$) | rate constant k (seconds $^{-1}$) |
|---|---|
| 0.03 | $5.28 \times 10^{-5}$ |
| 0.05 | $5.16 \times 10^{-5}$ |
| 0.10 | $5.30 \times 10^{-5}$ |

One explanation of the dependency of the reaction only upon the concentration of trifluoroacetic anhydride is the ionisation of the anhydride into trifluoroacetylium and trifluoroacetoxy ions.

$$(CF_3CO)_2O \xrightarrow{slow} CF_3CO^+ + CF_3COO^- \qquad (45)$$

This heterolysis is slow and is followed by the reaction of the trifluoroacetylium ions with methane sulphonate to give the unsymmetrical anhydride.

$$CF_3COO^- + CH_3SO_3H \xrightarrow{fast} CH_3SO_3^- + CF_3COOH \qquad (a)$$

$$CF_3CO^+ + CH_3SO_3^- \xrightarrow{fast} CH_3SO_2OCOCF_3 \qquad (b)$$

(46)

Although polar solvents assist ionisation in uni-molecular substitution ($S_{n1}$) reactions, they do not enter the rate expression since they are present in a large excess. The more polar the solvent, the faster the reaction proceeds. This phenomenon is exhibited here by carrying out the reaction in different mixtures of dichloromethane and nitromethane (Table 4.2.1 - 2). Figs.4.2.1. - 6 - 9 give kinetic plots and the graph of rate constants against volume percent of nitromethane in dichloromethane. Increasing the volume percentage of nitromethane in dichloromethane enhances the polarity of the solvent. By plotting the rate constant (k) against the volume percentage of nitromethane in nitromethane-dichloromethane mixtures, a straight line was obtained which on extrapolation a value of k in pure nitromethane corresponds to the unattainable rate constant of this reaction discussed previously. This rate constant was estimated to be approximately $3.95 \times 10^{-1} s^{-1} \pm 1.0$ although of course it could not be measured directly.

Table 4.2.1 -2

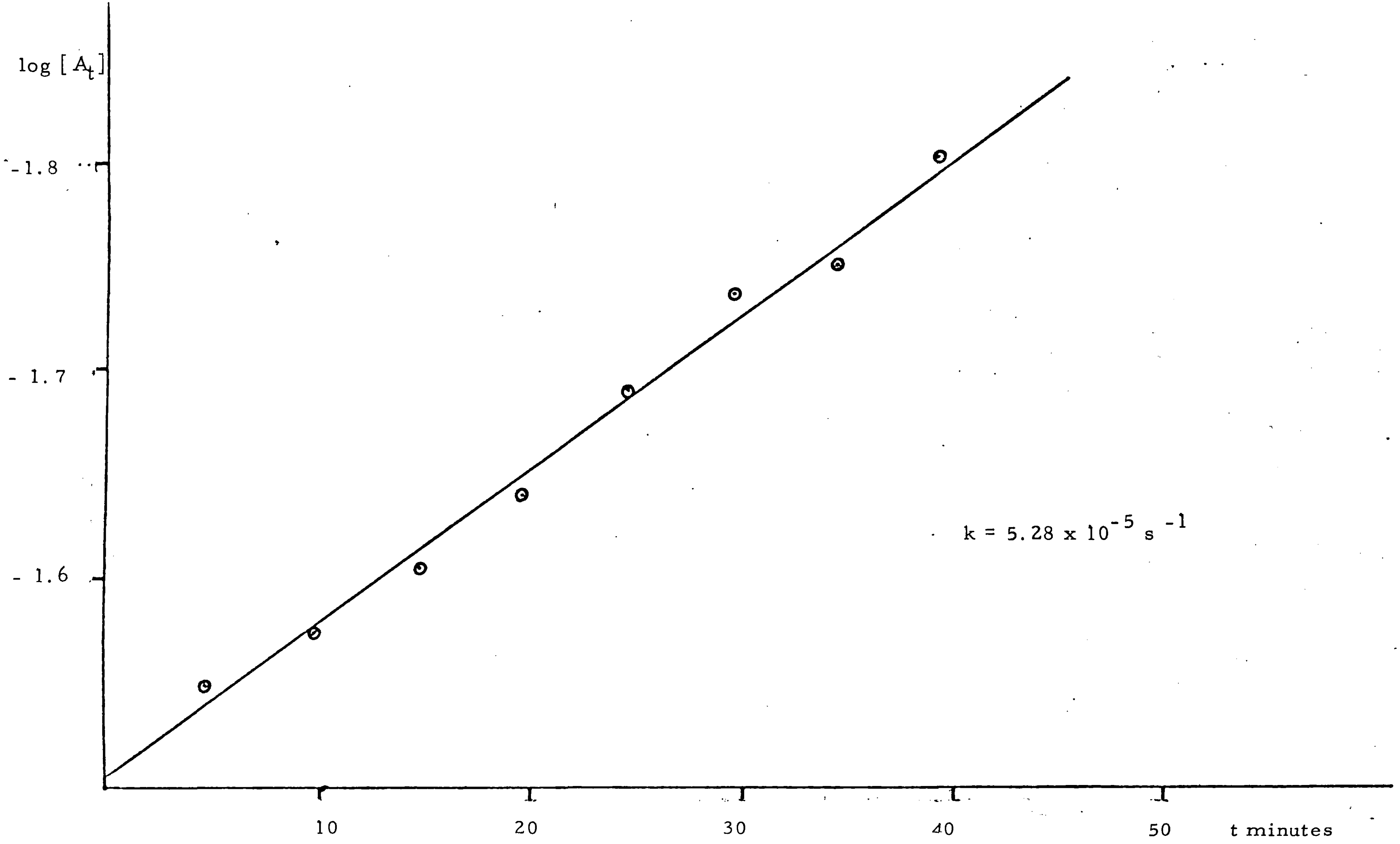
Rate constants against volume % nitromethane/dichloromethane

| k seconds$^{-1}$ | Volume % nitromethane |
|---|---|
| $5.25 \times 10^{-5}$ | 0 |
| $1.85 \times 10^{-4}$ | 10 |
| $4.85 \times 10^{-4}$ | 25 |
| $1.68 \times 10^{-3}$ | 37 |
| $4.30 \times 10^{-3}$ | 50 |

### 4.2.2. Kinetics of the reaction of mesitylene sulphonic acid with trifluoroacetic anhydride.

Aromatic sulphonic acids present considerable difficulties when used in kinetic studies that require anhydrous conditions because of their very hygroscopic nature. Further, most aromatic sulphonic acids in the solid state are associated with one or more molecules of water of crystallisation. When

Fig. 4.2.1 - 3. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. $dm^{-3}$) with $CH_3SO_3H$ (0.03 mol. $dm^{-3}$) in $CH_2Cl_2$.



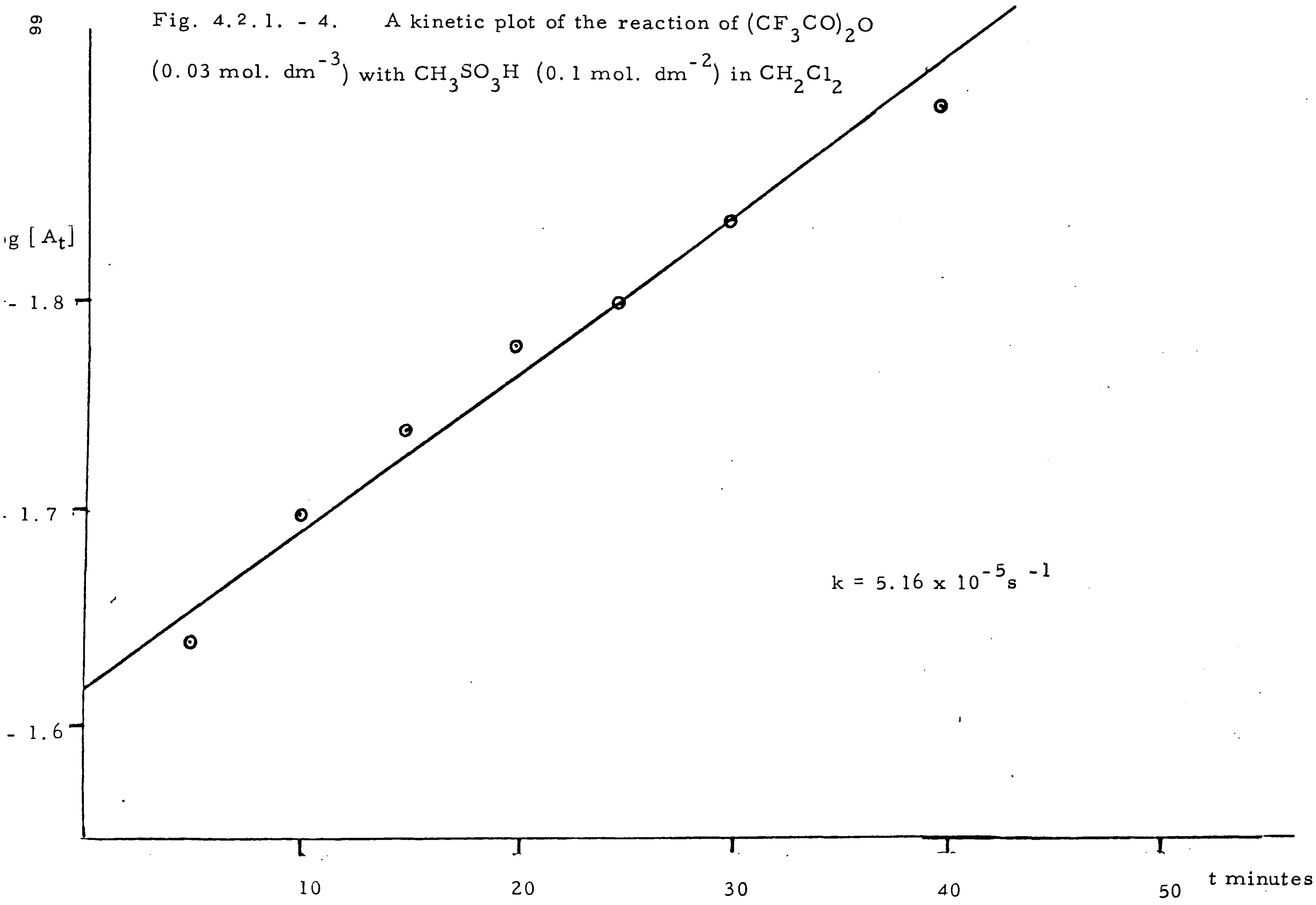


Fig. 4.2.1. - 4. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. $dm^{-3}$) with $CH_3SO_3H$ (0.1 mol. $dm^{-2}$) in $CH_2Cl_2$

$k = 5.16 \times 10^{-5} s^{-1}$

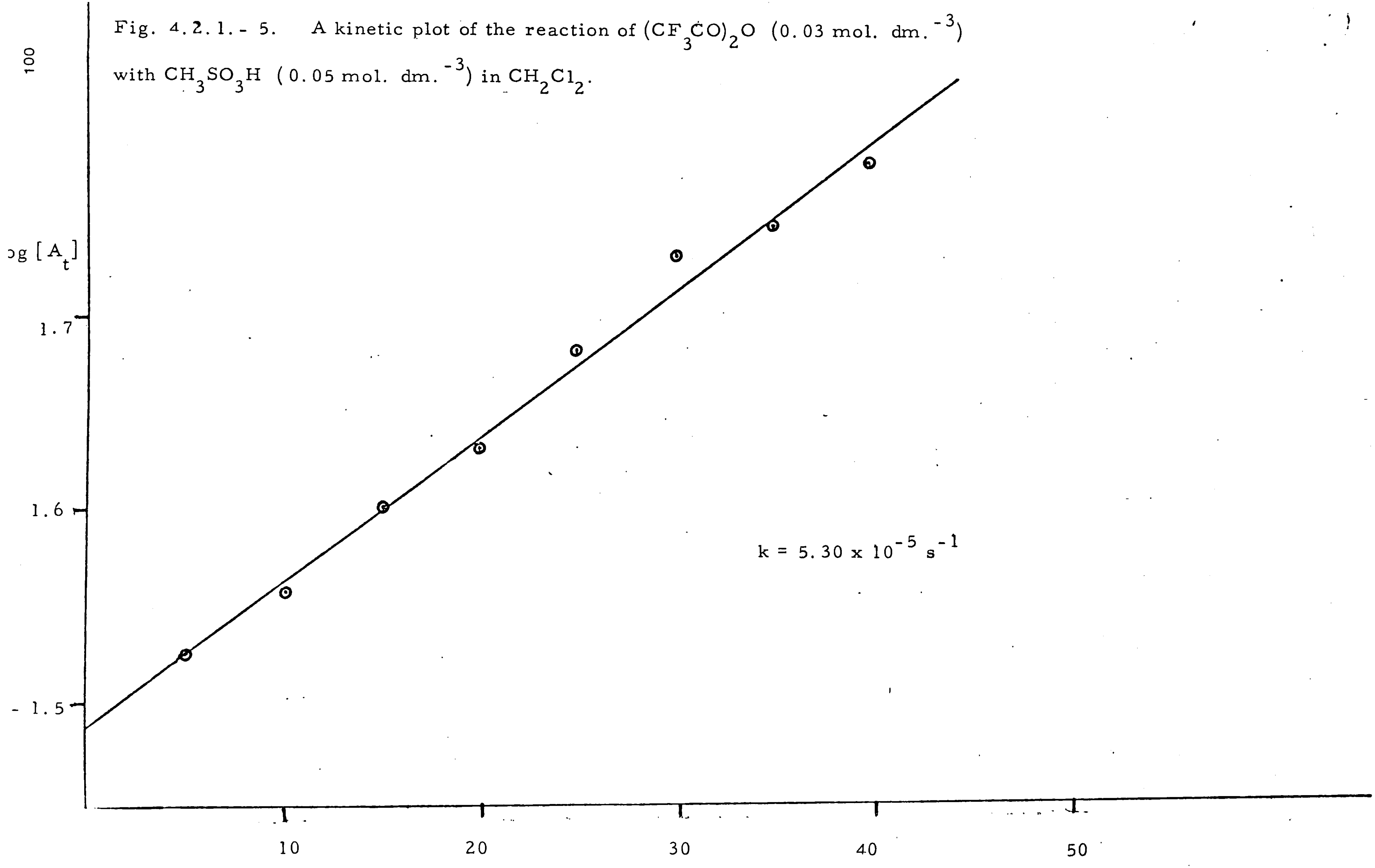


Fig. 4.2.1.- 5. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. dm.$^{-3}$) with $CH_3SO_3H$ (0.05 mol. dm.$^{-3}$) in $CH_2Cl_2$.

Fig. 4.2.1. - 6. A kinetic plot of the reaction of $CF_3CO)_2O$ (0.03 mol. dm$^{-3}$) with $CH_3SO_3H$ (0.03 mol. dm.$^{-3}$) in 10% $CH_3NO_3/CH_2Cl_2$ (V/V).

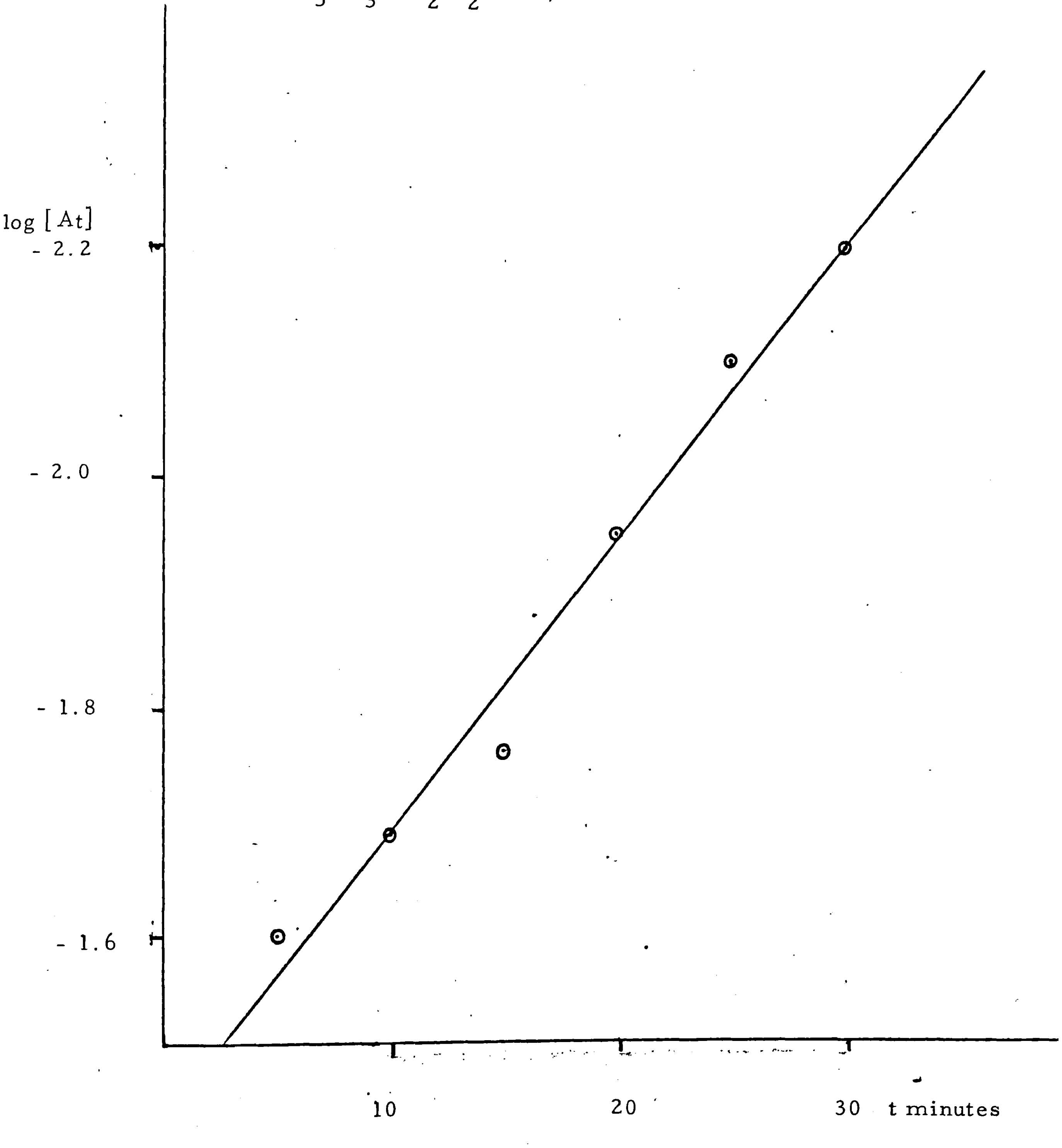
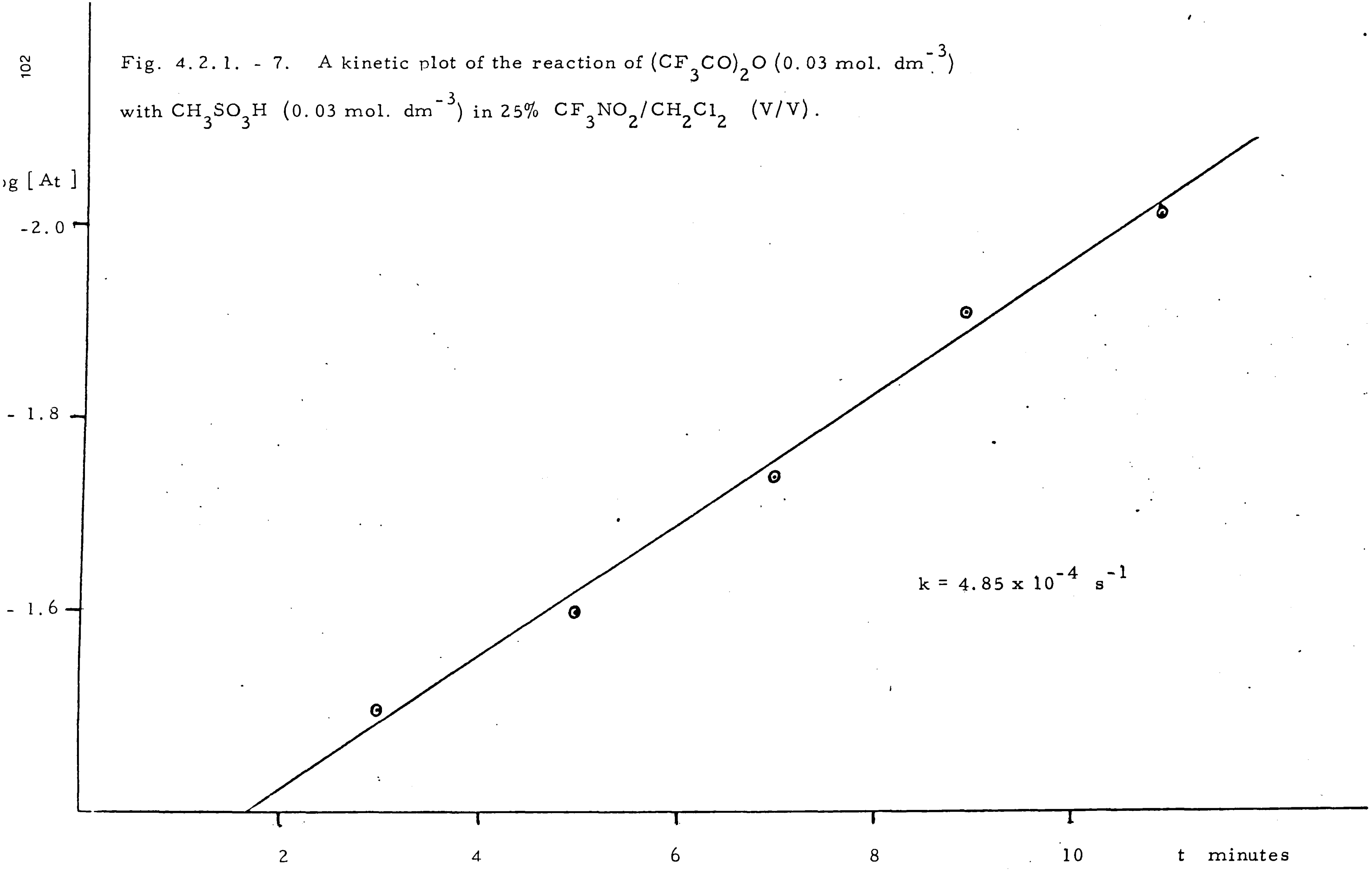


Fig. 4.2.1. - 7. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. dm$^{-3}$) with $CH_3SO_3H$ (0.03 mol. dm$^{-3}$) in 25% $CF_3NO_2/CH_2Cl_2$ (V/V).



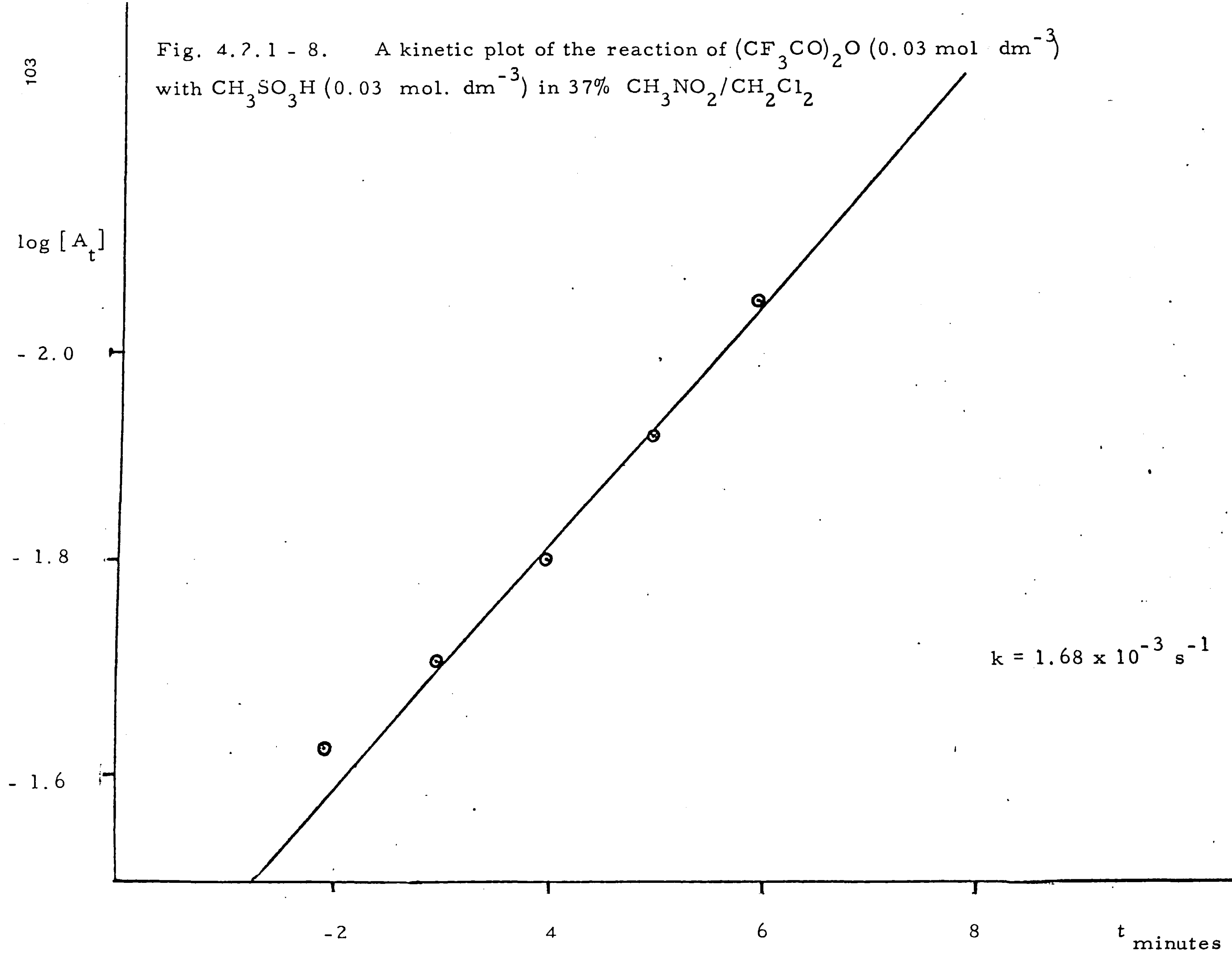


Fig. 4.7.1 - 8. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol dm$^{-3}$) with $CH_3SO_3H$ (0.03 mol. dm$^{-3}$) in 37% $CH_3NO_2/CH_2Cl_2$

$k = 1.68 \times 10^{-3}\ s^{-1}$

Fig. 4.2.1.-10 A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. dm$^{-3}$) with $CH_3SO_3H$ (0.03 mol. dm$^{-3}$) in 50% $CH_3NO_2/CH_2Cl_2$ (V/V).

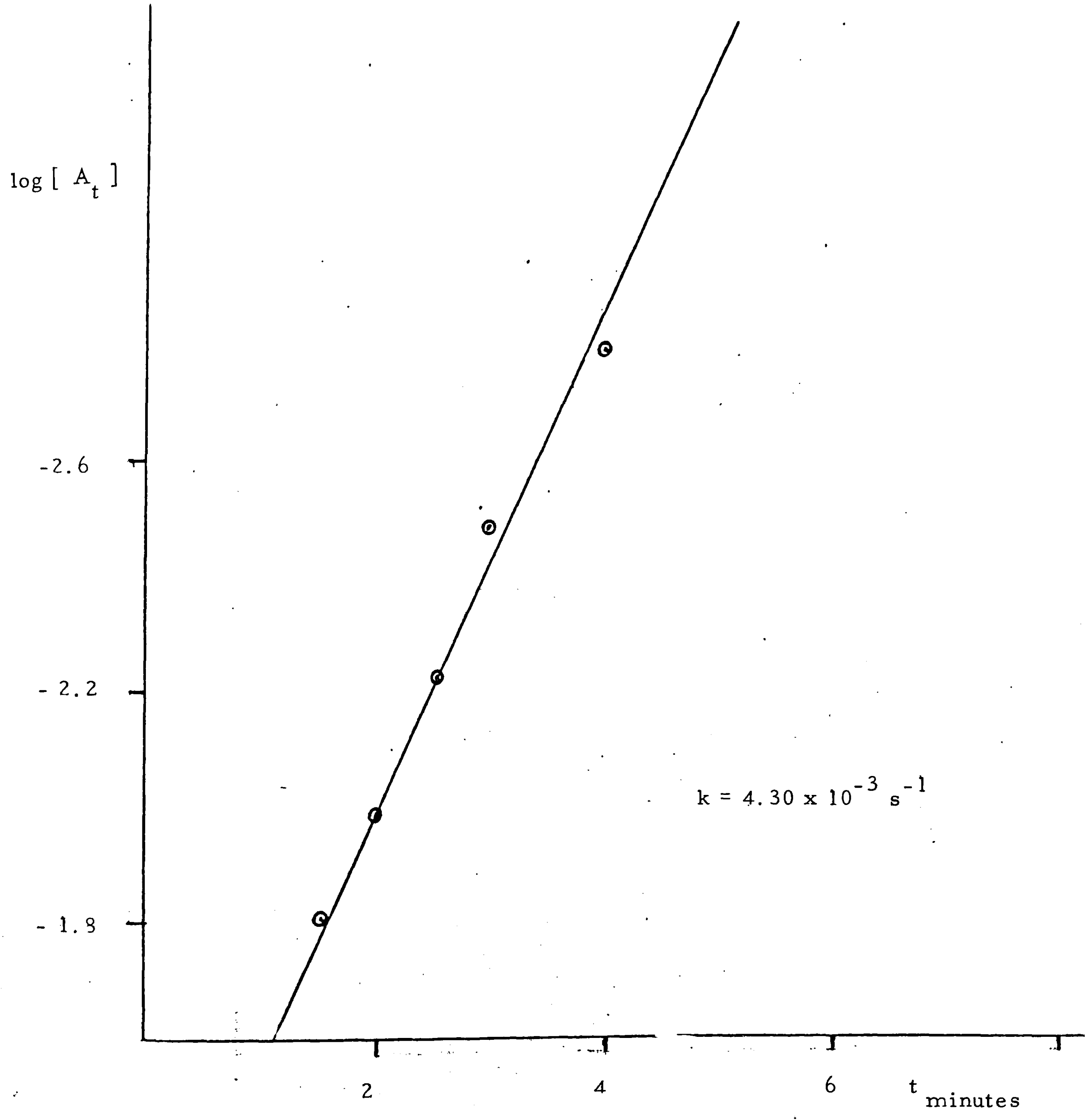
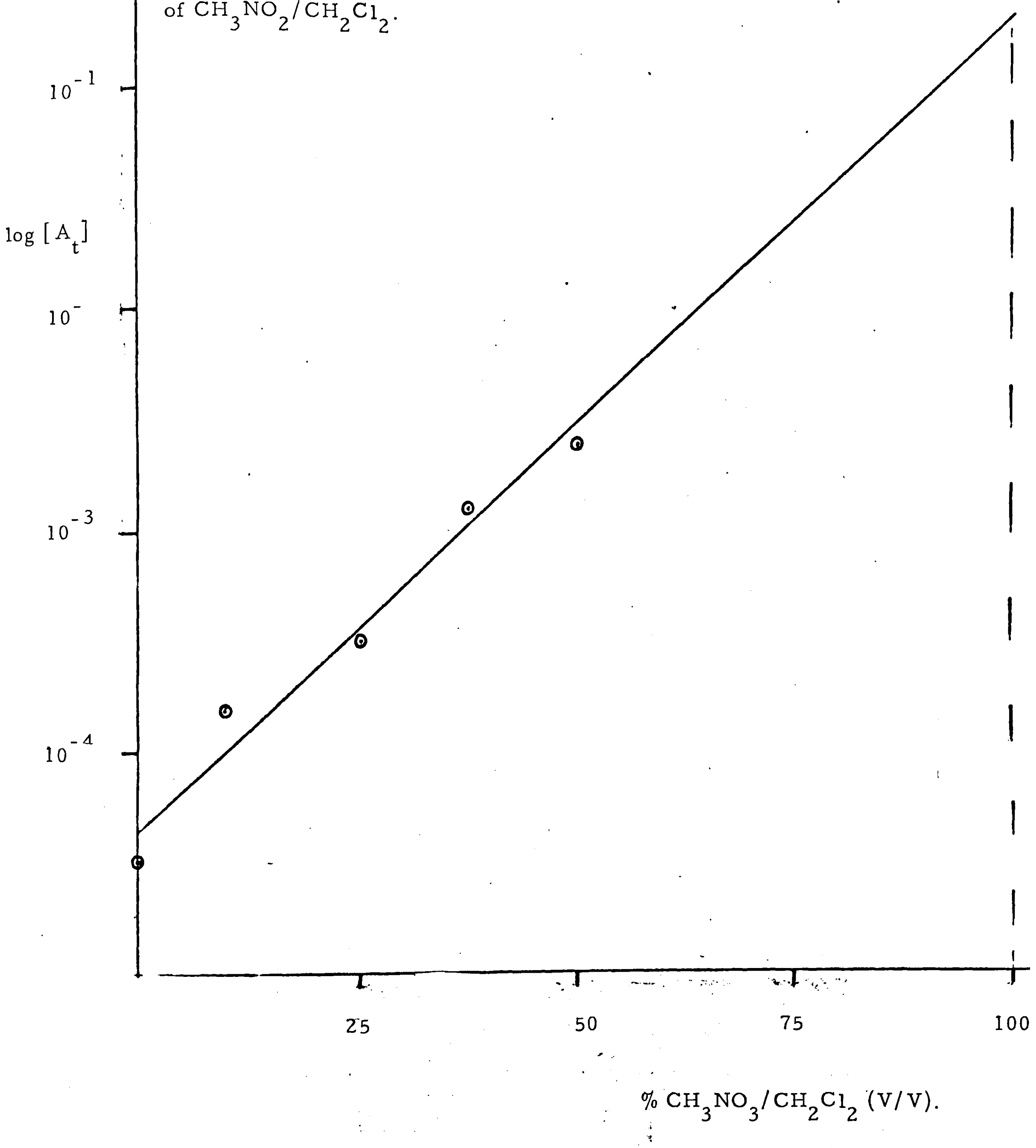


Fig. 4.2.1. - 9 A plot of rate constants (k) against volume per cent of $CH_3NO_2/CH_2Cl_2$.



attempts are made to remove this water, the processes used are often accompanied by decomposition leading to consequent contamination of the acid with undesirable products. p-Toluene sulphonic acid is a good example of this behaviour. In its crystalline form, it exists as a monohydrate. Even in this hydrated form, it is still very hygroscopic. Attempts to remove the water by azeotropic distillation with benzene resulted in an acid contaminated by 4 methyl diphenyl sulphone together with other sulphone isomers. Removal of water by distillation under reduced pressure and a subsequent distillation of the free acid itself, resulted in total decomposition. Another method, in which the sulphonic anhydride is first prepared and then subsequently hydrolysed with an exact amount of water in nitromethane solvent was also unsuccessful here. This may have been since p-toluene sulphonic anhydride is only slightly soluble in a nitromethane-water mixture and the rate of hydrolysis under these circumstances is very slow. However, mesitylene sulphonic acid dihydrate loses water easily under reduced pressure (14 mm. Hg) when heated to 100°C. in a drying pistol containing phosphorus pentoxide. The resulting anhydrous acid is red in colour and exists almost in a semi-solid state at room temperature.

Mesitylene sulphonic acid was found to react with trifluoroacetic anhydride in a similar way to methane sulphonic acid. The reaction was carried out at 24°C ± 0.5°C in 20% nitromethane in dichloromethane (volume %). Just as was found with the reaction between methane sulphonic acid and trifluoroacetic anhydride, the rate of this reaction is independent of the concentration of mesitylene sulphonic acid and dependent only on the trifluoroacetic anhydride concentration.

$$(CF_3CO)_2O \overset{slow}{\rightleftharpoons} CF_3CO^+ + CF_3COO^- \qquad (a)$$

$$CF_3COO^- + ArSO_3H \xrightarrow{fast} ArSO_3^- + CF_3COOH \qquad (b)$$

$$CF_3CO^+ + ArSO_3^- \longrightarrow CF_3COOSO_2Ar \qquad (c)$$

ArH = mesitylene

Below is a table of rate constants obtained at different concentrations of mesitylene sulphonic acid with the trifluoroacetic anhydride concentration at 0.03 mol.dm$^{-3}$. Figs.4.2.2 - 2 and 4.2.2 - 3 give kinetic plots obtained in these interactions.

Table 4.2.2 - 1

Rate constants at various concentrations of mesitylene sulphonic acid.

| concentration of mesitylene sulphonic acid | rate constant(k) seconds$^{-1}$ |
|---|---|
| 0.05 | $7.67 \times 10^{-5} \pm 0.20$ |
| 0.01 | $7.80 \times 10^{-5} \pm 0.15$ |

Average k = $7.74 \times 10^{-5} \pm 0.07$ s$^{-1}$

If the rate constants for the reactions with alkyl and aryl sulphonic acids depend only on the initial ionisation of trifluoroacetic anhydride, the overall process should be independent of the nucleophilic sulphonate. The rate constant of reaction of methane sulphonic acid in 20% $CH_3NO_2/CH_2Cl_2$ is $3.25 \times 10^{-4} \pm 0.1$ s$^{-1}$. This value is extrapolated from the graph of rate constants vs volume percentage of $CH_3NO_2/CH_2Cl_2$ curve (Fig.4.2.1. - 9). The rate constant measured for the reaction of mesitylene sulphonic acid with trifluoroacetic anhydride is $7.74 \times 10^{-3} \pm 0.07$ s$^{-1}$ under the same conditions. This apparent inhibition of ionisation is not yet fully understood. However, it should be noted that solutions of mesitylene sulphonic acid in 20% $CH_3NO_2/CH_2Cl_2$

are slightly turbid while those of methane sulphonic acid are clear. It is possible therefore that this inhibition might be related to the smaller change in polarity of solvent owing to the presence of the sulphonic acid. The reaction rates would be expected to be the same in 100% nitromethane in which the solubility of both acids is high.

From these results one can safely conclude that aliphatic and aromatic sulphonic acids resemble carboxylic acids in their reactions with trifluoroacetic anhydride. The products of these interactions are unsymmetrical anhydrides. Further these anhydrides are formed very fast in suitable polar solvents such as nitromethane. These anhydrides therefore can be expected to play an important role in the reactions of sulphonic acids with various compounds in the presence of trifluoroacetic anhydride. This will be discussed later in this chapter with special reference to their reactions with aromatic hydrocarbons.

### 4.2.3. Kinetics of the reactions of sulphuric acid with trifluoroacetic anhydride.

The reaction of sulphuric acid with trifluoroacetic anhydride is more complicated than that of sulphonic acids. This is probably due to the dibasic nature of this acid. Because of its low solubility in dichloromethane, most of the measurements were carried out in 1:1 mixture(by volume) of dichloromethane and nitromethane as a solvent.

The first experiments involved measuring the rate of the reaction of 0.03 mol. dm$^{-3}$ of trifluoroacetic anhydride with a varied but excess amount of sulphuric acid (0.15, 0.25, 0.4 mol. dm$^{-3}$). The behaviour of these solutions was found to be identical to that of the sulphonic acids. The rate of the reaction showed no dependence on the concentration of sulphuric acid but merely trifluoroacetic anhydride. The first order rate constant was calculated to be approximated $9.22 \times 10^{-5} \pm 0.6$ s$^{-1}$.

Fig. 4.2.2.-2. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol.dm.$^{-3}$ with $(CH_3)_3C_6H_2SO_3H$ (0.05 mol.dm$^{-3}$) in 20% $CH_3NO_2/CH_2Cl$ (V/V)

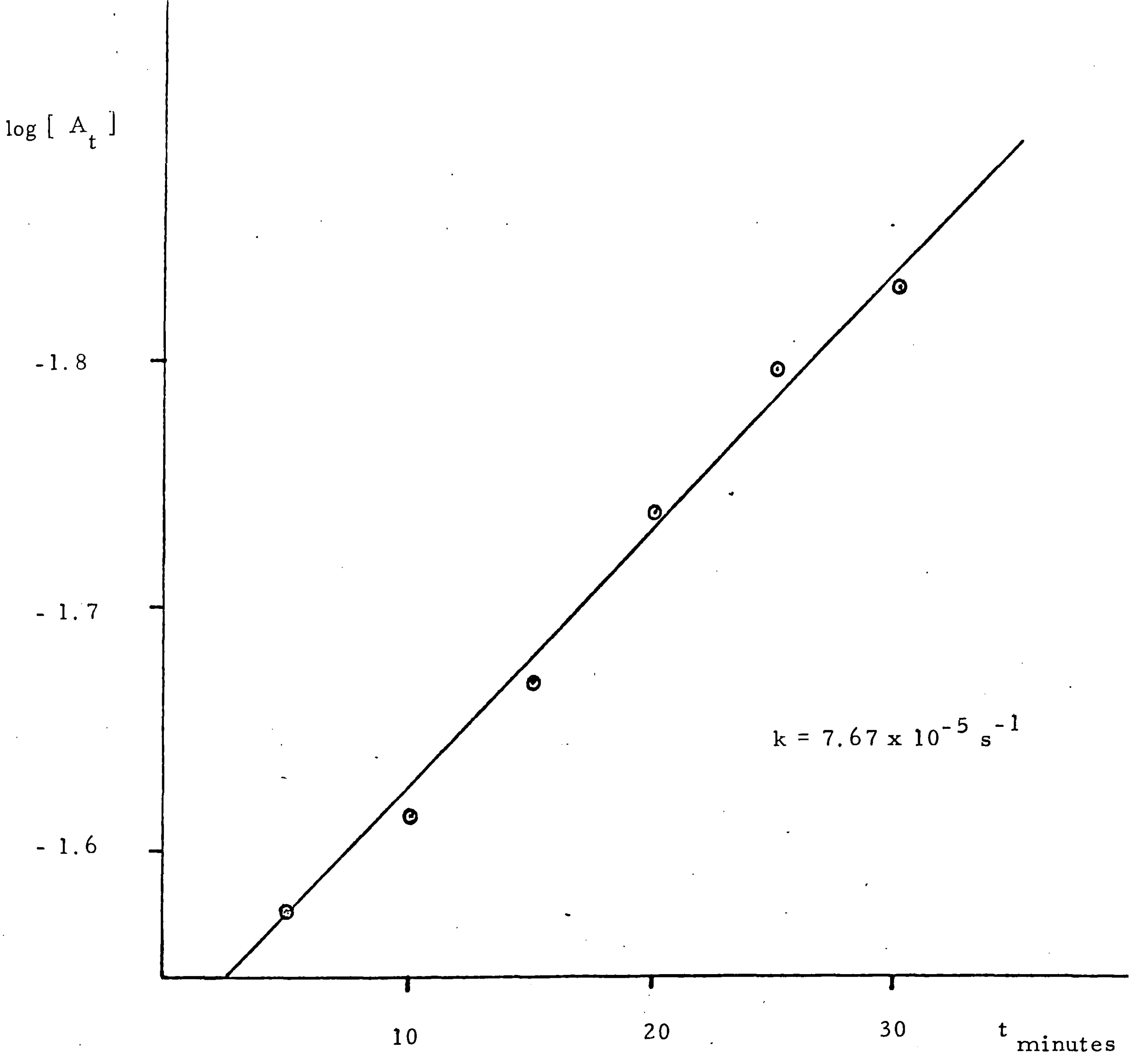
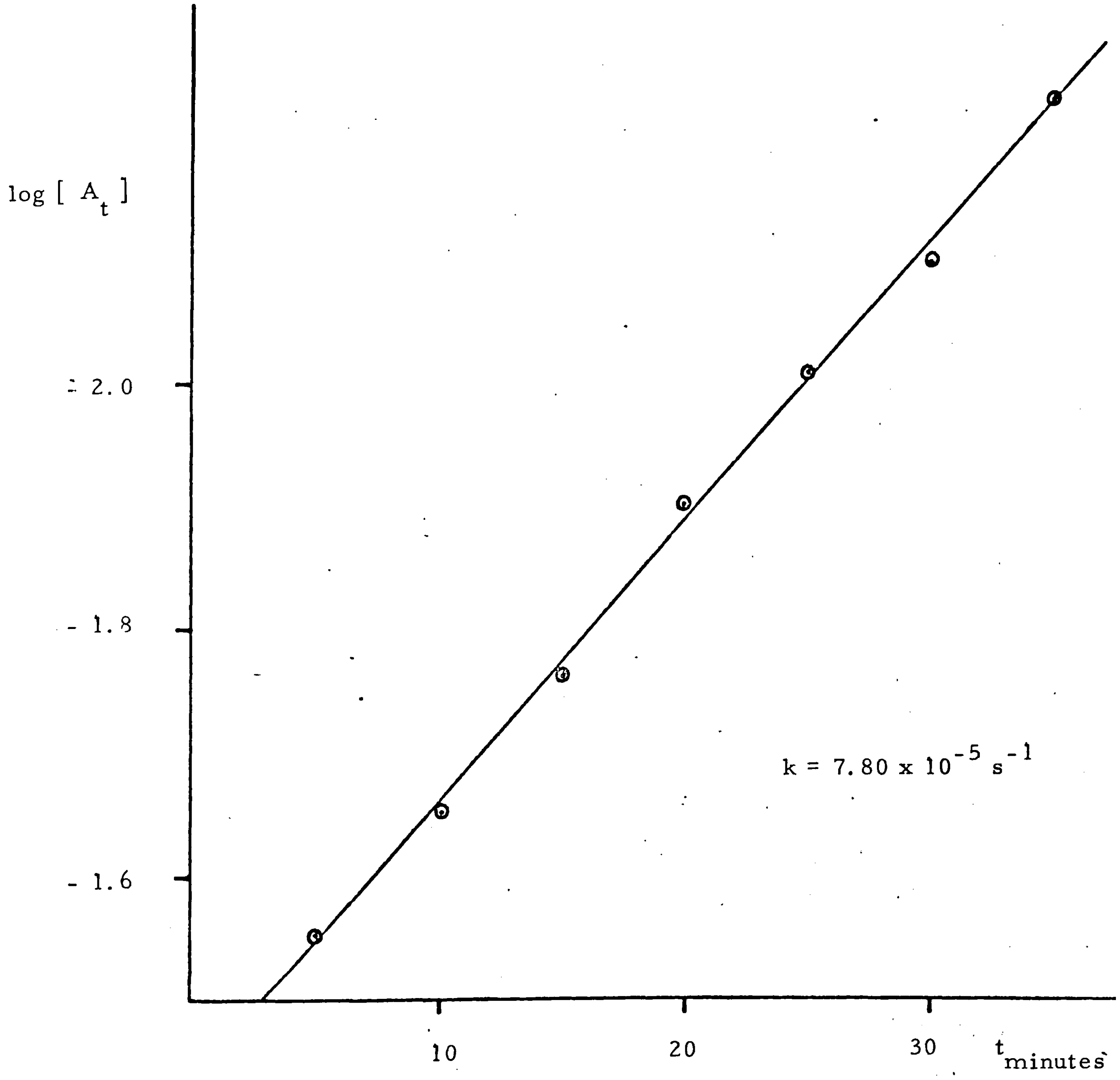


Fig. 4.2.2. - 3. A kinetic plot of the reaction of $(CF_3CO)_2O$ with $(CH_3)_3C_6H_2SO_3H$ (0.1 mol.dm$^{-3}$) in 20% $CH_3NO_2/CH_2Cl_2$ (V/V).



This behaviour was anticipated since in excess sulphuric acid only one unsymmetrical anhydride product would be expected to be formed.

$$(CF_3CO)_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CF_3CO^+ + CF_3COO^- \qquad \text{(a)}$$

$$CF_3CO^+ + CF_3COO^- + H_2SO_4 \xrightarrow{k_2} CF_3COSO_2OH + CF_3COOH \qquad \text{(b)}$$

(48)

Table 4.2.3. - 1 gives the rate constants and the various concentrations of sulphuric acid. Figs. 4.2.3 - 2, 4.2.3 - 3 and 4.2.3 - 4 give kinetic plots in these interactions.

However, as in reaction 47, the reaction rate was much slower than the expected rate in found methane sulphonic acid. Therefore probably the same explanation given for the slower rate of reaction 47 applies in this case as well.

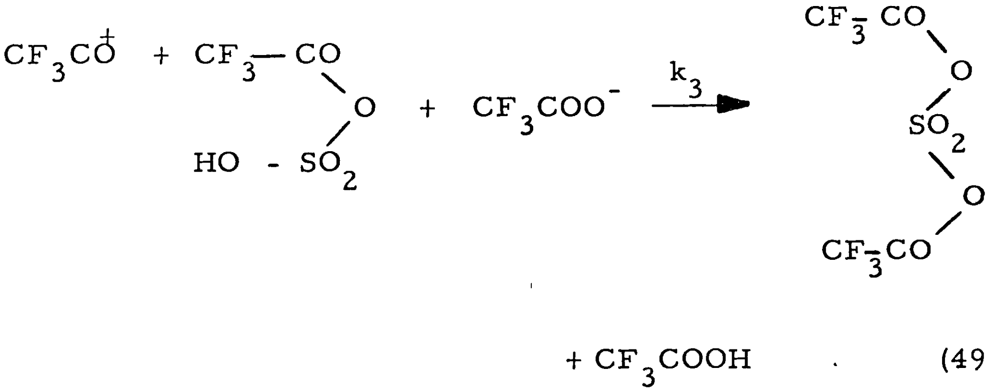
Table 4.2.3 - 1

Rate constants obtained at various concentrations of sulphuric acid

| concentration of sulphuric acid (mol dm$^{-3}$) | rate constant (k) seconds$^{-1}$ |
|---|---|
| 0.15 | $8.68 \times 10^{-5} \pm 0.1$ |
| 0.25 | $9.63 \times 10^{-5} \pm 0.1$ |
| 0.40 | $9.36 \times 10^{-5} \pm 0.1$ |

Average k = $9.22 \times 10^{-5} \pm 0.6$ sec$^{-1}$

When the concentration of sulphuric acid was reduced to 0.06 mol dm$^{-3}$ that is twice the concentration trifluoroacetic anhydride the rate constant became smaller (approximately $4.67 \times 10^{-5} \pm 0.1$) (Fig. 4.2.3 - 5). When equimolar quantities (0.03 mol dm$^{-3}$) of both sulphuric acid and the anhydride or an excess of the anhydride is used, the decrease in the concentration of the anhydride deviates from the first order rate law, i.e. the reaction rate becomes slower as the reaction approaches the end point (Fig.4.2.3 - 6). Figs.4.2.3 - 7 and 4.2.3 - 8 also show these reactions slowed down in 10% nitromethane/dichloromethane. The rate constants for the initial reactions were calculated and found to be approximately $1.65 \times 10^{-5} \pm 0.05\ s^{-1}$. When the concentration of $H_2SO_4$ is 0.015 mol $dm^{-3}$, the deviation occurs before 30% of the anhydride (0.03 mol $dm^{-3}$) is consumed. For equimolar quantities 0.03 mol $dm^{-3}$ the deviation does not occur until just over 50% of the reaction has taken place. Here it is probable that the dibasic nature of sulphuric acid becomes important. Under the conditions trifluoracetyl sulphuric acid may react further to give the di-(trifluoroacetyl) sulphate.



(49)

If now this reaction is slower than the formation of the trifluoroacetyl sulphuric acid ($k_2$) the overall removal of the trifluoroacetylium ion ($k_2$ and $k_3$) will become significant and be reflected in the slower rate of decrease in the concentration of trifluoroacetic anhydride. The derivation of the kinetic relationship is given using symbols for the reactants.

Trifluoroacetic anhydride = RX

Sulphuric acid = Y

$R^+ = CF_3CO^+$

$X^- = CF_3COO^-$

The reaction can be represented symbolically thus:-

$$RX \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} R^+ + X^- \qquad (50)$$

$$R^+ + Y \xrightarrow{k_2} RY + H^+ \qquad (51)$$

$$RY + R^+ \xrightarrow{k_3} R_2Y + H^+ \qquad (52)$$

$$\frac{-d[RX]}{dt} = k_1[RX] - k_{-1}[R^+][X^-] \qquad (53)$$

$$\frac{d[R_2Y]}{dt} = k_3 [RY][R^+] \qquad (54)$$

$$\frac{d[R^+]}{dt} = k_1[RX] - k_{-1}[R^+][X^-] - k_2[R^+][Y] - k_3[R^+][RY] \qquad (55)$$

$$\frac{d[RY]}{dt} = k_2[R^+][Y] - k_3[RY][R^+] \qquad (56)$$

Applying the stationary state approximation one can assume that the concentrations of the intermediates [R+] and [RY] do not change effectively with time i.e.

$$\frac{d[R+]}{dt} = \frac{d[RY]}{dt} = O \qquad (57)$$

$$[R+] = \frac{k_1[RX]}{k_{-1}[X^-] + k_2[Y] + k_3[RY]} \qquad (58)$$

$$[RY] = \frac{k_2[R+][Y]}{k_3[R+]} = \frac{k_2}{k_3} \cdot [Y] \qquad (59)$$

Substituting [RY] in equation (58)

$$[R+] = \frac{k_1 [RX]}{k_{-1}[X^-] + 2 k_2[Y]} \qquad (60)$$

and substituting [R+] in equation (53)

$$\frac{-d[RX]}{dt} = k_1[RX] - \frac{k_1\,k_{-1}[RX]\,[X^-]}{k_{-1}[X^-] + 2k_2[Y]} \tag{61}$$

$$= \frac{2k_1k_2[RX]\,[Y]}{k_{-1}[X^-] + 2\,k_2[Y]} \tag{62}$$

A similar expression can be derived for $R_2Y$

$$\frac{d[R_2Y]}{dt} = k_3[R^+]\,[RY]$$

$$= \frac{k_1k_2[Y][RX]}{k_{-1}[X^-] + 2k_2[Y]} \tag{63}$$

This equation shows that the rate of formation of the dianhydride should be half the rate of decrease of trifluoroacetic anhydride. Equation 63 can be rearranged to give

$$\frac{-d[RX]}{dt} = \frac{k_1[RX]}{\dfrac{k_{-1}[X^-]}{2k_2[Y]} + 1} \tag{64}$$

From equation 65 one can see that when $k_2[Y] \gg k_{-1}[X^-]$

$$\frac{-\,d\,[RX]}{dt} = k_1[RX] \tag{65}$$

This is observed experimentally at the beginning of the reaction and when the concentration of sulphuric acid is in large excess, i.e. when $2k_2[Y]$ is large. However as $2k_2[Y]$ becomes smaller, the equation predicts that the rate should decrease. This has been found to be the case when the initial concentration of sulphuric acid is twice, equal or less than that of trifluoroacetic anhydride. Therefore in order to account for the complete reaction it is necessary that the concentration of sulphuric acid be measured with time. In the case where the reaction goes as far as the formation of the monoanhydride, this retardation of the reaction can also be expected.

$$RX \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} R^+ + X^- \tag{50}$$

$$R^+ + Y \xrightarrow[k_2]{} RY \tag{51}$$

The expression for the decrease in the concentration of trifluoroacetic anhydride is:-

$$\frac{-d[RX]}{dt} = \frac{k_1[RX]}{\dfrac{k_{-1}[X^-] + 1}{k_2[Y]}} \tag{66}$$

In this case the rate of decrease of trifluoroacetic anhydride would be lower by a factor of 2 compared to equation (65).

From these results, one can conclude that trifluoroacetic anhydride reacts very readily with sulphuric acid in nitromethane. The initial product is trifluoroacetyl sulphuric acid which in excess trifluoroacetic anhydride is slowly converted to the di(trifluoroacetyl) sulphate in a slower reaction than the first. This information will be used later in this chapter to explain the mechanisms of sulphonylation of aromatic hydrocarbons in the presence of trifluoroacetic anhydride.

Fig. 4.2.3. - 2. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. $dm^{-3}$) with $H_2SO_4$ (0.4 mol. $dm^{-3}$) in 50% $CH_3NO_2/CH_2Cl_2$ (V/V)

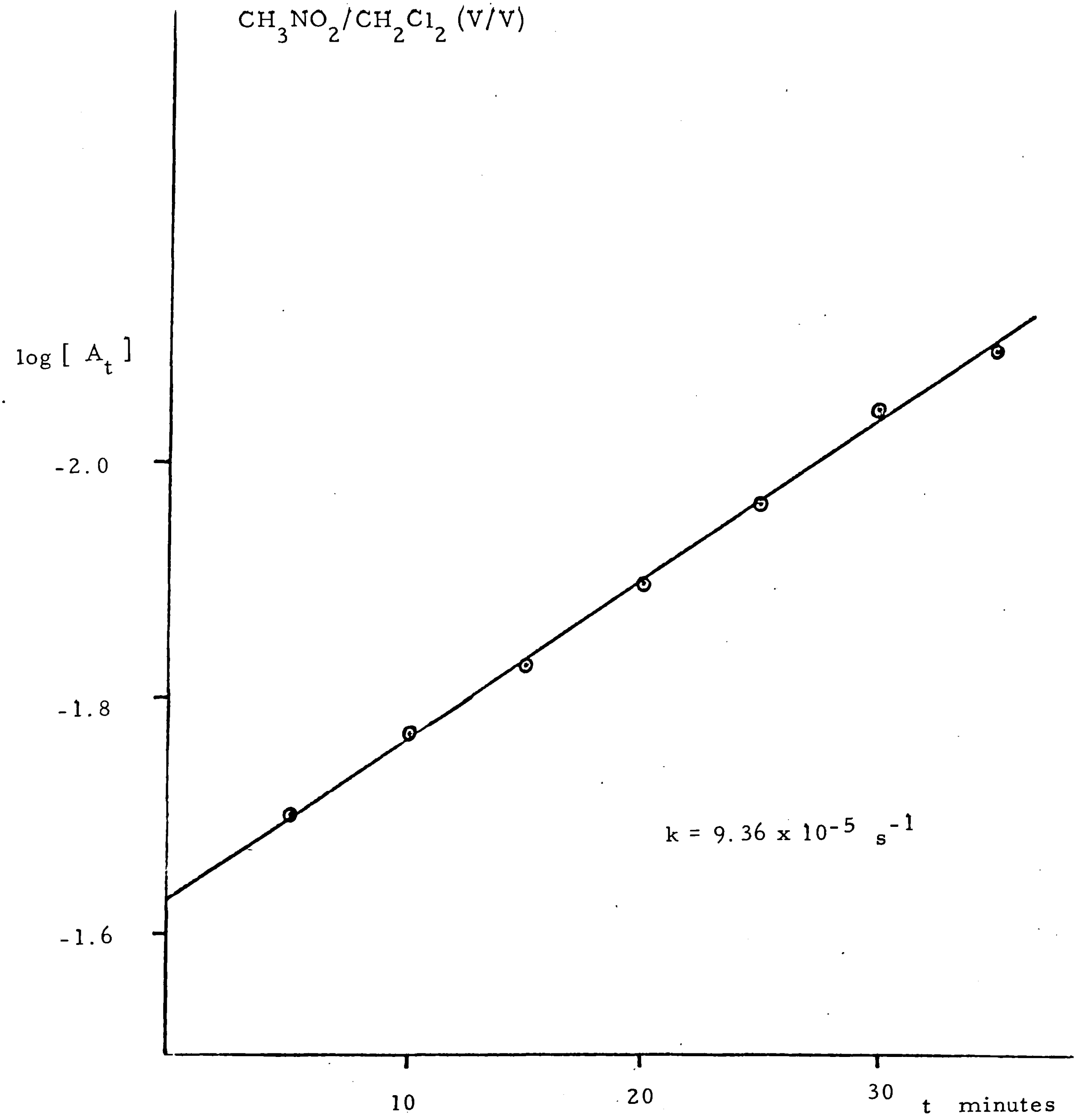


Fig. 4.2.3. - 2. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. $dm^{-3}$) with $H_2SO_4$ (0.25 mol. $dm^{-3}$) in 50% $CH_3NO_2/CH_2Cl_2$ (V/V)

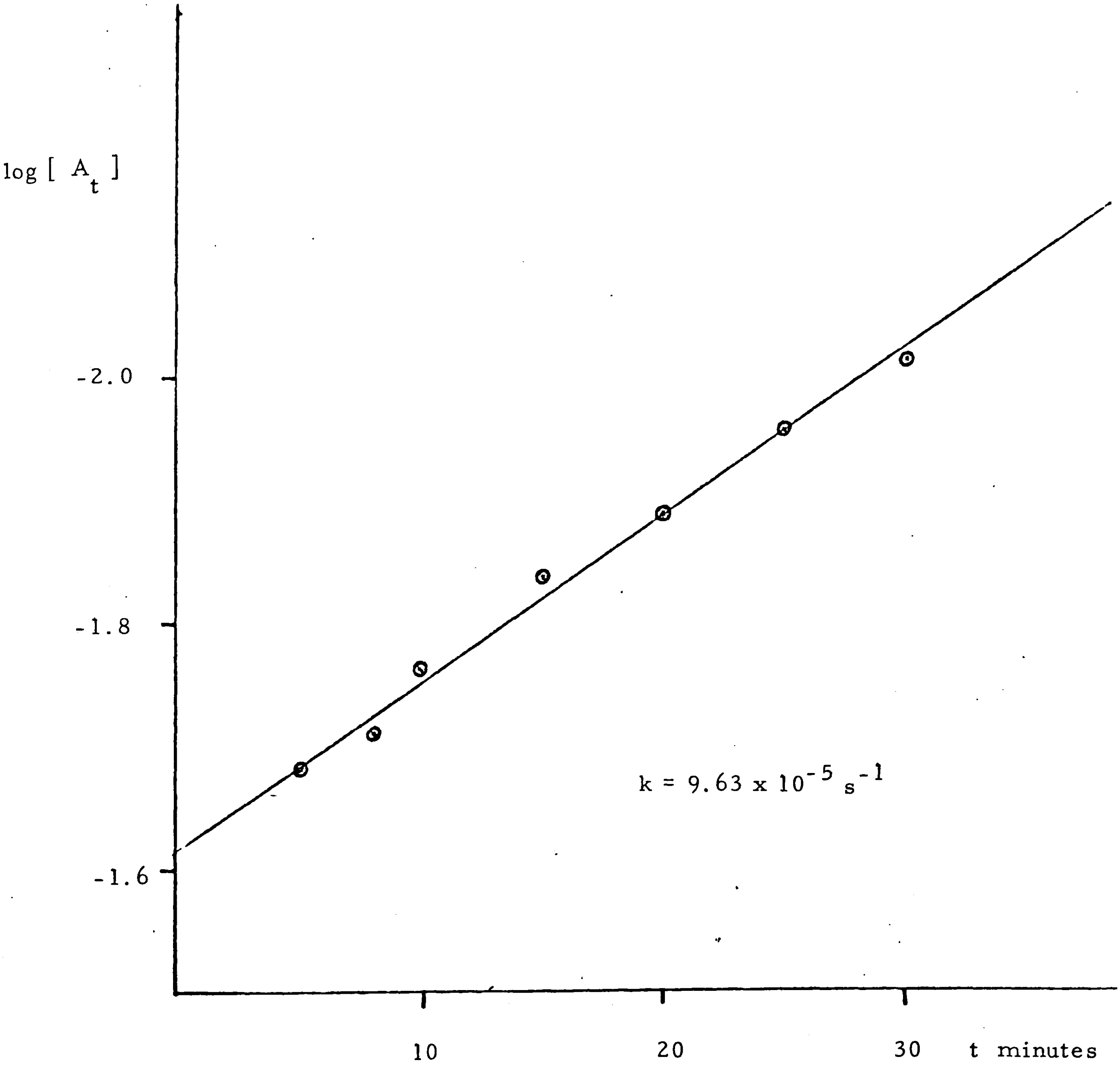
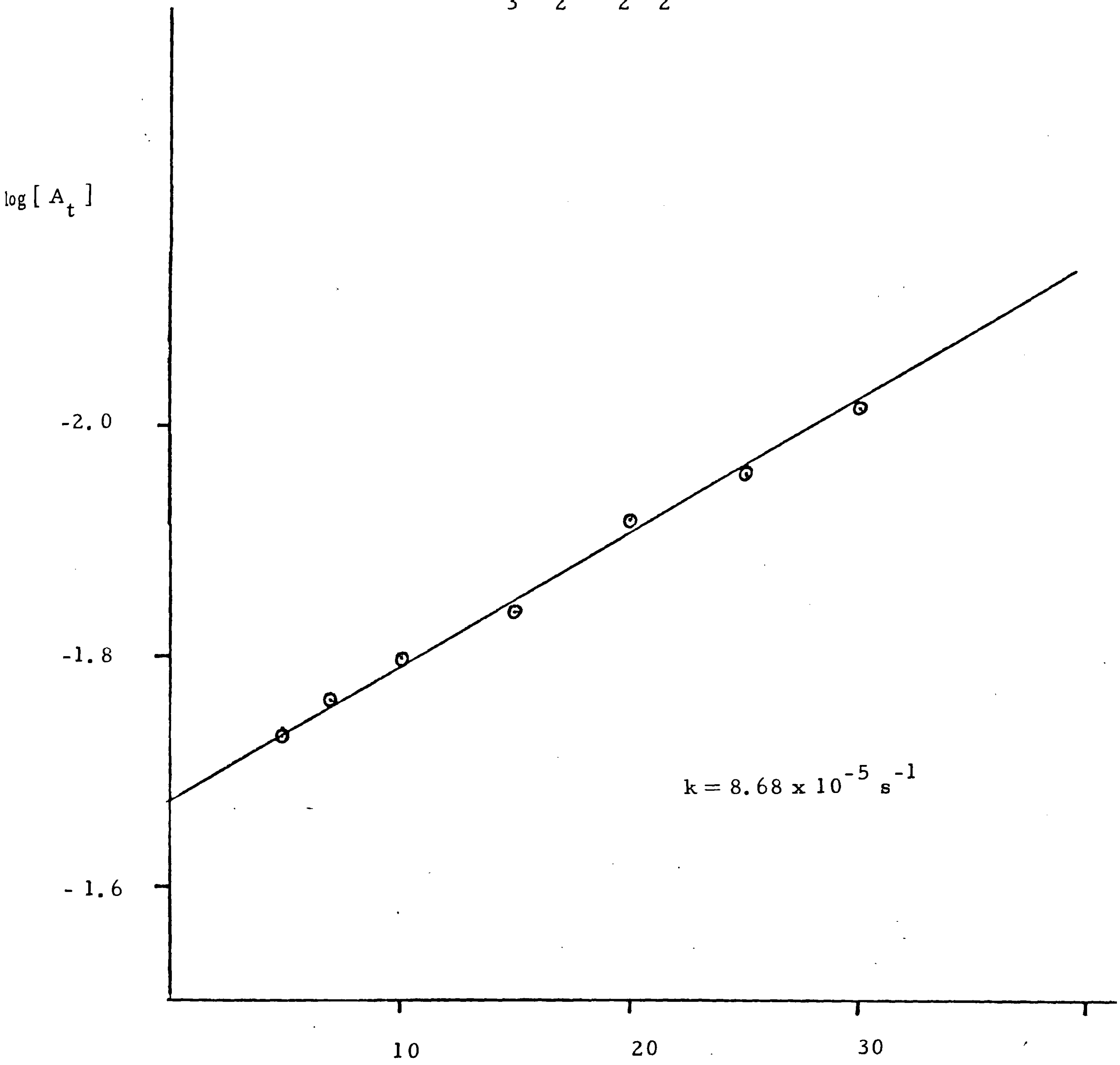


Fig. 4. 2. 3. - 4. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0. 03 mol. dm$^{-3}$) with $H_2SO_4$ (0.15 mol. dm$^{-3}$) in 50% $CH_3NO_2/CH_2Cl_2$ (V/V)



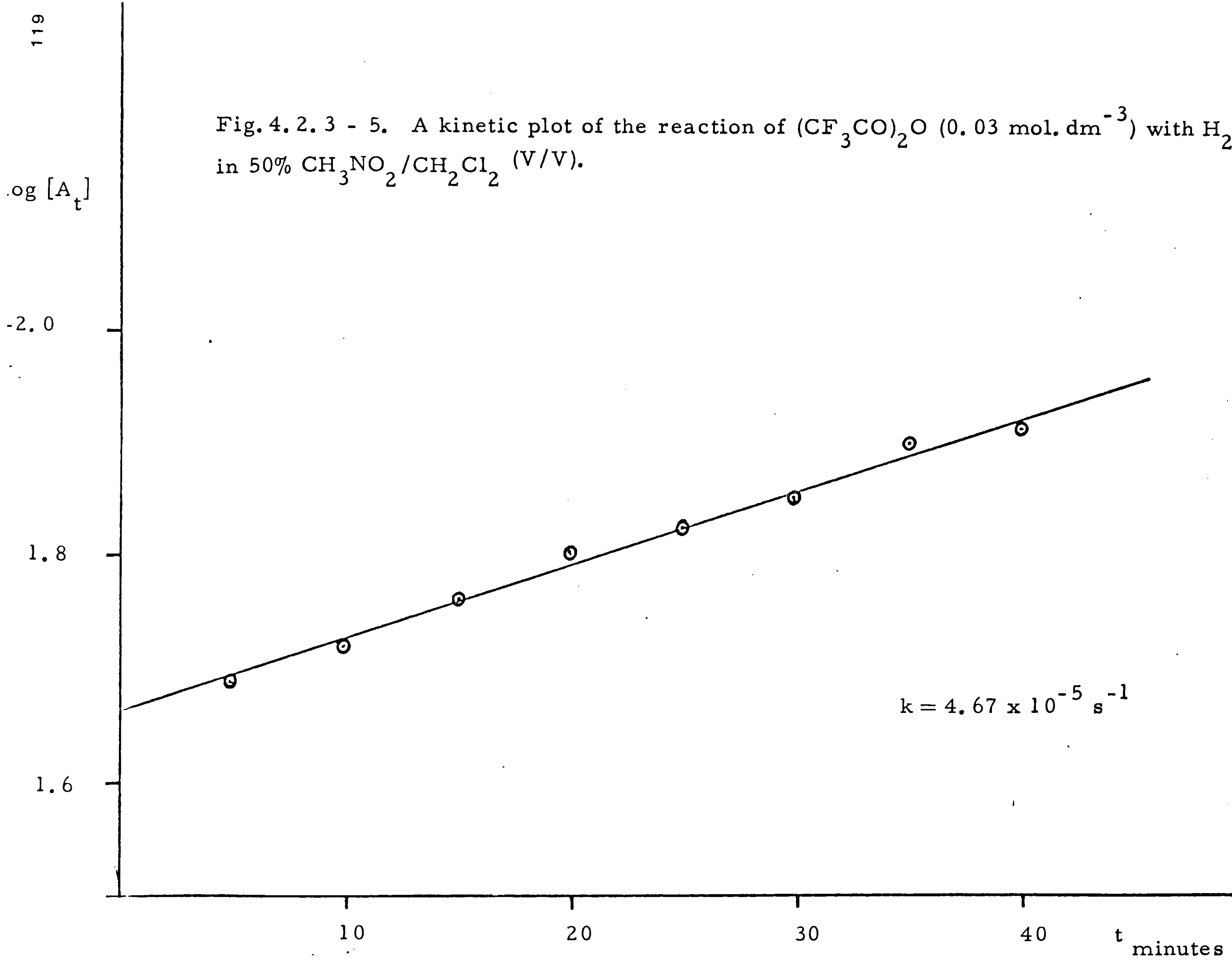


Fig. 4. 2. 3 - 5. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0. 03 mol. $dm^{-3}$) with $H_2SO_4$ (0. 06 mol. $dm^{-3}$) in 50% $CH_3NO_2/CH_2Cl_2$ (V/V).

Fig. 4.2.3 - 6. Kinetic plots of the reaction of $(CF_3CO)_2O$ (0.03 mol. dm$^{-3}$) with $H_2SO_4$ in 50% $CH_3NO_2/CH_2Cl_2$ (V/V)

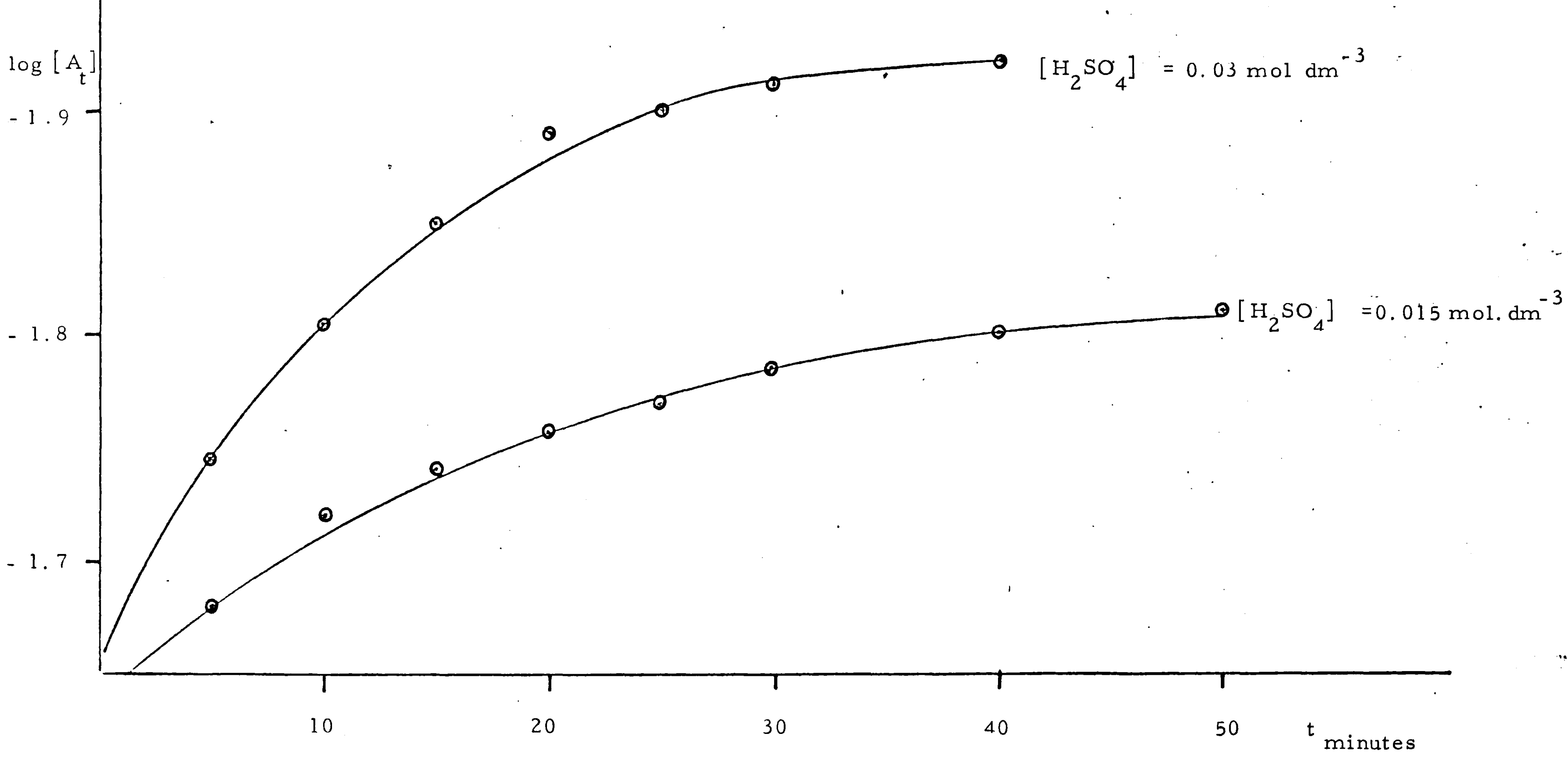


Fig. 4.2.3 - 7. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. dm$^{-3}$) with $H_2SO_4$ (0.015 mol. dm$^{-3}$) in 10% $CH_3NO_2/CH_2Cl_2$ (V/V).

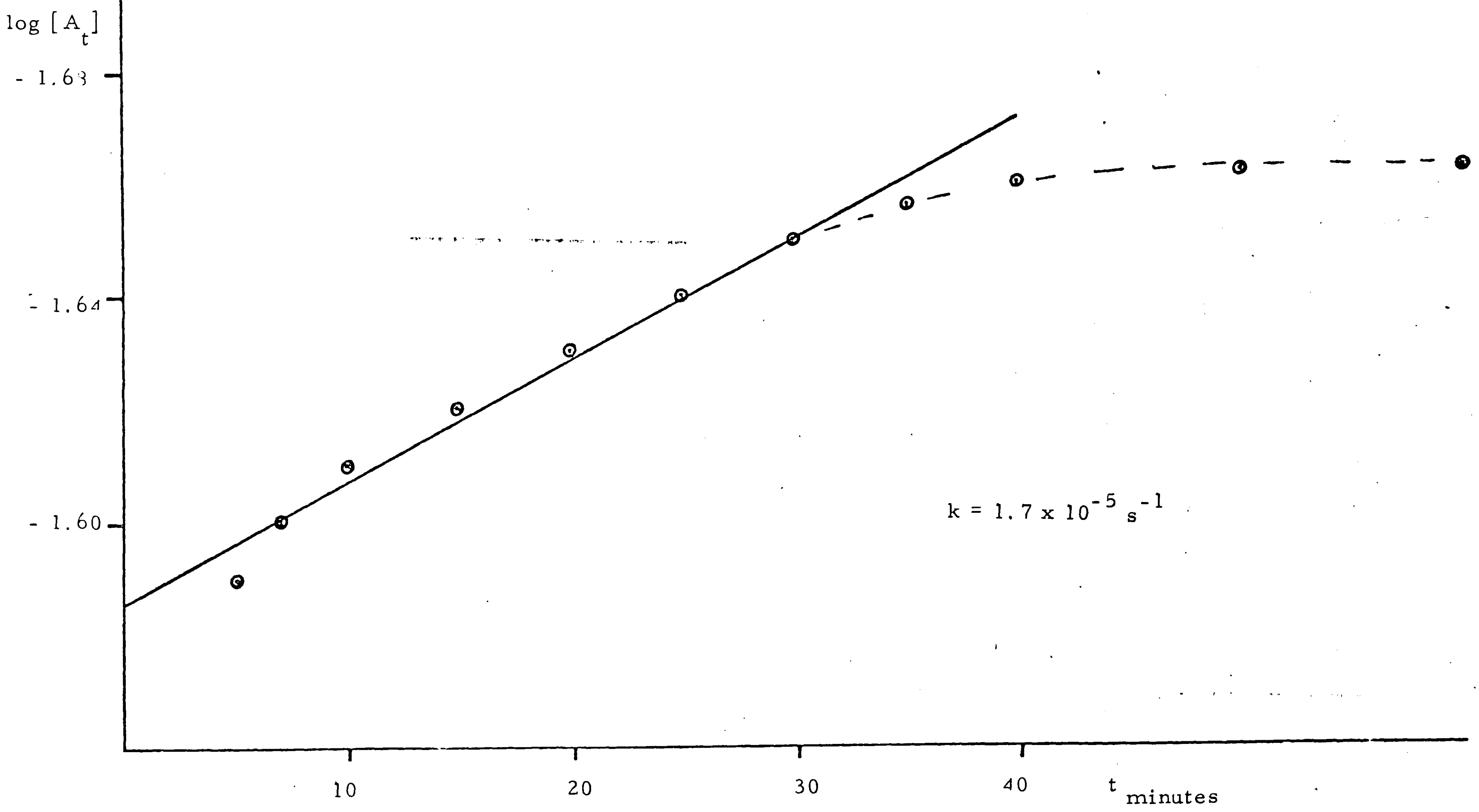
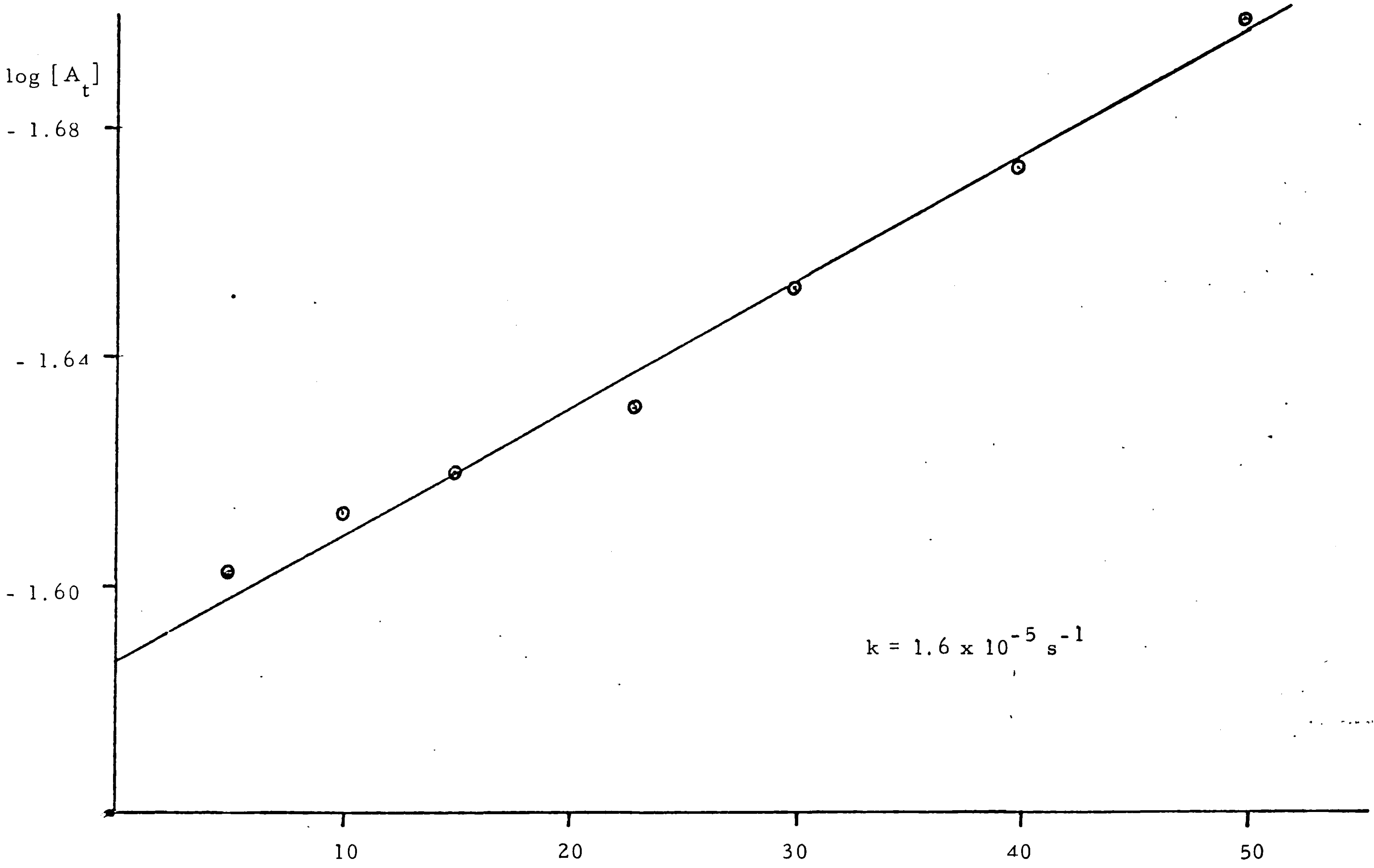


Fig. 4.2.3 - 8. A kinetic plot of the reaction of $(CF_3CO)_2O$ (0.03 mol. dm$^{-3}$) with $H_2SO_4$ (0.03 mol. dm$^{-3}$) in 10% $CH_3NO_2/CH_2/Cl_2$ (V/V).



## 4.3. MECHANISMS OF SULPHONE FORMATION.

### 4.3.1. Sulphonylation of aromatic hydrocarbons with sulphonic acids in the presence of trifluoroacetic anhydride.

Following the interpretation of the interactions of aryl sulphonic acids with trifluoroacetic anhydride, it is possible to suggest the mechanism for sulphone formation in the reactions of these solutions with aromatic hydrocarbons. The interactions between aryl sulphonic acids and trifluoroacetic anhydride are fast in solvents such as nitromethane and result in the formation of trifluoroacetyl aryl sulphonates as follows.

$$(CF_3CO)_2O + ArSO_3H \longrightarrow CF_3COOSO_2Ar + CF_3COOH \qquad (67)$$

Although the kinetics of the reactions of these particular unsymmetrical anhydrides with aromatic hydrocarbons have not yet been studied, some related unsymmetrical anhydrides have been investigated by F. Effenberger and K. Huthmacher.[46] These are trifluoromethane sulphonyl aryl sulphonates ($CF_3SO_2OSO_2Ar$). The formation of sulphones was found to be dependent on both the concentration of the anhydride and the aromatic hydrocarbon. This therefore implies that the rate determining step is the attack by the electrophile on the aromatic hydrocarbon. An identical behaviour might therefore be expected for the trifluoroacetyl sulphonates.

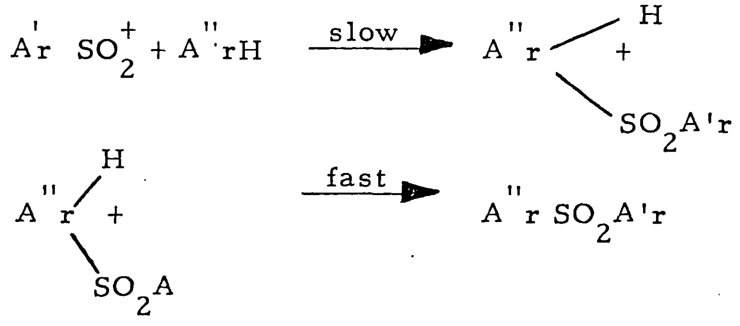
The dependence of the rate on the concentration of anhydride and the aromatic hydrocarbon suggests that these anhydrides can either be polarised and thus reacting with the aromatic hydrocarbon to form $\sigma$-complex thus,

$$\overset{\delta+}{ArSO_2} - \overset{\delta-}{O}\,COCF_3 + ArH \longrightarrow \sigma\text{-complex} \qquad (68)$$

or the attack is carried out by the aryl sulphonylium ion ($ArSO_2^+$). If the latter is the only effective electrophile present, then there must be a rapid rate of dissociation of the unsymmetrical anhydride prior to the attack upon the aromatic hydrocarbon.

$$ArSO_2OCOCF_3 \overset{fast}{\rightleftarrows} ArSO_2^+ + \bar{O}COCF_3 \qquad (69)$$

In this event the aromatic substitution follows the scheme (70) with the intermediacy of a $\sigma$-complex.



(70)

Although the $\sigma$-complex is stabilised by resonance, it no longer has the great stability associated with an aromatic sextet since a pair of electrons is removed by the electrophiles. Therefore the $\sigma$-complex intermediate will be rapidly converted into the sulphone by the expulsion of a proton. The kinetic behaviour of the trifluoromethane aryl sulphonates unfortunately cannot distinguish whether the attack is carried out by the polarised species of the anhydride or the sulphonylium ions since the kinetics would be identical. However evidence for the participation of the sulphonylium ions in this reaction is provided by the determination of the yields of the isomeric sulphone products. It is observed that the isomer distributions of these products corresponds to those prevailing in the reactions with other sulphonylating reagents like sulphonyl perchlorates (known to be dissociated in solution) and Friedel-Crafts species.

Methane sulphonic-trifluoroacetic anhydride mixtures do not react with aromatic hydrocarbons. This probably due to the instability of the mixed anhydride which if formed would disproportionate to the corresponding symmetrical anhydrides (methane sulphonic acid and trifluoroacetic anhydrides).

### 4.3.2. Sulphonylation of aromatic hydrocarbons with sulphuric acid in the presence of trifluoroacetic anhydride.

The experimental observations reported in Chapter 2 have led to two conclusions.

Firstly in the formation of sulphones, by treatment of aromatic hydrocarbons with sulphuric acid in the presence of trifluoroacetic anhydride, two consecutive electrophilic substitution reactions occur, the first of which is regiospecific. Secondly, as deactivated aromatic compounds, such as chlorobenzene and nitrobenzene, gave either only low yields of sulphones or did not react at all, the electrophile reacting in the first substitution reaction seems to be a weak electrophilic reagent. These facts must be borne in mind when discussing the mechanism of the reactions leading to sulphones. There exists various alternative pathways to diaryl sulphone formation by the reaction of sulphuric acid and aromatic hydrocarbons in the presence of trifluoroacetic anhydride. All these possibilities are diagrammatically represented in Fig. 4.3.2 - 1. Path 1 is an ordinary dehydration process involving the removal of water by a dehydrating agent (trifluoroacetic anhydride) between two molecules of an aromatic hydrocarbon and sulphuric acid. The intermediate in this case would be a sulphonic acid. However reactions performed using other dehydrating either do not give sulphones or else give them in reduced yields when the reactions are carried out under similar conditions. - These reactions and products are given on Table 4.3.2 - 2.

Fig. 4.3.2 - 1. POSSIBLE ROUTES TO DIARYL SULPHONE.

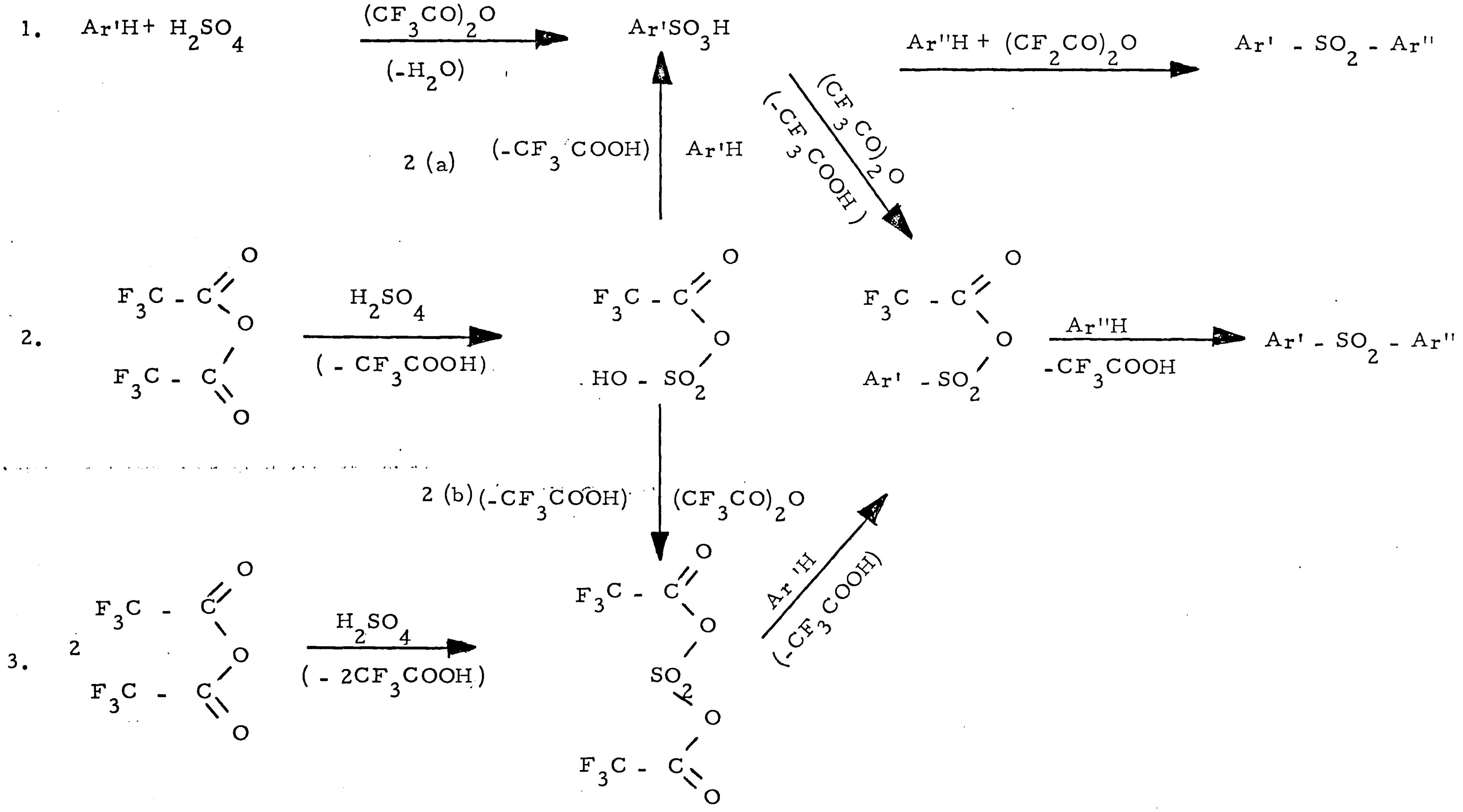


Table 4.3.2 - 2

Yields of major products from reactions of sulphuric acid in the presence of dehydrating agents.

| Dehydrating agent | Product | Yield |
|---|---|---|
| $P_2O_5$ | no neutral product | - |
| $(CH_3CO)_2O$ | $CH_3COAr$ | 53.3% |
| $(CH_3SO_2)_2O$ | $ArSO_2Ar$ | 32% |
| $(CF_3CO)_2O$ | $ArSO_2Ar$ | 87.6% |

$$\text{Reaction:- } 2ArH + H_2SO_4 \xrightarrow[\text{agent}]{\text{Dehydrating}} \text{products} \qquad (71)$$

$$ArH = CH_3\text{-}C_6H_5$$

When phosphorus pentoxide is present in place of trifluoroacetic anhydride, no neutral product could be isolated. Acetic anhydride on the other hand resulted in the formation of the corresponding aryl methyl ketone.. Only methane sulphonic anhydride reacted similarly to trifluoroacetic anhydride giving sulphones. Evidence from the isomer distribution of the sulphone products completely disagrees with a mechanism of a dehydration process but rather suggests the participation of sulphonylium ion in the reaction. The dehydration route must therefore be rejected.

E.A. Jeffery and D.P.N. Satchell[100, 101] have already shown that sulphuric acid reacts with acetic anhydride to form acetyl and diacetyl sulphate and that both these anhydrides are capable of acetylation of phenol (reaction 72(a) and (b)).

$$H_2SO_4 + (CH_3CO)_2O \rightleftharpoons CH_3COOSO_3H \qquad (a)$$

$$CH_3COOSO_3H + (CH_3CO)_2O \rightleftharpoons (CH_3COO)_2SO_2 \qquad (b)\ (72)$$

$$CH_3COOSO_3H + ArH \longrightarrow ArCOCH_3 + H_2SO_4 \qquad (a)$$

$$(CH_3COO)_2SO_2 + ArH \longrightarrow ArCOCH_3 + CH_3COOSO_3H \qquad (b)\ (73)$$

This is therefore consistent with the acetylation of aromatic hydrocarbon observed in the above reaction of acetic anhydride and aromatic hydrocarbons in the presence of sulphuric acid (reaction 73 (a) and (b)).

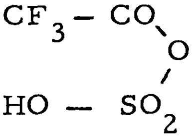
In Fig. 4.3.2 - 1, path 2 shows the formation first of the trifluoroacetyl sulphuric acid which in the presence of an aromatic hydrocarbon is then converted into a sulphonic acid (path 2 (a)). Evidence for this pathway is provided by the fact that aromatic sulphonic acids in the presence of trifluoroacetic anhydride react easily with aromatic hydrocarbons to give sulphones. However evidence from the isomer distribution of the sulphone isomers does not agree with this pathway. In the synthesis of unsymmetrical diaryl sulphones with sulphuric acid and two different aromatic hydrocarbons in the presence of trifluoroacetic anhydride, the results suggest that the first electrophilic step is regiospecific (Table 4.3.2 - 3).

Table 4.3.2. - 3.

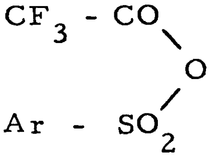
Isomer distribution of the sulphone products in the reactions of toluene and benzene with sulphuric acid in the presence of trifluoroacetic anhydride.

| Aromatic hydrocarbon added first | Aromatic hydrocarbon added second | Substituted diphenyl sulphone isomer | Abundance |
|---|---|---|---|
| benzene | toluene | 4-methyl | 49.90 |
| | | 2-methyl | 42.20 |
| | | 3-methyl | 7.9 |
| toluene | benzene | 4-methyl | 100 |

There appears to be no apparent reason why trifluoroacetyl sulphuric acid I should not react similarly to the unsymmetrical anhydride II formed from the aryl sulphonic acid and trifluoroacetic anhydride. If more than one isomer is formed from II the same should be the case with I. This therefore suggests

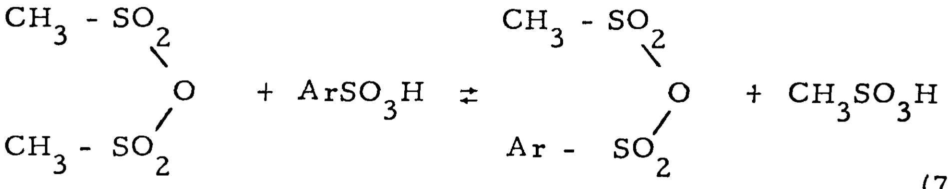


I



II

that both these anhydrides should give the same number of isomers in their reactions with aromatic hydrocarbons so that if path 2(a) was correct, and if $Ar'H$ and $Ar''H$ are monosubstituted aromatic hydrocarbons, a total number of nine isomers of diaryl sulphones would be expected. However only three isomers are formed. Further, although methane sulphonic anhydride in the presence of sulphuric acid, reacts with aromatic hydrocarbon to give sulphones, no reaction is observed when sulphuric acid is replaced by an aryl sulphonic acid, thereby suggesting that the unsymmetrical methane arenesulphonic anhydride is not formed in this way (reaction 74).

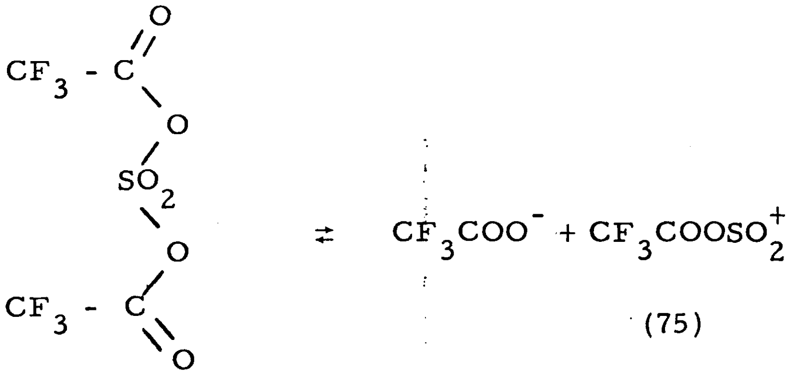


III

(74)

The formation of such a species would be a logical requirement for the sulphone forming steps from the intermediate aryl sulphonic acid for the overall reaction between the sulphonic acid and a hydrocarbon in the presence of methane sulphonic anhydride assuming of course, there is an analogous reaction to Path 2 in the scheme. There is therefore strong evidence for the rejection of Path 2(a).

The kinetic experiments carried out on the reaction of trifluoroacetic anhydride with sulphuric acid show that a mono anhydride is formed in a very fast reaction and this is immediately converted into the dianhydride in a slower reaction even with equimolar quantities of sulphuric acid and trifluoroacetic anhydride. Therefore in excess trifluoroacetic anhydride, the dianhydride will be exclusively formed. The heterolytic dissociation of the dianhydride may be represented thus:-



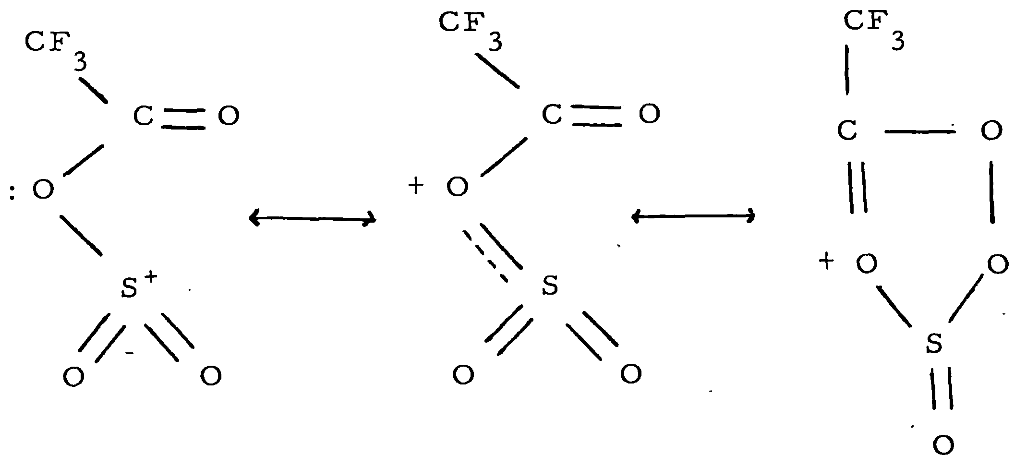
IV

(75)

The order of electrophilicity for sulphuric acid, the trifluoroacetyl sulphuric acid and the di(trifluoroacetyl sulphuric acid and the ditrifluoroacetyl sulphate is as follows:-

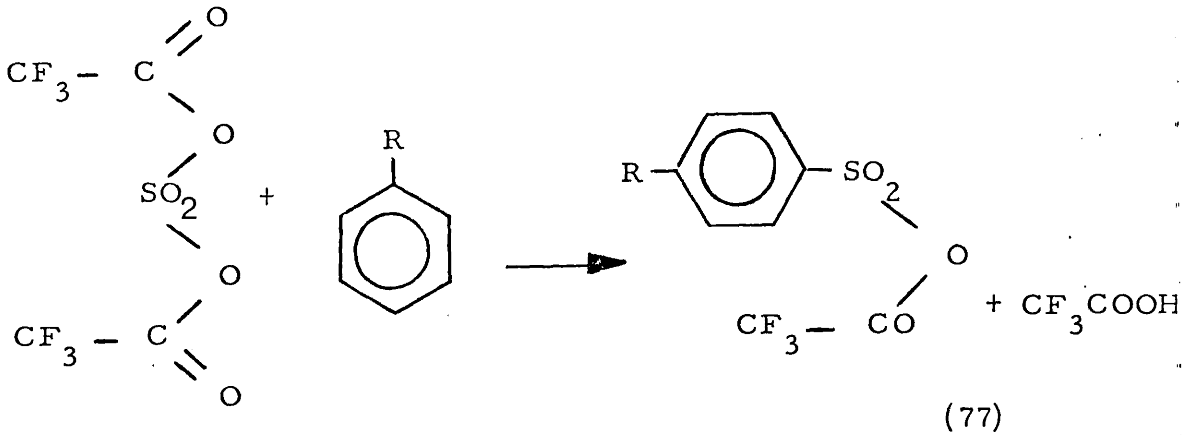
$$H_2SO_4 \angle CF_3COOSO_3H \angle (CF_3COO)_2SO_2$$

If the dianhydride is not dissociated but merely polarised when it attacks the aromatic hydrocarbon, the regiospecificity can be explained in terms of the size of the electrophilic reagent. This species is so large that its attack could be sterically hindered at the ortho position. However if this species dissociates, then this specificity has then to be explained in terms of charge delocalisation and/or its existence takes up a cyclic form. The charge delocalisation would considerably weaken the electrophile and thus make it more selective.



(76)

Isomer distribution of the sulphone products in this reaction is similar to that of the reaction of aryl sulphonic acids and aromatic hydrocarbons in the presence of trifluoroacetic anhydride (Table 4.3.2 - 4). It is logical therefore to suggest that the reaction of the dianhydride of sulphuric acid would lead to the formation of a trifluoroacetyl sulphonate (reaction 77).



(77)

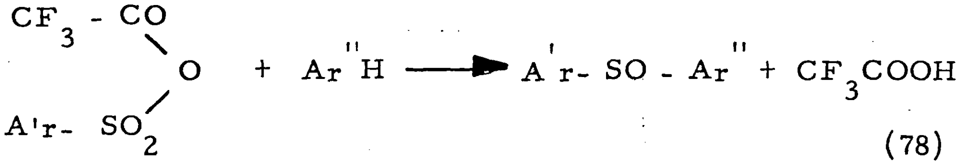
Table 4.3.2 - 4.

A comparison of the isomer abundance of the sulphone products from the reaction of sulphuric acid with those found in the reaction of p-toluene sulphonic acid and aromatic hydrocarbons.

$(CF_3CO)_2O + C_6H_5CH_3$

| $+ H_2SO_4$ | $+ CH_3C_6H_4SO_3H$ | Products |
|---|---|---|
| 62.2 | 67.3 | p, p-ditolyl sulphone |
| 36.2 | 20.8 | p, o-ditolyl sulphone |
| 1.6 | 12.9 | p, m-ditolyl sulphone |

Such unsymmetrical anhydrides are known[46] to react with aromatic hydrocarbons to give sulphones with the usual pattern of isomer distribution.



$$CF_3\text{-}CO\text{-}O\text{-}SO_2\text{-}A'r + Ar''H \longrightarrow A'r\text{-}SO\text{-}Ar'' + CF_3COOH$$

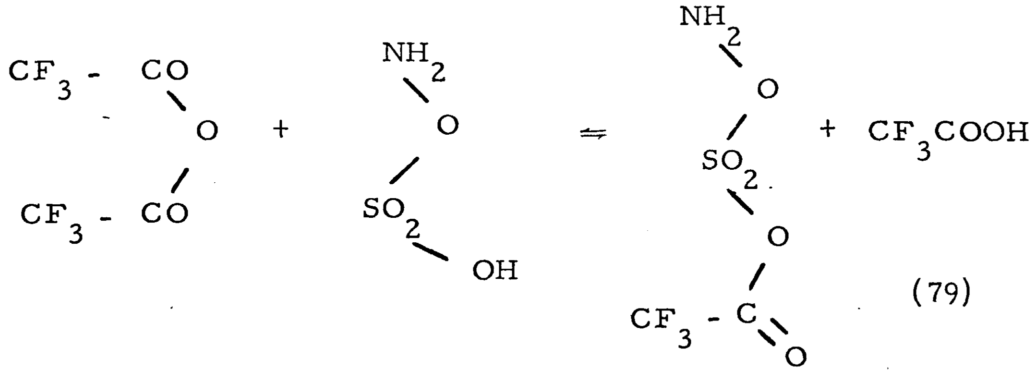
(78)

Path 2(b) in the scheme is also consistent with the formation of unsymmetrical diaryl sulphones when two different aromatic hydrocarbons are added to the dianhydride. The condition for the exclusive formation of these unsymmetrical sulphones is that the rate of addition of the first aromatic hydrocarbon should always be slower than the rate of formation of the trifluoroacetyl aryl sulphonate.

### 4.3.3. The reaction of hydroxylamine-O-sulphonic acid with aromatic hydrocarbons in the presence of trifluoroacetic anhydride.

Although the kinetics and mechanisms of the reaction of trifluoroacetic anhydride with hydroxylamine-O-sulphonic acid have not been studied, it is possible to postulate a mechanism for the sulphone formation in the reaction of these reagents with aromatic hydrocarbons from the experience gained from the studies made in the previous subsections, viz 4.3.1 and 4.3.2.

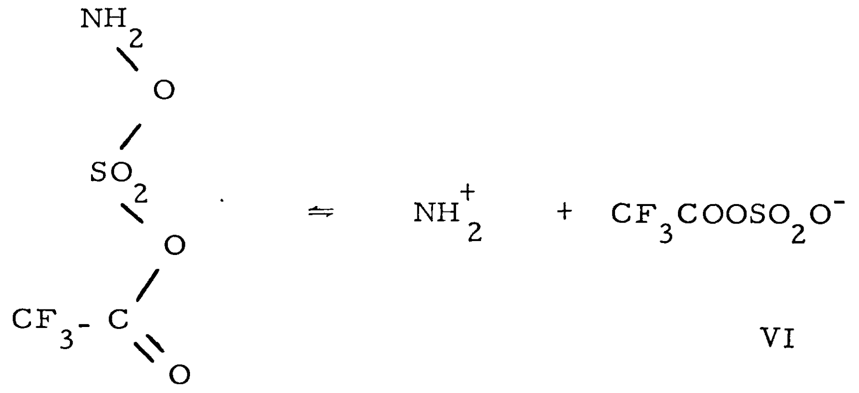
First if hydroxylamine-O-sulphonic acid were to behave like sulphuric acid, then the following reaction might be expected to take place



(79)

V

This mixed anhydride could then ionise in a similar way giving the trifluoroacetyl sulphate ion and an $\overset{+}{NH_2}$ ion.



VI

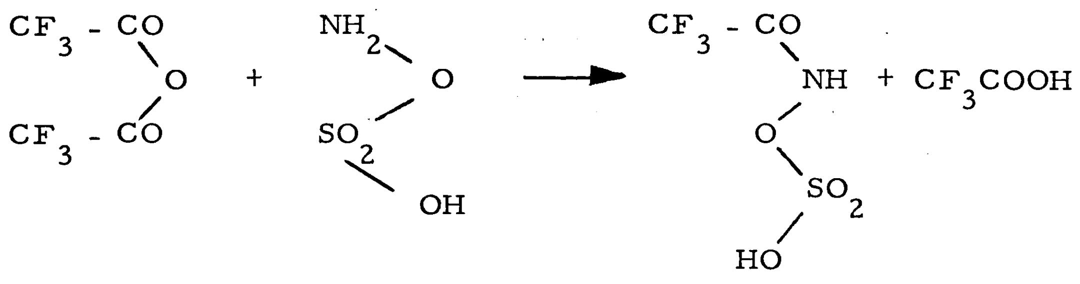
(80)

The electrophilic $NH_2^+$ would then be able to attack the aromatic ring to give an amine while the trifluoroacetyl sulphate ion would react further with another molecule of trifluoroacetic anhydride to give the dianhydride (IV) and with two molecules of aromatic hydrocarbons this could give the sulphone as described in subsection 4.3.2.

$$CF_3COOSO_2{}^-O + (CF_3CO)_2O \rightleftharpoons (CF_3COO)_2SO_2 + CF_3COO^-$$

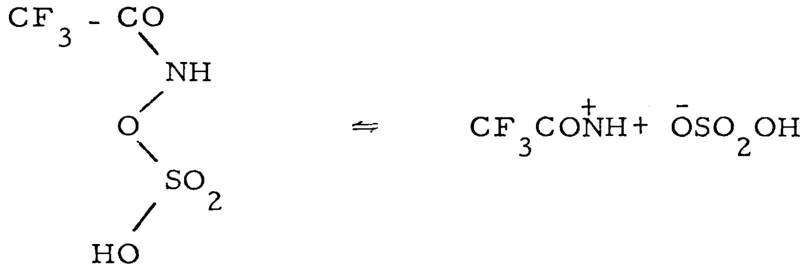
IV (81)

However the above sequence of reactions would appear rather unlikely owing to the nucleophilicity of the $NH_2$- group in the hydroxylamine-*O*-sulphonic acid. The most probable route therefore involves the reaction of trifluoroacetic anhydride with the amino group of hydrooxylamine sulphonic acid thus:-



VII VIII (82)

This intermediate might ionise to release the sulphate ion and the $CF_3CO\overset{+}{N}H$ ion thus:-



$$CF_3-CO-NH-O-SO_2-OH \rightleftharpoons CF_3CO\overset{+}{N}H + \overset{-}{O}SO_2OH$$

(83)

The sulphate ion would be expected to react further with trifluoroacetic anhydride giving IV and this with an aromatic hydrocarbon would again be able to form sulphones as already described in subsection 4.3.2.

$$\overset{-}{O}SO_2OH + (CF_3CO)_2O \rightleftharpoons CF_3COOSO_2OH + CF_3COO^-$$

$$CF_3COOSO_2OH + (CF_3CO)_2O \rightleftharpoons IV \longrightarrow \text{sulphones}$$

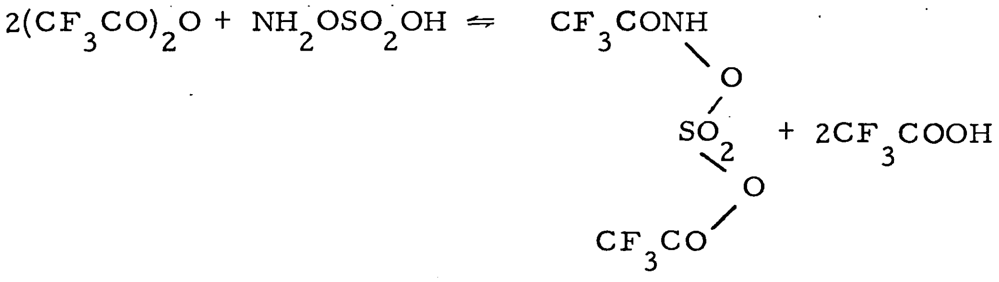
(84)

This time the $CF_3CO\overset{+}{N}H$ ion is an even stronger electrophilic and and should therefore attack an aromatic centre thus:-

$$Ar-H + CF_3CO\overset{+}{N}H \longrightarrow ArNHCOCF_3 + H^+ \qquad (85)$$

The trifluoroacetonitride has been isolated in this reaction described in chapter 3 and identified by mass spectroscopy.

Finally there must be the possibility of both N and O-trifluoroacetylation.



$$2(CF_3CO)_2O + NH_2OSO_2OH \rightleftharpoons CF_3CONH-O-SO_2-O-COCF_3 + 2CF_3COOH$$

IX (86)

The species IX could act both as a sulphonylating agent and an N-trifluoroacetyl aminating agent according to its mode of ionisation or at least charge separation prior to attack by an aromatic compound.

## 4.4. CONCLUSION.

The synthesis of diaryl sulphones from p-toluene sulphonic acid trifluoroacetic anhydride and aromatic hydrocarbons which was discovered by E. J. Bourne et al[2] has been studied in detail. The synthetic procedure has been improved by the use of anhydrous p-toluene sulphonic acid and carrying out the reaction in nitromethane. This has resulted in very good yields of these sulphones. The various isomeric sulphone products obtained by these means have been separated by g.l.c. and their distribution found to be similar to those of reactions carried out by sulphonylium ions, e.g. in Friedel Crafts processes. The study of the interactions between sulphonic acids (methane sulphonic acid and mesitylene sulphonic acid) and trifluoroacetic anhydride has been carried out using infra-red spectroscopy. The results show that a reaction takes place resulting in the formation of a mixed anhydride (the sulphonyl trifluoroacetate). The rate of decrease of the concentration of trifluoroacetic anhydride is only dependent on the concentration of trifluoroacetic anhydride and not upon the concentration of the sulphonic acid. An explanation for this kinetic behaviour has been suggested to be the ionisation of trifluoroacetic anhydride which is slow and is therefore the rate determining step. Although the kinetics of the formation of sulphones have not been studied here, work on similar mixed anhydride reactions by K. Hutmacher and F. Effenberger[46] suggests that sulphonyl trifluoroacetates should dissociate into sulphonylium and trifluoroacetate ions. These sulphonylium ions are the ones responsible for the electrophilic attack on the aromatic hydrocarbons.

Secondly, a new method for the synthesis of symmetrical diaryl sulphones has been discovered. This method involves the reaction of sulphuric acid with aromatic hydrocarbons in the presence of trifluoroacetic anhydride. The sulphone yields are very high and better than those of conventional methods such as the Friedel-Crafts Lewis acid catalysed reactions; they are comparable to those obtained with strong sulphonylating reagents such as the sulphonyl perchlorates and trifluoromethane sulphonyl sulphonates. The isomeric sulphone products of this reaction were also separated by gas chromatography and the isomer distribution found to be similar to those of other reagents involving sulphonylium ions. An important observation from the isomer distribution of the sulphone products is that of the two electrophilic reactions necessary for product formation, one is regiospecific. The first involves the reaction of the reagent, formed from the reaction of trifluoroacetic anhydride and sulphuric acid, with the first aromatic hydrocarbon. The second involves the reaction of this intermediate product with the second aromatic hydrocarbon.

In order to find out which of these steps was regiospecific an experiment was designed in which two different aromatic hydrocarbons were sequentially added to a solution of sulphuric acid and trifluoroacetic anhydride in nitromethane and the isomeric products analysed. The sequence of addition of the aromatic hydrocarbons was reversed and the product analysed again. The addition of the first aromatic hydrocarbon was carried out dropwise. The intention was that the rate of addition should exceed the rate of formation of the first intermediate product so as to minimise contamination due to symmetrical diaryl sulphone by-products. The analysis of the products from both sequences showed that the first step was regiospecific and the position that is selectively attacked is the para position. The sulphone yields in these processes were also good and contamination by symmetrical diaryl sulphone by-products minimal. Thus a new and easy method for the synthesis of unsymmetrical diaryl sulphones had been discovered.

The study of the interactions between sulphuric acid and trifluoroacetic anhydride in mixtures of nitromethane and dichloromethane showed that a monoanhydride (trifluoroacetyl sulphuric acid) is exclusively formed in a large excess of sulphuric acid. The reaction in excess sulphuric acid is identical to that of sulphonic acids in that it is only dependent on the concentration of trifluoroacetic anhydride and independent of the concentration of sulphuric acid. Therefore the rate determining step must be the ionisation of trifluoroacetic anhydride into trifluoroacetylium and trifluoroacetate ions. However as the initial concentration of sulphuric acid is decreased towards equimolar quantities, there is a deviation from the first order rate law. This has been attributed to the dibasic nature of sulphuric acid. The monoanhydride is converted into the dianhydride (di-trifluoroacetyl sulphate ) by a reaction with another molecule of trifluoroacetic anhydride in a slower reaction than the formation of the monoanhydride.

An attempt has been made to explain whether the monoanhydride or the dianhydride is responsible for the electrophilic attack on the first aromatic hydrocarbon. No evidence could be found for the monoanhydride's regiospecificity since it is similar to sulphonyl trifluoroacetates which give normal patterns of isomer distributions. However the dianhydride, being a larger molecule could be sterically hindered at the <u>ortho</u> position especially if it is not fully dissociated but is merely polarised. Secondly, if it does dissociate into ion pairs the trifluoroacetylsulphonium ion could be stabilised by resonance which would effectively reduce its electrophilicity. This weaker electrophile would therefore be more selective than a stronger electrophile.

The reaction of the dianhydride with the first aromatic hydrocarbon should lead to the formation of an aryl sulphonyl trifluoroacetate if sulphones are to be formed. This intermediate is the same as that proposed for the reactions of a sulphonic acid, trifluoroacetic anhydride and aromatic hydrocarbons. The distribution of the isomeric sulphone products observed suggests that this intermediate is formed; the aryl sulphonyl trifluoroacetate reacting with the second aromatic hydrocarbon to give sulphones with the normal pattern of distribution of the isomeric products.

The synthetic value of this reaction is that it provides a method for the preparation of a variety of diaryl sulphones under very mild conditions. This has been made possible by the discovery of a new technique for the separation of these isomers on a preparative scale. This technique is medium pressure chromatography. It is a simple and fast column chromatography technique in which excellent separation can be obtained in less than 30 minutes.

Some symmetrical diaryl sulphones have also been prepared with hydroxylamine-O-sulphonic acid, an aromatic hydrocarbon and trifluoroacetic anhydride. The yields in these reactions were not as good as those discussed above due to contamination by other products. One such by-product is believed to be the N-trifluoroacetyl aryl amino compound. The study of this reaction still needs to be carried further since it could lead to a new reaction for the direct ammination of aromatic hydrocarbons.

The polymerisation of diphenyl methane with sulphuric acid and trifluoroacetic anhydride has also been carried out. However the properties of the polymer and its structure have not been studied. This might prove to have commercial implications in the future.

Lastly, attempts to synthesize unsaturated sulphones from sulphonic acids, trifluoroacetic anhydride and alkenes have proved to be unsuccessful. The failure was due to the fast reaction between the sulphonic acid and the alkene to give an alkyl sulphonate in a route which does not require the participation of trifluoroacetic anhydride. Attempts to use a mixed anhydride, free from sulphonic acid contamination, have also ended in failure due to considerable polymerisation.

# 5. EXPERIMENTAL

## 5. 1. KINETIC EXPERIMENTS

### 5. 1. 1. Purification of reagents.

Spectroscopic grade nitromethane (Aldrich Chemicals) (1 $dm^3$) was washed three times with a solution containing 2.5% (by weight) sodium carbonate and 2.5% sodium bisulphate, then with 5% sulphuric acid, followed by aqueous sodium bicarbonate, and lastly with water. It was dried with calcium sulphate (Drierite) overnight and then distilled. The distillate was kept in a brown bottle over molecular sieve type 4A for one week.

### 5. 1. 1. 2 Dichloromethane.

Dichloromethane was shaken with portions of concentrated sulphuric acid until the acid layer remained colourless. It was washed with water, then with aqueous sodium bicarbonate and again with water. It was pre-dried in calcium chloride and then distilled from calcium sulphate (Drierite). The resulting distillate was stored in a brown bottle over molecular sieve of the type 4A.

### 5. 1. 1. 3 Methane sulphonic acid.

The water was removed by an azeotropic distillation with benzene. The methane sulphonic acid was then carefully distilled under reduced pressure (b.p. 106°C, 0.1 mm. Hg) and the distillate kept in a brown bottle in a dry box.

### 5. 1. 1. 4 Mesitylene sulphonic acid.

Mesitylene sulphonic acid dihydrate was heated to 100°C in a drying pistol containing phosphorus pentoxide. under reduced pressure (approx. 14 mm/Hg). On cooling red semi-solid crystals were formed. The crystals were weighed and immediately used for the kinetic experiments.

### 5. 1. 1. 5 Sulphuric acid.

Sulphur trioxide was distilled from a strong (45-60% $SO_3$) commercial oleum into 'Analar' sulphuric acid (98%) in an all glass apparatus until a strong 'Analar' oleum was obtained.

This colourless 'Analar' oleum was distilled into a known weight of 'Analar' sulphuric acid to make a weak oleum (approx. 102%). This oleum was standardised by titrating with standard sodium hydroxide using methyl orange as indicator. The value obtained was used as a rough guide for the amount of water required to convert the oleum to 100% sulphuric acid. Successive amounts of water were added from a microburette until a maximum freezing point was obtained (10, 3$^{\circ}$C).

### 5.1.1.6 Trifluoroacetic anhydride.

Trifluoroacetic anhydride (100g) (Aldrich Chemicals) was distilled over phosphorus pentoxide (87 g) and the distillate collected over phosphorus pentoxide. The product was redistilled (b.p. 38-39$^{\circ}$C) and again collected over fresh phosphorus pentoxide. To remove dissolved gases, the anhydride was frozen with liquid nitrogen and then evacuated to about 0.1 mm of mercury and then allowed to return to room temperature and the vacuum released.

### 5.1.2. Method of analysis.

All the reagents were kept in a dry-box. Inside the dry-box was a large dish containing phosphorus pentoxide. The dry box had an inlet and an outlet through which nitrogen, pre-dried by passing it through a series of drying towers containing calcium chloride and indicating silica gel, was pumped in to replace the moist air. The preparation of all the solutions was carried in the dry-box.

Next to the dry-box was an infrared spectrophotometer (Perkin-Elmer Model 177 grating spectrophotometer). The infra red cells were fitted with balanced silver chloride windows and 1 mm teflon spacers. The reaction cell had an adaptor fitted with a water jacket through which water from a water bath can be circulated. The temperature of the water-bath was adjusted to be the same as that of the dry-box; i.e. $24^{\circ}C + 0.5^{\circ}C$.

The reference cell containing the solvent was fitted with an ordinary adaptor.

Before the analysis, the pipettes volumetric flasks syringes and the reaction cell were dried in an oven at 100°C, and then allowed to cool down to room temperature and thereafter placed inside the dry-box. They were left for 30 min to equilibrate to the temperature of the dry-box. The solutions of trifluoroacetic anhydride and the acids made inside the dry-box were mixed and the clock started when half of the anhydride had been added. The resulting solution was quickly injected into the reaction cell and the cell transferred to the spectrophotometer. The spectrophotometer was used to measure the decrease in the concentration of trifluoroacetic anhydride by monitoring the carbonyl stretching absorption appearing at 1910 $cm^{-1}$. The extinction coefficient of this absorption was estimated using solution of trifluoroacetic anhydride whose concentration ranged from 0.01 - 0.03 $mol.\,dm^{-3}$.

### 5.1.2.1. The reaction of trifluoroacetic anhydride with methane sulphonic acid.

The first experiment was carried in dichloromethane as solvent. The concentration of trifluoroacetic anhydride was kept constant and that of methane sulphonic acid varied as shown below.

| Run | Concentration of $(CF_3CO)_2O$ | Concentration of $MeSO_3H$ |
|---|---|---|
| 1 | 0.03 $mol.\,dm^{-3}$ | 0.03 $mol.\,dm^{-3}$ |
| 2 | " | 0.05 " |
| 3 | " | 0.10 " |

see pages 98-100

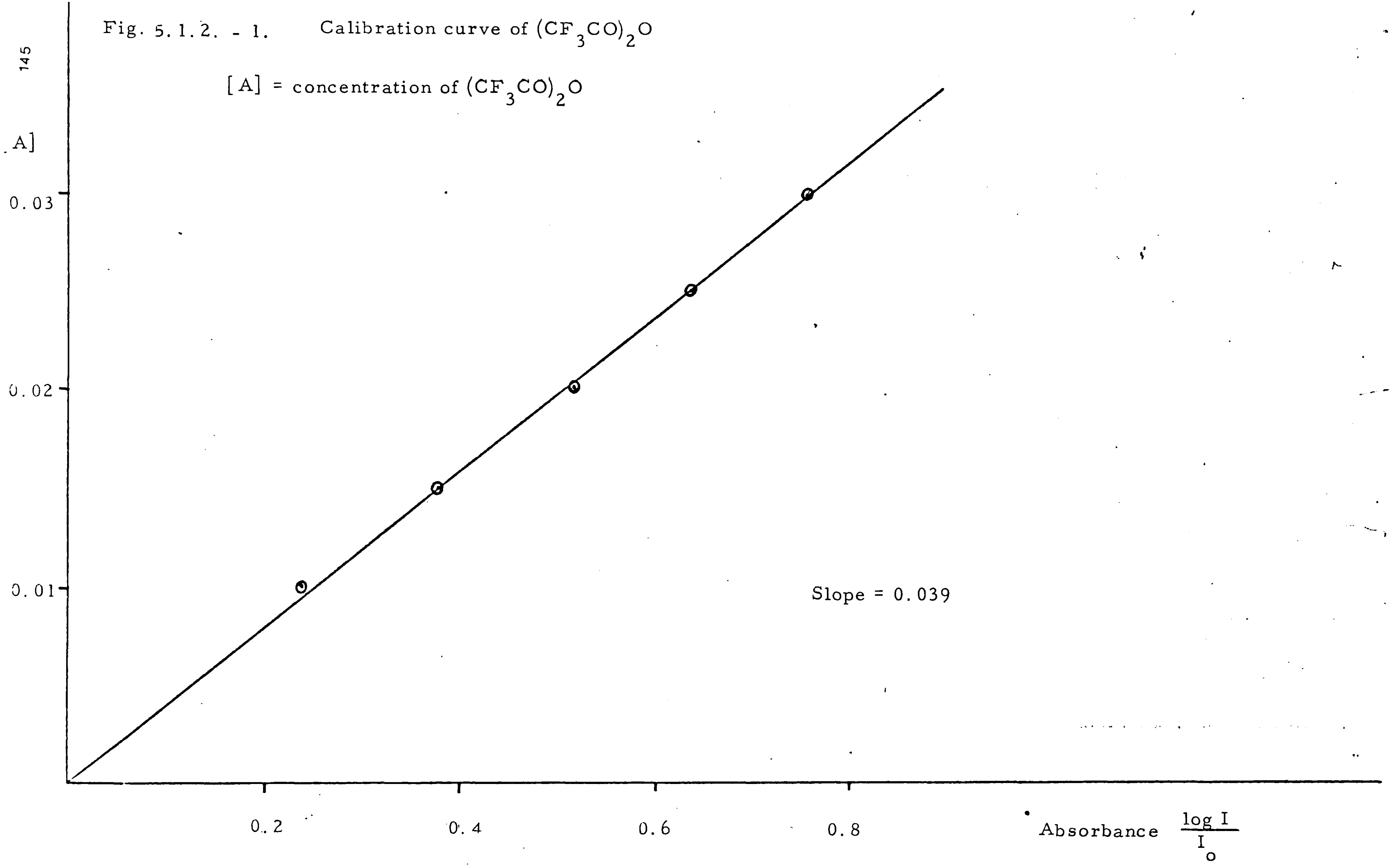


Fig. 5.1.2. - 1. Calibration curve of $(CF_3CO)_2O$

[A] = concentration of $(CF_3CO)_2O$

The second experiment involved the reaction of equimolar quantities of trifluoroacetic anhydride and methanesulphonic acid (0.03 mol. dm$^{-3}$) in different solvent mixtures.

| Run | % $CH_3NO_2$ in $CH_2Cl_2$ |
|---|---|
| 1 | 10 |
| 2 | 25 |
| 3 | 37 |
| 4 | 50 |

see pages 101-6

5.1.2.2. The reaction of trifluoroacetic anhydride with mesitylene sulphonic acid.

This experiment was carried out in 20% $CH_3NO_2$ in $CH_2Cl_2$ as solvent.

| Run | Concentration of $(CF_3CO)_2O$ | Concentration of $(CH_3)_3$-$C_6H_2SO_3H$ |
|---|---|---|
| 1 | 0.03 mol. dm$^{-3}$ | 0.05 mol. dm$^{-3}$ |
| 2 | " | 0.10 " |

see pages 109-10

5.1.2.3. The reaction of trifluoroacetic anhydride with sulphuric acid.

The first experiment was carried out in 50% $CH_3NO_2$ in $CH_2Cl_2$.

| Run | Concentration of $(CF_3CO)_2O$ | Concentration of $H_2SO_4$ |
|---|---|---|
| 1 | 0.03 mol. dm$^{-3}$ | 0.040 mol. dm$^{-3}$ |
| 2 | " | 0.25 " |
| 3 | " | 0.15 " |
| 4 | " | 0.06 " |
| 5 | " | 0.03 " |
| 6 | " | 0.015 " |

see pages 116-20

The second analysis was carried out in 10% $CH_3NO_2$ in $CH_2Cl_2$.

| Run | Concentration of $(CF_3CO)_2O$ | Concentration of $H_2SO_4$ |
|---|---|---|
| 1 | 0.03 mol. dm$^{-3}$ | 0.03 mol. dm$^{-3}$ |
| 2 | " | 0.015 " |

see pages 121-2

## 5.2. GENERAL TECHNIQUES

### 5.2.1. Gas-Liquid Chromatography (g.l.c. )

### 5.2.1.1. Packing material.

5% Silicone S.E.30 on Chromosorb W (100-120 mesh) was used as a packing material. To prepare the packing material 5 g of the stationary phase was dissolved in A.R. chloroform (50 $cm^3$). The inert support (95 g) was placed in a large conical flask and the solution of the stationary phase added to the inert support. The mixture was stirred thoroughly and the chloroform removed under reduced pressure in a rotary evaporator.

### 5.2.1.2. Instrumentation.

G.l.c. was carried out using a Pye 104 double column gas chromatograph with nitrogen as the carrier gas (flow rate = 45 $cm^3$/min), a flame ionisation detector using oxygen and hydrogen for ionising the sample and a glass column (1 64 x 2 mm). The temperature at which the separations were carried out was 225°C. The peak areas and retention time were obtained from an HP3370B/71B integrator.

### 5.2.2. Thin layer chromatography ( t.l.c. )

T.l.c.was performed on Camlab Polygram Sil.G. pre-coated chromatographic plates. The solvent system employed in the separations was ethyl acetate: toluene (1:19 by volume). The compounds were located with iodine vapour.

### 5.2.3. Medium pressure chromatography.

The diagram for setting up the apparatus for medium pressure chromatography has already been given in Chapter 2.2.5. A glass column was used, its length was 50 cm and diameter 4 cm. For the packing of the column Kieselguhr G for t.l.c. made by Merck (Germany) (90g) was was made into a slurry by adding (19:1 by volume) toluene: ethyl acetate. The slurry was carefully poured down the column making sure that no air bubbles were trapped between the glass and the packing material. When the packing material had settled, the solvent was drained by application of pressure with the pressure pump to about 5 mm above the packing material. The sample to be analysed was then carefully pipetted on to the surface of the packing material. The pressure was again applied until the sample was adsorbed to the surface of the packing material. The eluting solvent (toluene: ethyl acetate 19:1 by volume) was carefully poured down the column to about twice the volume of the packing material and such that the surface of the packing material was not disturbed. The pressure was applied and the eluate collected by a fraction collector. The fractions containing the different sulphone isomers were detected by t.l.c. chromatography.

### 5.2.4. Spectroscopic techniques.

### 5.2.4.1. Infra-red spectroscopy.

All the infra-red spectra of sulphones were recorded on a Perkin-Elmer Model 177 grating spectrophotometer.

### 5.2.4.2. Nuclear Magnetic Resonance (N.M.R.)

All 60 MHz $^1H$ n.m.r. spectra were recorded on a Varian EM360 spectrometer. The sulphones were dissolved in $CDCl_3$ and tetramethylsilane was used as an internal standard.

### 5.2.4.3. Mass spectroscopy.

Mass spectra were recorded on a VG micromass 12F spectrometer with an ionisation potential of 70eV. Chemical ionisation (c.i.) spectra were used for the determination of the relative molecular mass while electron impact (e.i.) spectra were used for the determination of structure.

## 5.3. SYNTHESIS

### 5.3.1. Synthesis of sulphones from p-toluene sulphonic acid, trifluoroacetic anhydride and an aromatic hydrocarbon.

Trifluoroacetic anhydride (8.4 g) was added to p-toluene sulphonic acid monohydrate (3.8 g) in a round-bottomed flask fitted with a condenser and a drying tube. The resulting solution was warmed to 40-50°C. An aromatic hydrocarbon (0.04 moles) was slowly added to the solution and the temperature raised to 80°C. for 4 hrs. The hot solution was then pured into a mixture of ethanol: water, 1:1. The sulphone crystallises out on cooling, Table 2.2.1- 1. gives the yields and melting points of these compounds.

### 5.3.2. Improved Method.

p-Toluene sulphonic and monohydrate was heated to 140°C in an oven for 15 minutes and was transferred into a dessicator and allowed to cool. This anhydrous toluene sulphonic acid (3.44 g) was dissolved in nitromethane (10 cm$^3$) in a two-necked round-bottomed flask fitted with a condenser with a drying tube on top and a separating funnel. Trifluoroacetic anhydride (4, 2 g) was added and the mixture warmed to 40°C until all the sulphonic acid had dissolved. Through the separating funnel, the hydrocarbon (0.02 moles) was added slowly. When the addition was complete the reaction mixture was refluxed for 1 hr. On cooling, the reaction mixture was neutralised with 10% sodium bicarbonate and extracted three times with 10 cm$^3$ portions of chloroform. The extracts were washed several times with water and dried over magnesium sulphate (dried). The chloroform was removed under reduced pressure and the sulphone crystallised. The results here are given in Table 2.2.1 - 2.

### 5.3.3. Preparation of symmetrical diaryl sulphones from sulphuric acid, trifluoroacetic anhydride and an aromatic hydrocarbon.

In a two-necked flask fitted with a condenser with a drying tube on top and a separating funnel was dissolved sulphuric acid ( 2 g) in nitromethane (10 cm$^3$). Trifluoroacetic anhydride (8, 4 g) was added to the solution and the reaction mixture allowed to equilibrate for 15 minutes. An aromatic hydrocarbon (0, 04 moles) was placed in the separating funnel and added dropwise over a period of 15 minutes to the reaction mixture. When the addition was complete, the solution was refluxed for 30 minutes. On cooling the reaction mixture was neutralised with 10% aqueous sodium carbonate and extracted with three 10 $cm^3$ portions of chloroform. The combined extracts were washed several times with water and dried over magnesium sulphate (dried). The chloroform was removed under reduced pressure and the crude sulphone crystallised. All these sulphones were recrystallised from ethanol. The results are given in Table 2.2.2.-1.

### 5.3.4. Preparation of unsymmetrical sulphones from sulphuric acid, trifluoroacetic anhydride and two different hydrocarbons.

To a solution of sulphuric acid (2 g) in nitromethane (10 $cm^3$) was added trifluoroacetic anhydride (8.4 g) and the mixture allowed to equilibrate at room temperature for 15 minutes in a three-necked round-bottomed flask fitted with a condenser with a drying tube on top and two separating funnels. The two aromatic hydrocarbons (each 0.02 moles) were placed in both separating funnels and the first added dropwise over a period of 30 minutes to the reaction mixture. This was followed by the dropwise addition of the second aromatic hydrocarbon. The flask was warmed to about 40 °C whilst the addition of the second hydrocarbon was carried out. When the addition was complete, the solution was refluxed for 30 minutes. On cooling the reaction mixture was neutralised with 10% aqueous sodium carbonate and extracted with three 10 $cm^3$ portions of chloroform. The combined chloroform extracts were washed several times with water and then dried over magnesium sulphate (dried). The chloroform was removed by evaporation under reduced pressure and the sulphone crystallised. Most of these sulphones were recrystallised from ethanol. The results are tabulated in Table 2.2.3 - 1.

### 5.3.5. Preparation of hydroxylamine-O-sulphonic acid.

65% Fuming sulphuric acid (50 ml) and concentrated sulphuric acid (50 $cm^3$) were placed in a large beaker. To this was added hydroxylamine-O-sulphonic acid (20 g). The mixture was cooled to 0°C in an ice bath with constant stirring. After 30 minutes, diethyl ether was added dropwise to precipitate out the hydroxylamine-O-sulphonic acid. The white crystals were filtered off and subsequently washed several times with diethyl ether. The crystals were thereafter dried in a dessicator. The yield obtained was 27.12 g and the melting point of these crystals was 208-209 °C (Litt. m.p. 210°C)[145].

### 5.3.6. Preparation of sulphones with hydroxylamine-O- sulphonic acid, trifluoroacetic anhydride and an aromatic hydrocarbon.

In a two-necked round-bottomed flask fitted with a separating funnel, a condenser with a drying tube on top was dissolved hydroxylamine-O-sulphonic acid (1.15 g) and trifluoroacetic anhydride (6.3 g) in 1, 1, 1-trichloroethane (20 $cm^3$). The mixture was warmed gently for 15 minutes until all the hydroxylamine-O-sulphonic acid had dissolved. At this point, an aromatic hydrocarbon (0, 06 mol) was gradually added through a separating funnel When the addition was complete, sometimes the solution refluxed unaided, but if not so, a gentle warming was applied and the reaction mixture refluxed for a further 30 minutes. The reaction mixture was placed in a separating funnel and neutralisation of the strongly acidic solution carried out with 10% aqueous sodium carbonate. The organic compounds were extracted three times with 10 cm portions of chloroform. The combined extracts were washed several times with water and the washings dried over magnesium sulphate (dried). The chloroform was removed under reduced pressure and the sulphone allowed to crystallise. The crude sulphone product was then recrystallised from ethanol. The results are given in Table 3 - 1.

### 5.3.7. Polymerisation of diphenyl methane.

In a round-bottomed flask fitted with a condenser and a drying tube on top, was dissolved sulphuric acid (2 g) in nitromethane (10 $cm^3$). Trifluoroacetic anhydride (8.4 g) was added and the solution allowed to equilibriate for 15 minutes. Diphenylmethane (3.54 g) was added to the reaction and the resulting solution refluxed for one hour. On cooling, the reaction mixture was washed with 10% aqueous sodium carbonate and then carefully extracted with chloroform. The chloroform extracts were dried with magnesium sulphate (dried) and chloroform was removed by evaporation under reduced pressure. A solid light green polymeric compound was left in the flask.

### 5.3.8. Attempted preparation of ditolyl sulphone from sulphuric acid and toluene in the presence of phosphorus pentoxide.

Sulphuric acid (2 g) was dissolved in nitromethane (40 $cm^3$). Phosphorus pentoxide (5.7 g) was added followed by toluene (3.7 g). The mixture was refluxed with vigorous swirling for 1 hr until the phosphorus pentoxide had dissolved. The resulting mixture was cooled and then neutralised with 10% sodium aqueous carbonate. The neutral solution was extracted three times with 10 $cm^3$ portions of chloroform. The combined extracts were washed thoroughly with water and dried over magnesium sulphate. The chloroform was removed under reduced pressure. There was no crystalline product found in this organic layer.

### 5.3.9 Attempted preparation of dianisyl sulphone with sulphuric acid and anisole in the presence of acetic anhydride.

In a two-necked round-bottomed flask fitted with a separating funnel and a condenser with a drying tube on top, was added sulphuric acid (4 g ) and acetic anhydride (8.2 g) in nitromethane (20 $cm^3$). The mixture was allowed to establish an equilibrium at room temperature for 15 minutes. Anisole

(9.6 g) was added dropwise through the separating funnel. When the addition was complete, the reaction mixture was refluxed for 30-45 minutes. The cooled solution was neutralised with 10% aqueous sodium carbonate, the organic compounds extracted three times with 10 $cm^3$ portions of chloroform and the combined extracts washed several times with water. The washings were dried over magnesium sulphate (dried). The resulting oily product was then distilled under reduced pressure, the distillate coming at 85°C (0.01 mm). On cooling the distillate crystallised giving yellow crystals with a melting point of 32°C. The yield of p-acetyl anisole was 53.3%.

### 5.3.10. Attempted preparation of methyl-tolyl sulphone from methane sulphonic acid trifluoroacetic anhydride and toluene.

In a round-bottomed flask fitted with a condenser and a drying tube,was dissolved methane sulphonic acid (1.92 g) in nitromethane (10 $cm^3$). Trifluoroacetic anhydride (4.2 g) was added and the mixture stirred and allowed to equilibriate for 15 minutes. Toluene (1.82 g) was then added to the reaction mixture and it was refluxed for a further 30 minutes. The resulting solution was transferred to a separating funnel and neutralised with 10% aqueous sodium carbonate. The neutral solution was extracted three times with 5 $cm^3$ portions of chloroform and the combined extracts washed several times with water. The washings were dried over magnesium sulphate (dried). The chloroform was removed under reduced pressure. No sulphone was isolated from the extract.

### 5.3.11. Preparation of dianisylsulphone from methane sulphonic anhydride sulphuric acid and toluene.

To a solution of sulphuric acid (1 g) in nitromethane (10 $cm^3$) was added methane sulphonic anhydride (3.44 g) in a two-necked round-bottomed flask fitted with a separating funnel and a condenser with a drying tube on top. The mixture was warmed up until all the anhydride had dissolved. Anisole (2.16 g ) was slowly added through the separating funnel and the reaction mixture refluxed for 30 minutes. The reaction mixture was neutralised with 10% aqueous sodium carbonate, extracted three times with 10 $cm^3$ portions of chloroform and the combined extracts washed with water. The washings were dried over magnesium sulphate (dried). After the chloroform had been removed under reduced pressure, the sulphone crystallised out. It was recrystallised from ethanol. Its melting point was 129°C and the yield was 80%. This experiment was repeated with toluene instead of anisole and a yield of 32% of ditoyl sulphone was obtained.

### 5.3.12. Attempted preparation of ditoyl sulphones from methane sulphonic anhydride, p toluene sulphonic acid and toluene.

To a solution of anhydrous p toluene sulphonic acid (3.44 g) in nitromethane (10 $cm^3$) was added methane sulphonic anhydride (3.44 g ) in a two-necked round-bottomed flask fitted with a separating funnel and a condenser with a drying tube on top. The mixture was warmed up until both the anhydride and the acid had dissolved. Toluene (1.84 g) was added and the reaction mixture refluxed for 1 hour. The resulting solution was cooled and then neutralised with 10% aqueous sodium carbonate. The product was extracted three times with 3 $cm^3$ portions of chloroform and washed several times with water. The chloroform extracts were dried over magnesium sulphate (dried) and the chloroform removed by evaporation under reduced pressure. No sulphone product was isolated from the residue.

### 5.3.13. Attempted preparation of trifluoroacetyl methane sulphonate.

Methane sulphonic acid (1.92 g ) was dissolved in nitromethane (10 mls). To this solution was added an excess of trifluoroacetic anhydride (5.0 g ). The reaction mixture was allowed to react to completion for 30 minutes. Trifluroacetic acid and excess trifluoroacetic anhydride were then removed by evaporation under reduced pressure. The resulting oil immediately crystallises in white crystals of methane sulphonic anhydride with a melting point of 71°C. (Litt. m.p. 71°C).[95] The crystals were dried in a sulphuric acid dessicator and the yield was quantitative. The infra-red spectrum was compared to that of an authentic sample.

### 5.3.14. Preparation of p-toluene sulphonic anhydride.

A mixture of phosphorus pentoxide (107 g ), Kieselguhr gel (7 g ) Gooch asbestos (3.5 g ) and p-toluene sulphonic acid monohydrate (85 g ) was heated on an oil bath to about 100°C with occasional mixing. After six hours, pure dichloroethane (150 $cm^3$) was added and the mixture refluxed for 10 minutes. The stoppered flask was well shaken and then decanted into another flask through a plug of glass wool. This extraction was repeated twice and the combined extracts concentrated. The resulting solid was recrystallised twice from ether-benzene giving light grey crystals with a melting point of 127-129°C. The yield was 40%.

### 5.3.15. Attempted preparation of unsaturated sulphones with trifluoroacetic anhydride, p-toluene sulphonic acid and cyclohexene.

In a round-bottomed flask fitted with a condenser and a drying tube on top was placed p-toluene sulphonic acid monohydrate (3.8 g) and trifluoroacetic anhydride.(8.4 g). The resulting mixture was warmed to about 40° until the sulphonic acid had dissolved. Cyclohexene (1.64 g ) was added to the reaction mixture and the resultant solution allowed to react to completion at room temperature for 1 hr. The reaction mixture was poured on to crushed ice and neutralised with 10% aqueous sodium carbonate. The organic materials were extracted several times with ether and the combined extracts washed with water.

The washings were dried over magnesium sulphate (dried) and the ether removed by evaporation under reduced pressure. The resulting product was a polymer mass and could not be crystallised.

However when the addition of cyclohexene to the mixture of toluene sulphonic acid and trifluoroacetic anhydride was carried out at 0°C and the same procedure followed, cyclohexyl-p-toluene sulphonate was exclusively formed; m.p. 40°C.

### 5.3.16. Preparation of p-toluene sulphonyl bromide.

p-Toluene sulphonyl chloride (38 g) was dissolved in dimethyl formamide. Hydrazine hydrate ( 10 g ) was slowly added with constant stirring to avoid the reaction mixture becoming too hot. When the reaction mixture had cooled down, the p-toluene sulphonyl hydrazone was precipitated. The crystals were filtered off and washed with cold dimethyl formamide and dried. The yield is 35 g. The hydrazone was transferred into a beaker ( 1 $dm^3$) containing water 200 $cm^3$ and crushed ice. Bromine (32 g) was added dropwise to the hydrazone until efferversence had stopped. The resulting reaction mixture was extracted several times with dichloromethane. The combined extracts were washed first with 10% aqueous sodium carbonate followed by 10% aqueous sodium carbonate and lastly with water. The washings were dried over magnesium sulphate (dried) and the dichloromethane removed by evaporation under reduced pressure. The sulphonyl bromide crystallised. The crude product was recrystallised from carbon tetrachloride. The yield was 78% and the melting point of the crystals 96°C.

### 5.3.17. Attempted preparation of unsaturated sulphones with trifluoromethane sulphonyl sulphonate and cyclohexene.

Silver trifluoromethane sulphonate (2.57 g) was dissolved in nitromethane (50 $cm^3$). p-Toluene sulphonyl bromide (2.35 g) was added to the solution and the mixture stirred for 15 minutes until all the silver bromide had precipitated. Cyclohexene (0.82 g) dissolved in nitromethane (10 $cm^3$) was added dropwise and the mixture allowed to react to completion for a further 30 minutes. The silver bromide was filtered off and the filtrate neutralised with 10% aqueous sodium carbonate. The neutral reaction mixture was extracted three times with 10 $cm^3$ portions of chloroform. The combined extracts were washed thoroughly with water and dried over magnesium sulphate (dried). The chloroform and the nitromethane was removed by evaporation under reduced pressure (N.B. nitromethane reacts violently with sodium hydroxide and therefore must be removed completely).

The resulting oily product was redissolved in chloroform (20 $cm^3$) and 10% aqueous sodium hydroxide (20 $cm^3$) added to the solution. The resulting mixture was refluxed for 30 minutes. The chloroform layer was separated washed with water and dried over magnesium sulphate dried. The chloroform was evaporated under reduced pressure. The crystals formed were treated with charcoal in ethanol and then when the ethanol was removed white crystals were formed with a melting point of 115-117°C. The yield was 41%.

When this reaction was repeated with other alkenes e.g. cyclopentene, 2 methyl butene, styrene and stilbene, considerable polymerisation took place and no crystalline product was isolated.

### 5.3.18 Attempted preparation of unsaturated sulphones with *p*-toluene sulphonyl perchlorate and cyclohexene.

Silver perchlorate (2.07 g) was dissolved in dry nitromethane (50 $cm^3$). Toluene sulphonyl bromide (2.35 g) was added and the reaction mixture stirred until all the silver bromide had been precipitated. Cyclohexene (0.82 g) dissolved in 10 $cm^3$ nitromethane was then added dropwise to the reaction mixture and the resulting mixture allowed to react to completion at room temperature for 1 hr. The silver bromide was filtered off and the filtrate neutralised with 10% sodium bicarbonate. The organic products were extracted three times with 5 $cm^3$ portions of chloroform, the combined extract washed was washed several times with water and the washings dried over magnesium sulphate dried. When the chloroform was removed by evaporation under reduced pressure, a crystalline product was formed which slowly decomposed and eventually got charred on being left overnight.

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