STUDIES ON NOVEL MACROCYCLIC SULPHUR COMPOUNDS

by

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SUMMARY

This thesis describes the synthesis and properties of 2,2'-bridged biphenyls in which sulphur or oxygen functions are incorporated into the bridging unit. Seven-, eight-, nine-, ten- and eleven-membered ring systems were prepared by nucleophilic substitution of alkylene α , ω -dihalides, xylylene dihalides or dialkyl ether α, ω-dihalides by alkali metal dimercaptides or 2,2'- biphenoxide. A homologous series of cyclic disulphones has been prepared by oxidation of the parent disulphide systems with hydrogen peroxide.

The nuclear magnetic resonance spectra of appropriate compounds are discussed and related to the optical stability of these disymmetric systems. Partial optical resolution of the dithia-heterocycles and the relation between their stereochemistry and optical stability is described. The ultraviolet spectra of the bridged and unbridged biphenyls is discussed and related to the conformation of the biphenyl rings.

The thermal degradation of some "acyclic" disulphonium salts with the formation of dibenzothiophen is discussed.

The preparation of fourteen-, sixteen-, eighteen- and twenty-four-membered tetrathia-heterocyclic systems containing the _o_- xylylene bridge is described.

A brief description of the divalent palladium and platinum complexes of the "acyclic" disulphides is given.

Finally, the mass spectra of many of the compounds are discussed.

ACKNOWLEDGEMENTS

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I would like to thank Professor I. T. Millar for his guidance and encouragement throughout my work, and to Dr. J. C. Tebby and Dr. D. W. Allen for helpful discussions.

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All the work reported in this thesis was carried out by the Author under the supervision of Professor I. T. Millar.

CONTENTS

INTRODUCTION

General

Since the beginning of this century organic sulphur chemistry has undergone a continuous expansion. Organic chemistry is itself growing at a breath-taking rate, but the growth of sulphur chemistry is double that of the whole. In 1924 one-sixth of the compounds listed in the formulae index of Chemical Abstracts contained sulphur, but in 1954 this number had risen to one-third. Ever-increasing demands for new and better drugs, detergents, dyes, fungicides and elastomers provide a constant stimulus for the development of organo-sulphur chemistry.

Sulphur, although having a formal resemblance to oxygen as indicated by its position in the periodic table, differs markedly from oxygen in both the elemental state and in its organic compounds. The ability of sulphur to form successive sulphur-sulphur bonds in both its elemental state and in its organic compounds has no parallel in the chemistry of oxygen. The almost universal divalency of oxygen in its organic compounds is in complete contrast with the stable divalent, tetravalent and hexavalent states known for sulphur in its organic chemistry.

The organic chemistry of divalent sulphur has been reviewed by Reid,[1] and a number of specialised aspects of organic sulphur chemistry are reviewed in a series edited by Kharasch and Meyers.[2]

Formation of carbon-sulphur bonds

Carbon-sulphur bonds may be formed by a variety of methods[3] which in many cases are similar to those used for the formation of carbon-oxygen linkages. However in practice only a few of these preparative techniques are used to prepare the vast majority of sulphur compounds in the laboratory, and only these latter methods will be discussed.

The most general synthetic process for the formation of a carbon-sulphur bond is the nucleophilic attack of an alkali metal sulphide on a reactive alkyl halide to form the dialkyl sulphide:

$$2RX + S^{--} \longrightarrow R_2S + 2X^-$$

If an alkali metal hydrosulphide is used in this reaction the product is an alkyl thiol, which is the sulphur analogue of an alcohol:

$$RX + HS^- \longrightarrow RSH + X^-$$

An aryl or alkyl thiol dissolves in an alkaline solution to form a mercaptide anion, which on treatment with a reactive alkyl halide yields an alkyl aryl or dialkyl sulphide:

$$RX + R'S^- \longrightarrow RSR' + X^-$$

The sulphide, hydrosulphide and alkyl or aryl sulphide anions are very much more nucleophilic than their oxygen analogues, and for this reason sulphides are more readily prepared than the ether analogues. Halogens which are attached directly to a benzene nucleus are not in general displaced by a sulphide nucleophile, and therefore the sulphur must be introduced into the aromatic ring by another method.

This problem can be overcome by utilising an aryl sulphonyl chloride, which can be easily reduced to the aryl thiol with the aid of zinc and acid:

$$ArSO_2Cl \longrightarrow ArSH$$

The aryl thiol can then be used in the usual manner to synthesise alkyl aryl sulphides.

Although alkyl thiols can be prepared as shown above, the instability of the alkaline hydrosulphides makes a second synthetic method desirable. A more convenient synthesis can be achieved via the S-alkyl isothiouronium salt. Thus an active alkyl bromide on treatment with thiourea yields an isothiouronium salt, which on alkaline hydrolysis yields the appropriate alkyl thiol in good yield:

$$RBr \longrightarrow R{\cdot}S{\cdot}C{:}HN(NH_2{\cdot}HBr) \longrightarrow RSH$$

Having discussed some important methods of forming sulphur-carbon bonds it remains to describe another important, if rather limited method of sulphide formation. Thiols condense readily with suitable carbonyl compounds in the presence of acid catalyst to yield stable disulphides:

$$2RSH + R_2C{=}O \longrightarrow R_2C(SR)_2 + H_2O$$

The condensation product is known as a mercaptal if an aldehyde is used, and a mercaptol if a ketone has been used in the reaction. The ease with which the thiols react with aldehydes and ketones reflects the intense nucleophilicity of the sulphur compounds. This contrasts with the reluctance of alcohols to condense with ketones and aldehydes.

Reactions of sulphur functions

The second-row element sulphur can achieve the higher oxidation numbers +4 and +6, and so there are stable series of sulphur compounds for which there are no oxygen analogues. It should be borne in mind that strong oxidising agents such as nitric acid will oxidise the lower valency sulphur compounds to the hexavalent state.

Thiols (formerly known as mercaptans) are stable to air, but are easily oxidised by air or other mild oxidants to the disulphide when in an alkaline solution. Stronger oxidants (e.g. nitric acid) rupture the sulphur-sulphur bond to give the sulphonic acid:

$$2RSH \longrightarrow RS\text{-}SR \longrightarrow 2RSO_3H$$

Thiols can add to olefins to give sulphides:

$$RSH + RCH{=}CH_2 \longrightarrow RCH(SR)CH_3$$

Heavy metal oxides and salts, such as mercuric oxide, form stable compounds (mercaptides) with thiols, which are covalent, e.g.

$$HgO + 2RSH \longrightarrow (RS)_2Hg$$

Thiols are more acidic than alcohols, and thiophenols are likewise more acidic than the corresponding phenols.

Sulphides are only oxidised by stronger oxidising agents such as peracetic acid. The oxidation proceeds in two stages, the rapid formation of the sulphoxide, which is then more slowly oxidised to the hexavalent sulphone:

$$R_2S \longrightarrow R_2SO \longrightarrow R_2SO_2$$

"Desulphurization" by Raney nickel is a useful reductive reaction of organic sulphides:

$$R_2S + H_2(Ni) \longrightarrow 2RH + NiS$$

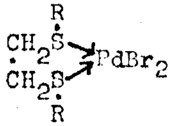
The nucleophilic nature of dialkyl sulphides enables them to form sulphonium salts with reactive alkyl halides.

$$R_2S + R'X \longrightarrow [R_2R'S^{+}]\,X^{-}$$

However aryl alkyl sulphides are less nucleophilic due to the possibility of delocalisation of one of the sulphur 3p electron pairs into the aromatic ring. Very reactive quaternizing reagents such as dimethyl sulphate are needed, to form salts with aryl alkyl sulphides.

A feature of organic sulphides is their ability (comparable with that of the ethers) to form co-ordination compounds with many types of transition metal cations, e.g. mercury (II), platinum (II) and palladium (II): e.g.

$$(R_2S)_2PtBr_2 \;,\; (R_2S)_2PdCl_2 \;,$$



$$\begin{array}{l} CH_2\overset{R}{S} \\ CH_2\underset{R}{S} \end{array} \rightrightarrows PdBr_2$$

Aryl alkyl sulphides do not complex with divalent mercury; the donor ability of sulphur is diminished by the aryl group.

<u>Disulphides and polysulphides</u> are less stable than the sulphides, and are increasingly difficult to obtain as more sulphur atoms are included in the chain. Polysulphides can be made by treating a thiol with a sulphur chloride:

$$2RSH + S_nCl_2 \longrightarrow RS(S)_nSR + 2HCl$$

$$(n > 1)$$

Alkyl polysulphides are produced on treating an alkyl halide with alkaline polysulphide:

$$2RX + K_2S_n \longrightarrow RS_nR + 2KX \qquad (n > 1)$$

It must be emphasised that alkaline polysulphides and sulphur chlorides are mixtures of compounds, whose complexity rises with increasing sulphur content, and these procedures are usually limited to the lower polysulphides. Aryl polysulphides up to $Ar.S_4.Ar$ are known; the sulphur chain is known to be unbranched. The main reactions of polysulphides involve the loss of sulphur from the polysulphide linkage. Such reactions are of importance in the vulcanisation of rubber. The disulphide link is of great importance in proteins and in biochemistry generally.

Sulphonium salts: on heating, sulphonium halides readily break down to their constituents:

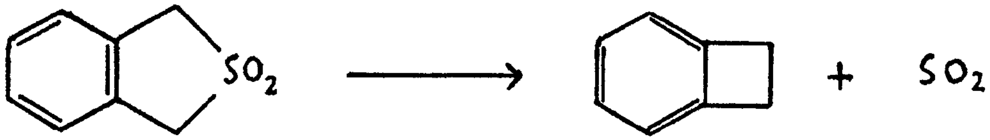
$$[R_3S^+]\,X^- \longrightarrow R_2S + RX$$

Sulphonium hydroxides containing suitable alkyl groups can undergo a Hofmann-type elimination reaction to yield an olefin: e.g.

$$[CH_3CH_2S^+R_2]\,OH^- \longrightarrow R_2S + CH_2 = CH_2 + H_2O$$

Sulphoxides are moderately stable sulphur compounds obtained by partial oxidation of sulphides. Sulphoxides are easily oxidised to sulphones, or reduced to sulphides, and form complexes with transition metals.

Sulphones are the most stable organic sulphur compounds; they are only reduced with lithium aluminium hydride with extreme difficulty. Certain sulphones decompose on heating with the expulsion of sulphur dioxide:

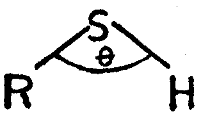


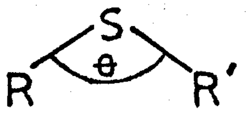
The pyrolysis is known to take place by a free radical process.[4]

A range of organic derivatives of oxy-acids of sulphur is known, e.g. sulphonic, sulphinic and thiosulphonic acids, and their esters and amides, halogen derivatives etc; these normally contain only one C-S bond, and since the work described in this thesis is mainly concerned with compounds containing two such bonds, they will not be discussed here.

Bonding and geometry of sulphur linkages: Sulphur has the electronic structure $[Ne]3s^2 3p^4 3d^0$ giving a total of six electrons with which it can form bonds. The vacant 3d orbitals can accommodate donated bonding electrons as in the higher valency state sulphur compounds. There is rapidly growing evidence that in certain compounds such expansion above the octet does occur.[5]

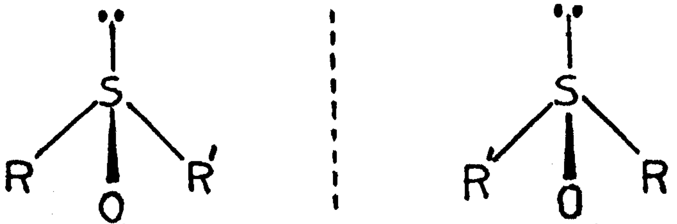
Thiols and sulphides are bent molecules:





and the angle θ is dependent on the group adjoining the sulphur atom. Thus for H_2S $\theta = 90^\circ$; in MeSH $\theta = 100^\circ$; in Me_2S $\theta = 105^\circ$ and in $p(BrC_6H_4-)_2S$ $\theta = 109^\circ$. The sulphur atom is thought to have varying degrees of s-p hybridisation in these compounds.[6]

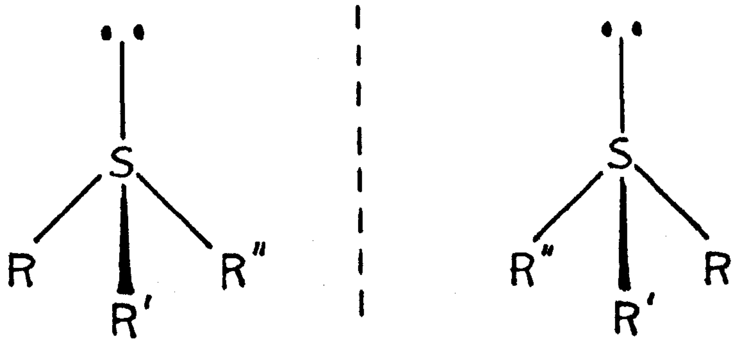
Sulphoxides are pyramidal molecules, which have a pseudo-tetrahedral geometry because of the lone pair of electrons. They can exist as stable optical isomers:



In dimethyl sulphoxide the sulphur atom can be considered to give up a major share of a pair of its 3p electrons, the electronic deficiency on the sulphur atom being compensated by back π-bonding between the $2p_y$ and $2p_x$ oxygen lone pairs of electrons and two of the empty 3d orbitals of the sulphur atom. The sulphur-oxygen bond has a bond energy of about 125 kcal. which is roughly the strength of a double bond, and can be written as a double bond even though it is electronically a triple bond:[6] $R_2S = O$ (cf. Carbon monoxide, $\overset{+}{C} = \bar{O}$). In basicity dimethyl sulphoxide is similar to acetone, whereas a far stronger basicity would be expected on the single bond formulation $R_2\overset{+}{S} \text{—} O^-$

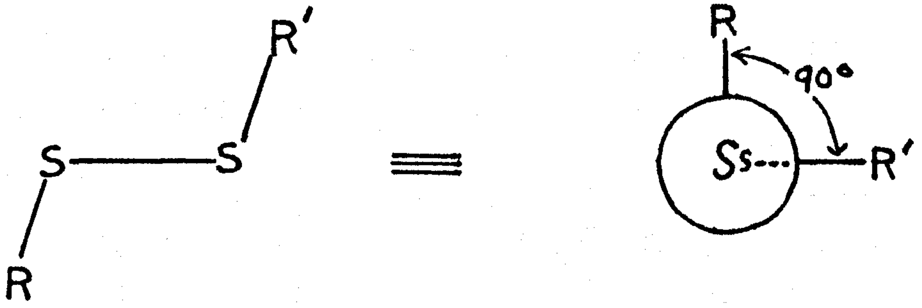
Sulphones are tetrahedral molecules, and like the sulphoxides the donation of the sulphur 3p lone pairs to form sulphur-oxygen σ-bonds, is compensated by π-bonding from oxygen to sulphur.[6] Chemical and physical evidence suggests that the π-bond character of sulphones is larger than that of sulphoxides.[5]

Sulphonium salts are pyramidal, but the sulphur lone pair of 3p electrons give a pseudo-tetrahedral system, which is resolvable; the enantiomers are stable.



Presumably the sulphur has some degree of s-p hybridisation as was suggested for the simple sulphides.

Disulphides are non-planar, with a dihedral angle of about 90° between the planes of the valencies of the adjacent sulphur atoms:[7]

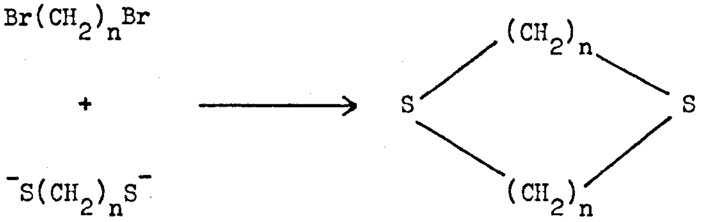


The barrier to rotation about the sulphur-sulphur bond has been estimated spectroscopically to be 9.5 kcal in dimethyl disulphide. It has been suggested that the greater stability of the non-planar form may have its origin in sulphur-sulphur π-bonding. Similar dihedral angles have been found in tri- and tetra-sulphide molecules and in elemental sulphur (α-form: cyclo-S_8).

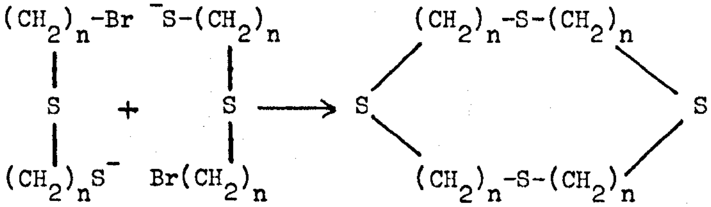
Synthesis of macrocyclic organo-sulphur compounds

Relatively few sulphur macrocyclic compounds are known and recorded in the literature, doubtless because of the synthetic difficulties involved.

Cyclic sulphur compounds can be made by reacting an α,ω-alkylene dibromide with either an alkaline sulphide or an alkaline dimercaptide, but with alkylene bridging units only the five-, six- and seven-membered rings are produced in respectable yields:

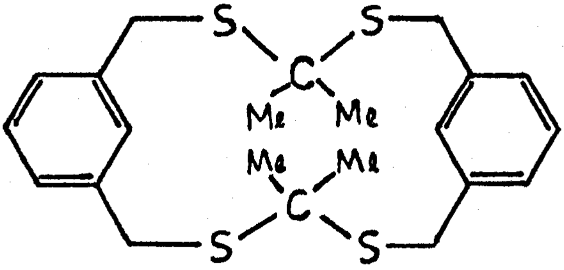


Since the cyclisation process requires two separate nucleophilic substitutions a 'dimeric' heterocycle may be formed by union of two intermediate molecules:

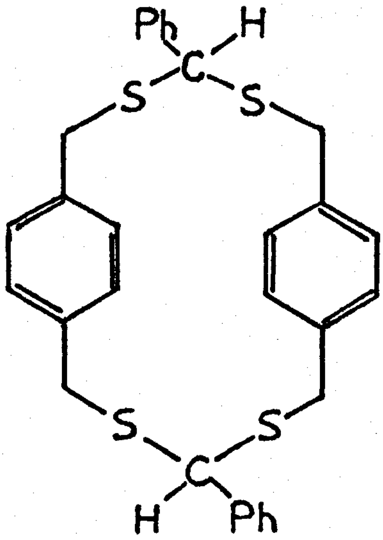


Naturally the formation of a dimeric heterocycle is usually made more difficult by the tendency of the longer flexible monomer intermediates to polymerise by successive reaction with their own species. Needless to say, the isolation of macrocycles and medium sized rings by this method is not easy when polymeric material is likely to form over 99% of the total product.

Autenrieth and Beuttel were the first workers to overcome this problem by using rigid m-and p-xylylene bridges to form thia-macrocycles. [8,9] Thus m-xylylene dithiol (I) and acetone condense together in the presence of hydrogen chloride in an acetal type of reaction to yield the sixteen-membered tetrathia-metacyclophane (II) in a 40% yield.[8] Similarly condensation of p-xylylene dithiol (III) and benzaldehyde yielded the eighteen-membered tetrathia-paracyclophane (IV):[9]



(II)



(IV)

Objectives of the present work

These were:

(a) To prepare novel types of macrocyclic structures containing only carbon and sulphur in the ring, and to study their simple chemical reactions;

(b) to study the degradation of those compounds by heat and in the mass spectrometer;

(c) to investigate their stereochemistry by nuclear magnetic resonance, ultraviolet spectrometry and polarimetry;

(d) also, since certain sulphur compounds are of value as additives in the rubber-processing industries, and others show biological activity of value in agriculture, this exploratory chemistry has been undertaken, in part, to provide new types of sulphur compounds for examination and testing for purposes such as these (preliminary results of such tests are given in Appendix (III));

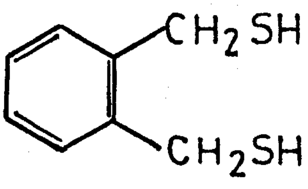
(e) in the course of the work it proved illuminating to prepare the previously unknown oxygen analogues of a number of these sulphur compounds, for examination by physical methods and for comparison.

PART I

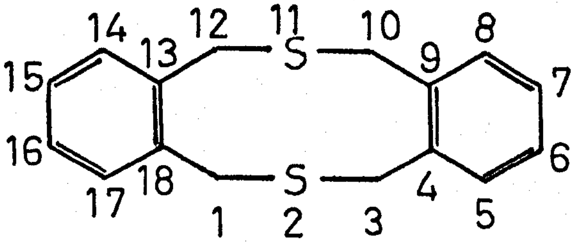
The Synthesis and Properties of Biphenyls with 2,2'- Bridges containing Carbon, Sulphur and Oxygen atoms, and the Preparation of some Macrocyclic Tetrasulphides

The compounds o-xylylene dithiol (V) and o-xylylene dibromide would appear to be useful potential intermediates in the synthesis of sulphur macrocycles, and for the preparation of novel chelating reagents. (For the latter see page 148). Their value arises both from the 'benzylic' reactivity of the compounds, and from the fact that the functional groups are held in a favourable orientation for cyclisation.

Autenrieth and Bruning first demonstrated the use of the o-xylylene bridge in macrocylic syntheses of sulphur compounds, when they treated the disodium salt of the dithiol (V) with o-xylylene dibromide to yield the ten-membered heterocycle (2,11)-dithia [3.3] orthocyclophane (VI).[10]

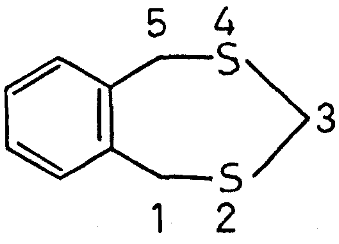


(V)

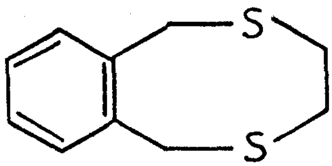


(VI)

Although the seven-[11] and eight-[12] membered dithia systems (2,4)-dithia [5] orthocyclophane (VII) and (2,5)-dithia [6] orthocyclophane (VIII) respectively, have been previously prepared, the corresponding "dimeric" macrocycles had not been isolated.



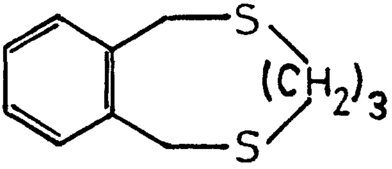
(VII)



(VIII)

The dithiol (V) was originally prepared by Kötz,[13] but Autenrieth and Hennings[14] were the first workers to describe the synthesis, which involved treating o-xylylene dibromide with an ethanolic solution of potassium hydrosulphide to give the dithiol (V) in a 50% yield. This synthesis is very tedious, and it is difficult to isolate a pure product. We have found the S-alkyl isothiouronium salt method (as adapted by Fletcher and Pan[15]) to be applicable to this preparation and to be a much superior method. Thus o-xylylene dibromide and thiourea in dimethyl sulphoxide are allowed to stand overnight, the resulting solution is then hydrolysed with aqueous sodium hydroxide, and the dithiol (V) liberated by adding hydrochloric acid. On ether extraction the pure dithiol (V) was obtained in almost quantitative yield. (N.B. All the reactions which involve alkaline solutions of thiols were performed under nitrogen.)

In the present work we have found that the dithiol (V) and o-xylylene dibromide react with methylene iodide and alkylene dithiols respectively, to yield both monomeric and dimeric cyclic systems. Thus the disodium salt of the dithiol (V) on treatment with methylene iodide in alcoholic media, gave the seven-membered dithia heterocycle (VII) (15%) together with the fourteen-membered tetrathia macrocycle (X;n=1), the latter in a yield of 3%.



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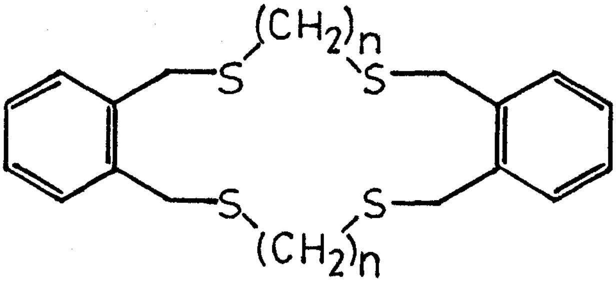
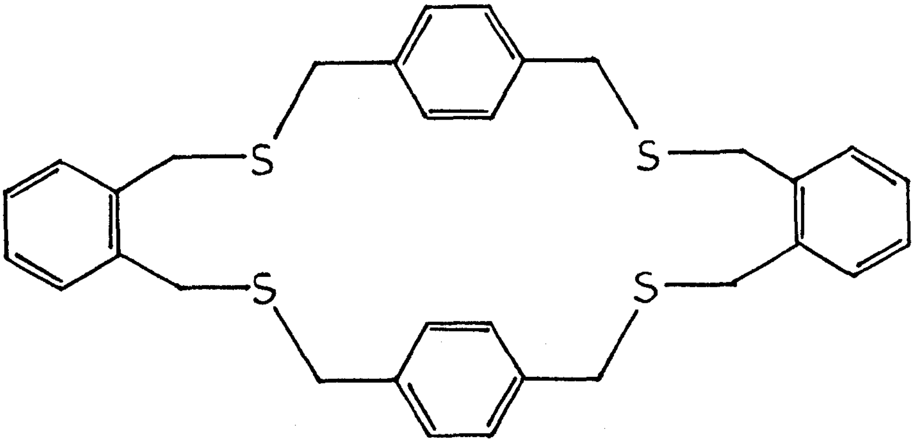


(X)

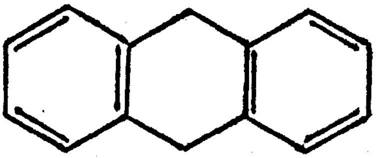
In a similar reaction with p-xylylene dibromide the twenty-four-membered tetrathia paracyclophane (XI) was isolated as the only crystalline product, in 10% yield.



(XI)

By treating o-xylylene dibromide with the disodium salts of dimethylene and trimethylene dithiols certain higher homologues, i.e. the eight- and nine-membered dithia heterocycles (VIII) and (IX), and the sixteen- and eighteen-membered tetrathia macrocycles (X; n=2 and 3) respectively were obtained. The yield of both the latter macrocycles was about 5%.

An interesting difference between the monomeric and dimeric sulphur heterocycles occurs in the aromatic region of their n.m.r. spectra. For the monomeric heterocycles (VII), (VIII) and (IX) and the twenty-four-membered paracyclophane (XI), the aromatic protons of the o-xylylene bridges all give sharp singlets in their n.m.r. spectra, showing the aromatic protons for a given system to have similar chemical shifts. For the dimeric macrocycles (X; n=1—3) however, the aromatic absorption signals occur as A_2B_2 multiplets. This phenomenon has been reported by Shoulders and Smith[16] for the compound 9,10-dihydroanthracene (XII). They postulate that this effect is due to the ring current effect of one aromatic ring upon the protons in the other aromatic ring, made possible because of the "butterfly wing" shape of the molecule.



(XII)

Since the related di(o-xylylene) disulphide (VI) also exhibits a similar effect, we suggest that the methylene bridged macrocycles (X; n=1—3) are sufficiently flexible to allow the aromatic rings to approach one another and cause a similar effect to that described for 9,10-dihydroanthracene (XII). It is interesting to note that for the twenty-four-membered metacyclophane (XI) no such interaction is observed, perhaps due to a more sterically rigid system with the two o-xylylene units well separated.

The mass spectra of these compounds were determined primarily to establish the molecular weight of the molecules, especially important for distinguishing between the monomeric and dimeric heterocycles. In addition it has proved of interest to examine some of the mass spectra in a qualitative way and to suggest possible mechanisms for some of the fragmentation processes.

It must be made quite clear at the outset that the interpretation of the mass spectra described in this thesis is essentially speculative. At the same time it was thought that at least some tentative ideas on interpretation should be developed.

Metastable ions are of great importance in deducing the path of a fragmentation process. Thus if an ion *A* decomposes in the accelerating region of the mass spectrometer to a second ion *B* and an uncharged fragment, a diffuse low intensity peak of mass below *B* is observed. This low intensity peak m* is known as a metastable ion and its position may be calculated by the simple formula: $\frac{m^*}{e} = \frac{B^2}{A}$. The nature of the formula is indicative that the fragmentation of *A* to *B* is a one-step process.

A feature of the mass spectra of these sulphur heterocycles is the presence of a very abundant ion of mass 135. In most of the compounds examined, including some *o*-xylylene di(alkylsulphide) compounds, this ion is the base peak in the spectra, and in the other cases had a very high abundance relative to the base peak.

The mass spectra of the dithia heterocycles (VII), (VIII) and (IX) are characterised by two abundant ions of mass 104 and 135, and the molecular ion. (See Figures 1 - 3). That the ion of mass 135 is formed directly from the molecular ion in each case is confirmed by the presence of the appropriate metastable ions in their spectra. Two possible

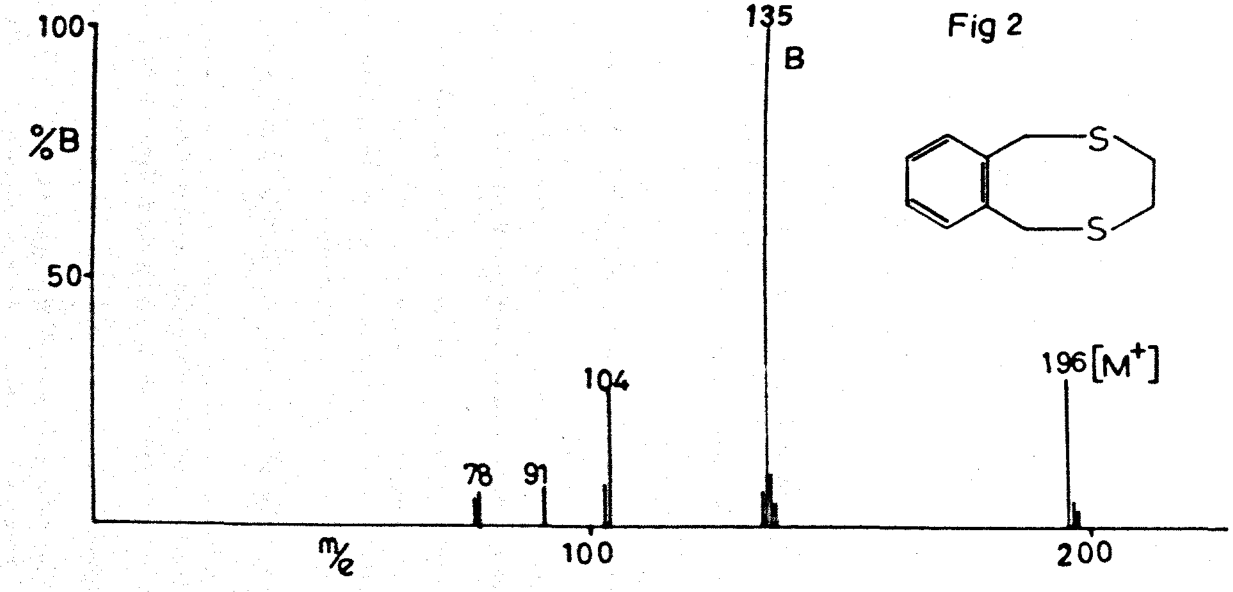


Fig 2

100
%B
50
135
B
104
78
91
196[M⁺]
m/e
100
200

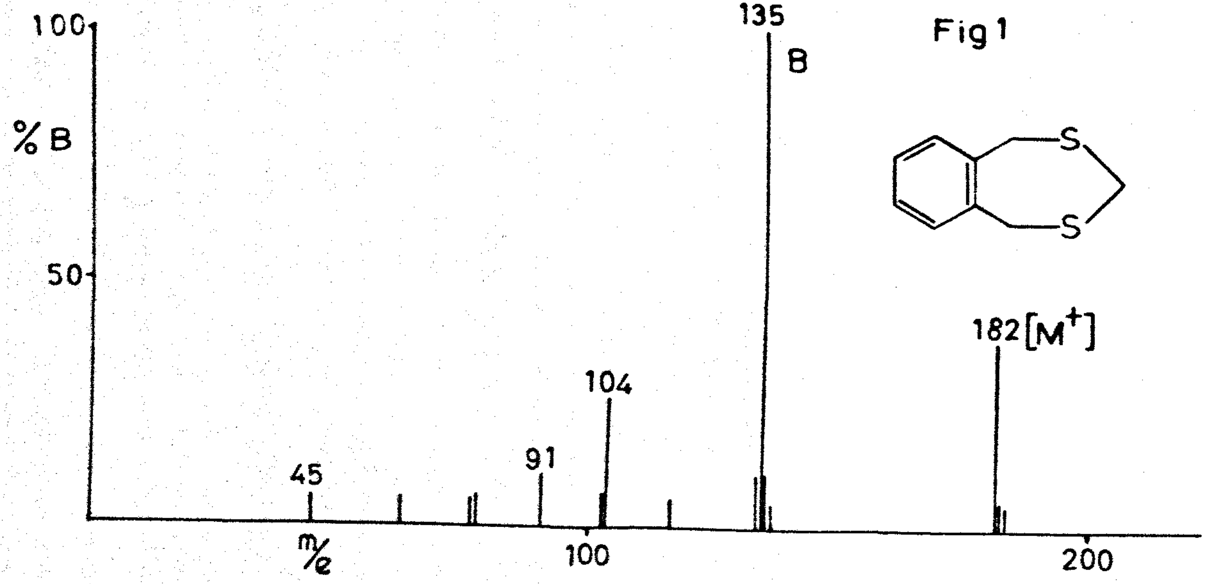
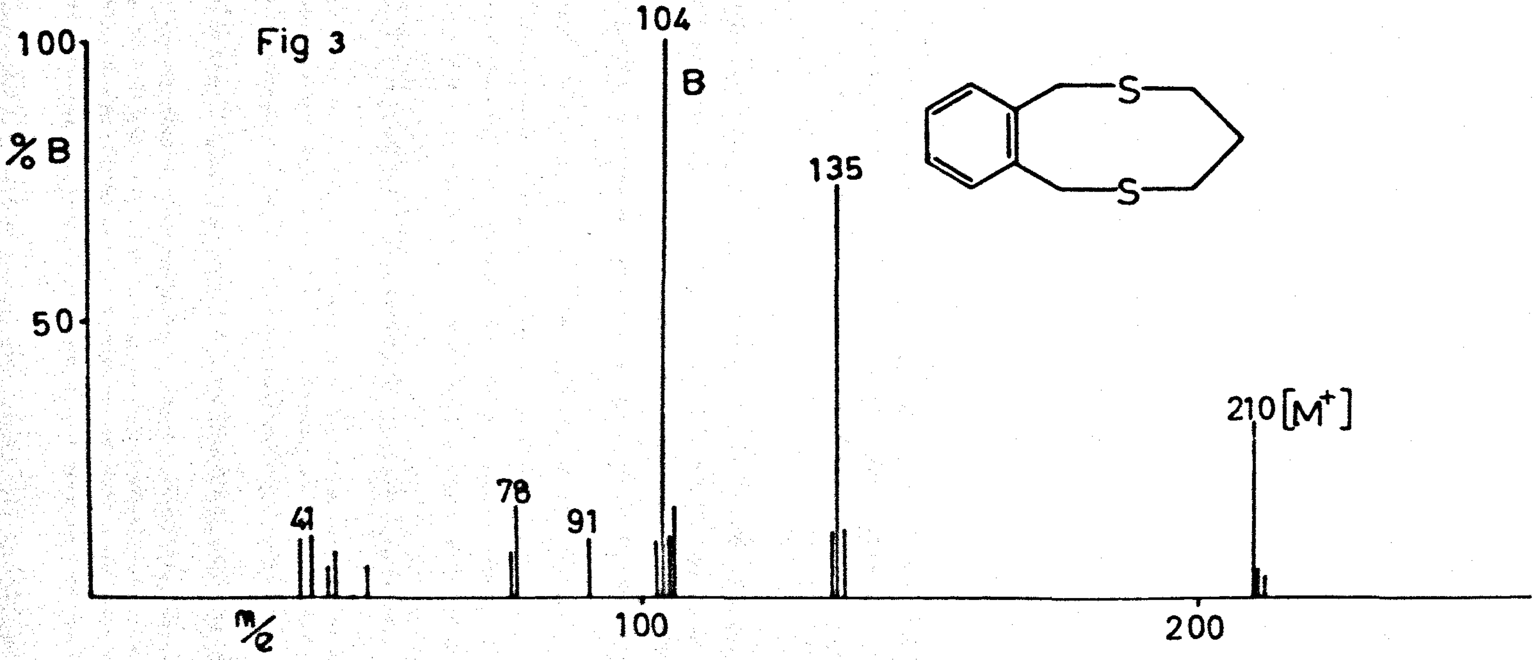


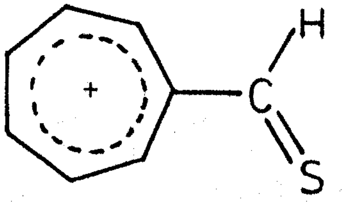
Fig 1

100
%B
50
135
B
104
91
45
182[M⁺]
m/e
100
200

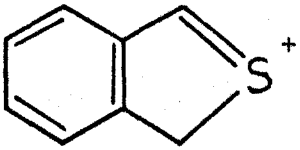
Fig 3



structures for the ion of mass 135 are: the substituted tropylium ion (XIII); and the cyclic sulphonium ylide (XIV):

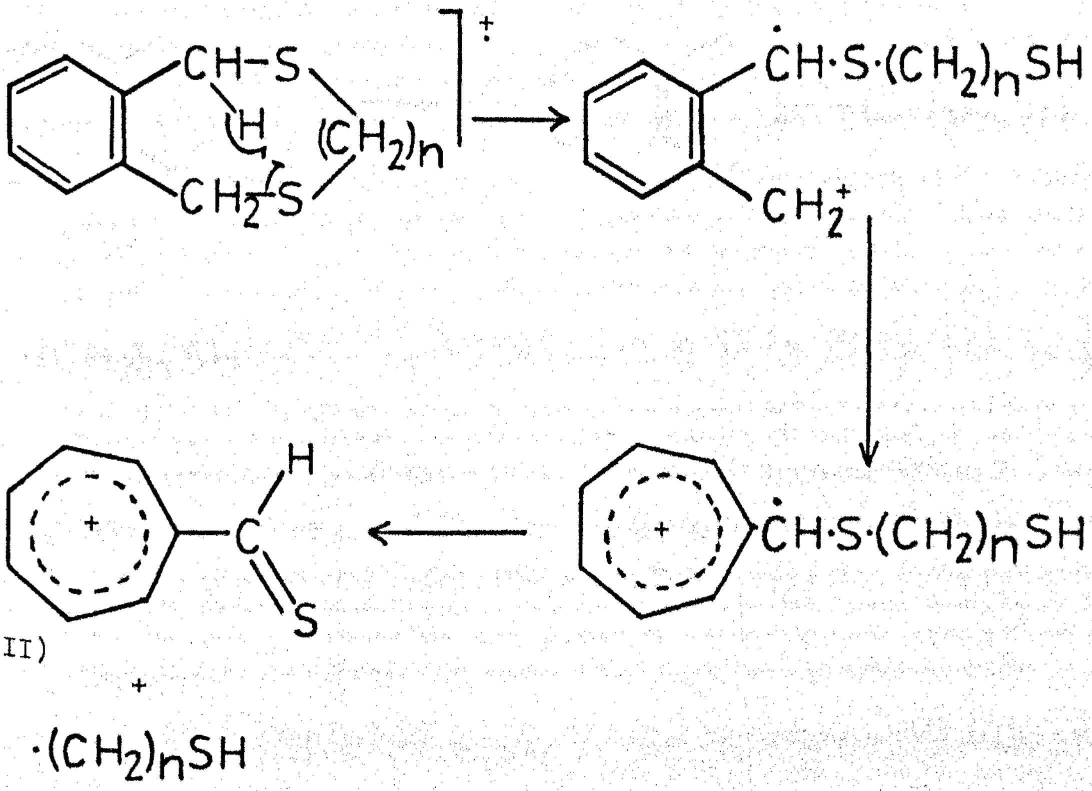


(XIII)

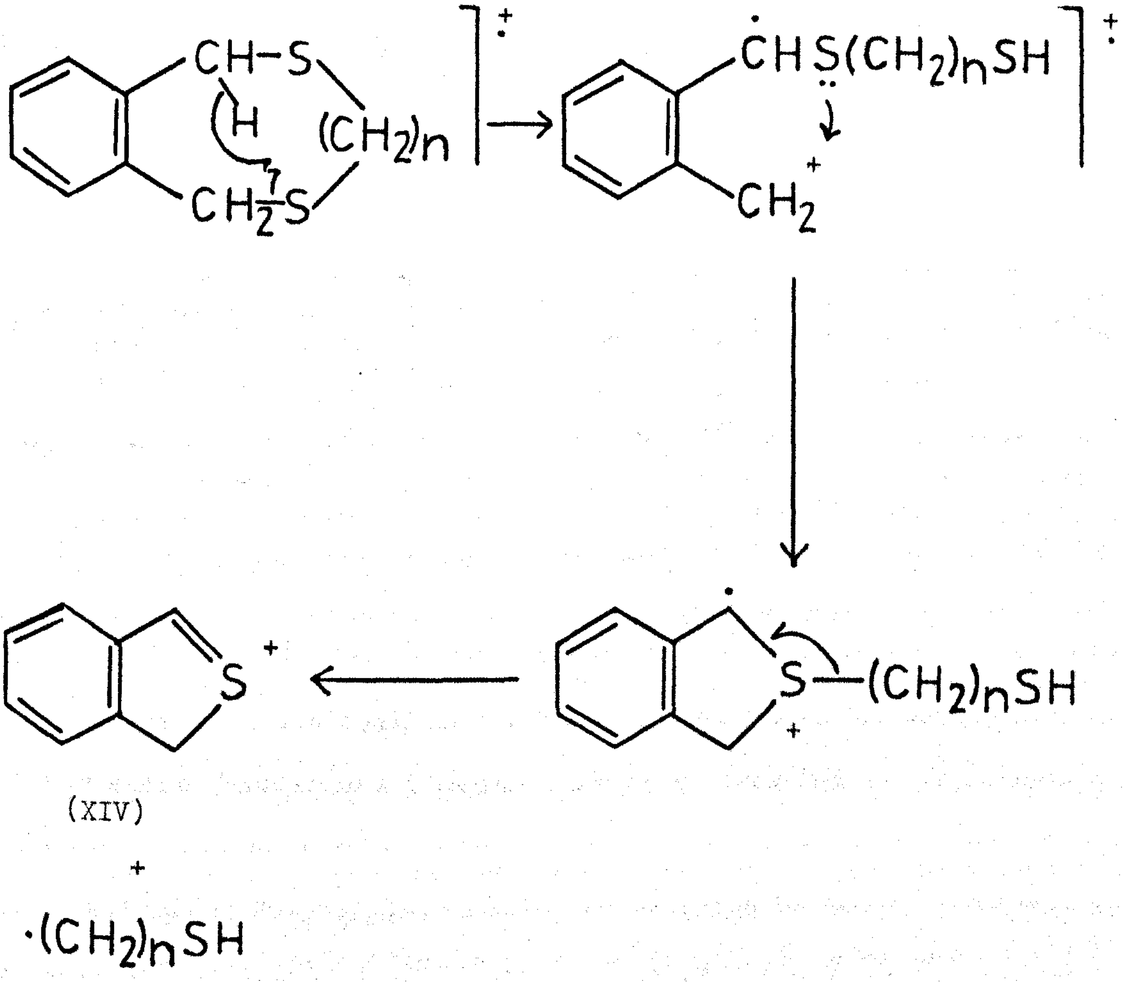


(XIV)

The molecular ion may rearrange to give a substituted benzyl ion which rearranges to a substituted tropylium ion of the same mass. This ion could then lose an uncharged fragment to give the tropylium ion (XIII):

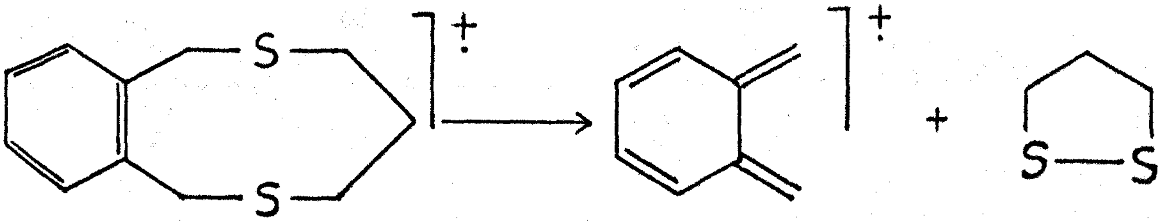


Alternatively the first rearranged ion could react in its substituted benzyl ion form to give the cyclic sulphonium ylide (XIV), i.e.



(XIV)

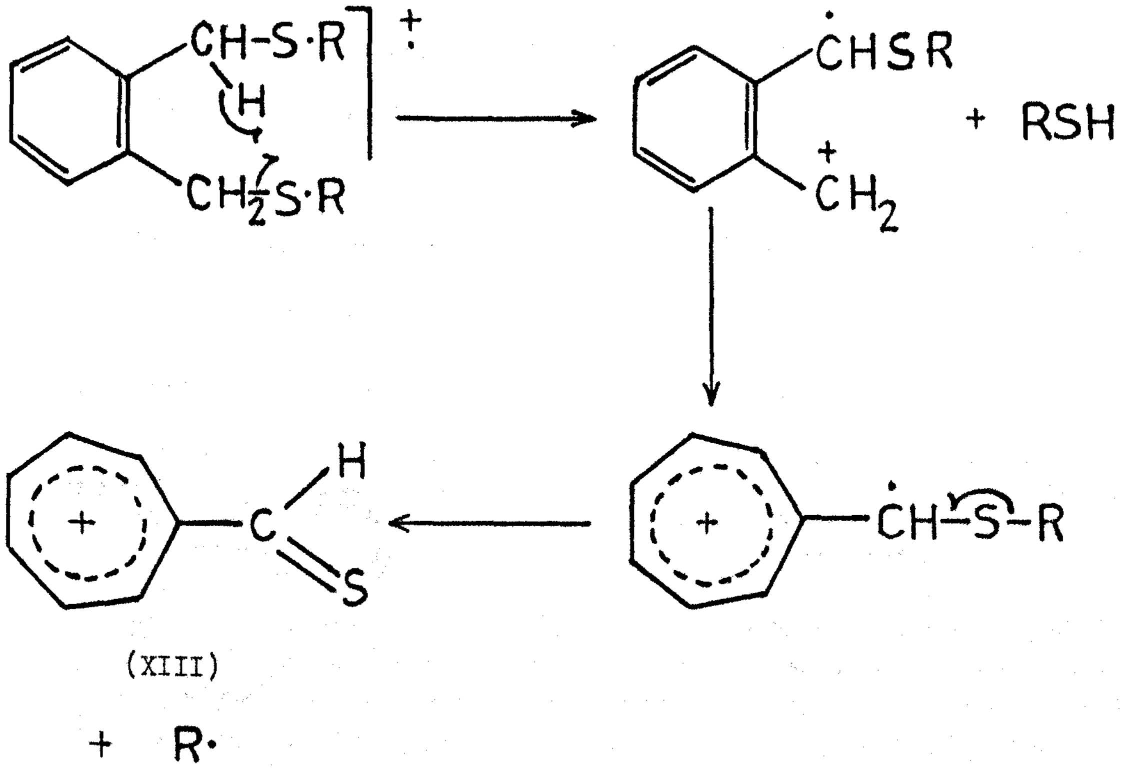
The formation of the ion of mass 104 is particularly favourable for the largest dithia heterocycle (IX), which has this ion as its base peak. (See Figure 3). A suggested fragmentation path which involves the elimination of a neutral molecule of trimethylene disulphide, is as follows:



$\frac{m}{e}$ 104

On the other hand the smaller mono- and di-methylene bridges hold the sulphur atoms further apart making such a cyclisation reaction less probable.

The "acyclic" compounds, <u>o</u>-xylylene di(ethyl or methylsulphide) also fragment to the stable ion at $\frac{m}{e}$ 135. A single step process does not appear to occur since the required metastable ions are absent. It is possible that the acyclic compounds degrade in a similar way to that suggested for the dithia heterocycles, the process now being a two step one. Thus for the tropylium ion (XIII):



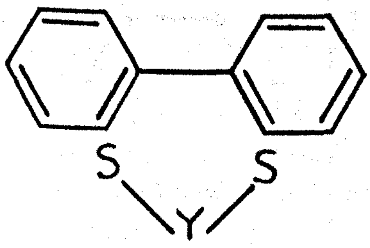
(XIII)

The sulphonium ylide ion is formed as above by cyclisation of the first intermediate ion by a two-step process.

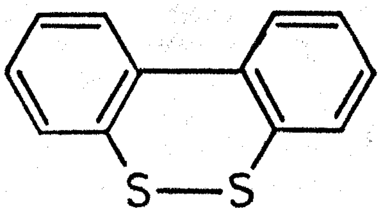
Since it has been observed that both benzyl and tropylium type ions are preferentially stabilised according to the substituents on the aromatic ring,[17] one cannot say which species is the more stable in these cases. The mass spectra of the *m*- and *p*-xylylene compounds may throw more light on the problem, and establish if the ion of mass 135 is a common intermediate. Also deuterium substituted compounds would need to be studied to establish whether a tropylium species was formed.

The major part of this synthetic work is concerned with the preparation of 2,2'-bridged biphenyl systems, which have yielded much interesting chemistry. Since few biphenyls with 2,2'-bridges containing oxygen and sulphur atoms are known, this whole area is open to exploration.

The previously-known sulphur compounds of skeletal type (XV) are limited to the seven-membered ring system (XV; Y= ·(C<)·), and the six-membered cyclic disulphide [18] (XVI).

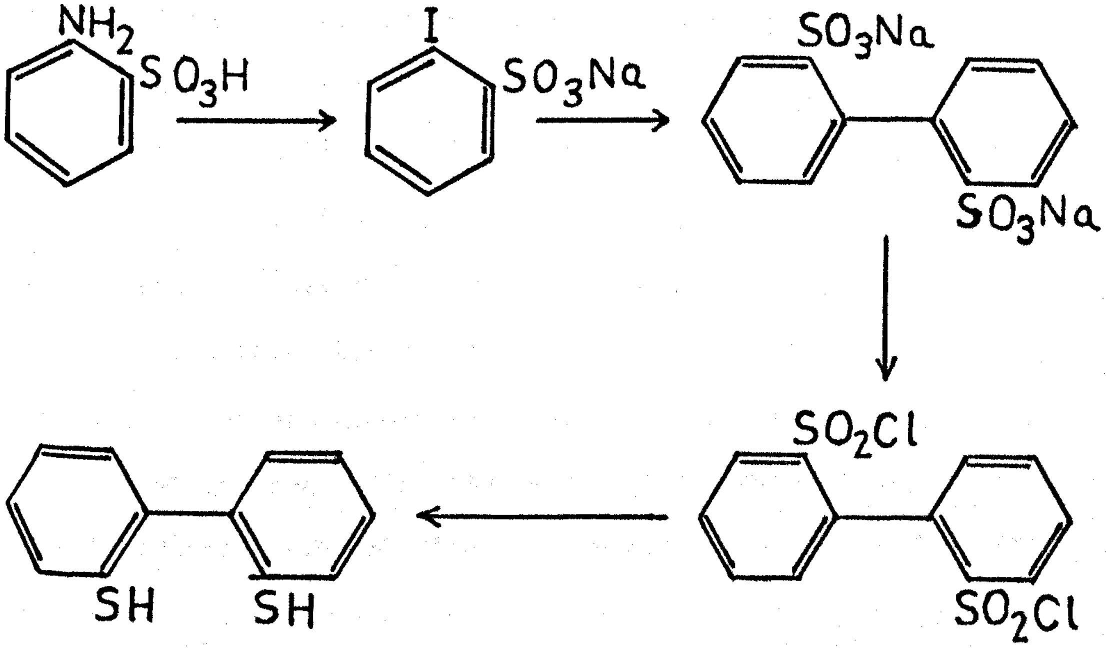


(XV)



(XVI)

The important synthetic intermediate biphenyl 2,2'-dithiol (XVII) was first synthesised by Barber and Smiles in 1928.[18] They iodinated the diazonium salt of orthanilic acid, and the resulting sodium o-iodobenzene sulphonate was converted to the biphenyl compound by boiling it in aqueous solution with copper bronze. Subsequent treatment with phosphorus pentachloride gave the 2,2'-biphenylylenebis-sulphonylchloride, which on reduction with zinc dust and hydrochloric acid in ethanol gave the dithiol (XVII) in overall yield of 35%:



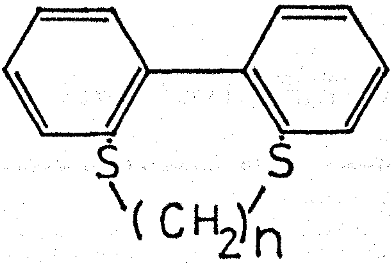
(XVII)

The dithiol (XVII) was found to condense with the carbonyl function of aldehydes and ketones in the presence of an acid catalyst to give the seven-membered ring system (XV; Y=CMe_2, CHPh or CPh_2).[18] The same system was formed when the disodium salt of the dithiol (XVII) was treated with phosgene in toluene, i.e. (XV; Y=($>$C=O)).[18] Barber and Smiles tried to form the eight-membered ring system by treatment of the disodium salt of the dithiol (XVII) with oxalyl chloride and ethylene dibromide, without success.

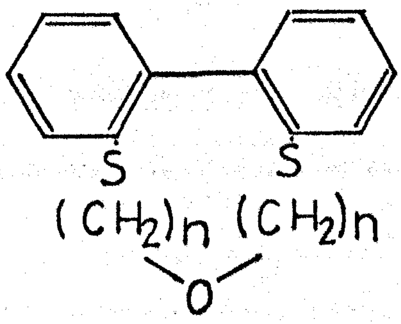
A subsequent preparation of the dithiol (XVII) by Armarego and Turner[19] in 1956 failed at the Ullmann stage in the synthesis, and they proceeded to modify the Ullmann reaction by using the phenyl ester of o-iodobenzene sulphonic acid. This new synthesis brought the number of synthetic stages to six without increasing the original yield.

In our work we have successfully repeated the original synthesis, but we also found difficulty with the Ullmann reaction, which was overcome by activating the copper bronze before use, by the method due to Kleiderer and Adams.[20]

We have found the disodium salt of the dithiol (XVII) to undergo reactions in dilute alcoholic solutions with a variety of reactive alkylene and dialkyl ether α,ω-dihalides and xylylene dibromides, to give a range of 2,2'-bridged biphenyl dithia heterocycles in good yields. Thus methylene iodide, dimethylene-, trimethylene-, tetramethylene- and pentamethylene dibromides gave a homologous series of dithia heterocycles of general formulae (XVIII; $n = 1—5$).



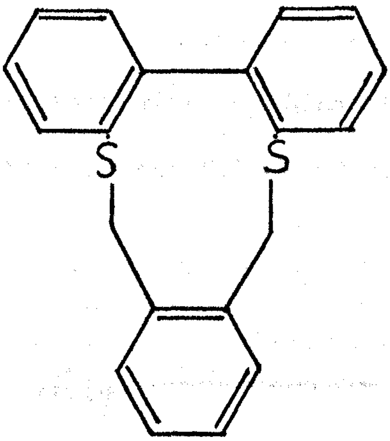
(XVIII)



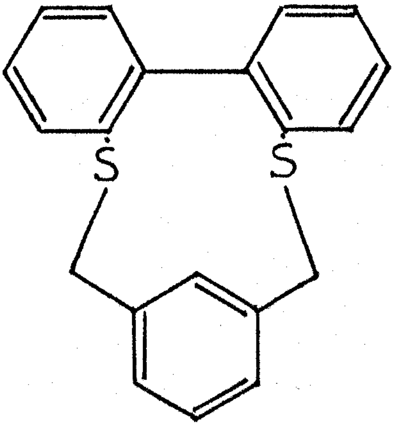
(XIX)

Surprisingly, the yields (35% - 70%) did not diminish as the longer bridges were employed; on the contrary the highest yields (60% - 70%) were achieved using the two longest bridges.

In a similar reaction, di(chloromethyl) ether and di(β-chloroethyl) ether gave the two dithia-oxa heterocyclic systems of the type (XIX; n=1 and 2) both in a yield of 60%. Finally o- and m-xylylene dibromide gave the ortho- and metacyclophanes (XX) and (XXI), respectively, in this reaction, in 70% and 50% yields. In contrast, p-xylylene dibromide in this reaction gave a polymeric solid.

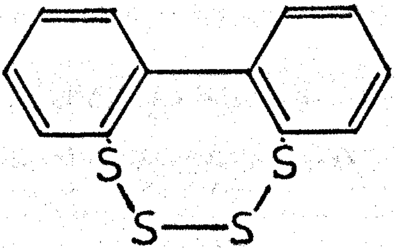


(XX)



(XXI)

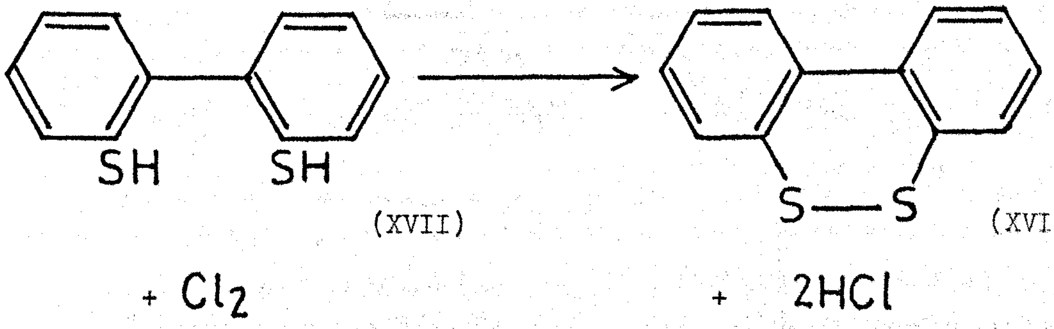
On investigating the reaction of the dithiol (XVII) with sulphur dichloride (SCl_2) and "sulphur monochloride" (S_2Cl_2) in benzene, the novel cyclic tetrasulphide (XXII) was isolated in both cases.



(XXII)

With sulphur dichloride the tetrasulphide (XXII) and the cyclic disulphide (XVI) were isolated in a 1:1 ratio, whereas with sulphur monochloride (S_2Cl_2)the major product was the cyclic tetrasulphide. The formation of the eight-membered ring structure as the only polysulphide from SCl_2, may imply that the corresponding seven-membered trisulphide ring is very unstable. On the other hand it is possible that since disproportionation of the sulphur dichloride takes place readily in solution, and any liberated chlorine would be removed readily by reaction with the dithiol (XVII), the compound (XVI) arises in this reaction in the following way:

$$2\ SCl_2 \longrightarrow S_2Cl_2 \quad + \quad Cl_2$$



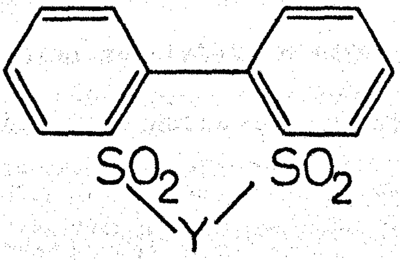
(XVII)

(XVI)

The known high stability of the eight-membered ring in elemental (α) sulphur is also noteworthy in this context.

The synthesis of a relatively wide range of 2,2'-bridged dithia biphenyls provided a valuable opportunity to examine the stereochemistry of the systems. A full account of the ultraviolet spectra of these dithia compounds and its relation to their stereochemistry is given in Part II of this thesis. The use of n.m.r. spectra in predicting the optical stability of suitable sulphur compounds, and their partial optical resolution, is described in Part III of this thesis.

Each of the dithia heterocycles was oxidised to the corresponding disulphone, using hydrogen peroxide in acetic acid, to give a second series of heterocycles of general structure (XXIII). The ultraviolet spectra are described in Part II of this thesis.

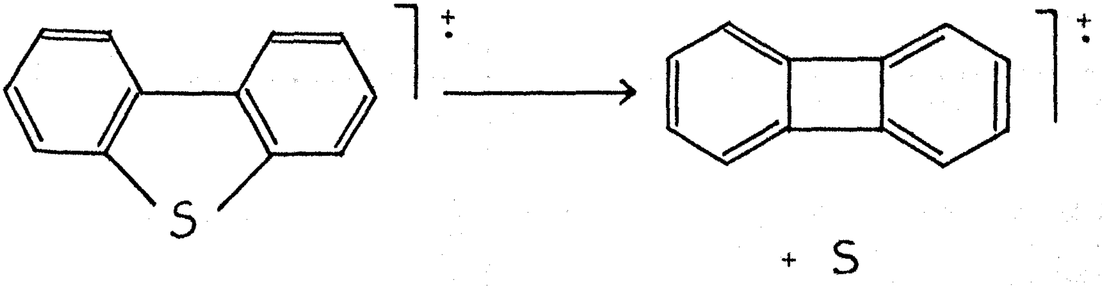


(XXIII)

The n.m.r. spectrum of the simple 2,2'-bridged biphenyl, 9,10-dihydrophenanthrene, shows two multiplets in the aromatic region at 2.31τ (2H) and 2.80τ (6H) and this has been attributed to deshielding effects which are operating on the 6,6' protons.[21] The two ortho 6,6' protons are deshielded by the opposite aromatic ring, and give rise to the two-proton multiplet at 2.31τ. In the n.m.r. spectra of the 2,2'-bridged dithia biphenyls (XVIII; n = 1—5), the aromatic protons are partially split into two multiplets, which become completely separated in the case of the dimethylene bridged disulphide (XVIII; n = 2). The multiplets for the aromatic protons of this compound at 2.2τ and 2.7τ, integrated for two and six protons respectively and it appears that this is another example of the type of deshielding effect already observed for 9,10-dihydrophenanthrene. It is noteworthy that approximate integration of the partially separated aromatic proton multiplets in the other compounds gave roughly the same ratio of protons as in the case of the disulphide (XVIII; n = 2). The n.m.r. spectra of all the disulphone analogues show the aromatic protons to be generally deshielded, but again split into two multiplets integrating for two and six protons. The two proton multiplet is shifted down field relative to the six-proton multiplet. This extra deshielding effect is the result of diamagnetic deshielding of the aromatic protons ortho to the sulphonyl group; the situation is similar to the deshielding which occurs with the carbonyl group in benzaldehyde.

The mass spectra of the bridged and unbridged dithia biphenyls have been recorded and qualitatively interpretated. The mass spectrum of dibenzothiophen, which is an important fragment ion in the spectra of these compounds, is discussed by Danby and Eland.[22] The mass spectra of the 2,2'-bridged dithia biphenyls are such that they are best considered by examining these compounds in separate classes.

The formally similar polymethylene bridged and methylene(O) ether bridged compounds have mass spectra which are dominated by the base peak at $\frac{m}{e}$ 184. (See Figures 4 and 5) Comparison with authentic material shows the peak to be that of the very stable dibenzothiophen ion. A metastable ion at $\frac{m}{e}$ 125.5 occurs in all the spectra and is due to the formation of the excited biphenylene ion from dibenzothiophen:[22]



The molecular ions of all these heterocycles fragment in one step to dibenzothiophen, the process being verified by their metastable ions. The path by which the rearrangement takes place is thought to occur as follows:

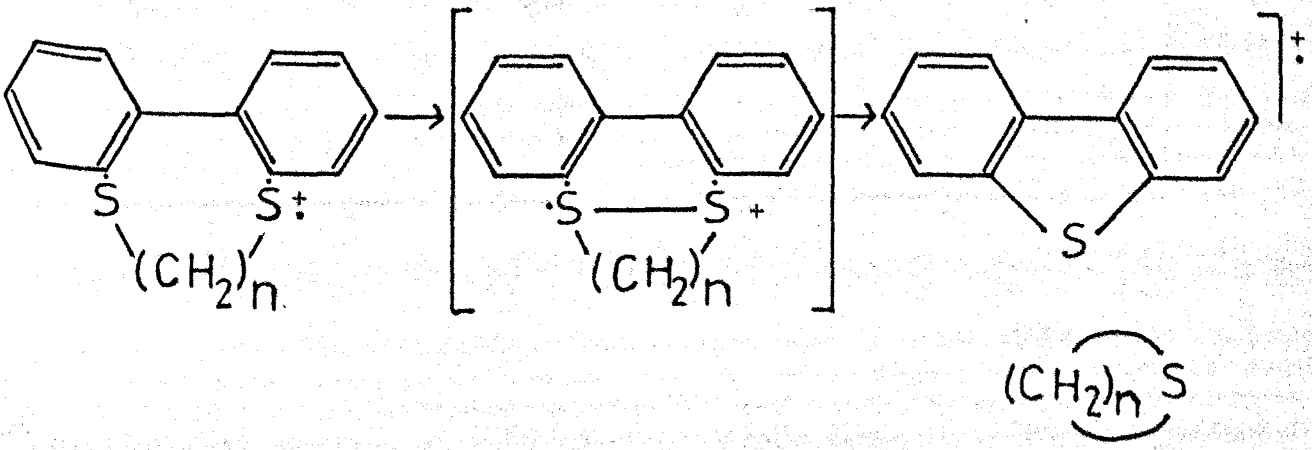


Fig 5

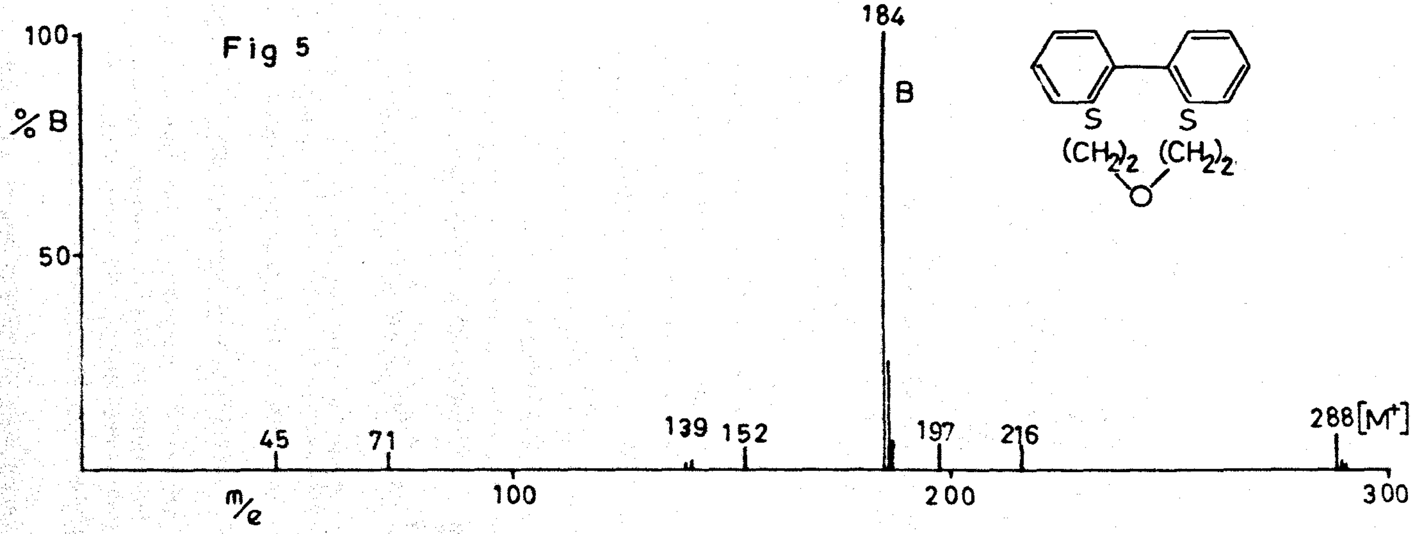
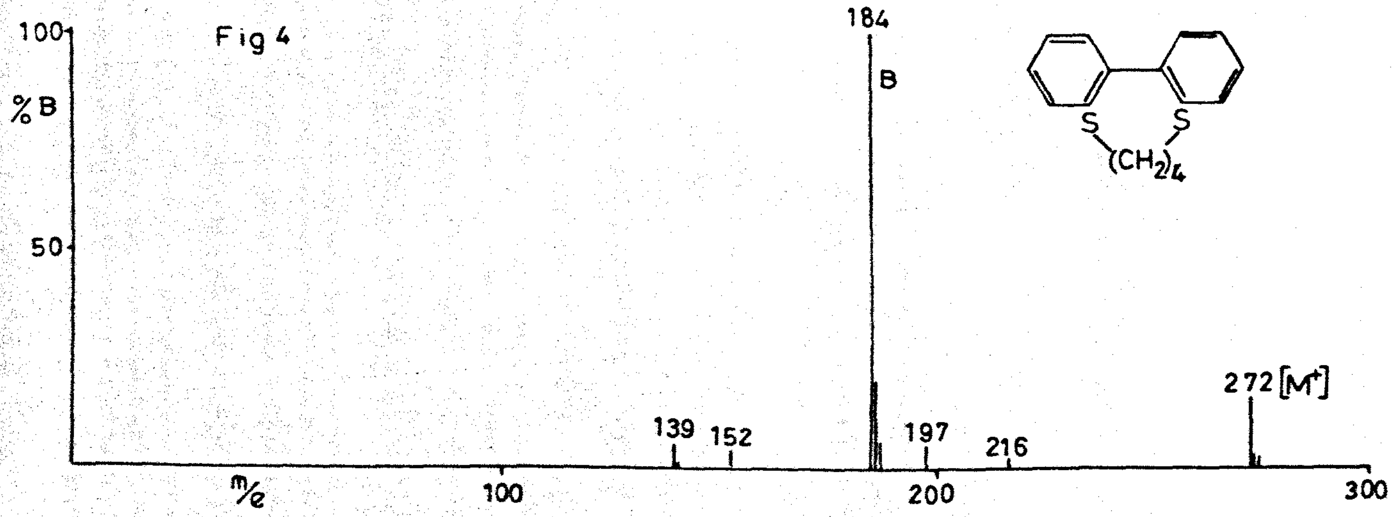
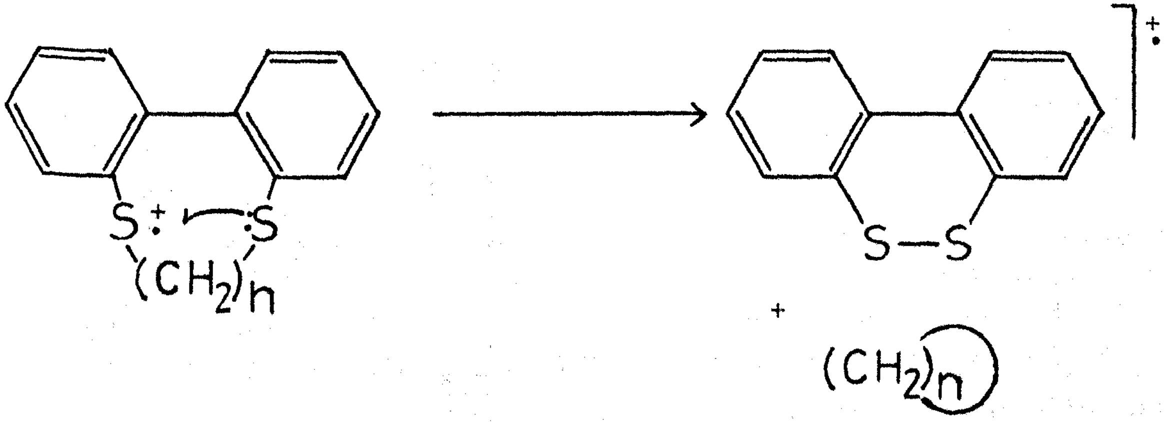

100
%B
50
184
B
45
71
139
152
197
216
288[M+]
m/e
100
200
300
S
S
(CH2)2
(CH2)2
O

Fig 4


100
%B
50
184
B
139
152
197
216
272[M+]
m/e
100
200
300
S
S
(CH2)4

The hypothetical intermediate ion is suggested to have a transient sulphur-sulphur bond as shown, to stabilise the charge and radical by delocalisation. It is noticeable that the larger polymethylene and five-membered (O) ether bridged biphenyls show a small peak at $\frac{m}{e}$ 216 which corresponds to the cyclic disulphide (XVI). This may be caused by the direct formation of a new sulphur-sulphur bond within the molecular ion:



When the bridge is replaced by an o-xylylene group the spectrum closely resembles those of the corresponding compounds with the polymethylene bridges. (See Figure 6) The usual ions of mass 104 and 135 for the o-xylylene group are also present. (See page 18). Drieding models suggest that the o-xylylene bridged biphenyl (XX) is quite flexible and there is little steric hindrence to the formation of the dibenzothiophen ion by the process previously described. In contrast the m-xylylene bridge forces the sulphur atoms apart to a transoid configuration, which will clearly prohibit a mechanism such as that suggested for the other bridged biphenyls. That this is the case

Fig 7

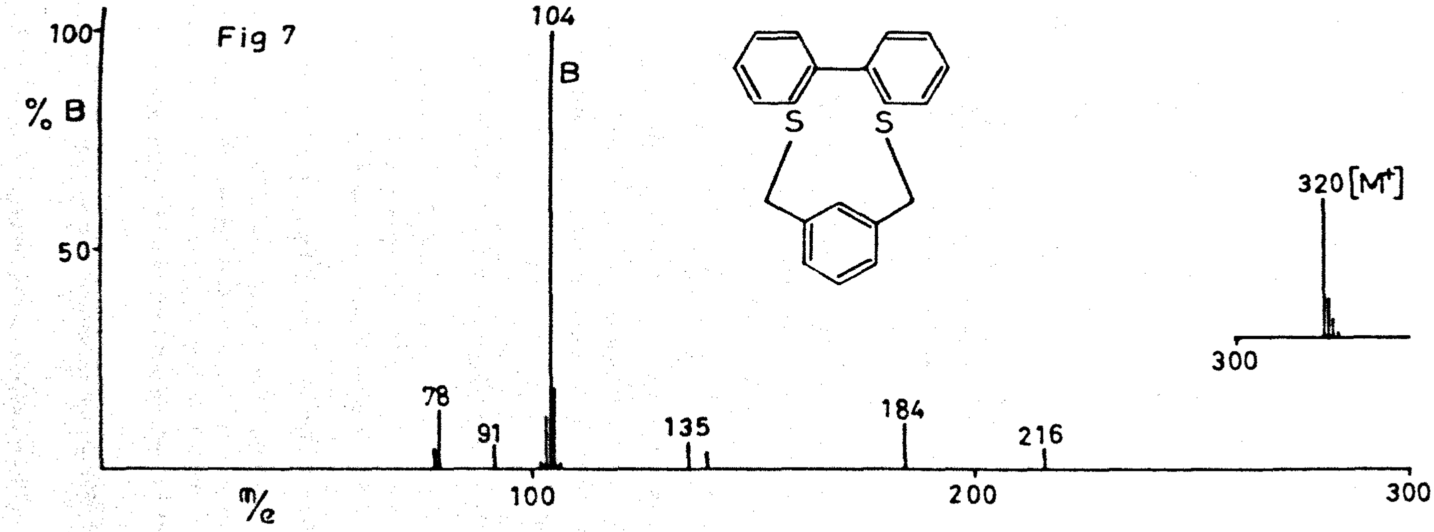
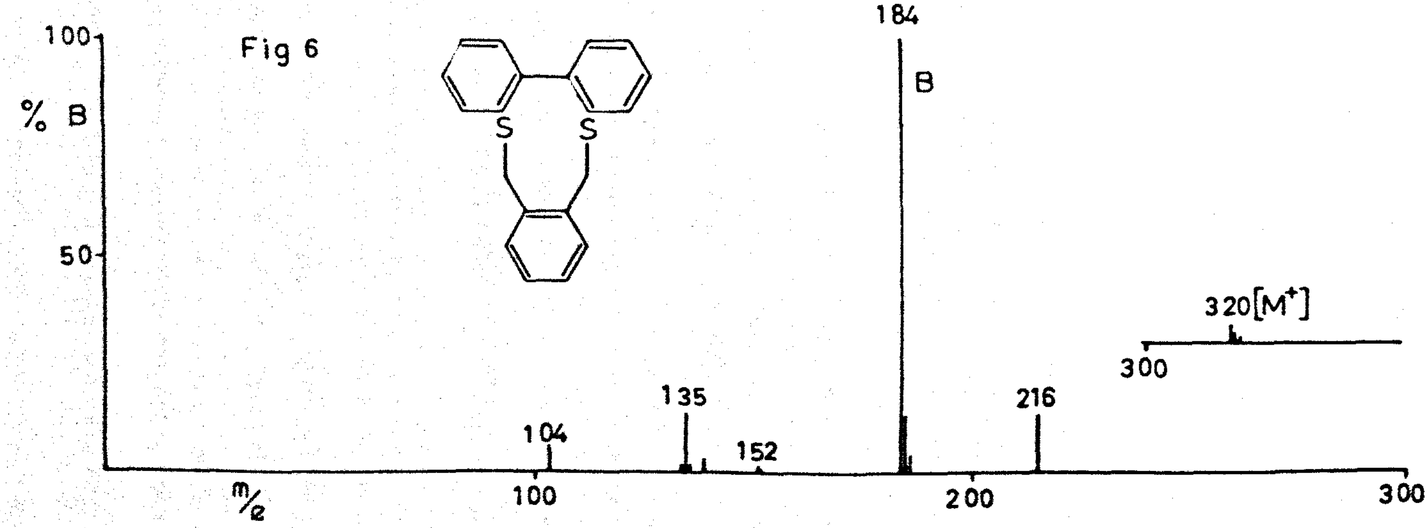
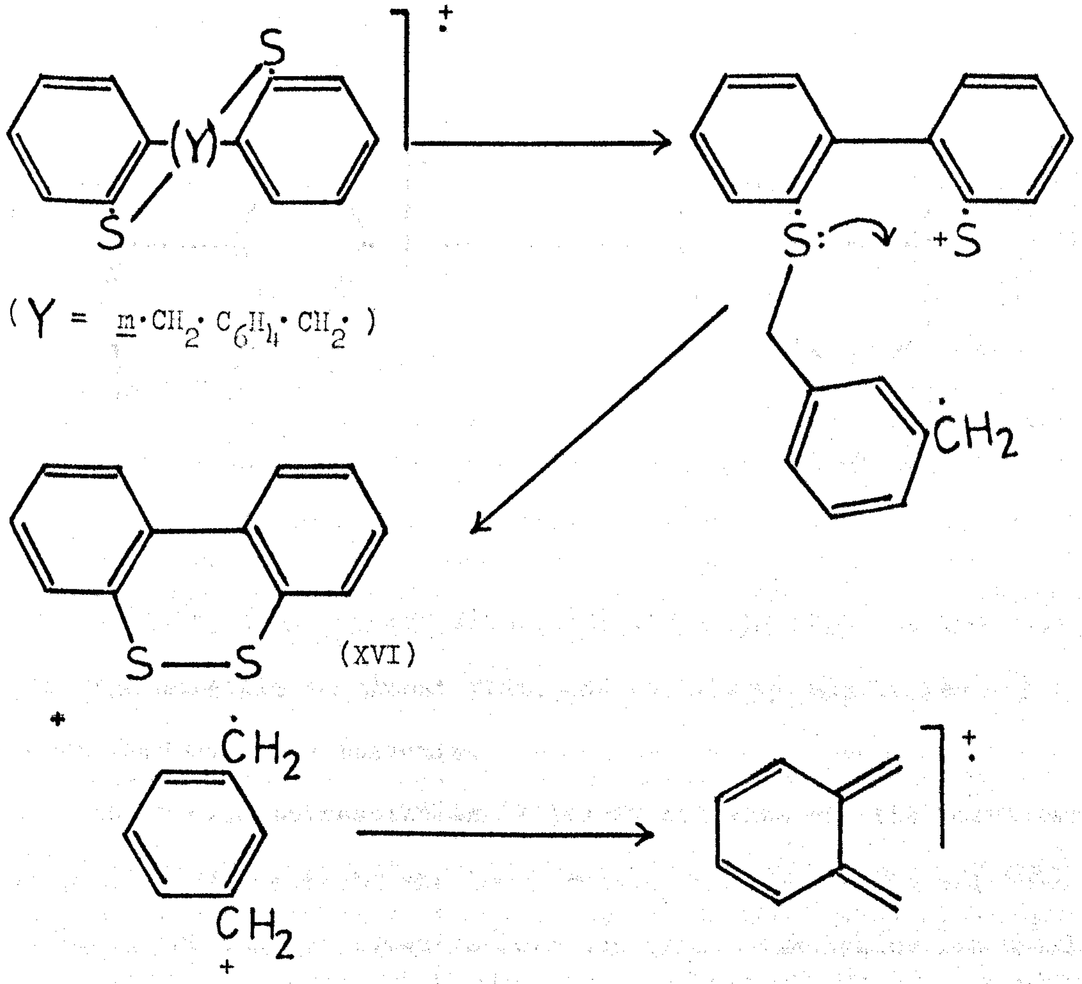

100
% B
50
104
B
78
91
135
184
216
S
S
320[M⁺]
300
m/e
100
200
300

Fig 6


100
% B
50
184
B
S
S
320[M⁺]
300
104
135
152
216
m/e
100
200
300

can be readily seen by examination of its spectrum, which has a new base peak at $\frac{m}{e}$ 104, and the dibenzothiophen ion at $\frac{m}{e}$ 184 is reduced to a peak of modest intensity. (See Figure 7). The appearance of a metastable ion at $\frac{m}{e}$ 34 indicates that the stable ion of mass 104 is formed directly from the molecular ion. The ion of mass 104 may be formed by the following process:

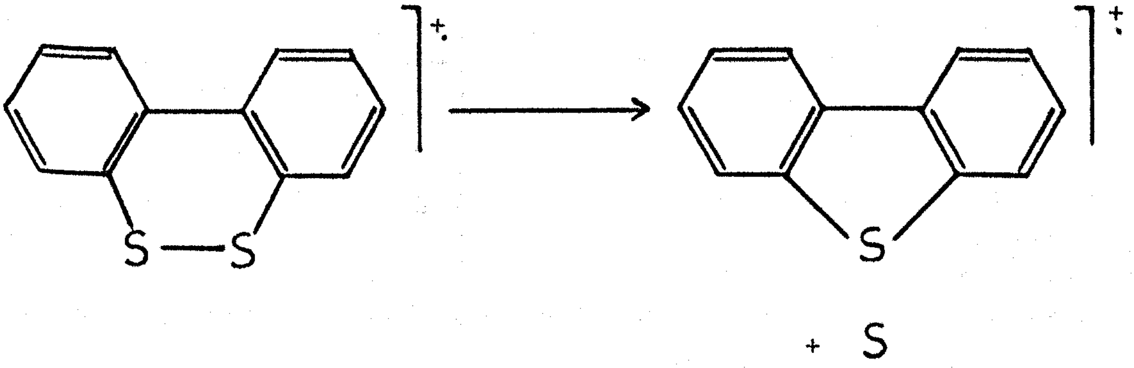


($Y = \underline{m}\cdot CH_2\cdot C_6H_4\cdot CH_2\cdot$)

(XVI)

The process involves fission of a methylene carbon-sulphur bond, the biphenyl rings rotating to enable a new sulphur-sulphur bond to be formed. The neutral disulphide (XVI) is eliminated together with the hydrocarbon fragment, which presumably rearranges into the o- or p-xylylene ion form.

When the bridge consists of two or four atoms of sulphur only, the spectra are again quite characteristic. (See Figures 8 and 9). For example the cyclic disulphide (XVI), has a very stable molecular ion (which is the base peak), which breaks down to the slightly less abundant dibenzothiophen ion by loss of a sulphur atom:



The stability of the cyclic disulphide ion is perhaps not too unexpected since the molecule is almost flat, and the charge can be readily delocalised over the molecule.

The cyclic tetrasulphide (XXII) is not flat and the molecular ion readily fragments to the lower cyclic sulphides. The molecular ion loses two sulphur atoms to form the cyclic disulphide ion which then eliminates a further sulphur atom to give the dibenzothiophen ion, which is also the base peak in the spectrum. A strong metastable peak at $\frac{m}{e}$ 156 indicates that fragmentation of the $\frac{m}{e}$ 216 disulphide ion to hydrocarbon fragment, which presumably rearranges into the _o_- or _p_-xylylene ion form.

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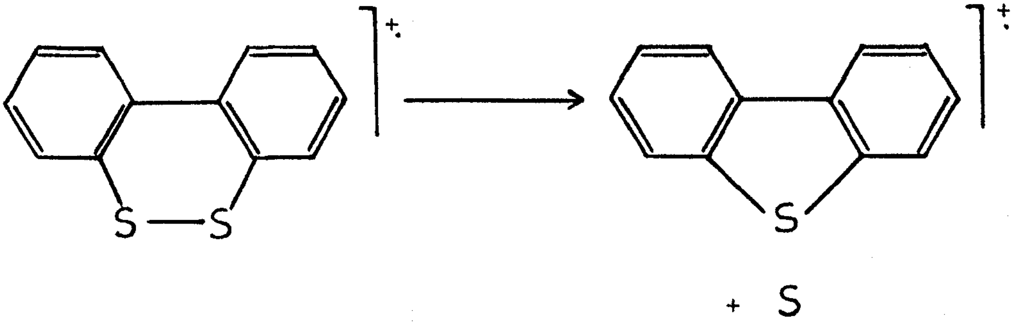

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Fig 9

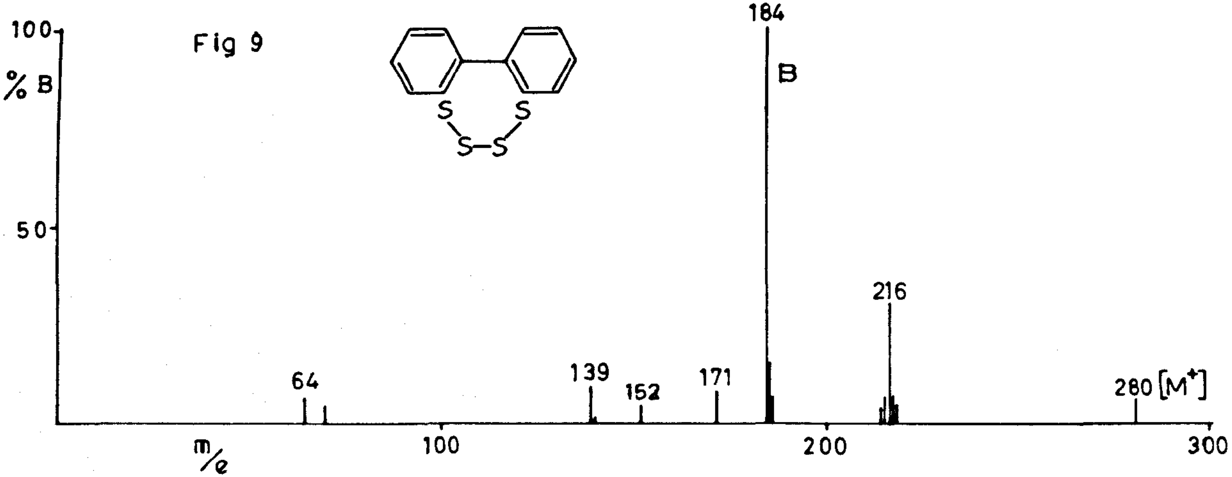
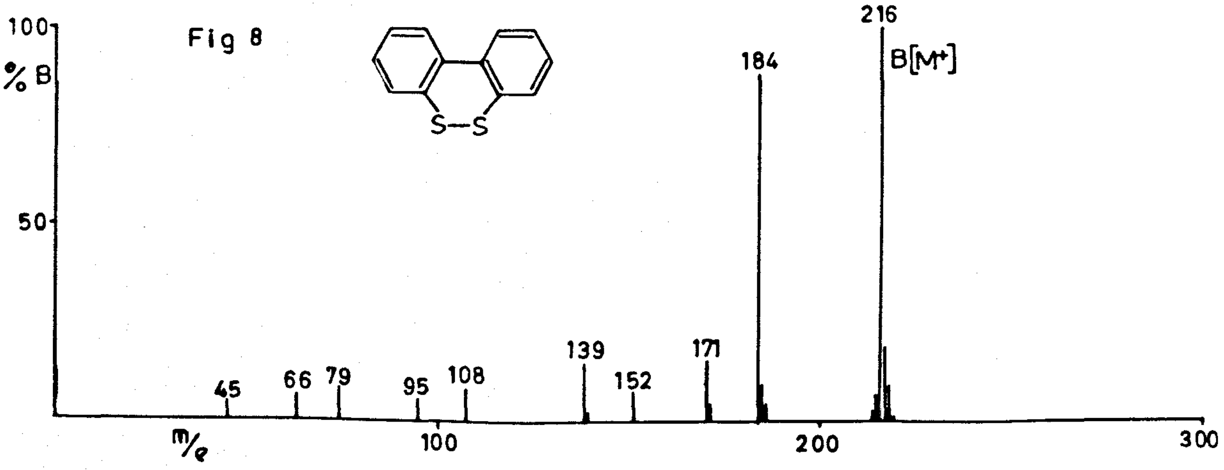
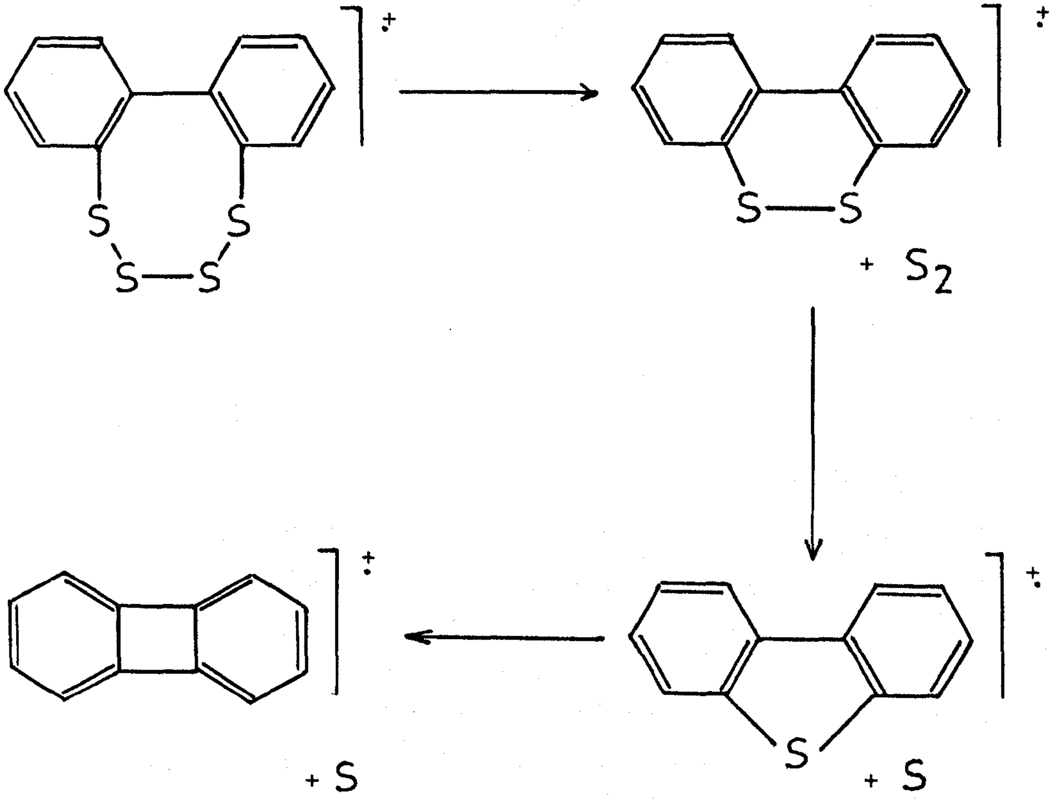

100
% B
50
184
B
216
64
139
152
171
280 [M⁺]
m/e
100
200
300
S
S
S
S

Fig 8

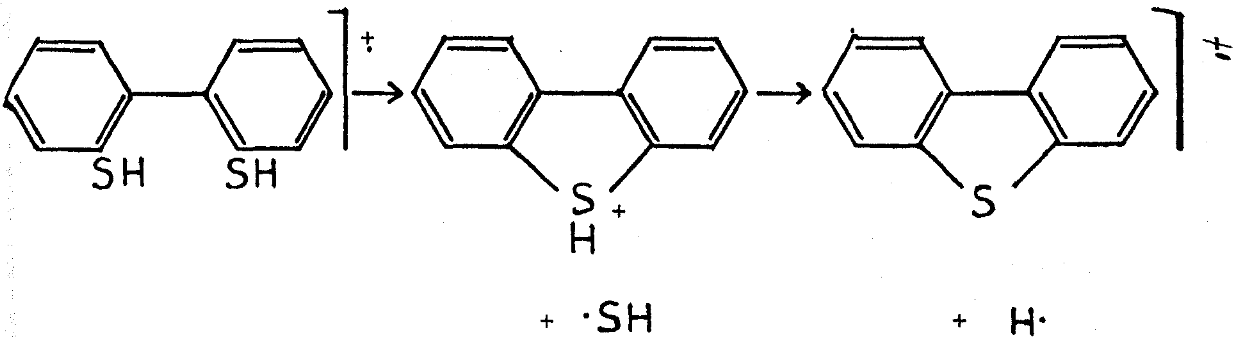

100
% B
50
216
B[M⁺]
184
45
66
79
95
108
139
152
171
m/e
100
200
300
S
S

the dibenzothiophen ion is occurring. Thus, one fragmentation path would appear to be a stepwise degradation process in which two, three and four atoms of sulphur are successively eliminated. The low abundance of the cyclic trisulphide ion is indicative of its instability, in accord with failure in the attempted preparation of the neutral molecule (see page 26). The cyclic tetrasulphide may fragment as follows:



The last class of compounds to be discussed are the "acyclic" 2,2'-biphenyl derivatives. These molecules all fragment in a similar fashion by processes presumably similar to those described earlier.

The dithiol (XVII) fragments to an ion at $\frac{m}{e}$ 185, which is of equal intensity to that of the dibenzothiophen ion at $\frac{m}{e}$ 184. (See Figure 10) These two ions are joint base peaks, and the metastable ion at $\frac{m}{e}$ 157 is expected for the formation of the ion of mass 185 directly from the molecular ion. Such a fragmentation is envisaged to occur by the following path:



the sulphonium ion losing a hydrogen atom to give the dibenzothiophen ion.

The methyl and ethyl derivatives of the dithiol (XVII) fragment in a very similar way (See Figures 11 and 12): in each case the alkyl sulphonium derivative of the dibenzothiophen ion is formed. These sulphonium ion derivatives of dibenzothiophen would be expected to be very stable because the positive charge can be delocalised by bonding between the carbon $2p_z$ and sulphur 3d orbitals, an example of the expansion of the octet of sulphur.

The fragmentation patten of 2,2'-biphenylylenebismethylsulphide

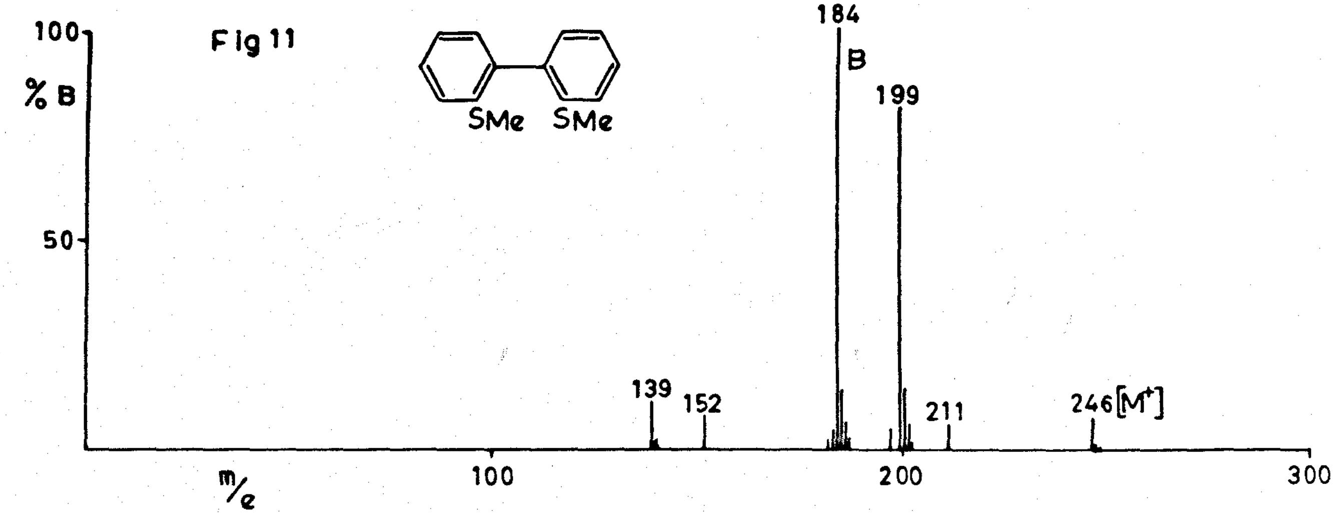


Fig 11

100
% B
50
SMe
SMe
184
B
199
139
152
211
246[M+]
m/e
100
200
300

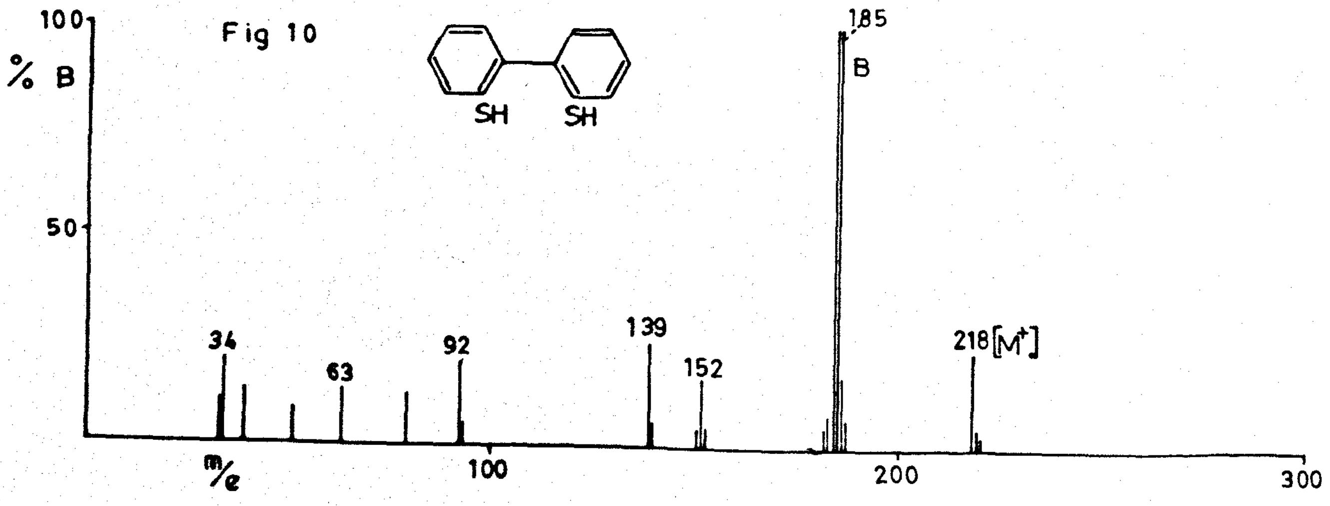


Fig 10

100
% B
50
SH
SH
185
B
34
63
92
139
152
218[M+]
m/e
100
200
300

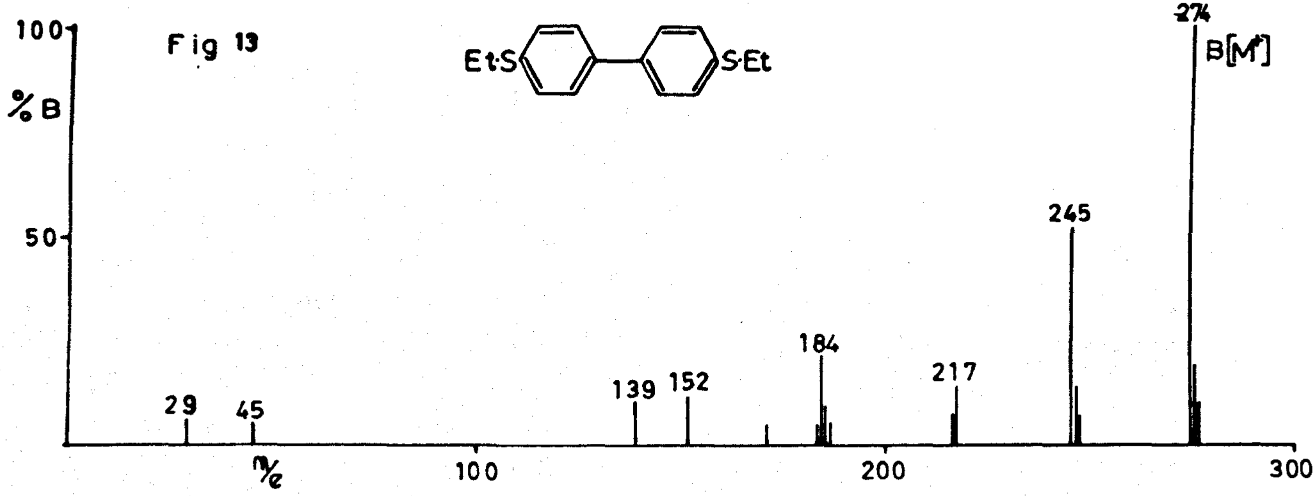


Fig 13
100
%B
50
EtS
SEt
274
B[M⁺]
245
184
217
139
152
29
45
m/e
100
200
300

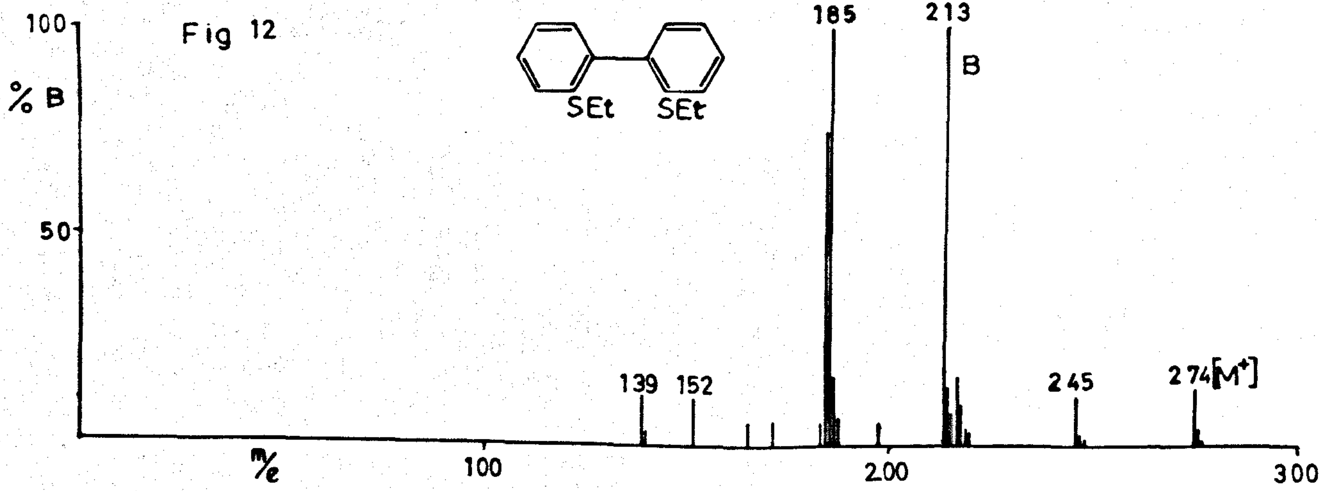
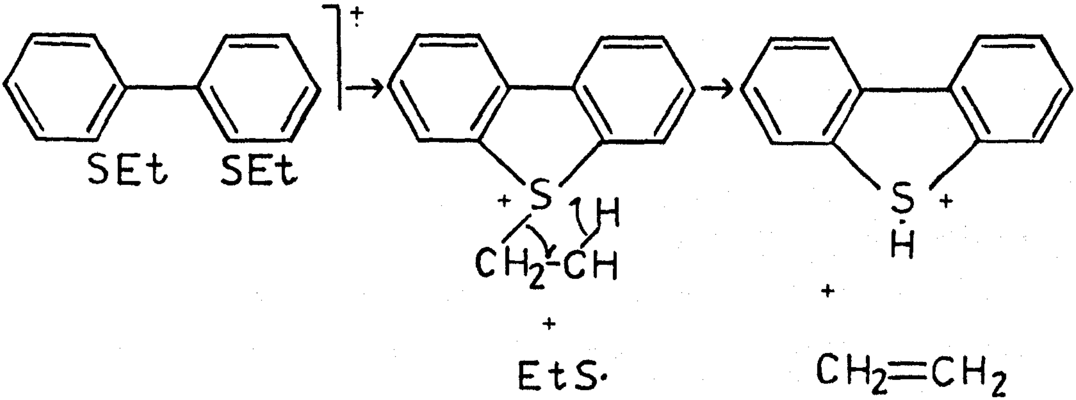


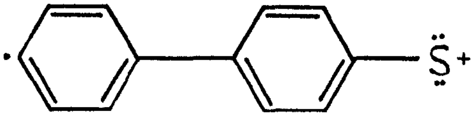
Fig 12
100
%B
50
SEt
SEt
185
213
B
139
152
245
274[M⁺]
m/e
100
200
300

(see Figure 11) is very similar to that of the dithiol (XVII); in this case a methylated dibenzothiophen ion is produced in place of the protonated species. Metastable ions indicate that one pathway involves a two-step process as shown for the dithiol (XVII). By contrast, 2,2'-biphenylylenebisethylsulphide fragments by a modification of the process described. The ethyl sulphonium ion of dibenzothiophen is formed in the usual manner but eliminates ethylene to give the protonated dibenzothiophen as the base peak of the spectrum:



The protonated dibenzothiophen presumably eliminates a hydrogen atom to give the dibenzothiophen ion as before.

By contrast with its 2,2'-isomer, 4,4'-biphenylylenebisethylsulphide (XXIV) fragments in an entirely different way. (See Figure 13). The molecular ion is the base peak in the spectrum, probably because the molecule cannot easily rearrange to give a stable heterocyclic ion as is the case for the 2,2'-biphenyl dithia compounds. The second most abundant ion represents loss of an ethyl radical from the molecular ion. A peak at $\frac{m}{e}$ 184 may be that of the dibenzothiophen ion caused by rearrangement during the fragmentation process, or the simple ion:

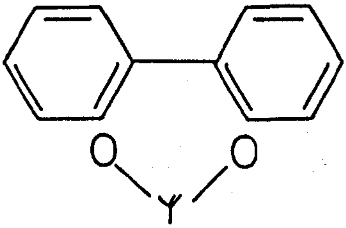


However if the ion of mass 152 is the biphenylene ion, its abundance relative to that of the ion of mass 184 suggests it is formed by a route other than that from dibenzothiophen. In any event it appears clear that the fragmentation path of the 4,4'-biphenyl disulphide (XXIV) is completely different from that of the 2,2'-substituted dithia biphenyls.

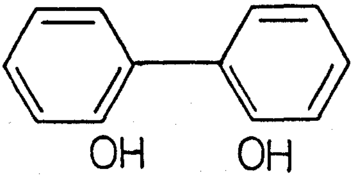
In conclusion we can say that wherever possible the 2,2'-biphenyl dithia compounds rearrange on ionisation to give the stable dibenzothiophen or dibenzothiophensulphonium ions, in which extensive delocalisation of the charge can occur.

The 2,2'-bridged biphenyls so far described contain the bulky sulphone and smaller sulphide groups and it was thought that the synthesis of the ether analogues would be of interest. As the oxygen atom is much smaller than sulphur, this would give three series of 2,2'-bridged biphenyls with a graded steric effect between the series.

The 2,2'-bridged dioxa biphenyl system of structure type (XXV) was first synthesised by Bibergeil and Diels in 1902.[23] Thus on heating 2,2'-biphenol (XXVI), potassium hydroxide, water and ethylene dibromide in a sealed flask at 150°C for sixteen hours, the eight-membered ring system (XXV; $Y=(CH_2)_2$) was isolated in unspecified yield. Methylene di-iodide and trimethylene dibromide in the same reaction gave polymeric solids.



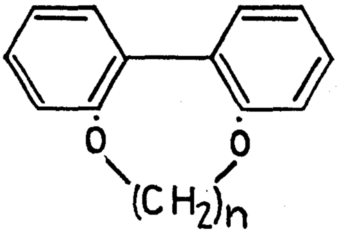
(XXV)

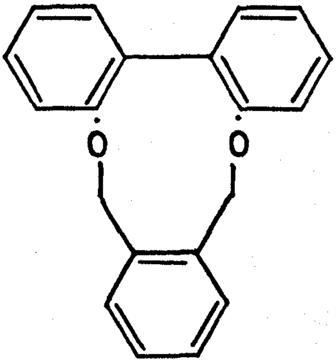


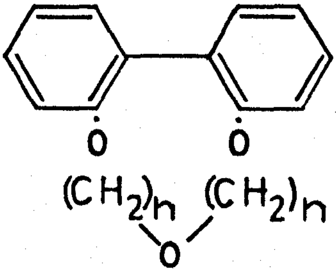
(XXVI)

In 1965 Hewgill and Hewitt synthesised the smallest bridged diethers by acid-catalysed condensation of 2,2'-biphenol (XXVI) with various ketones.[24] Thus with acetone the dioxapin (XXV; $Y=CMe_2$) was obtained in 30% yield.

The main problem in synthesising these ether heterocycles is the low reactivity of disodium 2,2'-biphenate, even under reflux conditions. Thus, use of a similar procedure to that for the synthesis of the sulphur heterocycles fails. We have however solved this problem by utilising aqueous dimethyl sulphoxide as solvent. Thus 2,2'-biphenol (XXVI), sodium hydroxide and the appropriate reactive alkylene- or ether α,ω-dihalide or xylylene dibromide, were heated in aqueous dimethyl sulphoxide for twenty-four hours. We have found that a range of heterocycles can be obtained in good yield by this method. Treatment of the disodium salt of 2,2'-biphenol (XXVI) with methylene iodide, dimethylene-, trimethylene-, tetramethylene- and pentamethylene dibromide gave the novel heterocycles (XXVII; n=1—5). o-Xylylene dibromide in this reaction gave the ten-membered ring system (XXVIII), but only polymer was formed when m-xylylene dibromide was used. Finally di(chloromethyl) and di(β-chloroethyl) ether in this reaction yielded the heterocycles (XXIX; n=1 and 2).


(XXVII)


(XXVIII)


(XXIX)

Yields of heterocycles are not strictly comparable since a number of these reactions were carried out under various conditions in order to improve the yields. The conditions used to prepare the trimethylene bridged heterocycle (XXVII; n=3) gave good results, though more dilute solutions and a slower addition of the trimethylene dibromide might give even better yields.

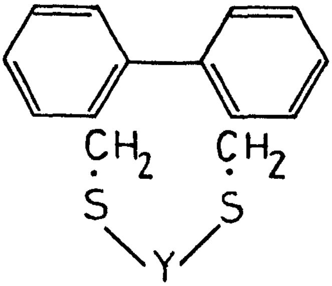
The oxygen heterocycles were synthesised mainly in order to examine their ultraviolet spectra (see Part II of this thesis); however, the n.m.r. spectra and mass spectra of the compounds also show some interesting features.

On examination of the n.m.r. spectrum of the methylene bridged compound (XXVII; n=1) the aromatic protons appear as two separate multiplets centred at 2.4τ and 2.85τ and integrating for two and six protons respectively. A similar observation has been made earlier with regard to the sulphur analogues, and the phenomena could similarly be attributed to the deshielding of the 6,6' protons. Interestingly, the partial separation of the aromatic multiplets observed in the 2,2'-bridged dithia biphenyls does not occur to the same extent in the corresponding ethers.

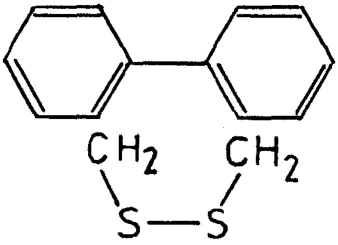
The mass spectra of the bridged and unbridged diethers have been recorded, to determine their molecular weights. Although the spectra has not been examined in detail, some preliminary comments are appropriate.

From the spectra of the ethers it is clear that cyclisation reactions to form the $\frac{m}{e}$ 168 dibenzofuran ion occur only to a limited extent. The molecular ion is the base peak in the spectrum of the 2,2'-biphenyl diethers, which is surprising when one considers the apparent ease with which the sulphur analogues fragment to the dibenzothiophen ion. The spectra of the diethers are much more complex than those of the sulphur compounds and interpretation is more difficult.

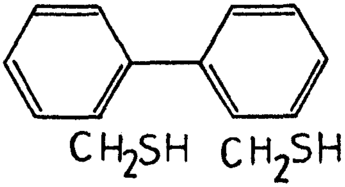
Finally a number of sulphur heterocycles of the general formulae type (XXX) have been synthesised mainly to study their optical (i.e. conformational) stability and to compare the optical stability of isomeric sulphur compounds.



(XXX)



(XXXI)



(XXXIII)

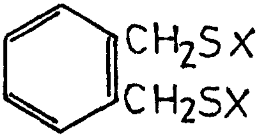
One member of this series, the eight-membered cyclic disulphide (XXXI) was synthesised by Hess, Luttringhaus and Rosenbaum in 1967.[25] Thus 2,2'-bis-(bromomethyl)-biphenyl (XXXII) on treatment with potassium thioacetate gave the di(thioacetomethyl) derivative, which on oxidation with ferric chloride in ether and acetic acid gave the cyclic disulphide (XXXI) in 50% yield. The same workers obtained the dithiol (XXXIII), by hydrolysis of 2,2'-di-(thioacetomethyl)-biphenyl with methanolic sodium methoxide in a yield of ca.50%.[25]

We have achieved a very simple synthesis of both the cyclic disulphide (XXXI) and the dithiol (XXXIII) (the former compound being necessary for the optical resolution work as described in Part III of this thesis). The disulphide (XXXI) may be obtained in 50% yield by treatment of the dibromide (XXXII) with sodium disulphide ("Na_2S_2") in aqueous methanol. This simple one-stage procedure gave a good yield of the required product. The dithiol (XXXIII) was obtained as a pale yellow oil by use of the general procedure described for the synthesis of *o*-xylylene dithiol (V) (see page 14), the yield being almost theoretical.

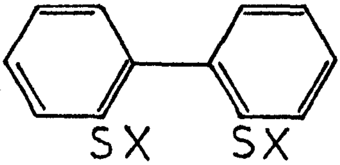
We have found the dithiol (XXXIII) condenses with acetone in the presence of hydrochloric acid, to give the nine-membered cyclic mercaptol (XXX; $Y=CMe_2$). When the disodium salt of the dithiol (XXXIII) is treated with methylene iodide in alcohol another nine-membered ring (XXX; $Y=CH_2$) is produced in good yield. Finally *m*-xylylene dibromide in the same reaction gave the thirteen-membered metacyclophane (XXX; $Y=$*m* $CH_2 \cdot C_6H_4 \cdot CH_2$) in good yield.

These heterocycles have been examined with regard to their optical stability and will be discussed in this context in Part III of this thesis. It would be of interest to synthesise the larger heterocyclic systems in this series and also their ether analogues, having different sequences within the bridge, and compare them with the isomeric compounds which are described in this thesis.

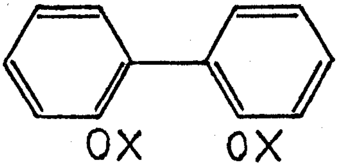
In addition to the heterocyclic systems a number of compounds were prepared in which the hetero-atom is not part of a ring, in order to compare them with the cyclic compounds. The compounds are of four formula types; (XXXIV), (XXXV), (XXXVI) and (XXXVII) where X represents an alkyl or benzyl group. In general these compounds were synthesised in a similar manner to the related heterocycles, except dilution problems associated with intra- and inter-molecular cyclisation do not arise.



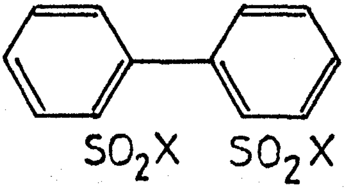
(XXXIV)



(XXXV)



(XXXVI)



(XXXVII)

EXPERIMENTAL

Compounds are colourless unless otherwise stated.

All melting points were measured on a Kofler hot stage apparatus.

Infrared absorption spectra were obtained using a Perkin-Elmer 257 grating spectrophotometer.

Nuclear magnetic resonance (n.m.r.) spectra were recorded on a Perkin-Elmer 60 megacycle instrument.

Mass spectra were recorded on a Perkin-Elmer/Hitachi R.M.U.-6 spectrometer.

Molecular weights were determined by mass spectrometry, or with a Mechrolab 301A vapour pressure osmometer.

Microanalyses were carried out by Mr. J. Boulton or Mrs. L. Thomas in the Department of Chemistry, University of Keele.

All heterocycles have been named on the "cyclophane" nomenclature devised and recommended by Smith.[26]

All operations involving alkaline solutions of dithiols were performed under nitrogen.

o-Xylylene dibromide

This was prepared by bromination of o-xylene, in 50% yield, as described by Stephenson.[27]

Trimethylene dithiol

Trimethylene dithiol was prepared by the S-alkyl isothiouronium salt method in 50% yield, by the method due to Hall and Reid.[28]

o-Xylylene dithiol (V) was prepared by modification of a method by Fletcher and Pan.[15]

o-Xylylene dibromide (13.2g) and thiourea (8.4g) were stirred overnight in dimethyl sulphoxide (150g) at room temperature. The S-alkyl isothiouronium salt solution was hydrolysed by stirring it for half an hour with aqueous 10% sodium hydroxide (600 ml). Ice and concentrated hydrochloric acid were then added to the solution at such a rate as to keep the solution at room temperature, until it became acidic. The milky solution was shaken with ether (3 x 300 ml), and the combined ether layers then thoroughly washed with water. After drying (with Na_2SO_4), the ether was removed to give a colourless oil, which on cooling gave crystalline o-xylylene dithiol, m.p. 45°, (Lit.[14] m.p. 44-46°), (8.2g., 96%).

Tetrathia macrocycles with o-xylylene bridges

(a) (2,4,13,15)-Tetrathia[5.5]orthocyclophane (X; n=1)

Methylene iodide (17.4g) was added to a stirred solution prepared from sodium (3.0g) in ethanol (500 ml) and the dithiol (V) (11.0g). The solution was stirred for one hour, refluxed for a further two hours, and the hot solution filtered to remove polymer.

On cooling the solution a white solid was obtained, which crystallised from ethanol to give an impure crystalline product. The mixture was chromatographed on preparative T.L.C. plates using a 1:1 benzene/60° - 80° light petroleum eluent, to give two bands on the plate. The higher band was scraped off and extracted with ethanol to yield the (known) (2,4)-dithia[5]orthocyclophane (VII) (needles from ethanol), m.p. 157-159°, (Lit.[11] m.p. 152-153°) (15%).

n.m.r. ($CDCl_3$): 2.6τ(singlet, 4 aromatic protons); 5.9τ(singlet, 4 methylene protons); 6.0τ(singlet, 2 methylene protons).

Extraction of the lower band yielded the macrocyclic dimeric compound (2,4,13,15)-tetrathia[5.5]orthocyclophane (needles from ethanol), m.p. 198-200°, (3%), (Found: C, 59.0; H, 5.5. $C_{18}H_{20}S_4$ requires C, 59.3; H, 5.5%), (m.wt. $\frac{m}{e}$ = 364 (364)).

n.m.r. ($CDCl_3$): 2.5τ (A_2B_2 multiplet, 8 aromatic protons); 5.75τ(singlet, 8 methylene protons); 5.95τ(singlet, 4 methylene protons).

(b) (2,5,14,17)-Tetrathia[6.6]orthocyclophane (X; n=2)

Finely powdered *o*-xylylene dibromide (13.2g) was added to a stirred solution prepared from sodium (2.3g) in ethanol (300 ml) and dimethylene dithiol (4.7g) over a period of ten minutes.. The reaction mixture was refluxed for one hour, and then filtered. The filtrate, on cooling, yielded a pale precipitate, which crystallised from benzene in fine needles to give the macrocycle

(2,5,14,17)-tetrathia[6.6]orthocyclophane, m.p. 142-144°, (5%), (Found: C, 60.9; H, 6.2. $C_{20}H_{24}S_4$ requires C, 61.2; H, 6.2%), (m.wt. $\frac{m}{e}$ = 392 (392)).

n.m.r. ($CDCl_3$): 2.55τ (A_2B_2 multiplet, 8 aromatic protons); 6.0τ (singlet, 8 methylene protons); 7.1τ (singlet, 8 methylene protons).

On adding water to the residual filtrate a mass of crystals of the known (2,5)-dithia[6]orthocyclophane (VIII) were deposited, m.p. 94-96°, (Lit.,[12] m.p. 93°) (40%).

n.m.r. ($CDCl_3$): 2.6τ (singlet, 4 aromatic protons); 6.1τ (singlet, 4 methylene protons); 7.1τ (singlet, 4 methylene protons).

(c) (2,6,15,19)-Tetrathia[7.7]orthocyclophane (X; n=3)

Powdered o-xylylene dibromide (13.2g) was added to a stirred solution prepared from sodium (2.3g) in ethanol (500 ml) and trimethylene dithiol (5.4g). After the addition of the dibromide, the solution was refluxed for two hours, and the clear solution decanted. The alcoholic solution was diluted with 2-3 volumes of water to yield a solid, which crystallised from 95% ethanol in needles to give the (2,6)-dithia[7]orthocyclophane (IX), m.p. 85° (40%), (Found: C, 63.1; H, 6.65. $C_{11}H_{14}S_2$ requires C, 62.85; H, 6.71%), (m.wt. $\frac{m}{e}$ = 210 (210))

n.m.r. ($CDCl_3$): 2.55τ (singlet, 4 aromatic protons); 6.15τ (singlet, 4 methylene protons); 7.35τ (triplet, 4 methylene protons); 8.1τ (multiplet, 2 methylene protons).

The residual polymer was extracted with hot benzene, which on cooling yielded crystals of *(2,6,15,19)-tetrathia[7.7]orthocyclophane*, m.p. 208-210°, (5%), (Found: C, 62.9; H, 6.8. $C_{22}H_{28}S_4$ requires C, 62.85; H, 6.71%), (m.wt. $\frac{m}{e}$ = 420 (420))

n.m.r. ($CDCl_3$): 2.55τ(A_2B_2 multiplet, 8 aromatic protons); 6.05τ(singlet, 8 methylene protons); 7.3τ(triplet, 8 methylene protons); 8.0τ(quintuplet, 4 methylene protons)

(d) (4,5:18,19)-Dibenzo-(2,7,16,21)-tetrathia[8.8]paracyclophane (XI)

A solution of *p*-xylylene dibromide (8.6g) in boiling ethanol (200 ml) was quickly added to a stirred solution prepared from sodium (1.5g) in ethanol (250 ml) and *o*-xylylene dithiol (V) (5.2g). After leaving overnight, the alcohol was decanted and the residue extracted with hot benzene. After many recrystallisations from benzene, *(4,5:18,19)-dibenzo-(2,7,16,21)-tetrathia[8.8]paracyclophane* was obtained in large rhombs m.p. 183-184°, (10%), (Found: C, 70.7; H, 5.85. $C_{32}H_{32}S_4$ requires C, 70.6; H, 5.9), (m.wt. $\frac{m}{e}$ = 544 (544)).

n.m.r. ($CDCl_3$): 2.62τ(singlet, 8 aromatic protons); 2.67τ(singlet, 8 aromatic protons); 6.4τ(two singlets, 16 methylene protons).

(e) (2,11)-Dithia[3.3]orthocyclophane (VI)

This compound was prepared according to the method due to Autenrieth and Bruning [10] in 50% yield.

n.m.r. ($CDCl_3$): 2.3 and 2.6τ(A_2B_2 multiplets, 8 aromatic protons); 6.55τ(singlet, 8 methylene protons).

The synthesis of alkyl and benzyl derivatives of o-xylylene dithiol (V)

(a) o-Xylylenebisbenzylsulphide (XXXIV; X = $PhCH_2$)

A solution prepared from sodium (0.46g) in ethanol (50 ml) and benzyl thiol (2.5g) and o-xylylene dibromide (2.64g) was stirred for two hours. On adding an equal volume of water, a solid was precipitated, which crystallised from aqueous ethanol to give the known o-xylylenebisbenzylsulphide,[11] m.p. 48-50°, (Lit.,[11] isolated as an oil) (3.4g., 95%).

(b) o-Xylylenebismethylsulphide (XXXIV; X = Me)

A solution of o-xylylene dithiol (V) (4.0g), methyl iodide (5.9g) and potassium hydroxide (2.6g) in ethanol (100 ml) was stirred for one hour. The solution was diluted with two volumes of water, and extracted with ether to give an oil. Distillation of the oil gave pure o-xylylenebismethylsulphide, b.p. 114° 1.0mm Hg, (3.0g., 65%), (Found: C, 60.6; H, 7.0. $C_{10}H_{14}S_2$ requires C, 60.6; H, 7.1 %)

n.m.r. ($CDCl_3$): 2.7τ (singlet, 4 aromatic protons); 6.1τ (singlet, 4 methylene protons); 8.1τ (singlet, 6 methyl protons).

(c) o-Xylylenebisethylsulphide (XXXIV; X=Et)

This compound was prepared in the same way as the methyl compound. The product, a colourless oil, was obtained in a 60% yield; its properties were in accord with the literature.[29]

Biphenyl 2,2'-dithiol (XVII)

This was prepared by modification of Barber and Smiles'[18] procedure, as follows:

(a) Sodium o-iodobenzene sulphonate

A solution of orthanilic acid (73g), sodium hydroxide (16.8g) and sodium nitrite (28g) in water (600 ml) at 0° was added dropwise to a stirred solution of conc. sulphuric acid (75 ml) in water (200 ml) at 0°, during ten minutes. After stirring for a further ten minutes, potassium iodide (94g) in water (200 ml) was added to the stirred diazonium salt suspension. The diazonium complex was gradually heated on a steam bath until most of the nitrogen was evolved. Evaporation of the solution to ca 500 ml (sulphurous acid being added as necessary during the evaporation to destroy the liberated iodine), deposited the crystalline product on cooling. The crude product was filtered off, and the acid removed by washing with saturated brine solution. Yield of damp product, 130-140g.

(b) Disodium 2,2'-biphenyl disulphonate

A solution of sodium *o*-iodobenzene sulphonate (350g) and saturated copper sulphate solution (10 ml) in boiling water (2l) was vigorously stirred under reflux with activated copper-bronze[20] (300g) for twenty-four hours. The hot aqueous solution was separated from excess copper-bronze, etc., by filtration, and evaporated to give the crude grey product in a yield of ca. 150g (dried at 150°).

(c) 2,2'-Biphenylylenebis-sulphonylchloride

Phosphorus pentachloride (300 g) and dry disodium 2,2'-biphenyl disulphonate (180g) were intimately mixed, the mixture rapidly becoming warm and mobile. The reactants were heated under reflux at 150° for one hour, the product then being cooled to 0°. The product was stirred with ice (1 kg) until all the phosphorus pentachloride was hydrolysed. The dense sludge-like product was filtered off, and the filter cake well washed with water, to yield 100gms of crude 2,2'-biphenylylenebis-sulphonylchloride. A liquid bye-product (80gms) was shown to be benzenesulphonylchloride.

(d) Biphenyl 2,2'-dithiol (XVII)

Conc. hydrochloric acid (200 ml) was added in small portions to a stirred suspension of crude 2,2'-biphenylylenebis-sulphonylchloride (100g), zinc dust (150g) and 95% ethanol (200 ml), the temperature being kept below 20°. When the acid had been added, the solution was carefully warmed to boiling, and more acid and ethanol were added at intervals until all the zinc had dissolved. The hot solution was quickly filtered and diluted with water to give on cooling copious needles of almost pure biphenyl 2,2'-dithiol (50gms). Overall yield was ca 40%.

Reactions of biphenyl 2,2'-dithiol with reactive alkylene α,ω-dihalides to give dithia heterocycles

(a) (1,3)-Dithia[3.0]orthocyclophane (XVIII; n=1)

A solution of methylene iodide (13.4g) in methylated spirit (200 ml) was added dropwise over a period of half an hour to a stirred solution from sodium (2.3g) in methylated spirit (1 l) and the dithiol (11g). The solution was stirred for two hours, then refluxed for fifteen minutes, and the hot solution filtered. The alcoholic solution was evaporated to 400 mls, and diluted with 2-3 volumes of water to give a pale yellow solid. The solid was dissolved in the minimum of benzene and eluted down a column containing 200 gms of "Woelm" neutral alumina (activity 1) with 1:1 60-80° light petroleum/benzene. Evaporation of the first fractions of product yielded colourless crystals of <u>(1,3)-dithia[3.0]orthocyclophane</u> which were recrystallised from 95% ethanol as prisms, m.p. 95-96°, (4.5g., 39%), ($\frac{m}{e}$ = 230; by osmosis in dioxan = 227, (230)), (Found: C, 67.7; H, 4.3. $C_{13}H_{10}S_2$ requires C, 67.8; H, 4.4%).

n.m.r. ($CDCl_3$): 2.4τ (multiplet, 2 aromatic protons); 2.65τ (multiplet, 6 aromatic protons); 5.8τ (singlet, 2 methylene protons).

A sample (300mg) was dissolved in hot glacial acetic acid (5 ml) and treated with "100 volume" hydrogen peroxide (5 ml). On standing for twenty-four hours crystals formed, which were recrystallised from aqueous acetic acid as prisms of <u>(1,3)-dithia[3.0]orthocyclophane tetra-oxide (XXIII; Y=CH_2)</u>, m.p. 254-255°, (Found: C, 53.5; H, 3.3. $C_{13}H_{10}S_2O_4$ requires C, 53.1; H, 3.4%).

i.r. (mull), 1325 and 1150 cm^{-1} ($S(=O)_2$).

2.5τ(multiplet, 6 aromatic protons); 6.4τ(A_2B_2, multiplet, 4 methylene protons).

(c) (1,5)-Dithia[5.0]orthocyclophane (XVIII; n=3)

A solution of trimethylene dibromide (4.6g) in methylated spirit (500 ml) was added overnight to a well-stirred solution from sodium (1.05g) in methylated spirit (1 l) and the dithiol (XVII) (5.0g). The resulting solution was evaporated down to ca 250 mls, and diluted with water to yield a yellow solid. On passing the product through an alumina column to remove the polymer (see preparation (a)) colourless crystals of (1,5)-dithia[5.0]orthocyclophane were isolated. Recrystallisation from 95% ethanol gave needles, m.p. 69-70°, (2.3g., 36%), ($\frac{m}{e}$ = 258 (258)), (Found: C, 69.5; H, 5.3. $C_{15}H_{14}S_2$ requires C, 69.8; H, 5.5%).

n.m.r. ($CDCl_3$): $2.3\text{-}2.9\tau$(multiplet, 8 aromatic protons); 7.3τ(triplet, 4 methylene protons); 7.9τ(multiplet, 2 methylene protons).

On oxidation of a sample (0.3g), (1,5)-dithia[5.0]orthocyclophane tetra-oxide (XXIII; $Y=(CH_2)_3$) was formed, (prisms from acetic acid), m.p. 256-258°, (Found: C, 56.0; H, 4.2. $C_{15}H_{14}S_2O_4$ requires C, 55.9; H, 4.4%), i.r. (mull), 1305 and 1120 cm^{-1} ($S(=O)_2$).

(d) (1,6)-Dithia[6.0]orthocyclophane (XVIII; n=4)

A solution of tetramethylene dibromide (7.2g) in methylated spirit (500 ml) was added overnight to a stirred solution from sodium (1.54g) in methylated spirit (1 l) and the dithiol (XVII) (7.4g). The evaporated solution was diluted with 2-3 volumes of water to give a white solid, which crystallised as needles (from 95% ethanol) of (1,6)-dithia[6.0]orthocyclophane, m.p. 143-144°, (6.0g., 66%), ($\frac{m}{e}$ = 272 (272)), (Found: C, 70.4; H, 5.8. $C_{16}H_{16}S_2$ requires C, 70.6; H, 5.9%).

n.m.r. ($CDCl_3$): 2.35τ(multiplet, 2 aromatic protons); 2.7τ(multiplet, 6 aromatic protons); 7.8τ(multiplet, 4 methylene protons); 8.6τ(multiplet, 4 methylene protons).

A sample (0.3g), was oxidised to the (1,6)-dithia[6.0]orthocyclophane tetra-oxide (XXIII; Y=$(CH_2)_4$), prisms from acetic acid, m.p. > 300°, (Found: C, 57.3; H, 4.7. $C_{16}H_{16}S_2O_4$ requires C, 57.1; H, 4.8%), i.r. (mull), 1305 and 1130 cm^{-1} ($S(=O)_2$).

(e) (1,7)-Dithia[7.0]orthocyclophane (XVIII; n=5)

A solution of pentamethylene dibromide (6.9g) in methylated spirit (500 ml) was added over four hours to a solution from sodium (1.4g) in methylated spirit (1 l) and the dithiol (XVII) (6.5g). The solution, after stirring overnight, was evaporated and diluted with water to give a crystalline product. The product was purified by percolating through an alumina column in the manner of preparation (a), and gave fine needles from 95% ethanol of (1,7)-dithia[7.0]orthocyclophane, m.p. 121-122°, (7.0g., 81%), ($\frac{m}{e}$ = 286 (286)), (Found: C, 71.6; H, 6.4. $C_{17}H_{18}S_2$ requires C, 71.3; H, 6.34%).

n.m.r. ($CDCl_3$): 2.6τ(multiplet, 2 aromatic protons); 2.85τ(multiplet, 6 aromatic protons); 7.4τ(multiplet, 4 methylene protons); 8.6τ(multiplet, 6 methylene protons).

A sample (0.3g), was oxidised to the <u>(1,7)-dithia[7.0]orthocyclophane tetra-oxide (XXIII; Y=$(CH_2)_5$)</u>, needles from acetone, m.p. > 300°, (Found: C, 58.8; H, 5.1. $C_{17}H_{18}S_2O_4$ requires C, 58.3; H, 5.2%), i.r. (mull), 1300 and 1150 cm^{-1} ($S(=O)_2$).

<u>The reactions of biphenyl 2,2'-dithiol (XVII) with α,ω-ether dihalides to give dithia-oxa heterocycles</u>

(a) <u>(1,5)-Dithia-(3)-oxa[5.0]orthocyclophane (XIX; n=1)</u>

Bis(chloromethyl)ether (3.83g) in methylated spirit (500 ml) was added overnight to a stirred solution from sodium (1.53g) in methylated spirit (1 l) and the dithiol (XVII) (7.4g). The solution was evaporated, and diluted with water in the usual way to give a white solid, which crystallised from 95% ethanol to give <u>(1,5)-dithia-(3)-oxa[5.0]orthocyclophane</u>, m.p. 150-152°, (5.1g., 59%), ($\frac{m}{e}$ = 260 (260)), (Found: C, 64.5; H, 4.5. $C_{14}H_{12}S_2O$ requires C, 64.6; H, 4.65%)

n.m.r. ($CDCl_3$): 2.7τ(multiplet, 8 aromatic protons); 5.15τ(AB doublets, J_{AB} = 11.3 c/s, $\Delta\nu_{AB}$ = 15.6 c/s, 4 methylene protons).

Oxidation of a sample (0.3g) gave <u>(1,5)-dithia-(3)-oxa[5.0]orthocyclophane tetra-oxide (XXIII; Y=$CH_2 \cdot O \cdot CH_2$)</u>, needles from acetic acid, m.p. 250°, (Found: C, 52.1; H, 3.6. $C_{14}H_{12}S_2O_5$ requires C, 51.9; H, 3.7%), i.r. (mull), 1300 and 1150 cm^{-1} ($S(=O)_2$).

n.m.r. ($CDCl_3$): 1.9τ(multiplet, 2 aromatic protons); 2.5τ(multiplet, 6 aromatic protons); 5.35τ(AB doublets,

J_{AB} = 12.5 c/s, $\Delta\nu_{AB}$ = 18.8 c/s, 4 methylene protons).

(b) (1,7)-Dithia-(4)-oxa[7.0]orthocyclophane (XIX; n=2)

Bis-(β-bromoethyl)ether (7.7g), the dithiol (XVII) (7.3g) and sodium (1.53g) were heated in alcohol as in the previous preparation to give a white solid, which crystallised from 95% ethanol to give *(1,7)-dithia-(4)-oxa[7.0]orthocyclophane*, m.p. 129°, (6.4g., 67%), ($\frac{m}{e}$ = 288 (288)), (Found: C, 67.1; H, 5.6. $C_{16}H_{16}S_2O$ requires C, 66.7; H, 5.6%).

n.m.r. ($CDCl_3$): 2.6τ (multiplet, 8 aromatic protons); 6.5τ (multiplet, 4 methylene protons); 7.0τ (multiplet, 4 methylene protons).

A sample (0.3g) on oxidation gave the *(1,7)-dithia-(4)-oxa[7.0]orthocyclophane tetra-oxide (XXIII; Y = $(CH_2)_2\cdot O\cdot(CH_2)_2$)*, crystals from acetic acid, m.p. 250°, (Found: C, 54.8; H, 4.8. $C_{16}H_{16}S_2O_5$ requires C, 54.6; H, 4.6%), i.r. (mull) 1310 and 1120 cm^{-1} ($S(=O)_2$).

Reactions between 2,2'-biphenyl dithiol (XVII) and xylylene dibromides to give dithia heterocycles

(a) (1,10)-Dithia[2,2,0]orthocyclophane (XX)

o-Xylylene dibromide (8.8g), the dithiol (XVII) (7.3g) and sodium (1.53g) were heated in methylated spirit as previously to give a yellow solid, which crystallised from 95% ethanol to give *(1,10)-dithia[2.2.0]orthocyclophane*, m.p. 102-103°, (7.3g., 69%) ($\frac{m}{e}$ = 320, also 302 by osmometry, (320)), (Found: C, 75.3; H, 4.8.

$C_{20}H_{16}S_2$ requires C, 75.0; H, 5.0%).

n.m.r. ($CDCl_3$): 2.5τ (multiplet, 2 aromatic protons); 2.8τ (multiplet, 10 aromatic protons); 6.37τ (AB doublets, J_{AB} = 14.5 c/s, $\Delta\nu_{AB}$ = 9 c/s, 4 methylene protons).

Oxidation of a sample (0.3g) gave (1,10)-dithia[2.2.0] orthocyclophane tetra-oxide (XXIII; Y = o- $CH_2 \cdot C_6H_4 \cdot CH_2$), crystals from acetic acid, m.p. 285°, (Found: C, 62.4; H, 3.8. $C_{20}H_{16}S_2O_4$ requires C, 62.5; H, 4.2%), i.r. (mull), 1310 and 1130 cm^{-1} ($S(=O)_2$).

n.m.r. ($CDCl_3$): 1.95τ (multiplet, 2 aromatic protons); 2.5τ (multiplet, 10 aromatic protons); 5.7τ (AB doublets, J_{AB} = 15 c/s, $\Delta\nu_{AB}$ = 20 c/s, 4 methylene protons).

(b) (3,4:5,6)-Dibenzo-(2,7)-dithia[8]metacyclophane (XXI)

A solution of m-xylylene dibromide (8.8g) in warm methylated spirit was added overnight to a stirred solution from sodium (1.53g) in methylated spirit (1 l) and the dithiol (XVII) (7,3g). Water (1 l) was added to the solution, and the resulting yellow solid crystallised from boiling acetone as pure (3,4:5,6)-dibenzo-(2,7)-dithia[8]metacyclophane, m.p. 164-165°, (6.1g., 57%), ($\frac{m}{e}$ = 320, (320)), (Found: C, 75.3; H, 4.7. $C_{20}H_{16}S_2$ requires C, 75.0; H, 5.0%).

n.m.r. ($CDCl_3$): 2.3-3.4τ (multiplet, 12 aromatic protons); 6.15τ (AB doublets, J_{AB} = 14 c/s, $\Delta\nu_{AB}$ = 12.8 c/s, 4 methylene protons).

A sample (0.3g) on oxidation gave (3,4:5, 6)-dibenzo-(2,7)-dithia[8]metacyclophane tetra-oxide (XXIII; Y = m- $CH_2 \cdot C_6H_4 \cdot CH_2$), crystals from acetic acid, m.p. 304°, (Found: C, 62.6; H, 4.2. $C_{20}H_{16}S_2O_4$ requires C, 62.5; H, 4.2%), i.r. (mull), 1310 and 1150 cm^{-1} ($S(=O)_2$).

n.m.r. ($CDCl_3$); 1.9-3.0τ(multiplet, 12 aromatic protons); 5.6τ(singlet, 4 methylene protons).

(c) When p-xylylene dibromide was heated with the disodium salt of the dithiol (XVII) under the usual conditions, a white polymer was formed. It had low solubility in common solvents and melted over a wide temperature range. No crystalline product was isolated from the reaction.

The reaction between biphenyl 2,2'-dithiol (XVII) and the lower sulphur chlorides to give polysulphide heterocycles

(a) Reaction with sulphur dichloride (SCl_2)

Sulphur dichloride (1.03g) was added to a stirred solution of the dithiol (XVII) (2.18g) in dry benzene (500 ml). A solution of triethylamine (2.0g) in benzene (250 ml) was added to the solution over a period of one hour. The resulting emulsion was shaken with water, and the benzene solution was separated, dried and evaporated, to yield a yellow solid. The solid was extracted with boiling acetone to yield the known cyclic disulphide (XVI),[18] m.p. 110-112°, (Lit.,[18] m.p. 113°), (1.05g).

The residual solid from the acetone extraction was extracted with boiling chloroform to yield pale yellow rhombs of (1,2,3,4)-tetrathia[4.0]orthocyclophane (XXII), m.p. 200°, (1.0g) ($\frac{m}{e}$ = 280, (280)), (Found: C, 51.5; H, 3.1. $C_{12}H_8S_4$ requires C, 51.4: H, 2.9%).

n.m.r. ($CDCl_3$): 2.1τ(multiplet, 2 aromatic protons); 2.6τ(multiplet, 8 aromatic protons).

(b) Reaction with sulphur monochloride (S_2Cl_2)

The dithiol (XVII) (2.8g), sulphur monochloride (1.7g) and triethylamine (2.6g) were reacted together as in the first preparation. The benzene solution on evaporation yielded a yellow solid, which crystallised from chloroform as pale yellow rhombs of (1,2,3,4)-tetrathia[4.0]orthocyclophane (XXII), m.p. = 200°, (2.5g). In this reaction none of the cyclic disulphide (XVI) was isolated.

The synthesis of the dialkyl and dibenzyl derivatives of the dithiol (XVII)

(a) 2,2'-Biphenylylenebismethylsulphide (XXXV; X=Me)

Methyl iodide (2.82g) was added to a stirred solution of the dithiol (XVII) (2.18g) and sodium hydroxide (0.8g) in ethanol (20 ml). After standing for one hour, the solution was diluted with two volumes of water to yield a solid, which crystallised from 95% ethanol as the known 2,2'-biphenylylenebismethylsulphide m.p. 155-157°, (Lit.[30] m.p. 155°) (2.2g., 85%).

A sample (0.3g) was oxidised to the tetra-oxide 2,2'-biphenylylenebismethylsulphone (XXXVII; X = Me), m.p. 170-172°, (Found: C, 54.5; H, 4.5. $C_{14}H_{14}S_2O_4$ requires C, 54.2; H, 4.55%).

n.m.r. ($CDCl_3$): 1.9τ(multiplet, 2 aromatic protons); 2.5τ(multiplet, 6 aromatic protons); 7.07τ(singlet, 6 methyl protons).

(b) 2,2'-Biphenylylenebisethylsulphide (XXXV; X =Et)

Ethyl iodide (2.0g) was added to a stirred solution of the dithiol (XVII) (2.2g) and sodium hydroxide (0.8g) in ethanol (20 ml). The solution was refluxed for two hours, diluted with water and extracted with ether. On evaporation of the dried ether extracts a white solid was isolated, which crystallised from 95% ethanol to give needles of 2,2'-biphenylylenebisethylsulphide, m.p. 54-55°, (2.1g., 77%), (Found: C, 69.7; H, 6.4. $C_{16}H_{18}S_2$ requires C, 70.0; H, 6.6%).

n.m.r. ($CDCl_3$): 2.8τ(multiplet, 8 aromatic protons); 7.2τ(quartet, 4 methylene protons); 8.8τ(triplet, 6 methyl protons).

A sample (0.3g) was oxidised to the tetra-oxide, 2,2'-biphenylylenebisethylsulphone (XXXVII; X = Et), m.p. 175°, (Found: C, 56.6; H, 5.3. $C_{16}H_{18}S_2O_4$ requires C, 56.8; H, 5.4%).

n.m.r. ($CDCl_3$), 1.9τ(multiplet, 2 aromatic protons); 2.5τ(multiplet, 6 aromatic protons); 6.95τ(quartet, 4 methylene protons); 8.8τ(triplet, 6 methyl protons).

(c) 2,2'-Biphenylylenebisisopropylsulphide (XXXV; X = Pr^i)

A solution of isopropyl bromide (2.46g), the dithiol (XVII) (2.2g) and sodium hydroxide (0.8g) in ethanol (50 ml) were refluxed overnight. The solution was diluted with water, and ether-extracted to yield an oil, which was bulb distilled to give pure 2,2'-biphenylylenebisisopropylsulphide, (Found: C, 71.8; H, 7.3. $C_{18}H_{22}S_2$ requires C, 71.5; H, 7.3%).

n.m.r. ($CDCl_3$): 2.8τ(multiplet, 8 aromatic protons); 6.8τ(heptuplet, 2 aliphatic protons); 8.8τ(doublet, 6 methyl protons).

(d) 2,2'-Biphenylylenebisbenzylsulphide (XXXV; X = $PhCH_2$)

Benzyl chloride (2.5g) was added to a solution of the dithiol (XVII) (2.2g) and potassium hydroxide (1.1g) in ethanol (50 ml). After one hour, the solution was heated to boiling; water was then added and on cooling a crystalline solid was formed. The solid was recrystallised from 95% ethanol to give 2,2'-biphenylylenebisbenzylsulphide, m.p. 116°, (3.4g., 85%), (Found: C, 78.7; H, 5.4. $C_{26}H_{22}S_2$ requires C, 78.4; H, 5.6%).

n.m.r. ($CDCl_3$): 2.9τ(multiplet, 18 aromatic protons); 6.1τ(singlet, 4 methylene protons).

A sample (0.3g) was oxidised to the tetra-oxide, 2,2'-biphenylylenebisbenzylsulphone (XXXVII; X = $PhCH_2$), m.p. 233-235°, (Found: C, 68.0; H, 4.7. $C_{26}H_{22}S_2O_4$ requires C, 67.5; H, 4.8%).

n.m.r. ($CDCl_3$): 1.8-3.2τ(multiplet, 18 aromatic protons); 5.4τ(singlet, 4 methylene protons).

The synthesis of 4,4'-biphenylylenebisethylsulphide is described in Part II of this thesis.

The reaction between 2,2'-biphenol (XXVI) and alkylene α,ω-dihalides

(a) (1,3)-Dioxa[3.0]orthocyclophane (XXVII; n=1)

2,2'-Biphenol (9.3g)was dissolved in a solution of sodium hydroxide (4g) in water (100 ml) and added to dimethyl sulphoxide (200 ml). The solution was heated on a steam bath, and a solution of methylene iodide (13.5g) in dimethyl sulphoxide (75 ml) added over half an hour. The reaction was heated under reflux overnight and then poured into 2-3 volumes of water. The emulsion was extracted with ether (3 x 250 ml) and the combined ether solution was thoroughly shaken with water (3 x 500 ml). Evaporation of the dried ether (sodium sulphate) gave a brown oil, which was stirred and warmed with aqueous 10% sodium hydroxide (100 ml). The residue was washed with water, and boiled with ether and charcoal, and evaporation of the filtered ether solution gave a pale yellow oil. On passing the oil through a column of Woelm neutral alumina using benzene as eluent a colourless crystalline product was isolated. A small sample was bulb-distilled to give pure (1,3)-dioxa[3.0] orthocyclophane, m.p. 35-36°, (2.5g., 25%), ($\frac{m}{e}$ = 198 (198)), (Found: C, 79.0; H, 5.05. $C_{13}H_{10}O_2$ requires C, 78.8; H, 5.1%).

n.m.r. ($CDCl_3$): 2.4τ(multiplet, 2 aromatic protons); 2.85τ(multiplet, 6 aromatic protons); 4.5τ(singlet, 2 methylene protons).

(N.B. In all the reactions between disodium 2,2'-biphenoxide and various alkylene, ether and o-xylylene dihalides, there was always an excess of the biphenoxide at the end of the reaction. The dihalides appear to be destroyed in a side reaction before they can react with the disodium 2,2'-biphenoxide. An excess of dihalide in these reactions may give improved yields of the heterocycles.)

(b) (1,4);Dioxa[4.0]orthocyclophane (XXVII; n=2)

1st Method

(By modification of the method due to Claret and Archer[31])

A solution of 2,2'-biphenol (18.6g), sodium hydroxide (8g) and dimethylene dibromide (18.6g) in methylated spirit (500 ml) was refluxed for twenty-four hours. On working up the solution, 99% of the original 2,2'-biphenol was recovered and 0.1gm of the desired heterocycle were isolated. The m.pt. was in agreement with the literature (m.p. 98°).[23]

2nd Method

The first method was repeated, and at the end of twenty-four hours, dimethyl sulphoxide (200 ml) was added to the solution, which was then heated on a steam bath overnight under reflux. Evaporation of the alcohol, followed by dilution with an equivalent volume of water, gave an emulsion, which was extracted with ether (2 x 200 ml). (On evaporating a small volume of the ether solution a pale yellow oil was formed. N.m.r. examination of the oil showed it to be composed mainly of 2,2'-biphenol with a smaller amount of the desired heterocycle. No dimethylene dibromide remained in the product.) The ether extracts were combined, and thoroughly shaken with aqueous 10% sodium hydroxide (2 x 100 ml), followed by water (2 x 100 ml). On evaporation of the dried ether solution a pale yellow oil was isolated, which crystallised from 95% alcohol as the known (1,4)-dioxa[4.0]orthocyclophane, m.p. 98°, (Lit. [23] m.p. 98°), (2.9g., 13%), ($\frac{m}{e}$ = 212 (212)).

n.m.r. ($CDCl_3$): 2.75τ (multiplet, 8 aromatic protons); 5.8τ (Collapsed A_2B_2 multiplet, 4 methylene protons).

(c) (1,5)-Dioxa[5.0]orthocyclophane (XXVII; n=3)

A solution of trimethylene dibromide (11 ml) in dimethyl sulphoxide (50 ml) was added over 1½ hours to a hot solution of 2,2'-biphenol (9.3g) and potassium hydroxide (5.6g) in water (75 ml) and dimethyl sulphoxide (50 ml). The solution was heated on a steam bath for a further three hours, and then poured into an ice cold 5% solution of aqueous potassium hydroxide (300 ml). After stirring, the emulsion was extracted with ether (2 x 200 ml), the combined ether solution was then shaken with water (3 x 400 ml). After shaking the ether layer with charcoal and sodium sulphate, the filtered etherial solution on evaporation gave a straw-coloured oil. The oil was passed down a column packed with Woelm neutral alumina (200g) using benzene eluent, to give a colourless oil, which crystallised from aqueous ethanol as pure (1,5)-dioxa[5.0] orthocyclophane, m.p. 67-69°, (3.1g., 27%), ($\frac{m}{e}$ = 226 (226)), (Found: C, 80.1; H, 6.3. $C_{15}H_{14}O_2$ requires C, 79.6; H, 6.25%).

n.m.r. ($CDCl_3$): 2.85τ(multiplet, 8 aromatic protons); 5.7τ(triplet, 4 methylene protons); 8.1τ(quintuplet, 2 methylene protons).

(d) (1,6)-Dioxa[6.0]orthocyclophane (XXVII; n=4)

2,2'-Biphenol (9.3g), potassium hydroxide (5.6g) and tetramethylene dibromide (11 ml) were heated in aqueous dimethyl sulphoxide under the conditions described for preparation (c), and gave a pale yellow oily product, which crystallised on cooling and scratching. Recrystallisation from 95% ethanol gave needles of (1,6)-dioxa[6.0]orthocyclophane, m.p. 110-111°, (4.1g., 34%), ($\frac{m}{e}$ = 240 (240)), (Found: C, 80.4; H, 6.8. $C_{16}H_{16}O_2$ requires C, 80.0; H, 6.7%).

n.m.r. ($CDCl_3$): 2.8τ(multiplet, 8 aromatic protons); 5.6τ(multiplet, 4 methylene protons); 8.1τ(multiplet, 4 methylene protons).

(e) (1,7)-Dioxa[7.0]orthocyclophane (XXVII; n=5)

2,2'-Biphenol (9.3g), potassium hydroxide (5.6g) and pentamethylene dibromide (11 ml) were heated together in aqueous dimethyl sulphoxide under the conditions described in preparation (c), to yield a colourless solid, which crystallised from 95% ethanol as pure (1,7)-dioxa[7.0]orthocyclophane, m.p. 109-110°, (3.1g; 24%), ($\frac{m}{e}$ = 254 (254)), (Found: C, 80.3; H, 6.7. $C_{17}H_{18}O_2$ requires C, 80.3; H, 7.1%).

n.m.r. ($CDCl_3$): 3.0τ(multiplet, 8 aromatic protons); 5.9τ(broad peak, 4 methylene protons); 8.35τ(broad peak, 6 methylene protons).

The reaction between 2,2'-biphenol and ether α,ω-dihalides to give trioxa heterocycles

(a) (1,3,5)-Trioxa[5.0]orthocyclophane (XXIX; n=1)

A solution of bis(chloromethyl) ether (11.4g) in dimethyl sulphoxide (50 ml), was rapidly added to a warm solution of 2,2'-biphenol (18.6g) and sodium hydroxide (8.0g) in dimethyl sulphoxide (200 ml) and water (200 ml). The solution was heated overnight, diluted with six volumes of water and acidified with hydrochloric acid. The turbid solution was ether extracted, the etherial solutions after shaking with water and drying yielded an orange oil. After stirring the oil with aqueous 10% sodium hydroxide (100 ml) a white solid was formed, which crystallised from 95% ethanol in small rhombs of pure (1,3,5)-trioxa[5.0]orthocyclophane, m.p. 144-145°, (1.5g; 14%), ($\frac{m}{e}$ = 228, (228)), (Found: C, 74.1; H, 5.4. $C_{14}H_{12}O_3$ requires C, 73.7; H, 5.3%).

n.m.r. ($CDCl_3$): 2.75τ(multiplet, 8 aromatic protons); 4.7τ(singlet, 4 methylene protons).

(b) (1,4,7)-Trioxa[7.0]orthocyclophane (XXIX; n=2)

2,2'-Biphenol (9.3g), potassium hydroxide (5.6g) and bis(β-bromoethyl) ether (12 ml) in aqueous dimethyl sulphoxide were treated as in preparation (c). On diluting the aqueous dimethyl sulphoxide solution with iced water a solid was precipitated. This solid crystallised from carbon tetrachloride as prisms of (1,4,7)-trioxa[7.0]orthocyclophane, m.p. 190-192°, (3.5g; 27%), ($\frac{\underline{m}}{e}$ = 256, (256)), (Found: C, 74.9; H, 6.15. $C_{16}H_{16}O_3$ requires C, 75.0; H, 6.3%).

n.m.r. ($CDCl_3$): 2.95τ(multiplet, 8 aromatic protons); 5.8τ(multiplet, 4 methylene protons); 6.2τ(multiplet, 4 methylene protons).

The reaction between 2,2'-biphenol and o-xylylene dibromide to give the dioxa heterocycle (XXVIII)

(a) (1,10-Dioxa[2.2.0] orthocyclophane (XXVIII)

Finely powdered o-xylylene dibromide (13.2g) was added directly to a solution of 2,2'-biphenol (9.3g) and sodium hydroxide (4.0g) in water (100 ml) and dimethyl sulphoxide (200 ml). During the first hour the reactants were warmed and shaken to dissolve the dibromide, after which the reactants were heated on a steam bath overnight. The resulting solution was poured onto ice (200g) the emulsion extracted with ether (2 x 250 ml) and the combined ether solution thoroughly shaken with water (3 x 200 ml). Evaporation of the dried ether solution gave an orange gum, which crystallised from 95% ethanol in needles of pure (1,10);dioxa[2.2.0.]orthocyclophane, m.p. 156-158°, (4.3g; 30%) ($\frac{m}{e}$ = 288, (288)), (Found: C, 82.9; H, 5.7. $C_{20}H_{16}O_2$ requires C, 83.3; H, 5.6%).

n.m.r. ($CDCl_3$): 2.8τ(multiplet,12 aromatic protons); 4.8τ(singlet, 4 methylene protons).

(b) m-Xylylene dibromide in the same reaction, gave a polymeric product only.

The synthesis of 2,2'-biphenylylenebisalkylethers (XXXVI; X = Me and Et).

(a) 2,2'-Biphenylylenebismethylether (XXXVI; X = Me)

A solution of 2,2'-biphenol (4.65g), sodium hydroxide (2g) and methyl iodide (6.6g) in water (100 ml) and dimethyl sulphoxide (100 ml) were heated overnight on a steam bath under reflux. On working up the solution in the usual way, a solid was isolated which was crystallised from aqueous ethanol to give the known 2,2'-biphenylylenebismethylether, m.p. 154-155°, (Lit.[32] m.p. 155°) (2.6g., 50%).

(b) 2,2'-Biphenylylenebisethylether (XXXVI; X =Et) was made under the same procedure as the methyl ether. The known product m.p. 36-37° (Lit.[33] m.p. 36-37°) was isolated in a yield of 55%.

The synthesis of 2,2'-bis-(mercaptomethyl)-biphenyl (XXXIII)

(a) 2,2'-Bis-(carbomethoxy)-biphenyl

Concentrated sulphuric acid (10 ml) was added to a solution of diphenic acid (100g) in methanol (500 ml), and the solution refluxed overnight. More sulphuric acid (20 ml) was added to the solution, which was refluxed for a further eight hours. After allowing to stand overnight 2-3 drops of water were added, and crystallisation of the ester commenced immediately. The product was filtered off and the filter cake washed with aqueous sodium hydroxide solution, followed by a thorough washing with water. On drying in a pistol at 50°, 95gms of the known 2,2'-bis-(carbomethoxy)-biphenyl were isolated of m.p. 73-75°. (Lit.[34] m.p. 73-74°).

(b) 2,2'-Bis-(hydroxymethyl)-biphenyl was prepared by the method due to Hall, Lesslie and Turner.[35]

A solution of 2,2'-bis-(carbomethoxy)-biphenyl (56g) in anhydrous ether (520 ml) was added as fast as refluxing would permit to a stirred solution of lithium aluminium hydride (12.5g) in anhydrous ether (450 ml). After the reaction was completed, water followed by dilute sulphuric acid were added to the suspension, and the ether was evaporated by heating on a steam bath. The products were cooled and filtered, and the filter cake washed well with water, to give the crude 2,2'-bis-(hydroxymethyl)-biphenyl as an off-white solid. (45 gms of damp product).

(c) 2,2'-Bis-(bromomethyl)-biphenyl (XXXII) was prepared by the method due to Hall, Lesslie and Turner.[35]

2,2'-Bis-(hydroxymethyl)-biphenyl (48g) was added to stirred 46-48% hydrobromic acid (2 l) at 90°. The mixture was then heated at 140° for two hours and allowed to cool. The solid product was filtered off and washed with water. The crude crystalline 2,2'-bis-(bromomethyl)-biphenyl was isolated (70 gms) m.p. 90-91°. The dibromide may be further purified by recrystallisation from 60-80° light petroleum.

(d) 2,2'-Bis-(mercaptomethyl)-biphenyl (XXXIII)

A solution of 2,2'-bis-(bromomethyl)-biphenyl (17.1g) and thiourea (8.4g) in dimethyl sulphoxide (150 ml), was stirred overnight. The solution was stirred with 10% sodium hydroxide solution (600 ml) for one hour, and then acidified by the addition of ice and hydrochloric acid, keeping the reaction at room temperature. The acidic solution was then extracted with ether (3 x 250 ml) and the combined extracts shaken with water (3 x 400 ml). The ether solution was dried with magnesium sulphate, and evaporated at 30° under vacuum to give the known 2,2'-bis-(mercaptomethyl)-biphenyl[25] as an almost colourless oil, (11.1g., 90%). N.m.r. examination showed the oil to be the pure dithiol.

(2,3)-Dithia[4.0]orthocyclophane (XXXI)

Methanol (500 ml) was added to a warm solution of sodium sulphide nonahydrate (12g) in water (100 ml). Sulphur (1.6g), was added to the stirred solution which was heated on a steam bath to give a yellow solution. A warm solution of 2,2'-bis-(bromomethyl)-dibromide (12g) in methanol (1 l), was added to the stirred solution overnight and at room temperature. The yellow precipitate was filtered off, and boiled with charcoal and chloroform (40 ml), and on evaporation of the filtered chloroform solution a pale yellow crystalline solid was obtained. Recrystallisation from 95% ethanol gave colourless needles of *(2,3)-dithia[4.0]orthocyclophane*, m.p. 167° (Lit.,[25] m.p. 169°), (4.4g., 51%).

Reactions of 2,2'-bis-(mercaptomethyl)-biphenyl with methylene iodide and with m-xylylene dibromide.

(a) (2,4)-Dithia[5.0]orthocyclophane (XXX; Y=CH_2)

A solution of methylene iodide (5·36g) in methylated spirit (500 ml) was added overnight to a stirred solution of the dithiol (XXXIII) (4.9g) and sodium (1.0g) in alcohol (500 ml). The alcoholic solution was evaporated to dryness, and the residue extracted with chloroform. After evaporating the chloroform solution to 10 ml, the solution was passed down a 65 x 3.5 cm column of "Woelm" neutral alumina with 1:1 benzene - light petroleum eluent. Evaporation of the fractions gave a colourless oil, which crystallised on cooling. The product recrystallised from aqueous ethanol as needles of *(2,4)-dithia[5.0]orthocyclophane*, m.p. 95-97°, (2.4g., 46%), (Found: C, 70.0; H, 5.75. $C_{15}H_{14}S_2$ requires C, 69.75; H, 5.45%).

n.m.r. ($CDCl_3$): 2.7τ(multiplet, 8 aromatic protons); 6.45τ(singlet, 2 methylene protons); 6.55τ(AB doublets, J_{AB} = 15 c/s, $\Delta\nu_{AB}$ = 28 c/s, 4 methylene protons).

(b) (4,5:6,7)-Dibenzo-(2,9)-dithia[10]metacyclophane

(XXX; m- $CH_2 \cdot C_6H_4 \cdot CH_2$)

A solution of m-xylylene dibromide (5.3g) in methylated spirit (1 l) was added overnight to a stirred solution of the dithiol (XXXIII), (4.9g) and sodium (1gm) in alcohol (500 ml). The resulting solution was evaporated to ca 100 ml diluted with water (200 ml), and the resulting solid boiled with acetone, and charcoal. The acetone solution yielded colourless crystals of the metacyclophane (XXX; Y = m- $CH_2 \cdot C_6H_4 \cdot CH_2$) m.p. 150-152°, (3.5g., 50%), (Found: C, 76.0; H, 5.75. $C_{22}H_{20}S_2$ requires C, 75.85; H, 5.8%).

n.m.r. ($CDCl_3$): 2.1-3.6τ (complex multiplets, 12 aromatic protons); 6.5τ (singlet, 4 methylene protons); 6.6τ (AB doublets, J_{AB} = 16 c/s, $\Delta\nu_{AB}$ = 37 c/s., 4 methylene protons).

Reaction of 2,2'-bis-(mercaptomethyl)-biphenyl with acetone

A solution of the dithiol (XXXIII) (2.46g), acetone (1 ml) and conc. hydrochloric acid (1 ml) in ethanol (15 ml) was allowed to stand overnight. On diluting the water a white solid was precipitated, which crystallised from 95% ethanol as needles of (3,3)-dimethyl-(2,4)-dithia[5.0]orthocyclophane (XXX; Y=CMe_2), m.p. 97-99°, (1.8g., 63%), (Found: C, 71.6; H, 5.9. $C_{17}H_{18}S_2$ requires C, 71.3; H, 6.3%).

n.m.r. ($CDCl_3$): 2.75τ(multiplet, 8 aromatic protons); 6.3τ(singlet, 4 methylene protons); 8.5τ(singlet, 6 methyl protons).

PART II

The Ultraviolet Spectra of Alkyl Phenyl Ethers and Sulphides and of 2,2'-Biphenyls with Bridges Containing Ether, Sulphide and Sulphone Groups and their Relation to Stereochemistry

The stereochemistry of 2,2'-bridged biphenyls has been extensively investigated during the past twenty years, and a wealth of interesting information has been obtained. These systems are of interest to chemists on two counts. Firstly, 2,2'-bridged biphenyls often exist in two skeletal conformers which are enantiomerically related; and secondly, the energy needed to interconvert the two conformers is often high enough to be measured.

It is intended to discuss the geometry of the 2,2'-bridged biphenyls in this section, and to discuss the thermodynamic stability of the systems in Part III of this thesis.

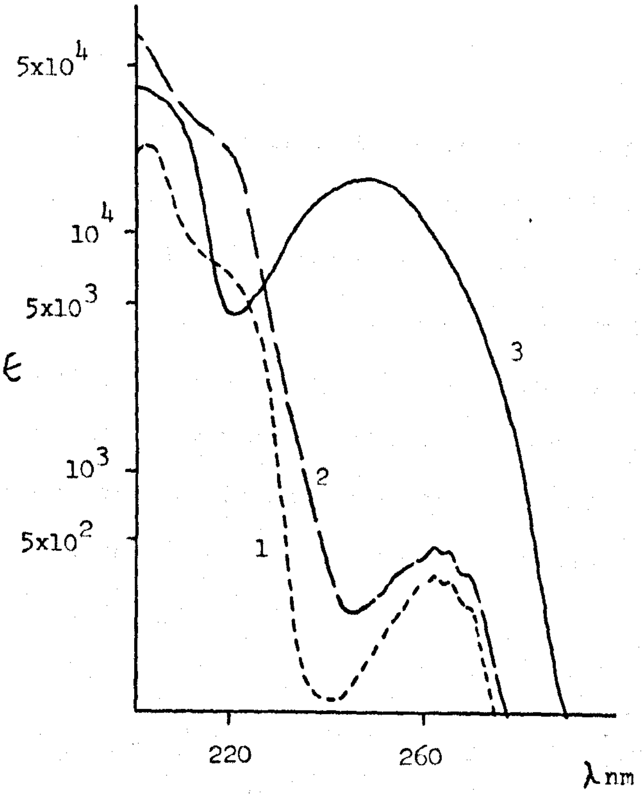
One of the earliest methods of obtaining information about the stereochemistry of 2,2'- substituted biphenyls was that of ultraviolet spectroscopy. Even today, ultraviolet spectroscopy plays a vital role in the understanding of the geometry of these systems, and is the most important method of assessing the dihedral angle between the planes of the biphenyl rings in such systems.

Biphenyl itself gives an ultraviolet spectrum which is characterised by an intense band at 249 nm ($\varepsilon \sim 18,000$), known as the "biphenyl band". This intense band is attributed to the conjugation which occurs between the two phenyl rings. O'Shaughnessy and Rodebush[36] in 1940 showed that the spectrum of bimesityl resembled that of mesitylene; in it the characteristic biphenyl band was absent, replaced by the structured low intensity benzenoid band known as the "secondary α-band" (See Figure 14). These authors considered the absence of the biphenyl band in bimesityl to be due to the inability of the phenyl rings to become coplanar. The view that coplanarity of the benzene rings was essential in order that the usual biphenyl band be observed in such compounds has since been somewhat modified, since it is now known that biphenyl itself in solution is non-planar.

In biphenyl itself, a Drieding model shows the two phenyl rings to be unobstructed and easily rotated relative to one another about the coannular bond. However in reality two factors are undoubtedly operating to hinder this free rotation.

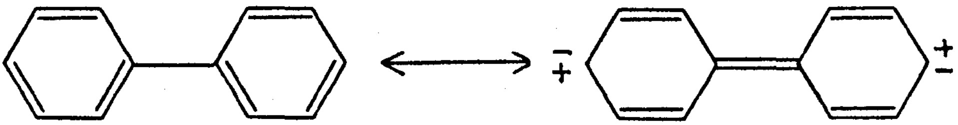
(a) Conjugation between the two phenyl rings, which lowers the electronic energy of the system, tends to hold the two rings coplanar in order that maximum overlap of the conjugating $2p_z$ π-electrons can occur:

Ultraviolet Spectra of Aromatic Compounds

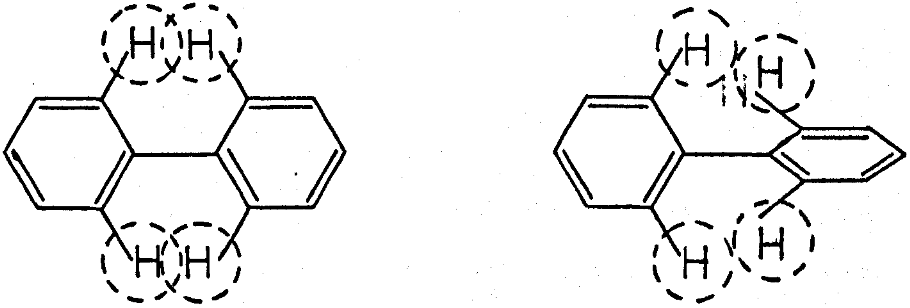


1. Mesitylene x 2
2. Bimesityl
3. Biphenyl

Figure 14



(b) However, a competing steric repulsion effect between the substituents in the four ortho positions of the biphenyl tends to force the phenyl rings into an antiplanar conformation. Even the small hydrogen atoms in the ortho positions of biphenyl, have sufficient repulsion between them to cause the phenyl rings to adopt a non-planar conformation in solution. (Suzuki[37] has calculated the dihedral angle θ between the planes of the phenyl rings of biphenyl in solution to be ca. 20°):

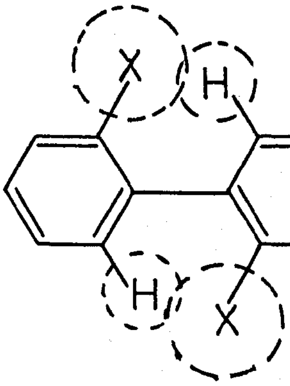


PLANAR ANTIPLANAR

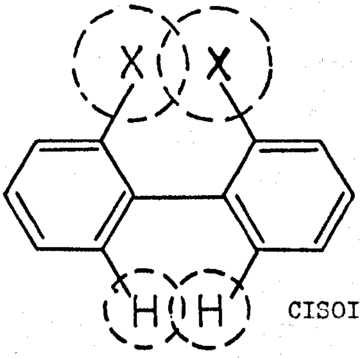
As can be seen above, biphenyl in an antiplanar configuration receives a reduced steric effect.

Clearly, substituents of greater size than the hydrogen atom in the ortho positions of biphenyl will exert a greater steric repulsion between the ortho groups, due to their larger Van de Waals' radii. As a general rule the more ortho substituents in the molecule, and the larger the size of the substituents, the greater will be the steric repulsive forces and the dihedral angle θ .

Unfortunately predictions based on simple logical energy considerations are not always in harmony with experimental evidence. For example the 2,2'-dihalo biphenyls would be expected to assume a transoid conformation, as that in which the least repulsive effects would be experienced:



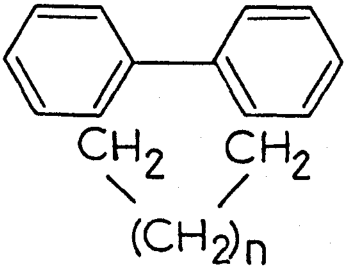
TRANSOID



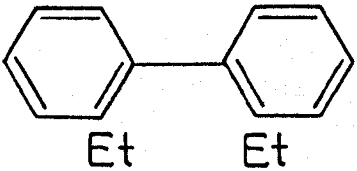
CISOID

However, Beaven[38] concluded from electron diffraction studies, and dipole moments, that a preference exists for the more sterically demanding cisoid conformation. This author suggests the same may be true of 2,2'-dimethylbiphenyl.

2,2'-Bridged biphenyls, on the other hand, have been investigated with a little more certainty; here the 2,2' positions are linked and the maximum distance between the α- and ω-atoms of the bridge is limited by the number of atoms in the bridge. In practice compounds with bridges of less than six members will be restricted to a cisoid configuration, while bridges of six or more atoms will have an option of either a cisoid or transoid conformation. As the bridge increases in length, the biphenyl usually increases its dihedral angle. Thus, Mislow in 1962[39] using ultraviolet spectral data showed that the 2,2'-bridged biphenyls (XXXVIII; n=0 - 3) underwent a steady increase in the dihedral angle as the value of n increased. (See Figure 15). The longest-bridged compound (XXXVIII; n=3) shows the biphenyl band as a mere inflection at short wavelength, and the structured benzene α-band is clearly visible at longer wavelength. The spectrum of the pentamethylene bridged biphenyl (XXXVIII; n=3) was found to be almost identical with that of 2,2'-diethylbiphenyl (XXXIX), indicating that both compounds have similar dihedral angles:



(XXXVIII)



(XXXIX)

Ultraviolet Spectra of Homocyclic 2,2'-Bridged Biphenyls

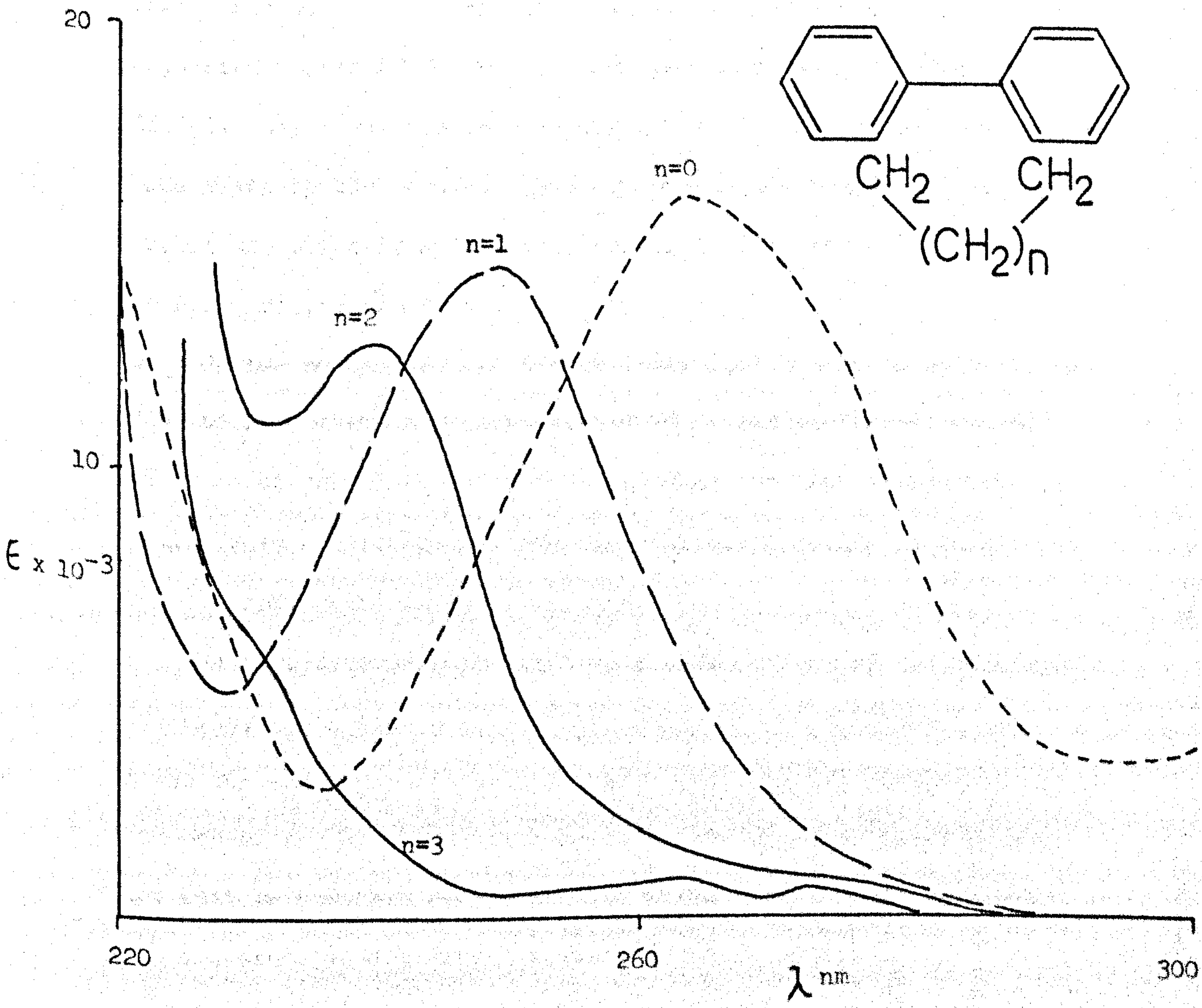


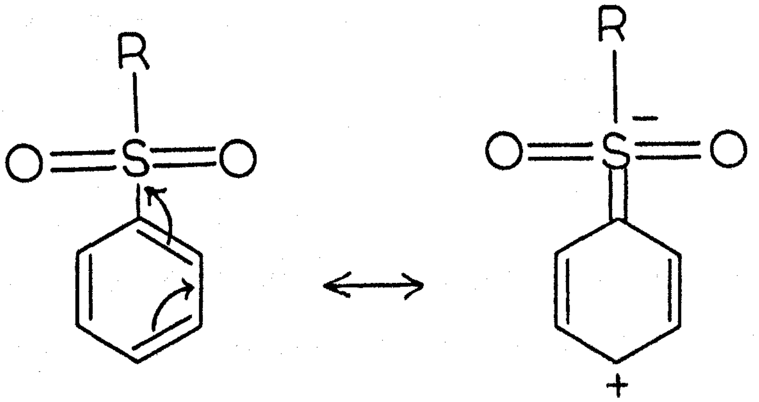
Figure 15

In continuing his work Mislow[40] made accurate models of derivatives of the polymethylene bridged compounds (XXXVIII; n=0 - 3), and found that for n = 0 and 1, the models gave single dihedral angles for strainless systems, for n = 2 two dihedral angles were obtained, whilst for n = 3 the dihedral angle is not fixed. Suzuki,[41] using the LCAO molecular orbital method, calculated values of θ for the homocyclic bridged biphenyls (XXXVIII; n=1 - 3); the results for n = 1 and 2 were in accord with those given by the models. This agreement gave confidence in the further use of scale models to investigate the stereochemistry of the 2,2'-bridged biphenyls.

Up to the time of our studies only 2,2'-biphenyls with bridges of up to five atoms had been studied by ultraviolet spectroscopy, and it is of considerable interest to find out what stereochemistry results when longer bridges are employed and a choice of cisoid or transoid conformations are available.

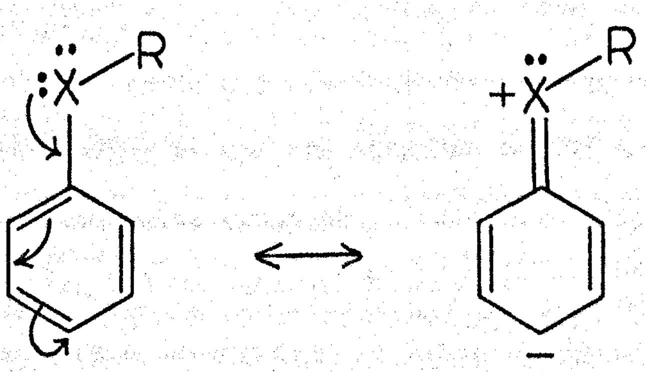
We have recorded the spectra of three series of 2,2'-bridged biphenyls, which incorporate ether, sulphide and sulphone functions in the α- and ω- positions of the bridge. Interpretation of the stereochemistry by ultraviolet spectroscopy is complicated by the fact that we now have groups present which can intereact strongly with the aromatic π electron system, by conjugation.

For the sulphone group, conjugation occurs between the aromatic π electron system and the sulphur 3d orbitals:



etc

Because the conjugation involves the sulphur 3d orbitals, there is little or no steric demand placed on the conjugation process and the system behaves as a modified benzene ring. In contrast, the sulphide and ether groups conjugate with the aromatic rings by delocalisation of one of their lone pairs of p electrons into the ring, a process which demands a coplanar state as a fundamental requirement:



X = O or S

etc

If the molecule cannot assume a planar state, then the conjugation process will be reduced and the spectra affected accordingly. This effect was noticed when the spectra of alkyl phenyl ethers or thio-ethers was recorded; the spectra of the tertiary butyl compounds were vastly different from those of the lower alkyl compounds. This difference is attributed primarily to increased steric effects between the larger alkyl group and the ortho hydrogen atoms, preventing the coplanar state from being achieved. Obviously since two steric effects are being measured simultaneously in our 2,2'-bridged biphenyl systems, it is important to consider both effects. We have, therefore, reinvestigated the ultraviolet spectra of some simple alkyl phenyl thio-ethers and alkyl phenyl ethers, in an attempt to get a better understanding of the electronic and steric processes that are occurring between the heteroatom and the benzene ring.

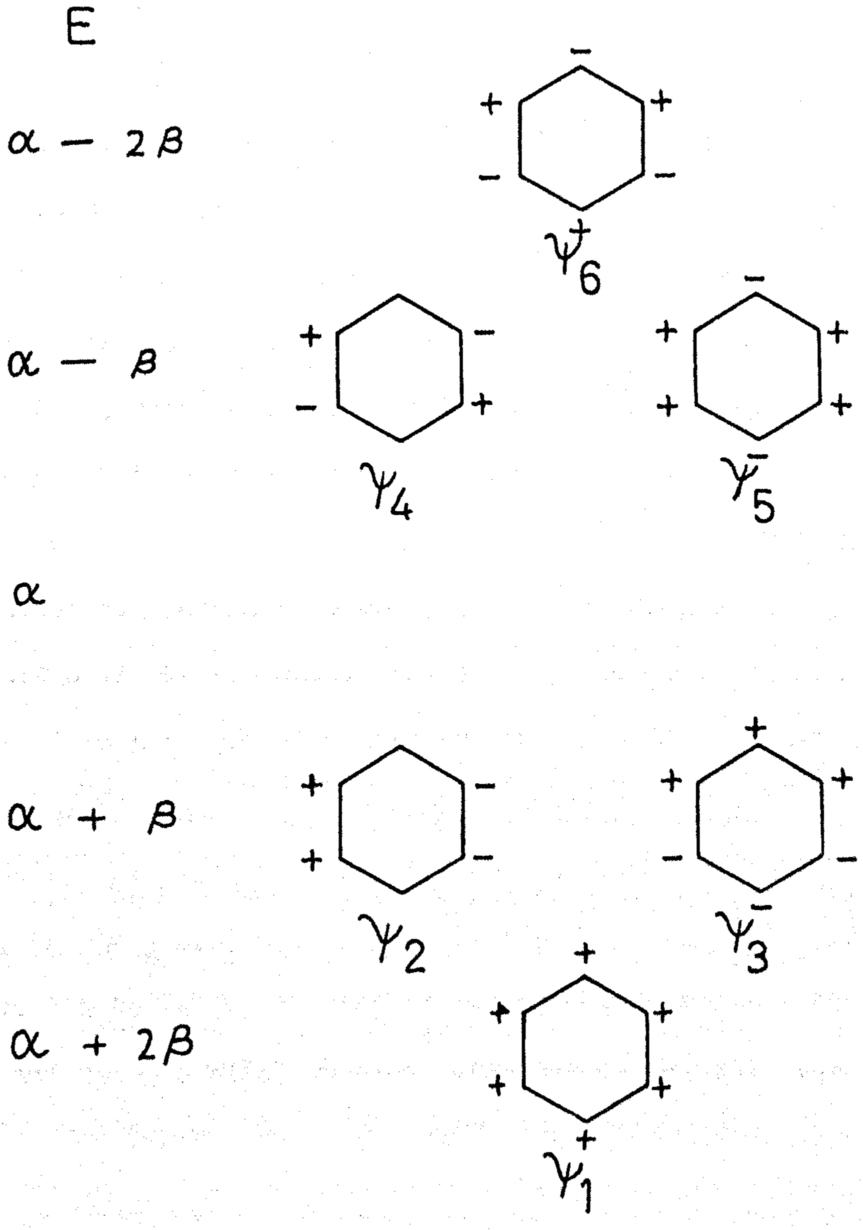
The u.v. spectra of aryl sulphides have been investigated by many workers[42, 43, 44] and the topic has been widely reviewed.[45, 46a] Steric inhibition of lone pair conjugation with the aryl ring together with large bathochromic and hyperchromic effects when para orientated electron-withdrawing groups are attached to the aryl ring, have shown that the sulphide group has a tendency to act as a lone-pair donor. The spectral changes which occur in a series of alkyl aryl sulphides have been interpreted in terms of the orientation of oscillating electric vectors.[42] Assignments of the bands have been made with the aid of molecular orbital and valence bond calculations[43] and also by comparison with the spectra of thiophenol, phenol and aniline.[44] The conclusions have not been consistent.

The spectrum of thioanisole in alcohol contains intense bands at ca 210 and 254 nm and a weak band at ca. 280 nm. The main difficulty in making assignments for the bands centres on the origin of the band at 254 nm. Although the wavelength and intensity of this band is consistent with it being a strongly perturbed primary band it does not undergo a hypsochromic shift when conjugation of the phenyl ring to the sulphur lone-pair of electrons is inhibited. Instead, a bathochromic shift occurs and the band eventually takes on the characteristics of an unstructured secondary α-band.

The spectra of alkyl aryl ethers are also well documented and a comparison of the effects on the spectra of changing the size of alkyl group has been made.[47] Steric inhibition of lone-pair conjugation with the aryl ring decreases the intensity and wavelength of the primary and secondary bands which appear at ca 220 and 270 nm. respectively.

There is general agreement that the bands which appear in the spectra of aryl sulphides and ethers are due to perturbed benzene transitions. The π molecular orbitals of benzene are shown in Figure 16.

Figure 16

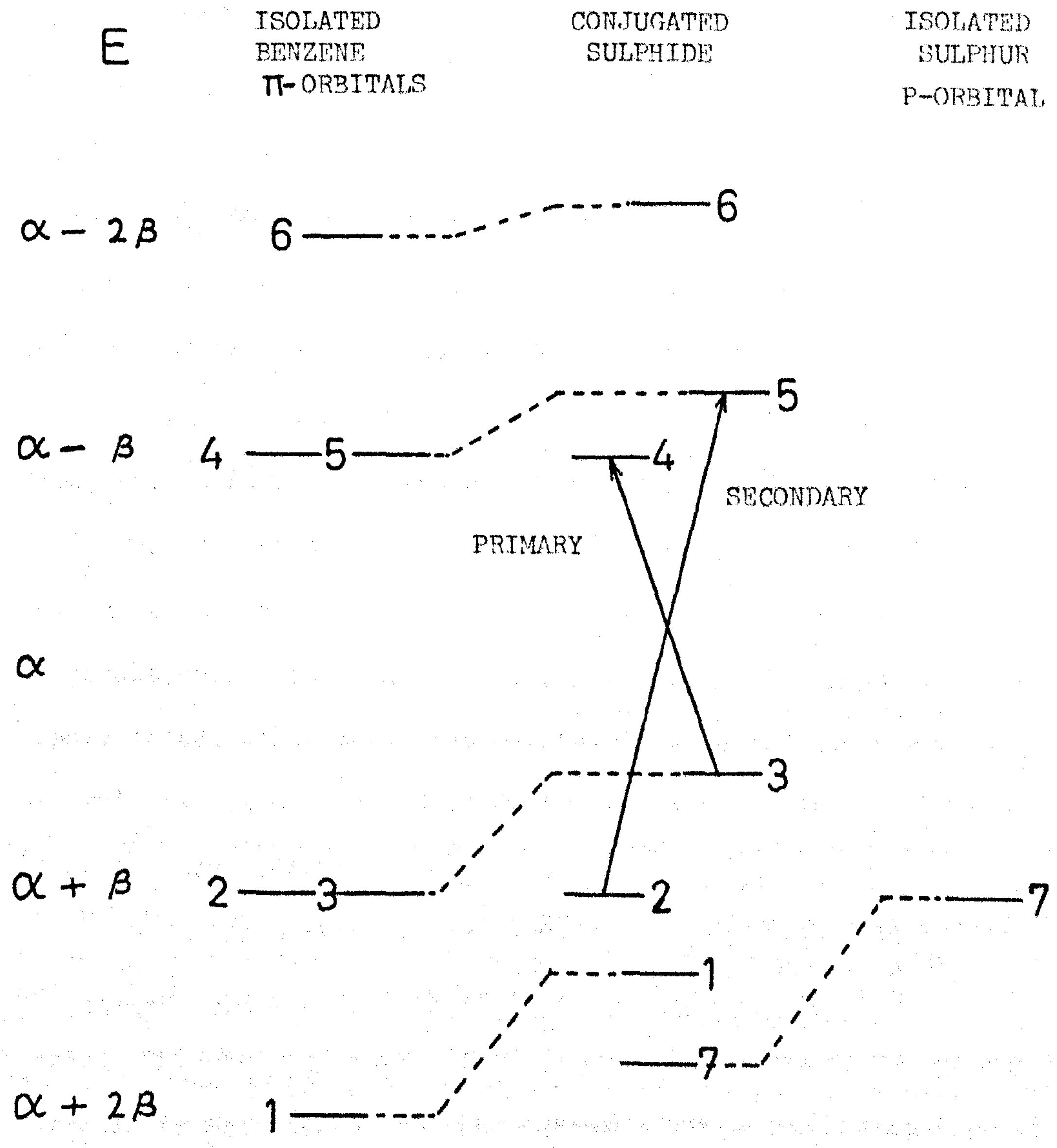


The pi molecular orbitals of benzene

The most intense band in the spectrum of benzene occurs at 180 nm., and is known as the second primary p band. It arises from the promotion of an electron from the ψ_2 to ψ_4 orbital or from the ψ_3 to ψ_5 orbital i.e. a transition which involves interconversion of bonding and antibonding orbitals. The transitions which involve promotion of an electron from the ψ_3 to ψ_4 orbital or from the ψ_2 to the ψ_5 orbital are both forbidden and give rise to the weaker primary and secondary bands at 200 and 260 nm. respectively.

If one considers the effect of conjugation only on the energies of the π orbitals of benzene one finds that one of the forbidden transitions is increased in energy while the other forbidden transition is decreased in energy. This would adequately explain the shifts of the secondary band in the spectra of the sulphides. Figure 17 is a diagramatic representation of the conjugation effect of the sulphide group on the energy of the π orbitals of benzene. The conjugative effect raises the energy levels of the ψ_1, ψ_3, ψ_5 and ψ_6 orbitals only since the ψ_2 and ψ_4 orbitals possess a node at the C_1 atom of the ring (see Figure 16). The ψ_1 and ψ_3 orbitals will be affected to greatest extent

Figure 17



Diagrammatic representation of the conjugation effects of a sulphide group on the benzene π -orbitals since their energy levels are closest to that of the sulphide p-orbital.[46b]

The secondary α-band is generally considered to arise from the promotion of an electron from the fully occupied ψ_2 orbital to the empty ψ_5 orbital and the primary p-band from a $\psi_3 - \psi_4$ transition. The hypsochromic shift of the secondary band, when conjugation to the sulphide group is permitted is in accord with this assignment, i.e. λ_{max} 266 for the t-butyl sulphide (conjugation inhibited) and 254 nm. for the methyl derivative.

The aryl ethers do not behave in this manner and both bands undergo a bathochromic shift when conjugation to the oxygen atom is permitted. This could be brought about by the operation of a dipole effect which lifts the degeneracy of the ψ_2 and ψ_3 π orbitals allowing conjugation to reduce the energy of both the forbidden transitions.

Conjugation removes the symmetry barrier to the forbidden transitions and produces an increase in intensity of the corresponding bands. This is very marked for the secondary band of the sulphides which is in accordance with the larger conjugative interaction with the ψ_3 and ψ_5 orbitals. Indeed the final energies and character of the π orbitals of the aryl sulphides may bear little relationship to those of benzene.

If the band at 254 nm. of thioanisole originates from the secondary band of benzene another assignment is needed for the weak band at 280 nm. However when the spectrum of a hexane solution of thioanisole is measured the weak band exhibits a structured nature, which is characteristic of a secondary band. Since donation of a lone-pair of electrons destroys the structured nature, the band may be due to the presence of conformer in which the lone-pair is out of conjugation.

The u.v. spectra of organic compounds do not usually reflect the presence of different conformers. However two distinct conformer populations could reasonably be present when the steric interactions are small; one conformer would be nearly planar (being stabilised by conjugation) and would produce the major bands in the u.v. spectrum, and the other conformer would be non-planar. Increased steric effects would raise the energy of the near planar conformer, and reduce the barrier between the near planar and non-planar conformer. It is of interest to note that the spectrum of thioanisole differs from the spectrum of the other alkyl derivatives in that it exhibits an additional band which occurs as a shoulder at 240 nm. In the vapour phase this is a well defined band in accordance with a reduced number of collisions and slower interconversion of rotamers. This band is in best accord with the p-band of the near planar conformer. In this case the band at ca.210 nm. would be attributed to the p-band of the non-planar conformer. If this is correct the 240 nm. band should merge with the 210 nm. band as the size of the alkyl group increases. In fact this is not observed and the 240 nm. band is absent from the spectra of the other alkyl sulphides, even in the vapour phase.

Solvent effects on the spectra have been examined; the position of the bands shows a marked dependence on the polarity of the solvent. The solvent shifts are similar to those observed for $n \rightarrow \pi$ transitions, i.e. there is a hypsochromic shift as the polarity of the medium is increased.[46c] A hypsochromic shift may be produced by packing strain or a decrease in dipole moment in the excitation process. However since the shift is at a maximum when there is least delocalisation of the lone pair of electrons, e.g. the tertiary butyl compounds, the predominant cause of the shift is attributed to hydrogen bonding to the lone pair of electrons on the heteroatom.

Table 1

U.v. spectra of phenyl alkyl sulphides and ethers: some solvent effects.

Compound	5% ethanol in water		95% ethanol		n-hexane	
PhSMe	[203]	250	207 213i	254	218	254 †
PhSEt	[203]	251	208 214i	255	215	256
$PhSCHMe_2$	[205]	252	210 215	257	217	258
$PhSCMe_3$	[200] 218	257	209i 219	266	220	268
PhOMe	217	268.5	220	271.5	220	271
PhOEt	217	269	221	272	221	272
$PhOCHMe_2$	218	270	222.5	273	223	273
$PhOCMe_3$	207	262	210	270	218	270

† the spectrum of thianisole in a n-hexane also contains an inflection at 240 nm. and a structured band is centred at 280 nm.

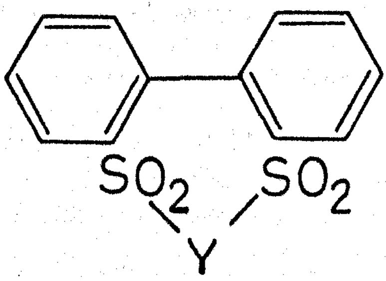
i = inflection. (Bracketed values are within the region of end-absorption of the solvent, and are therefore of limited significance.)

With the exception of the t-butyl derivatives the ethers show only a small solvent effect since donation of the lone pair of electrons to the phenyl rings reduces the electron density on the ether oxygen atom and consequently the hydrogen bonding. In the t-butyl ether, donation to the ring is inhibited and there is an appreciable hypsochromic shift in the hydroxylic solvents.

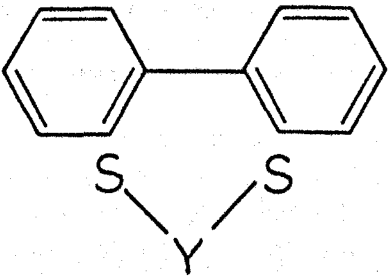
The spectral response of the sulphides and ethers to similar structural changes is different. Steric interactions change the wavelength and reduce the intensity only in the case of the t-butyl group for the ethers (See Table 1). In contrast the wavelength of the 254 nm. bond in thioanisole changes and its intensity is reduced as each extra methyl group is introduced. (See Table 1) This is in direct contrast with the expected decrease in steric interaction due to the longer carbon-sulphur bonds. A rational explanation may be found if one takes into account the fact that conjugation involving the larger orbitals on the sulphide group is not as sterically demanding as the corresponding smaller orbitals on the ether group. Thus $p\pi - p\pi$ conjugation in the ethers will change more rapidly with the orientation of the alkyl group and will resist steric forces to a greater extent.

The stereochemistry of 2,2'-bridged biphenyls has been investigated previously using ultraviolet and n.m.r. spectroscopy.[48,49,50] A comprehensive range of biphenyls with single and double three-membered bridges, and incorporating various hetero-atoms in the centre of the bridge, have been studied.[48, 49] More recently the 2,2'-bridged biphenyl (XXXI) has been prepared and is the first single-bridged dithia-biphenyl to be investigated spectroscopically.[25, 50]

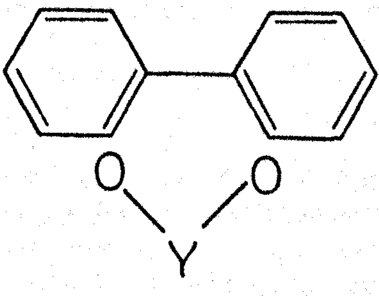
The present study is on three series of 2,2'-biphenyl heterocycles (XXIII), (XV) and (XXV) in which the heteroatoms or groups are directly attached to two positions _ortho_ to the coannular bonds of the biphenyl system. Eleven different bridging groups Y, having one to five members, provide a wide range of dihedral angles between the planes of the phenyl rings in the three series of heterocycles. The spectra of these compounds have been compared with the spectra of the unbridged biphenyl derivatives (XXXVII), (XXXV) and (XXXVI).



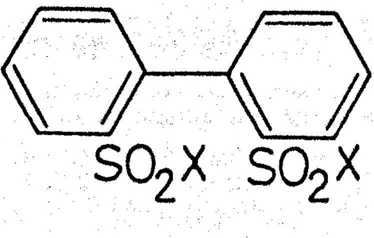
(XXIII)



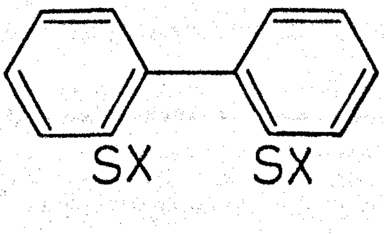
(XV)



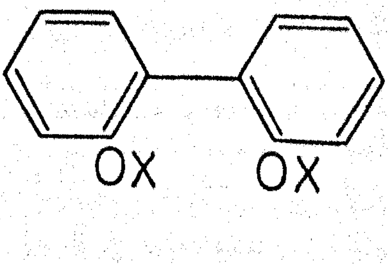
(XXV)



(XXXVII)



(XXXV)



(XXXVI)

The disulphides and diethers were prepared from the disodium salt of the dithiol (XXXV; X = H) and the diphenol (XXXVI; X = H) respectively, and the α, ω -dihalide of the bridging group Y. (See Part I). The disulphones were obtained by oxidation of the disulphides with hydrogen peroxide in acetic acid. (See Part I). The heterocyclic compounds were shown to be monomeric by mass spectral and solution vapour pressure measurements. (See Part I)

The u.v. spectra of phenyl methyl sulphone (XL; X = Me) (see Table 2) possesses two well-defined bands; an intense primary (p) band at ca 220 nm. and a structured secondary (α) band at ca 265 nm. The overall variation in λ_{max} of the p-band in the sulphone series of biphenyl compounds is little more than 5 nm. compared with 25 nm. for a α-band. The biphenyl disulphones which possess an extended bridge e.g. (XXIII; Y = $(CH_2)_{>1}$) or no bridge, i.e. (XXXVII), exhibit a p-band at shorter wavelength (ca 10 nm.) than the alkyl phenyl sulphones.[5] This shift reflects the presence of an out-of-plane aryl substituent in the phenyl sulphone chromophore of the biphenyl compounds. When the length of the bridge is reduced to a single methylene group, conjugation between the rings increases and the p-band undergoes a small bathochromic shift of ca 5 nm.

The structured secondary (α) band of the sulphones shows a more uniform behaviour than the p-bands with change in molecular structure (see Table 2). The band which is centred at 254 nm. in the spectrum of benzene, increases in intensity and is moved successively to longer wavelengths on substitution. A sulphone group (as in XL; X = Me)

Table 2

Ultraviolet spectra of sulphones in 95% ethanol

Compound	249 nm. Biphenyl Band		Secondary Benzenoid Band	
	λ max	$\epsilon \times 10^{-3}$	λ max	$\epsilon \times 10^{-3}$
(Benzene)	-	-	254	(0.2)
XL; X = Me	-	-	264	1.05
XXXVII; x = Me	-	-	271	3.5
XXXVII; X = Et	-	-	271	3.5
XXXVII; X = $PhCH_2$	-	-	271.5	2.8
XXIIIa;Y = $(CH_2)_2O(CH_2)_2$	240 (i)	6.00	282	4.1
XXIIIb;Y = $(CH_2)_5$	238 (i)	6.00	281.5	5.0
XXIIIc;Y = $(CH_2)_4$				
XXIIId;Y = CH_2-O-CH_2	-	-	272	4.0
XXIIIe;Y = $(CH_2)_3$	-	-	271	3.5
XXIIIf;Y = $\underline{O}$- $CH_2 \cdot C_6H_4 \cdot CH_2$	-	-	273	4.0
XXIIIg;Y = $(CH_2)_2$	240 (i)	5.35	272	4.6
XXIIIh;Y = $\underline{m}$- $CH_2 \cdot C_6H_6 \cdot CH_2$	-	-	287.5	4.7
XXIIIi;Y = CH_2	245	4.8	288.5	6.0
XXIIIj;Y = CHPh	245 (i)	16.0	289	6.6
XXIIIk;Y = $C(Me)_2$	246.5	5.3	289.5	6.8
XLIII	265	27.0	-	-

produces a 10 nm. shift and a non-planar ortho group as in (XXXVII; X = Me) increases λ_{max} by a further 7 nm. (see Figure 18 and Table 2).

Because the conjugation between the sulphone group and phenyl ring is stereo-independent,[51] the spectra of the biphenyl disulphones is governed mainly by the dihedral angle θ between the biphenyl rings. The unbridged disulphones all have similar spectra which are characterised by the structured α-band at ca 272 nm. This and the absence of the characteristic biphenyl band at ca 249 nm. suggest that the phenyl rings are roughly perpendicular to one another. This is supported by the spectra of the bridged compounds. In two examples, (XLI) and (XLII) a structureless intensified α-band occurs at ca 288 nm. which indicates that there is increased conjugation between the phenyl rings. Drieding models suggest that the methylene-bridged compound (XLI) is locked in a cisoid conformation with θ ca 60° and that the rigid m-xylylene bridged compound (XLII) has a transoid conformation with θ ca 120°, both compounds thus having similar deviations from planarity. The dimethylene-bridged compound has a dihedral angle of ca 80° and shows a reduction in the structured nature of the α-band even though the rings are close to being perpendicular to each other. Models indicate that the trimethylene and dimethylene ether bridges, (XXIIIe and XXIIId) and the o-xylylene bridge (XXIIIf) allow cisoid conformations up to a dihedral angle of ca 90°. However the bulky sulphone groups force the rings to their maximum dihedral angle, producing spectra similar

Ultraviolet Spectra of Sulphones

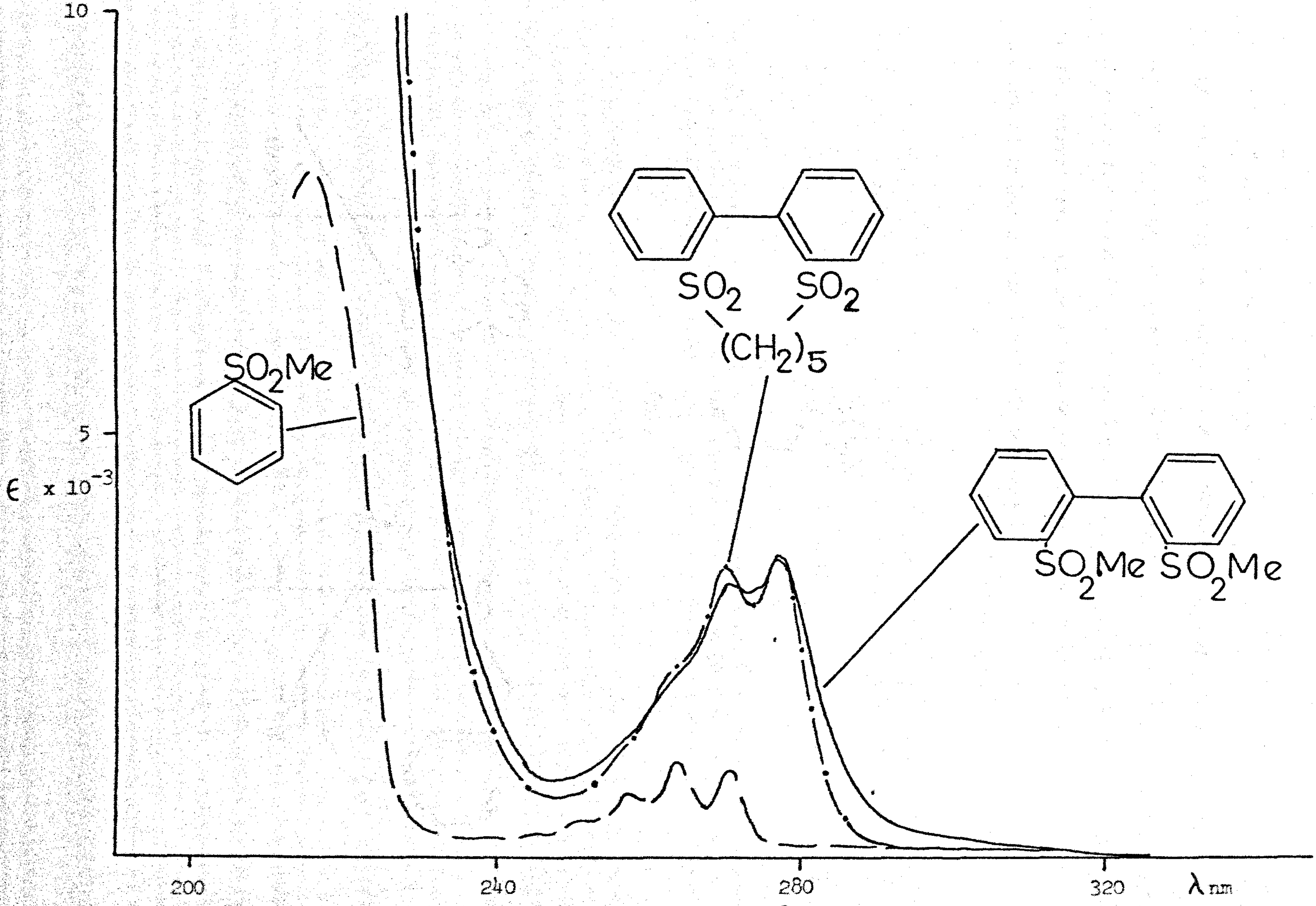
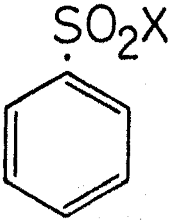
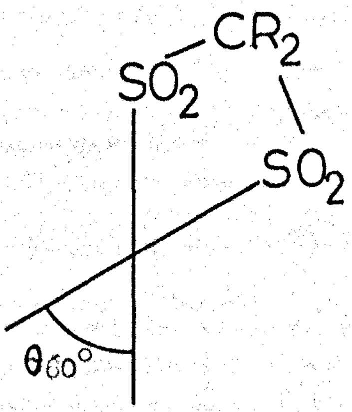


Figure 18

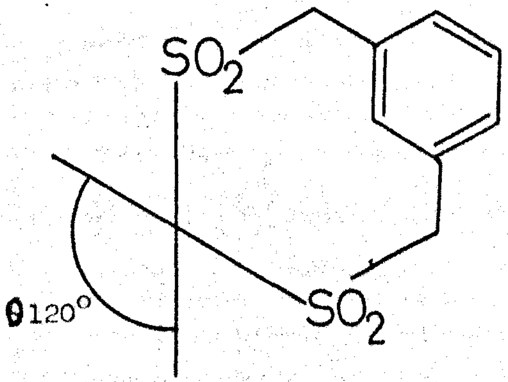
to those of the unbridged compounds (see Figure 18). Still longer bridges cause a gradual loss of the structure of the α-band, consistent with an increase in dihedral angle beyond 90° and a preference for transoid conformations (see Figure 19). Variation in the structured nature of the α -band was first observed in the spectra of 2-(or 2,6-di-) methylbiphenyls.[38]



(XL)



(XLI)



(XLII)

Ultraviolet Spectra of Sulphones

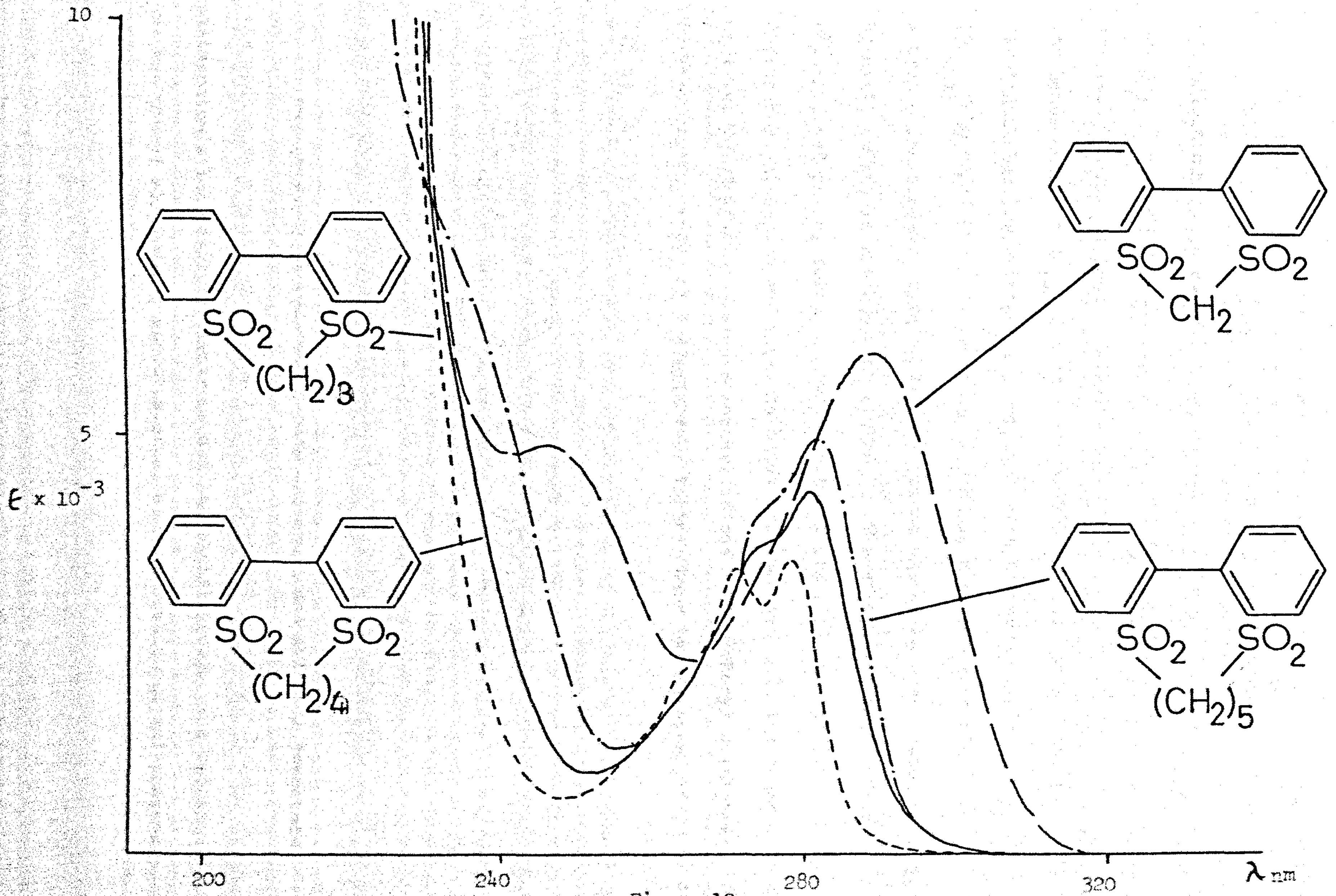
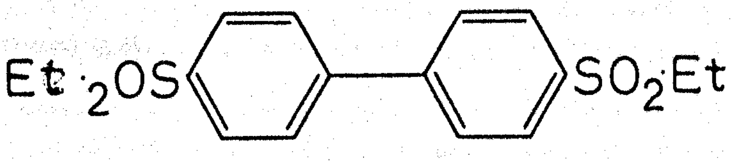


Figure 19

Bands which are attributed to the biphenyl chromophore appear as inflections at ca 240 - 245 nm. in the spectra of (XXIIIa, b, g and j). The bands are clearly defined only in the spectra of the smallest-bridged biphenyl sulphones (XXIIIi and k). (See Figure 19). The bands occur at λ_{max} 245 nm. ($\varepsilon \sim 5,000$) which is at a similar wavelength but lower intensity, compared with biphenyl itself (λ_{max} 249,$\varepsilon \sim 18,000$). This is in accordance with the recognised decrease in intensity with relatively little change in wavelength, caused by small twists in the biphenyl system.[52] The electric vectors of the biphenyl and phenyl sulphone chromophores of (XXIIIi) and (XXIIIk) approach right angles and separate bands are observed. On the other hand the corresponding electric vectors of the 4,4'-biphenyl disulphone (XLIII) are parallel and a single very intense band is observed at 265 nm. ($\epsilon \sim 27,000$).



(XLIII)

The ultraviolet spectra of both the ether and sulphide compounds are made more complex by the variation in p-orbital overlap of the heteroatom's lone pair of electrons and the phenyl group. The spectra of the phenyl alkyl ether and thio-ether compounds which do not possess a biphenyl group were discussed earlier.

The biphenyl disulphides which have an extended bridge e.g. (XV; Y = $CH_2)_{>2}$) or no bridge i.e. (XXXV) show an intense *p*-band at a similar wavelength to that of thioanisole (ca 205 nm.). For the shorter bridged biphenyls i.e. (XVi - k) and also (XVh), improved conjugation between the biphenyl rings produces a small bathochromic shift. In contrast the intense *p*-band of the biphenyl diethers at ca 210 nm. undergoes little change of wavelength with shortening of the bridge.

The spectrum of the unbridged biphenyl disulphide (XXXV; X = Me) shows that the additional phenyl group produces a small bathochromic shift in the 254 nm. thioanisole band and there is also a reduction in intensity if one takes into account the presence of two phenyl sulphide chromophores, which indicates that steric effects similar to those observed for the alkyl phenyl sulphides, are already operating (See Table 1, page 89).

Table 3

Ultraviolet spectra of sulphides in 95% ethanol

Compound	249 nm. Biphenyl Band		254 nm. Thioanisole Band	
	λ_{max}	$\varepsilon \times 10^{-3}$	λ_{max}	$\varepsilon \times 10^{-3}$
Thioanisole	-	-	254	9.9
XXXV; X = Me	239 (i)	13.3	255	13.0
XXXV; X = Et	240 (i)	12.0	259	10.5
XXXV; X = Pr^i	243 (i)	12.0	264	9.3
XXXV; X = $PhCH_2$	-	-	260 (i)	10.0
XVa; Y = $(CH_2)_2O(CH_2)_2$	240 (i)	8.0	270	7.8
XVb; Y = $(CH_2)_5$	242 (s)	10.0	271	8.7
XVc; Y = $(CH_2)_4$	238 (i)	6.7	272	5.5
XVd; Y = CH_2-O-CH_2	-	-	250	4.8
XVe; Y = $(CH_2)_3$	-	-	266	5.0
XVf; Y = <u>o</u>- $CH_2C_6H_4CH_2$	-	-	276	4.2
XVg; Y = $(CH_2)_2$	-	-	267	2.0
XVh; Y = <u>m</u>- $CH_2C_6H_4CH_2$	248 (i)	10.0	274	4.2
XVi; Y = CH_2	243 (i)	11.0	258 (s)	8.0
XVj; Y = CHPh	-	-	260 (s)	8.5
XVk; Y = $C(Me)_2$	243 (i)	9.7	256 (s)	8.0
XLV	-	-	247	15.0

Also similar is the effect of replacement of X = Me in (XXXV) by Et or Pr^i which causes further bathochromic shifts and decreases in intensity (see Figure 20 and Table 3). When the two sulphur atoms are connected by bridges, severe steric restraint is observed which prevents conjugation of the lone pair of electrons on sulphur with the phenyl ring and even with the most flexible bridges (XVa and XVb) the 254 nm. band is shifted to its longest wavelength at ca 270 nm. Shortening of the polymethylene chain to two members reduces the band at 270 nm. to its lowest intensity (see Figure 21) which is consistent with the increased twisting about the sulphur atoms indicated by Drieding models. For the smallest-bridged compounds (XVi - XVk) a number of overlapping bands occur. The biphenyl band of (XVi - XVk) is not well developed but it may well be represented by the inflection at ca 243 nm. This band appears at lower wavelength and is less intense than in the ether analogue (XXV) possibly indicating that the sulphides, due to the larger size of the sulphur atoms, do not achieve the same degree of planarity. However, conjugation of the sulphur atom with the aromatic ring is again comparable with that in the unbridged biphenyl disulphides as shown by the reappearance of the band at 258 nm.

By comparison, the spectra of the ether analogues are simpler to interpret since the biphenyl band (249 nm. in biphenyl) and the phenyl alkyl ether structured α-band (271.5 in anisole) are well separated, and the steric effects on the conjugation between the oxygen-atom and the phenyl ring are much smaller than those observed for the sulphides. The unbridged biphenyl ethers (XXXVI; X = Me or Et) are characterised by an almost structureless α-band at ca. 280 nm. which is about double the intensity of the isolated anisole chromophore (see Table 4 and Figure 22).

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Ultraviolet Spectra of Sulphides

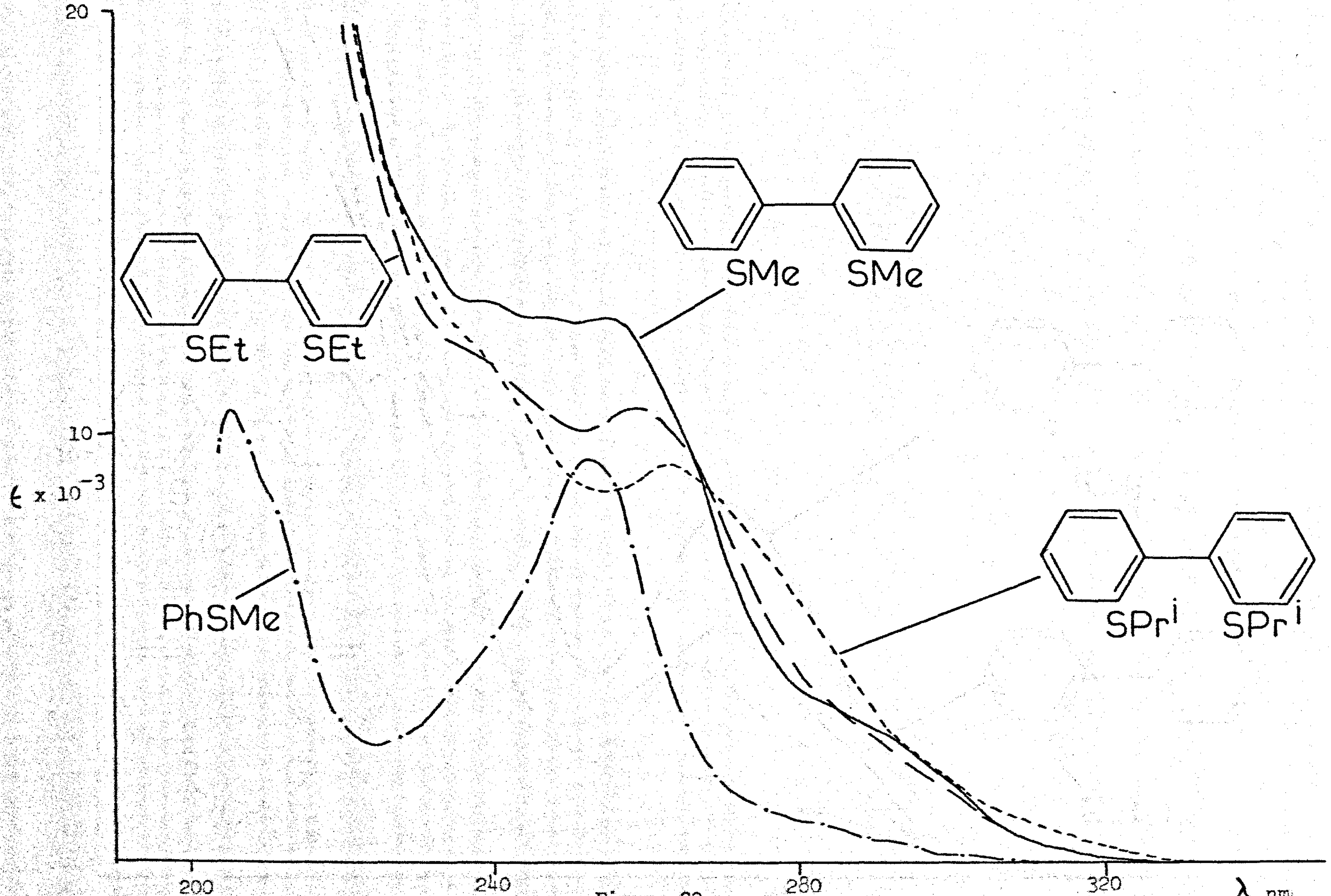


Figure 20

Ultraviolet Spectra of Sulphides

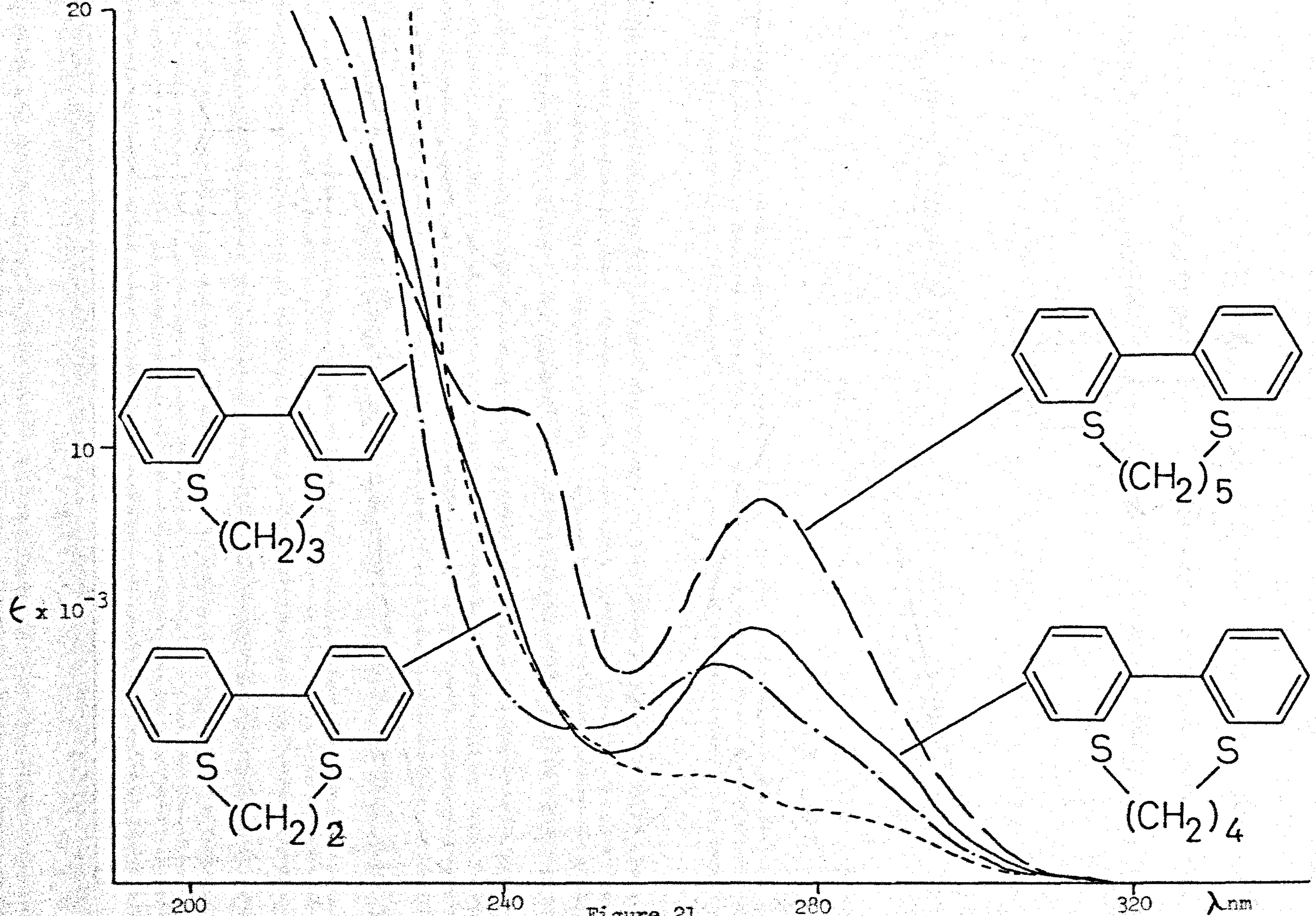


Figure 21

Ultraviolet Spectra of Ethers

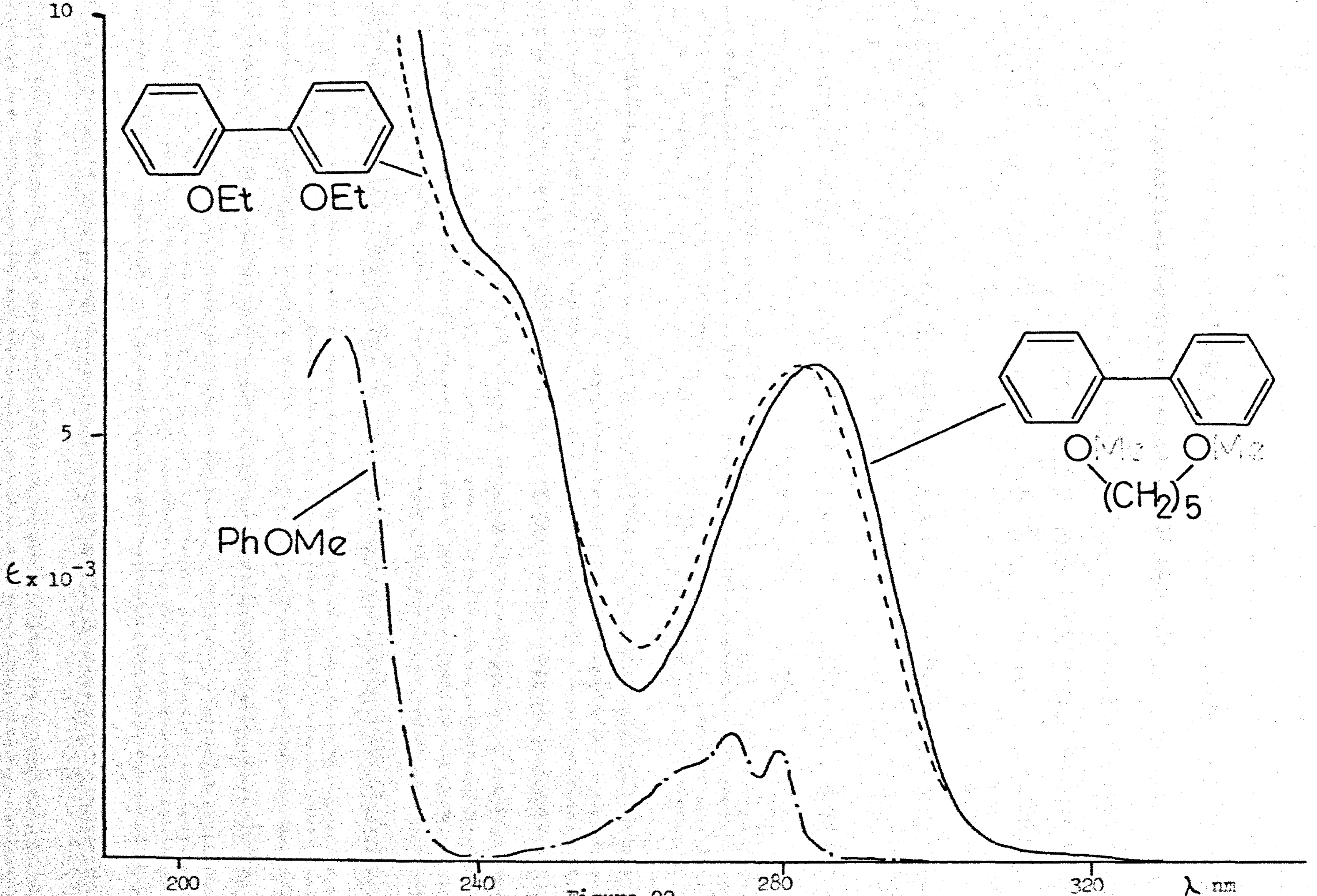


Figure 22

Table 4

Ultraviolet spectra of ethers in 95% ethanol

Compound	249 nm. Biphenyl Band		Secondary Benzenoid Band	
	λ_{max}	$\varepsilon \times 10^{-3}$	λ_{max}	$\varepsilon \times 10^{-3}$
Anisole	-	-	271.5	1.48
XXXVI; X = Me	242 (s)	6.5	280.5	6.0
XXXVI; X = Et	242 (s)	6.5	282	6.1
XXVa; Y = $(CH_2)_2O(CH_2)_2$	244 (s)	7.0	282	5.7
XXVb; Y = $(CH_2)_5$	245	7.3	282.5	6.0
XXVc; Y = $(CH_2)_4$	244	10.0	283	5.7
XXVd; Y = CH_2-O-CH_2	237.5	9.25	272.5	2.75
XXVe; Y = $(CH_2)_3$	241	8.0	279	4.0
XXVf; Y = *o*- CH_2 C_6H_4 CH_2	244 (s)	9.0	282	5.1
XXVg; Y = $(CH_2)_2$	241	11.25	271	2.5
XXVh; Y = CH_2	254	12.25	302	4.0
XLIV	-	-	268	2.35

Since the structured nature of the band is diminished by lone pair donation to the aryl ring as well as increased planarity of the biphenyl rings it is difficult to draw conclusions about the dihedral angle of the phenyl rings as was done for the disulphones. However, steric information is available from the biphenyl conjugation band at ca.249 nm. None of the diether bridges completely inhibit this band and therefore there is no evidence that the biphenyl rings, in any of the cases examined, prefer a perpendicular orientation; or undergo a change from a cisoid to a transoid conformation such as we suggest occurs in the disulphones. The longest-bridged diethers (XXVa) and (XXVb) have very similar spectra to the unbridged diethers (see Figure 22) which is in contrast with the disulphides. This is attributed to the difference in $p\pi - p\pi$ bonding; the larger $3p$ orbital of sulphur will conjugate over a wider range of twist about the phenyl heteroatom bond than the $2p$ orbital in the ethers. Consequently conjugation in the ethers has a higher steric demand and the spectra correspond to the conjugated system until the steric restraints are severe. The 280 nm. α-band undergoes a hypsochromic shift and decrease in intensity as the bridges are shortened (see Figure 23). However for the shortest bridge (XXVh) there is a large red shift to 302 nm. and restoration of much of the lost intensity. This observation indicates that the bridge achieves a considerable degree of planarity with the phenyl rings which allows a resumption of conjugation between the oxygen atoms and the phenyl rings. The

Ultraviolet Spectra of Ethers

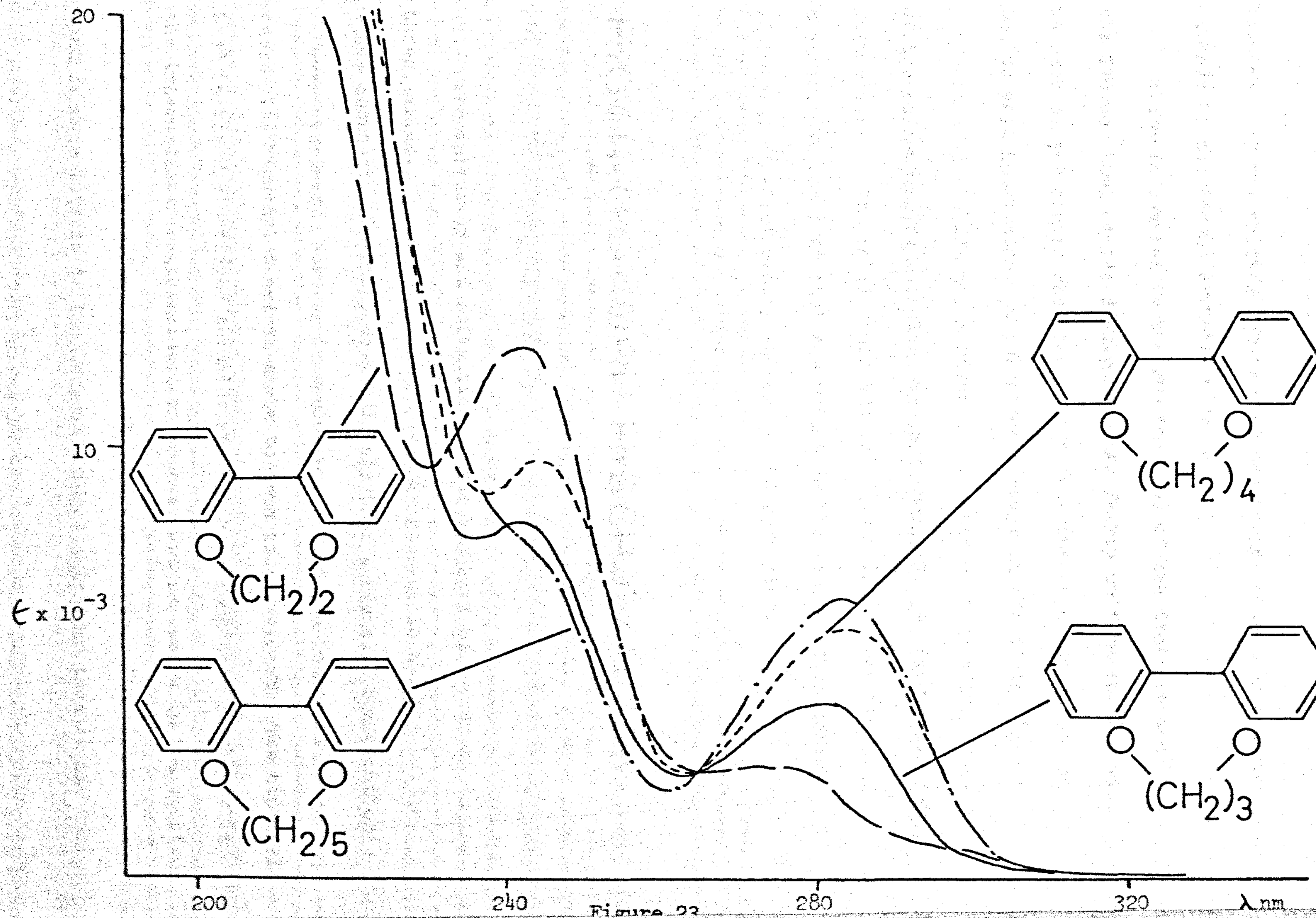


Figure 23

magnitude of the shift suggests that the phenyl ether conjugation extends to the second aromatic ring.

Although changes in the 280 nm. band of the diethers and the 270 nm. band of the disulphides are fairly uniform an exception in each series occurs when the bridge contains an oxygen atom β to the aryl heteroatom. The β-ether linkage in (XXVd) and (XVd) produces a blue shift and a reduction in intensity relative to that of the corresponding methylene-bridged compound i.e. (XXVe) and (XVe) respectively. The model compounds (XLIV) and (XLV) show the same changes. We conclude that the change is the result of inductive withdrawal of electrons by the central oxygen atom.

$Ph{\cdot}O{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}OPh$ $\quad$ $Ph{\cdot}S{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}S{\cdot}Ph$

(XLIV) (XLV)

The intensity and definition of the biphenyl band varies in the three series. Since the biphenyl band is present in all the bridged ether compounds, it would seem unlikely that a transoid conformation is ever attained. However it would appear that the longer bridges cause the biphenyl dihedral angle to open to its widest. The biphenyl band in the 2,2'-bridged sulphide and sulphone compounds is absent in the intermediate length bridged compounds, but reappears in the spectra of the oompounds having the longest bridges. However the biphenyl band is more intense in the longest bridged sulphides than in the sulphones. This indicates that both the bridged sulphides and sulphones, move from a cisoid to a transoid conformation as the length of the bridge is increased, the sulphides more readily than the sulphones. Of course, the return to a cisoid conformation in the longer bridged sulphides and sulphones cannot be ruled out, since cisoid and transoid biphenyl dihedral angles are indistinguishable from the spectra. However, by analogy with the bridged ethers, the larger sulphide and sulphone groups may be expected to lead to greater "biphenyl" dihedral angles and an eventual preference for a transoid conformation. In conclusion, the spectra show that steric effects which tend to maintain the biphenyl rings antiplanar decrease in the order: sulphone > sulphide > ether.

Experimental

Spectra were obtained in n-hexane, water (5% ethanol) and 95% ethanol solution with a Unicam SP.800 spectrophotometer. The 2,2'-biphenyl compounds were obtained as described in Part I of the thesis.

Preparation of sulphides and sulphones

Thiophenol

This was prepared by the reduction of benzene-sulphonyl chloride as described by Adams and Marvel.[53]

Sulphuric acid (435 ml) was added to crushed ice (2.6kgm) and the solution maintained between 0 - 5°. Benzenesulphonyl chloride (200g) was added over half an hour; zinc dust (400 gms) was then added in portions as rapidly as possible, with stirring, keeping the temperature below 5°. The mixture was warmed and then refluxed for three hours; the thiophenol was then removed by steam distillation. The product was separated from the distillate, dried and distilled to give thiophenol (b.p. 71°/15mm) (11.5g., 90%).

(a) Thioanisole

A solution of thiophenol (4.4g), sodium hydroxide (1.6g) and methyl iodide (5.3g) in alcohol (300 ml) were stirred for three hours. The solution was diluted with 2 - 3 volumes of water, and the product separated by ether extraction. Evaporation of the dried ether extracts gave the crude thioanisole (4.8g). A sample (1.0g) was bulb-distilled to give a purer product. Its properties were in accord with those described in the literature.[54]

A sample (500 mg) was oxidised to the sulphone by the procedure, described in the experimental section of Part I . The sulphone was isolated by evaporating off the solvent, and recrystallisation from water. Phenyl methyl sulphone m.p. 88°, had properties in accord with those described in the literature.[55]

(b) Ethyl phenyl sulphide

Prepared as for thioanisole. Its properties were in accord with those described in the literature.[56]

(c) Isopropyl phenyl sulphide

Prepared as for thioanisole, the solution being refluxed for three hours to effect reaction. The properties of the pure isopropyl phenyl sulphide were in accord with those described in the literature.[57]

(d) t-Butyl phenyl sulphide

This was prepared by the method due to Friedman, Ipatieff and Pines.[58]

t-Butyl alcohol (15.2g) was added to a stirred solution of sulphuric acid (80g) and ice (21.4g) at 0°. After stirring for fifteen minutes, thiophenol (11.0g) was added to the solution over half an hour, maintaining the temperature at 0°. After stirring for one hour at 0°, and a further hour at room temperature, the solution was poured on to ice, and the product extracted with ether. The ether solution was washed with aqueous sodium hydroxide followed by water. Evaporation of the dried ether extracts gave the almost pure t-butyl phenyl sulphide, (12.4g., 74%). Bulb-distillation of the crude sulphide gave the pure compound, the properties of which were in agreement with those described in the literature.[57]

(e) 4,4'-Biphenylylenebisethylsulphide

This compound was prepared by the method due to Adams and

Ferretti.[59]

Cuprous ethyl mercaptide

This compound was prepared by a modification of the method due to Adams, Nair and Reifschneider.[60]

Technical grade cuprous oxide (28.6g) was stirred with a refluxing solution of ethyl mercaptan (24.8g) in dry ether (500 ml) under nitrogen. After ten hours alcohol (100 ml) was added and the solution allowed to stand overnight. The product was filtered off as an off-white solid, and washed thoroughly with methanol to give the cuprous ethyl mercaptide (4.0g., 80%).

4,4'-Dibromobiphenyl

This was prepared by bromination of biphenyl in 60% yield, as described by Buckles and Wheeler.[61]

4,4'-Biphenylylenebisethylsulphide

This compound was prepared by the method due to Adams and Ferretti.[59]

A stirred mixture of 4,4'-dibromobiphenyl (6.2g), cuprous ethyl mercaptide (5.5g), quinoline (20 ml) and pyridine (2 ml) was heated at 200° for six hours. The product was cooled and poured on to a mixture of ice (100g) and hydrochloric acid (50 ml). The residue was washed with water, and crystallised from ethanol. The yellow product was recrystallised from benzene - light petroleum (after boiling with Norite) as colourless rhombs of 4,4'-biphenylylenebisethylsulphide, m.p. 133-135°, (Lit.[59] m.p. 135-136°), (90%).

A sample (0.5g) was oxidised to the disulphone, 4,4'-biphenylylenebisethylsulphone, m.p. 185-187°, (Lit.[62] m.p. 187°).

(f) (2,2)-Dimethyl-(1,3)-dithia[3.0]orthocyclophane (XV; Y = CMe_2)

This compound was prepared by the method due to Barber and Smiles [18] in 70% yield.

A sample (0.2g) was oxidised to (2,2)-dimethyl-(1,3)-dithia[3.0] orthocyclophane tetra-oxide (XXIII; Y = CMe_2) m.p. 227-229°, (Found: C, 55.6; H, 4.3. $C_{15}H_{14}S_2O_4$ requires C, 55.9; H, 4.4%).

i.r. (mull) 1320, 1050 cm^{-1} $(S(=O)_2)$

(g) (2)-Phenyl-(1,3)-dithia[3.0]orthocyclophane (XV; Y = CHPh)

This compound was prepared in a 60% yield, by the method due to Barber and Smiles.[18]

A sample (0.2g) was oxidised to (2)-phenyl-(1,3)-dithia[3.0] orthocyclophane tetra-oxide (XXIII; Y = CHPh), m.p. 236-238°, (Found: C, 62.0; H, 3.8. $C_{19}H_{14}S_2O_4$ requires C, 61.6; H, 3.8%).

i.r. (mull). 1320, 1050 cm^{-1} $(S(=O)_2)$

Di(phenylthiomethyl)ether (XLV)

A solution of thiophenol (11g) di(chloromethyl)ether (5.7g) and potassium hydroxide (5.6g) in ethanol (250 ml), was refluxed for two hours. Water (500 ml) was added to the solution, and the product extracted with ether. Evaporation of the dried ether and distillation gave di(phenylthiomethyl)ether, b.p. 134°/0.3mm Hg, (11g., 85%), (Found: C, 64.4; H, 64.1. $C_{14}H_{14}S_2O$ requires C, 64.1; H, 5.4%).

Synthesis of ethers

(a) Anisole and phenetole were commercial products.

(b) Isopropyl phenyl ether

Phenol (9.4g) and isopropyl bromide (12.3g) were added to a solution prepared from sodium (2.3g) in ethanol (300 ml). After refluxing for six hours, the alcoholic solution was evaporated (to 50 mls) and diluted with aqueous 10% potassium hydroxide (100 ml), and the product extracted with ether. Evaporation of the dried ether extracts gave a colourless liquid, a sample of which was bulb-distilled to give isopropyl phenyl ether.[63] (Yield = 70%) (b.p. 177°)

t-Butyl phenyl ether

This compound was prepared by the method due to Baddely, Smith and Vickars.[47]

Isobutene, generated by refluxing a solution of t-butanol (2 parts) and 30% sulphuric acid (1 part) was passed into a mixture of phenol (47g), carbon tetrachloride (250 ml) and sulphuric acid (two drops) at ca 8° until reaction was complete. The carbon tetrachloride solution was washed with aqueous 10% sodium hydroxide, dried and evaporated to give the ether. A sample was bulb-distilled to give t-butyl phenyl ether, (31g., 45%). (b.p. 60°/ 8mm Hg)

Di(phenoxymethyl)ether (XLIV)

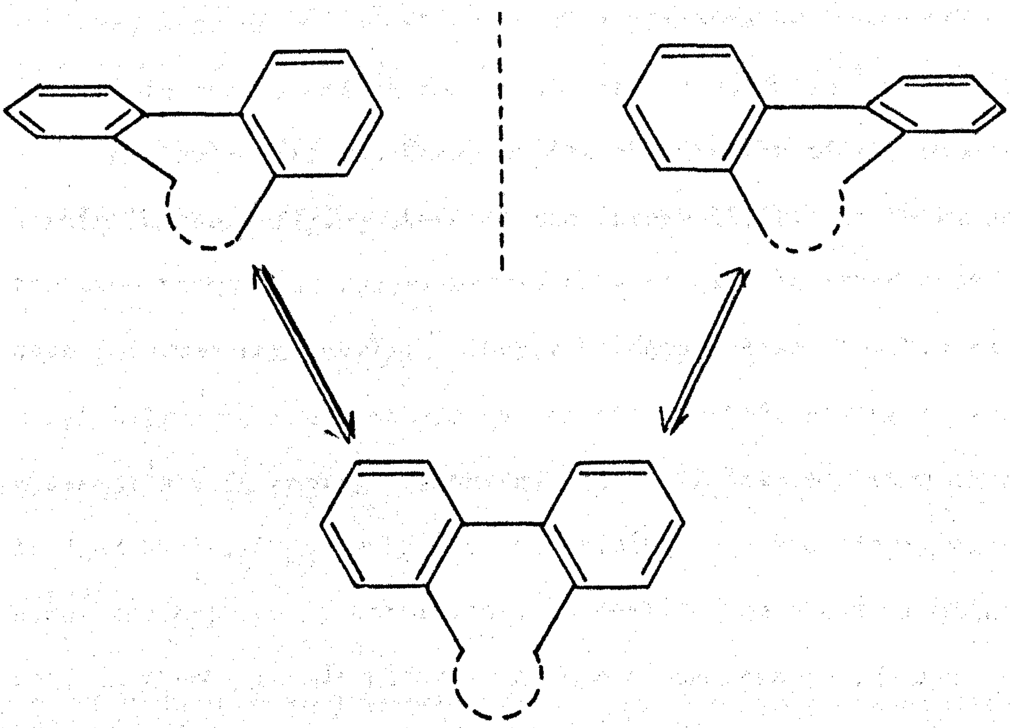
Phenol (9.4g) and di(chloromethyl)ether (5.7g) were dissolved in a solution from sodium (2.3g) in ethanol (250 mls), and then refluxed overnight. Filtration of the solution followed by evaporation of the alcohol gave a solid which crystallised from 95% ethanol as prisms of <u>di(phenoxymethyl)ether</u>; its properties were in accord with the literature.[64]

PART III

Partial Resolution of Optically Active 2,2'-Bridged Dithia Biphenyls. The Use of Variable Temperature N.M.R. and Polarimetric Measurements to Estimate Racemisation Energy Barriers

In Part II of this thesis the geometry of the 2,2'-bridged biphenyl systems was interpreted through the use of ultraviolet spectroscopy and Drieding models. Another parameter, which is related to the geometry of the molecules, is the energy barrier which separates the enantiomeric forms of the disymmetric biphenyl systems. This energy barrier, known as the energy of racemisation, is the energy required to convert one enantiomer into the other enantiomeric form. For conformational stability at room temperature the free energy $(\Delta G^{\ddagger})$ of the barrier must be at least ca 23kcals. mol^{-1}.[65]

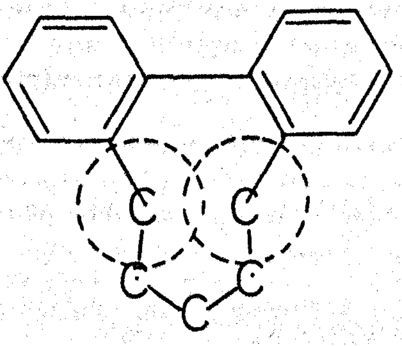
For the 2,2'-bridged biphenyls this process simply involves rotating the biphenyl rings, causing the α - and ω -bridging atoms to slip past each other. Normal bridges (from two to seven atoms) restrict the interconversion process to a 'cisoid racemisation' process although if a long enough bridge is present a choice of 'cisoid' or 'transoid racemisation' would obtain. The racemisation process may be represented as follows:

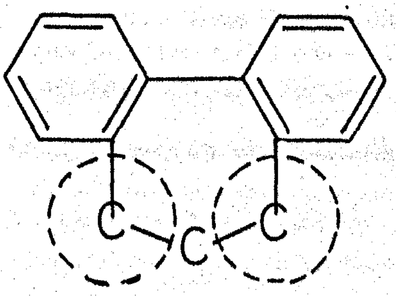


PLANAR INTERMEDIATE

The process is visualised to proceed via an intermediate in which the biphenyl rings are coplanar. This intermediate represents the molecule in its highest energy state during the racemisation process. By measuring the extent by which the bond angles of the bridging atoms are distorted from normality, in accurate models of various intermediates, estimates of the energies of racemisation were obtained by Mislow.[40] Although the calculations were in harmony with experimental results, determined by polarimetry, this may have been due to a fortunate cancellation of errors. Nevertheless, such an empirical approach represents an important step forward in understanding the nature of the racemisation process.

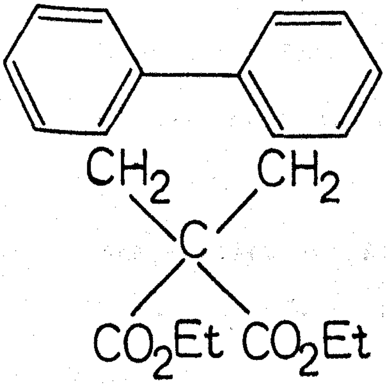
Mislow's work was based on the calculation of the bond angle strain in the bridging atoms of the intermediate. In fact, only the two-, three- and four-membered bridges give intermediates which have deformed bond angles. Longer bridges are so flexible that completely strainless models can be constructed, giving a zero apparent strain energy. Although models of intermediates of 2,2'-bridged biphenyls with bridges containing more than four bridging atoms are apparently strainless, in reality the steric repulsion between the α- and ω- atoms is at a maximum because of their close approach:

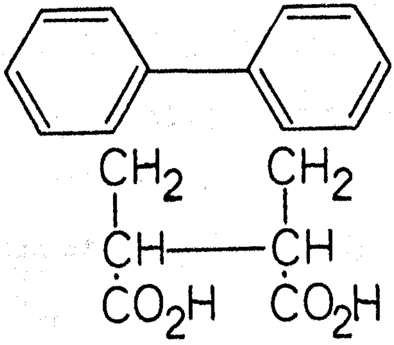


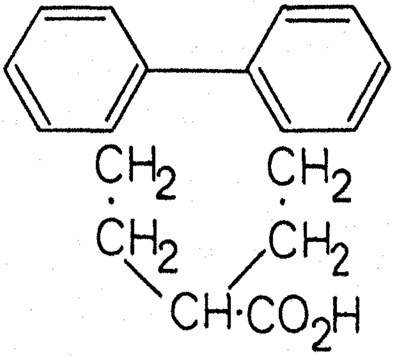


Thus new angle strain must be set up as the two conflicting atoms are forced apart by the opposing van der Waals' forces. In 1962, Mislow compared the energies of racemisation of the homocyclic

2,2'-bridged biphenyls (XLVI), (XLVII) and (XLVIII), and found the barriers to be of similar magnitude, i.e. $\Delta G^{\ddagger} \sim 24$ kcal. mol^{-1}.[40]


(XLVI)


(XLVII)


(XLVIII)

Although the effect of ring substituents on the racemisation process is unknown, Mislow suggested these effects should be small,[40] and that the similar energy barriers for the biphenyl systems were the result of two cancelling effects. Thus the bond angle strain which decreases with bridge length, and the repulsive van der Waals forces which increase with bridge length compensate each other, giving similar energy barriers within the homocyclic series.

However, since Mislow's earlier work the stereochemistry of three-membered 2,2'-bridged biphenyls which have heteroatoms incorporated into the centre of bridge, have been studied.[49, 66] A feature of all the three-membered bridge compounds is the readiness with which they undergo racemisation at room temperature, even when the large sulphone group is incorporated into the bridge. The three-membered 2,2'-bridged biphenyl (XLVI) claimed to have been prepared in optically active forms by Ifland and Siegel in 1958[67] and to have a $\Delta G^{\ddagger}$ of interconversion of 23.3 kcals.mol^{-1}, has in fact a very low racemisation barrier, i.e. $\Delta G^{\ddagger} \sim$ 14 kcal.mol^{-1}.[66] Such a low interconversion barrier implies that chemical resolution of the enantiomers as described by Ifland and Siegel would be impossible under the conditions described. As a consequence of this, the earlier conclusions of Mislow about the stability of the series of homocyclic 2,2'-bridged biphenyls (XLVI), (XLVII) and (XLVIII) were incorrect.

The thermal instability of the three-membered bridged biphenyls to racemisation may have its origin not in bond angle strain but in another phenomenon. Turner [68] in 1958 suggested that the steric interaction between the α - and ω- atoms of the bridge is of considerable importance. Thus bridged biphenyls which have the van der Waals' envelopes of the α - and ω - atoms in the bridge close or touching each other will racemise more easily than where the repulsive envelopes are well separated. This is demonstrated in the homocyclic 2,2'-bridged biphenyls compounds (XXXVIII; n=0), (XLVI), (XLVII) and (XLVIII). (See Table 5):

Table 5

Free energy barriers of racemisation: a series of homocyclic 2,2'-bridged biphenyls.

Compound	Dihedral Angle	$\Delta G^{\ddagger}$ kcals. mol^{-1}
XXXVIII; n = 0	20	< 9*
XLVI	45	14.5* (23.3)
XLVII (CIS)	60	23.3
XLVIII	> 60	24.5

* Determined by n.m.r.

A similar trend has also been noted by Mann et al.[60] for a series of 2,2'-bridged biphenyls having arsonium groups in the α- and ω-positions of the bridge.

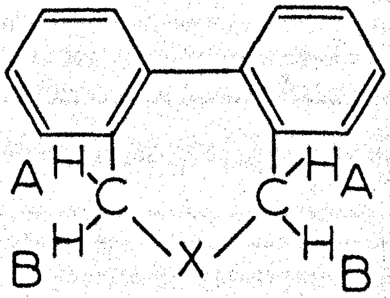
The interpretation of the energy of racemisation of 2,2'-bridged biphenyls is still not entirely clear. However, two factors appear to be important in increasing the stability of the conformers. Firstly, large heteroatoms or heteroatom groups stiffen the bridge, and also have a greater steric effect relative to the small carbon atom if in the α-, and ω- positions in the bridge. Secondly, optical stability is greatly increased if the bridge has four or more members.

Two methods are available for the measurement of the racemisation barrier; polarimetry and nuclear magnetic resonance. Polarimetry is usually used to study compounds which are optically stable at room temperature i.e. having an energy barrier $\Delta G^{\ddagger} > 23$ kcal .mol.$^{-1}$ On the other hand, n.m.r. can only determine lower energy processes, i.e. those for which $\Delta G^{\ddagger} < 23$ kcal.. mol^{-1}. Both methods are thus in a sense complementary to one another. Although each method suffers from certain disadvantages, much valuable information has been obtained by their use concerning the racemisation energy for bridged biphenyls.

The polarimetric method utilises the optical activity of suitable biphenyls. Thus a suitably bridged biphenyl is resolved (usually by the classical method using the formation of diastereoisomers) into its optically active components. The rates of interconversion between the two enantiomers are then followed by observing the loss of optical rotation with time, at each of several temperatures (suitable temperatures for use are obviously governed by the size of the energy barrier). With knowledge of the rate constants for the racemisation process at several temperatures, it is a simple matter to calculate the thermodynamic functions for the process. (For details of the method, see Luttringhaus and Rosenbaum.[50]).

Because the biphenyls must be resolved for this method to be used, suitable carboxy, hydroxy groups etc. must be present to act as "handles" for the classical diastereoisomer resolution method. This is a disadvantage, because of the unpredictable effect they will have in affecting the value of the energy barrier. A more generally advantageous method is partial optical resolution by column chromatography. Luttringhaus[25] achieved the partial resolution of several racemates using a chromotographic column packed with acetylcellulose, and the method is claimed to be of very general application. The method of separation involves the formation of unstable "diastereoisomers" at the absorbent surface, each of which elutes at a different rate. Thus compounds without "handles" on them can be successfully partially resolved, a considerable advantage over the classical method. (For the determination of rate constants, it is sufficient to have only partially resolved species present, providing that a reasonable optical rotation can be observed).

The n.m.r. method depends on the interconversion of magnetically non-equivalent protons. If we take as our example systems of the type (XLIX), each methylene group is magnetically identical, having two non-magnetically equivalent protons; H_A and H_B:



(XLIX)

The presence of two magnetically different protons can give rise to a symmetrical four-line AB pattern. When one enantiomer interconverts to its mirror image, the magnetically dissimilar protons switch positions, proton H_A becoming proton H_B, etc. Because the n.m.r. process measures the protons on a time average scale, i.e. a proton must remain in a given environment for a certain minimum period of time to be recorded as a distinct species, a rapid interconversion of the protons will only be recorded as a single peak in the spectrum. Thus by recording the spectrum at a low temperature where the interconversion rate is slower, a fully resolved AB pattern can be obtained, and at a sufficiently high temperature a sharp singlet may be recorded. Somewhere between these two temperatures the spectrum of the protons will appear as a broad peak (the coalescence temperature). From a knowledge of the coalescence temperature, the coupling constant and the chemical shift between the two protons in the resolved AB pattern, the free energy of the interconversion process can be calculated, by the use of two simple equations.

$$Kc = \frac{\pi(\Delta\nu^2 + 6J_{AB}^2)^{\frac{1}{2}}}{\sqrt{2}} \quad \text{---} \; ①$$

and $$\Delta G^{\ddagger} = 4.57\,Tc\,(10.32 + \mathrm{Log}\,\frac{Tc}{Kc}) \quad \text{---} \; ②$$

where Kc is the rate of proton exchange at the coalescence temperature Tc, and J_{AB} is the coupling constant and $\Delta\nu$ the chemical shift separation of the H_A and H_B protons in the resolved spectrum.

Unfortunately the AB pattern does not always occur in the spectrum, even when it is expected. The chemical shifts of the protons may be very similar, or the solvent can cause the shifts to be similar. Lack of an AB pattern in a spectrum does not necessarily mean the biphenyl system is interconverting rapidly at that temperature; it is important to observe the structure of the AB pattern change to a singlet.

A number of the 2,2'-bridged dithia biphenyls appeared excellent systems on which to attempt variable temperature n.m.r. studies. All the compounds with isolated methylene groups gave clearly resolved AB patterns at room temperature so the spectra were recorded at elevated temperatures to induce the patterns to collapse. In fact all the AB patterns remained fully resolved up to the instrumental limit of 200°. (A higher temperature might decompose the compounds, in any case). Calculation of the minimum energy of racemisation for these systems (using the highest temperature obtained in place of Tc, in formulae ②) showed that all the compounds would have a free energy barrier greater than the 23 kcal.mol^{-1} necessary for optical stability at room temperature. (See Table 6) Thus the following compounds would be optically stable at room temperature:

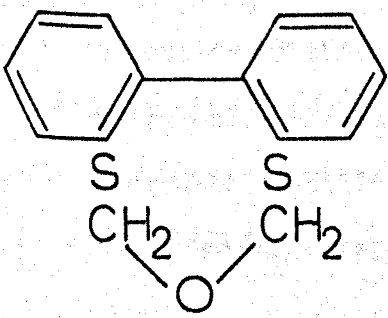
Table 6

Minimum free energy barriers of racemisation: some 2,2'-bridged dithia biphenyls.

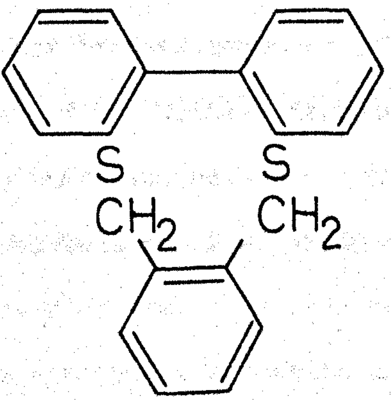
Compound	Solvent	$\Delta\nu_{AB}$ c/s	J_{AB} c/s	T max ^{o}K.	$\Delta G^{\ddagger}$ min. kcals.mol^{-1}
XIX; n = 1	DCB	18.5	11.5	473	24.0
XX	DCB	13.5	15	473	23.9
XXI	TCB	14.5	14.5	473	23.9
XXX; Y = CH_2	TCB	26	14.5	473	23.8
XXX; Y = *m* $CH_2 \cdot C_6H_4 \cdot CH_2$	TCB	30.5	16	473	23.7

TCB = 1,3,5-trichlorobenzene

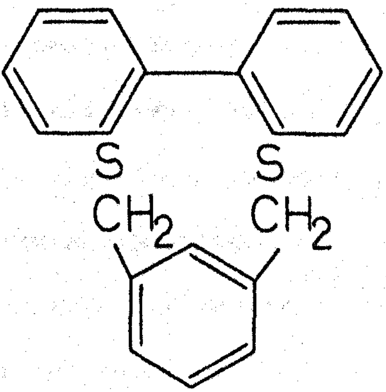
DCB = *o*-dichlorobenzene



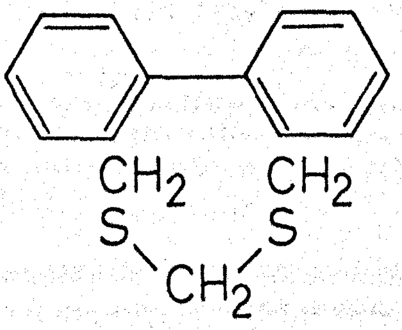
(XIX; n=1)



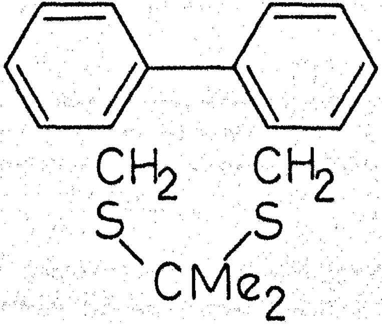
(XX)



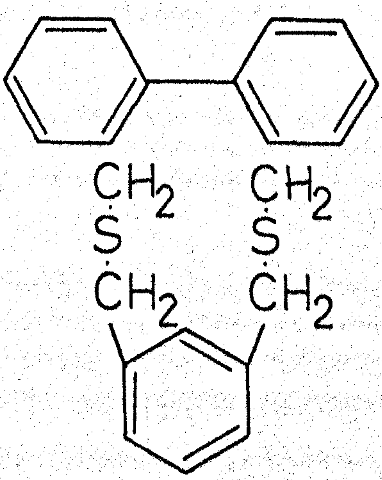
(XXI)



(XXX; Y=CH_2)



(XXX; Y=CMe_2)



(XXX; Y=$CH_2\cdot C_6H_4\cdot CH_2$)

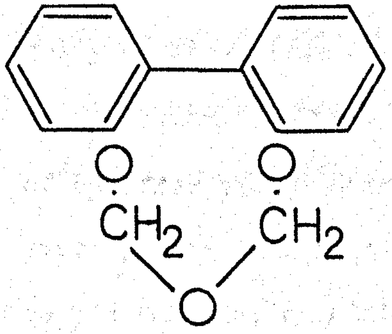
The dimethylene bridged dithia biphenyl (XVIII; n=2) also exhibits a complex A_2B_2 pattern which remains invariant up to 200°, and this compound is also likely to be optically stable at room temperature. These results gave confidence that all the 2,2'-bridged dithia biphenyls should be resolvable with the possible exception of the smallest bridged compound (XVII; n=1). The tetra-oxide derivatives of the dithia compounds should have increased stability to racemisation.

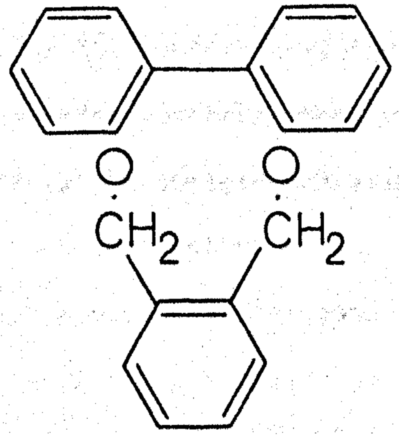
Having established that the 2,2'-bridged dithia biphenyls should be stable to interconversion at room temperature, it seemed logical to examine the variable temperature n.m.r. of the ether analogues to assess their stability. (See Table 7). The two 2,2'-bridged ether compounds with isolated methylene groups and the dimethylene bridged compound were selected as systems which would be most likely to yield information about the interconversion energy barrier, i.e. the compounds shown on the following page:

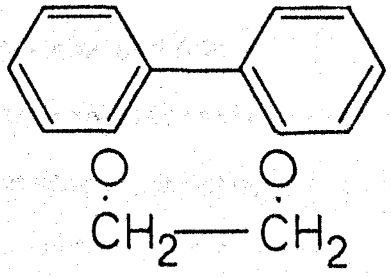
Table 7

Free energy barriers of racemisation: some 2,2'-bridged ether biphenyls

Compound	Solvent	$\Delta\nu_{AB}$ c/s	J_{AB} c/s	Tc ^{o}K	$\Delta G^{\ddagger}$kcal.mol^{-1}
XXIX; n = 1	$CDCl_3$	-	-	-	-
XXVII; n = 2	$CDCl_3$	15	-	311	$\sim$ 16
XXVIII	$CDCl_3$	7.6	11.2	299	15.0


(XXIX; n=1)


(XXVIII)


(XXVII; n=2)

The first compound to be examined was the dimethylene bridged diether (XXVII; n=2). The four methylene protons gave a structureless broad peak at 5.8τ at 38°. On cooling to 0° a resolved complex A_2B_2 pattern was obtained, while on heating the solution the methylene protons were observed as a singlet at 100°. (See Figure 24). Estimation of the free energy for the inversion process is very difficult because of the complexity of the spin coupling. However, the fact that interconversion on the n.m.r. time scale occurs at room temperature, indicates the extreme lability of the system compared with the more stable sulphur analogue. The energy barrier for the interconversion process was estimated to be ca 16 kcals.mol^{-1}, from the half peak width at the coalescence temperature using equations ② and ③.

$$Kc = \frac{\pi \Delta \nu}{\sqrt{2}} \quad --- \quad ③$$

where $\Delta\nu$ equals the half peak width at coalescence. (It is fully realised that equation ③ applies strictly to the unsplit H_A H_B system.[70]) Since the major governing factor in the estimation of the free energy barrier is the coalescence temperature, an error in the rate of exchange constant will be less serious, and such a calculation although approximate is meaningful.

The methylene protons of the o-xylylene bridged compound (XXVIII) gave a four line AB pattern at 0° which collapsed to a singlet at 100° (see Figure 25). From the temperature of coalescence (26°), the coupling constant and chemical shift separation of the two protons the free energy barrier of interconversion was calculated to be 15.0 $kcals.mol^{-1}$.

Finally, the methylene protons of the triether (XXIX; n=1) gave a singlet down to -60° in the solvent used ($CDCl_3$). This must be a case of chemical equivalence due to an effect other than a rate process. The calculated energy barriers of the two 2,2'-bridged diether biphenyls (XXVII; n=2) and (XXVIII) are well below that of the minimum free energy needed for optical stability at room temperature, i.e. $23kcal.mol^{-1}$. (See Table 7)

Having established the lability of the 2,2'-bridged diether biphenyls, and the stability of the 2,2'-bridged dithia biphenyls, it was decided to try and partially resolve the racemic compounds by the method used by Luttringhaus et al.[25] As mentioned on page 117 Luttringhaus succeeded in partially resolving several racemic compounds

N.m.r. of the dimethylene bridged diether (XXVII; n=1)

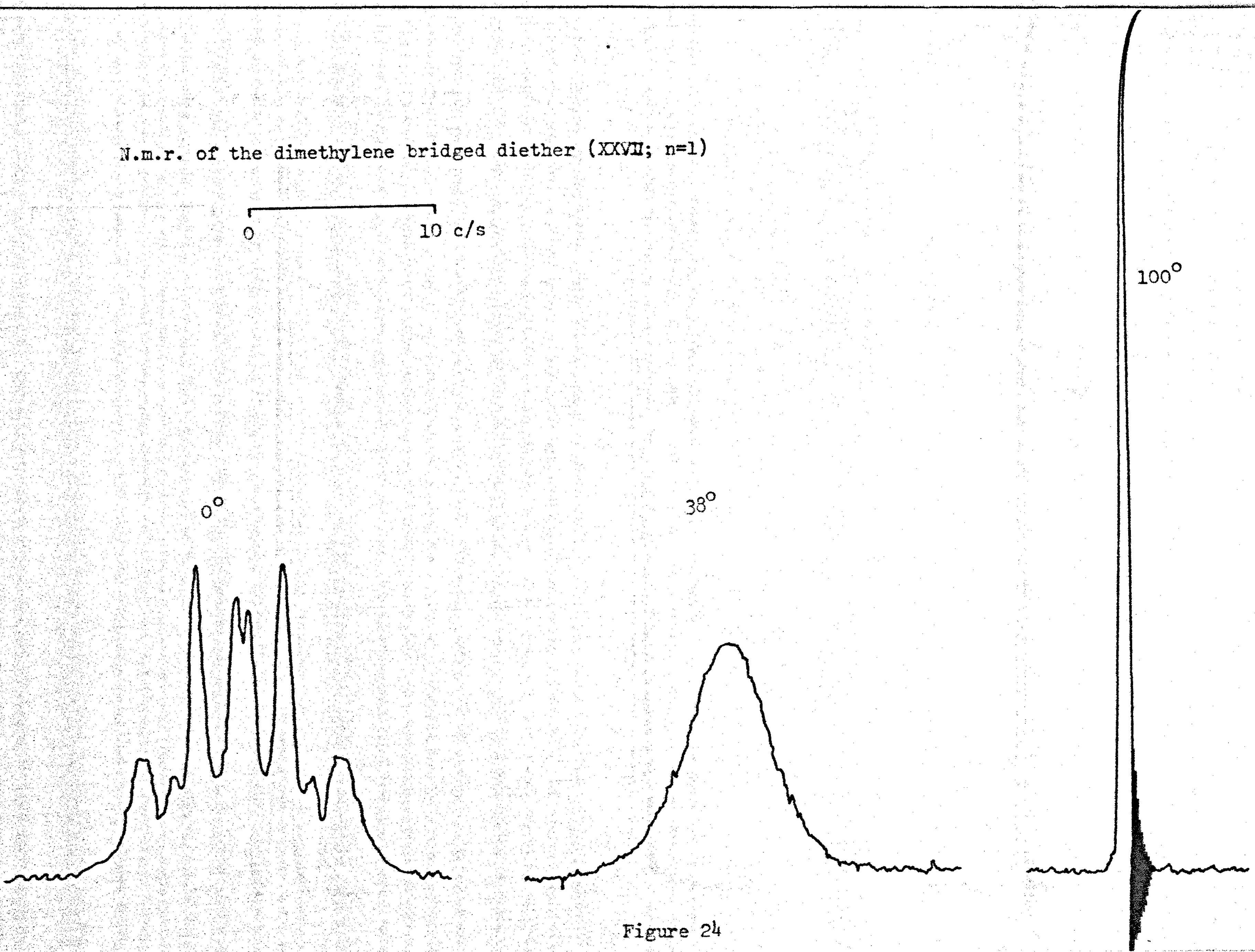


Figure 24

N.m.r. of the diether (XXVIII)

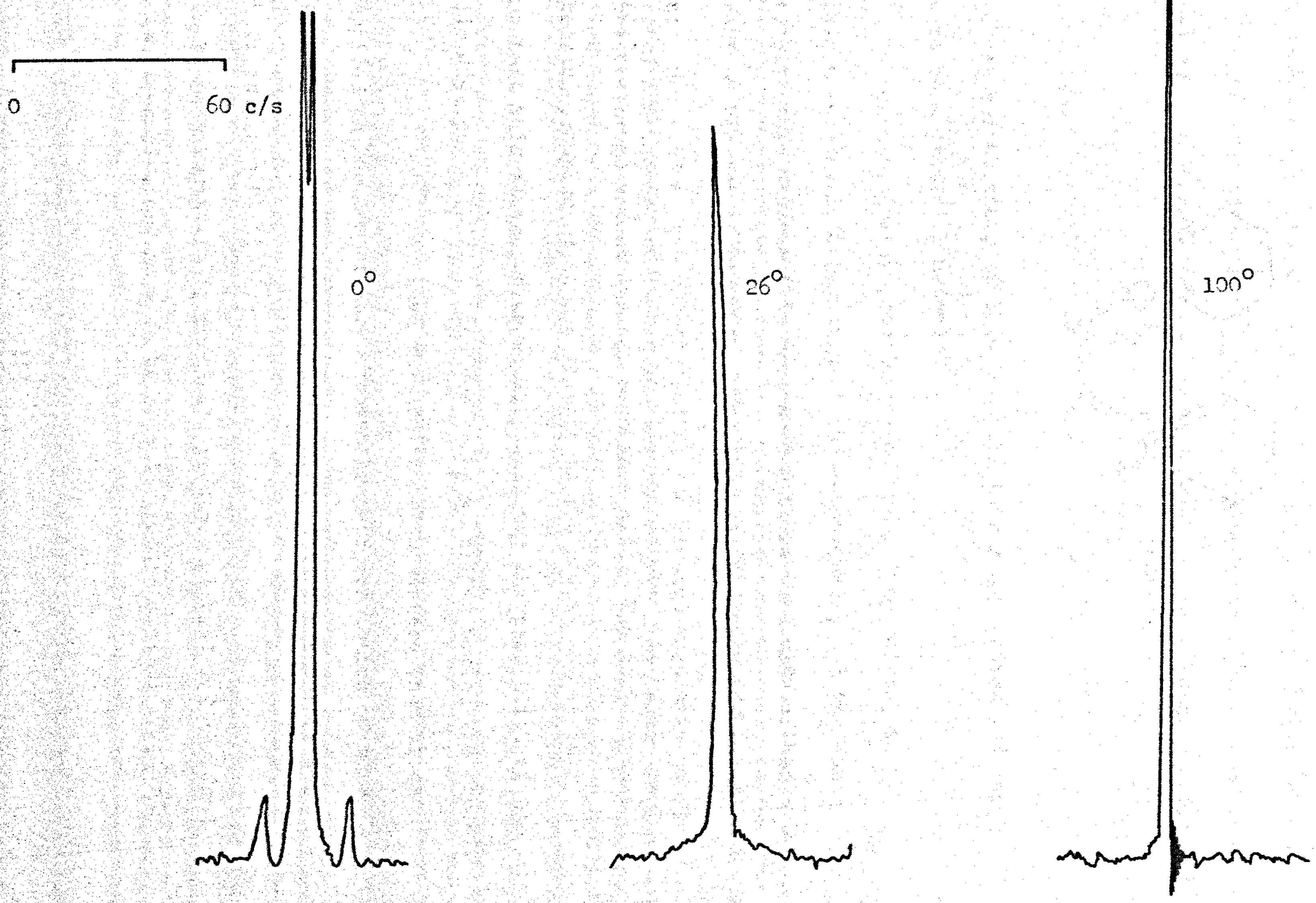
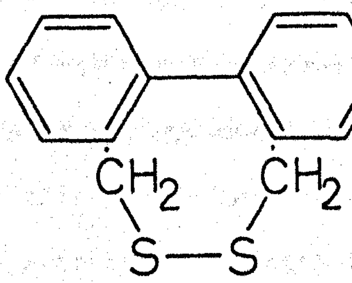


Figure 25

including the cyclic disulphide (XXXI):



(XXXI)

The close relationship of this compound to our own series indicated this to be a promising method.

The chromatography procedure requires a long column, to achieve a reasonable separation of the enantiomers; and the Woelm acetylcellulose absorbent is recommended to be used with either ethanol or benzene as eluents. For the cyclic disulphide (XXXI), benzene was used as the eluent, and it was assumed that this would be the preferred eluent for our compounds also. The toxic nature of benzene prompted us to use toluene in its place, and we have found that this eluent works equally well for the resolution of the cyclic disulphide (XXXI). Besides being much less toxic, the use of toluene (m.p. -95°) may have the additional advantage that it can be applied to low temperature chromatographic resolution of more labile compounds; this is impossible with benzene because of its high freezing point (5.5°).

We have successfully partially resolved several 2,2'-bridged dithia biphenyls, and hope to be able to resolve further compounds in future work. The method apparently fails with a number of compounds, but this may be due to the limitations of our polarimeter. As might be expected, the smallest three-membered bridged compound (XVIII; n=1) was one of the compounds which remained inactive after chromatography. In this particular oompound the failure to effect a separation may be attributed to inherent lability. We have measured the racemisation of one of the cyclic dithia compounds (XIX; n=1) at several temperatures, and from the resulting rate constants, have calculated the values of the thermodynamic functions for the process to be: $\Delta Ea = 27.1$ kcal.mol^{-1}, $\Delta G^{\ddagger} = 27.2$ kcal.mol^{-1}, $\Delta H^{\ddagger} = 26.4$ kcal.mol^{-1} and $\Delta S^{\ddagger} = -2.3$ cal.mol^{-1} deg.$^{-1}$ (For method see experimental section). The value of the free energy is higher than that of the homocyclic compound (XLVIII) which confirms the higher stability of the systems to interconversion, when carbon atoms are replaced by the larger sulphur atoms. This effect has also been reported by Luttringhaus in the four-membered 2,2'-bridged biphenyl compounds.[50]

Obviously the next stage will be to carry out optical rotation studies on the other partially resolved compounds, and calculate the barriers of racemisation. This would supply some very important information, especially if the barriers of the longest bridged compounds can be measured.

In conclusion, the lability of the 2,2'-bridged ether biphenyls in comparison with the very much higher optical stability of the sulphur compounds has been established. This large difference in stability may be attributed in part to the large difference between the size of the sulphur and oxygen atoms. So far it has been assumed that the sulphones will be the most optically stable compounds, and to show that this is the case it may be worth while oxidising the partially resolved disulphides to their disulphone derivatives, and measuring the barriers to inversion of the optically active disulphones.

Experimental

Variable temperature n.m.r. experiments were performed on a Perkin-Elmer 60 megacycle instrument fitted with a variable temperature probe. Temperatures were measured with a thermocouple.

Optical rotations were measured on a Bellingham and Stanley visual polarimeter fitted with a sodium lamp.

Optical rotations kinetic studies were performed at Sheffield University on a Bellingham and Stanley Polarimatic 62 instrument, using a 0.5 cm quartz cell.

All the 2,2'-bridged dithia biphenyls were prepared as described in Part I of this thesis.

The 'Woelm' acetylcellulose was obtained from Koch Light Ltd.

Shell 'technical' grade toluene, pre-dried over calcium chloride, and then dried over sodium wire, was used as eluent.

Partial resolution of the racemic dithia compounds

(a) (1,3)-Dithia[3.0]orthocyclophane (XVIII; n=1)

Acetylcellulose (200g) was ground in an alumina ball-mill and passed through a 100 mesh B.S. sieve. The fines were allowed to stand under dry toluene for 48 hours in order to allow the cellulose to swell. The resulting slurry was poured into a 120 x 2 cm column, and dry toluene (200 ml) allowed to percolate through. The dithia compound (XVIII; n=1), in toluene (10 ml) was admitted to the column, and eluted with dry toluene at a rate of 12.5 mls an hour. After 350 mls of eluent had passed through the column, 10 mls fractions were collected under pressure until all the product was eluted from the column. The fractions containing the dithia compound were located by t.l.c. and examined polarimetrically, using 10.0 cm tubes. Rotations were measured using the sodium D line and are direct readings, not specific rotations. (Unnecessary evaporation processes were avoided, to minimise racemisation of the compounds.)

Results (w - weak, m - medium, s - strong)

Fraction	Volume ml	Rotation α_D°	Solution Strength
1	10	0.0	w
2	"	"	w
3	"	"	m
4	"	"	s
5	"	"	s
6	"	"	s
7	"	"	s
8	"	"	m
9	"	"	m
10	"	"	w
11	"	"	w
12	"	"	w

(b) (1,4)-Dithia[4.0]orthocyclophane (XVIII; n = 2)

A solution of the dithia compound (XVIII; n=2) (1.0g) in toluene was eluted down the above column (a column can be used repeatedly, provided pure compounds are used) in the same manner to give the following results:

Fraction	Volume ml	Rotation α_D°	Solution Strength
1	10	0.0	w
2	"	+0.2	m
3	"	+0.4	s
4	"	+0.2	s
5	"	0.0	s
6	"	-0.1	s
7	"	-0.2	s
8	"	-0.2	s
9	"	-0.2	m
10	"	-0.1	m
11	"	0.0	w

(c) (1,5)-Dithia[5.0]orthocyclophane (XVIII; n=3)

A solution of the dithia compound (XVIII; n=3) (0.7g) in toluene (10 mls) was eluted down the above column in the usual manner. On examination of the active fractions by polarimetry the following results were obtained:

Fraction	Volume ml	Rotation $\alpha_D{}^{\circ}$	Solution Strength
1	10	0.0	
2	"	+0.1	m
3	"	+0.45	s
4	"	+0.2	s
5	"	-0.1	s
6	"	-0.2	s
7	"	-0.2	s
8	"	-0.2	s
9	"	-0.1	m
10	"	0.0	w

(d) (1,6)-Dithia[6.0]orthocyclophane (XVIII; n=4)

A solution of the dithia compound (XVIII; n=4) (1.0g) in toluene (20 mls) was eluted through the column as above. On examination of the fractions no optical rotation was recorded. (Possibly due to lack of sensitivity of the instrument.)

(e) (1,5)-Dithia-(3)-oxa[5.0]orthocyclophane (XIX; n=1)

The dithia compound (XIX; n=1) (1.0g) in toluene (10-20 mls) was eluted through the column as usual. On examination of the active fractions by polarimetry the following results were obtained.

Fraction	Volume ml	Rotation $\alpha_D{}^o$	Solution Strength
1	10	+0.3	w
2	"	+3.3	s
3	"	+2.0	s
4	"	+0.5	s
5	"	-0.5	s
6	"	-1.0	s
7	"	-1.1	s
8	"	-1.1	s
9	"	-0.7	s
10	"	-0.7	s
11	"	-0.5	s
12	"	-0.3	m
13	"	-0.2	w

(f) (1,7)-Dithia-(4)-oxa[7.0]orthocyclophane (XIX; n=2)

A solution of the dithia compound (XIX; n=2) (1.0g) in toluene (10-20 mls) was eluted through the column, and the fractions gave the following rotations:

Fraction	Volume ml	Rotation α_D°	Solution Strength
1	20	+0.35	s
2	"	+0.05	s
3	10	-0.15	s
4	"	-0.2	s
5	"	-0.15	s
6	"	-0.1	s
7	"	-0.1	s
8	"	-0.05	m
9	"	0.0	w

(g) (1,10)-Dithia[2.2.0]orthocyclophane (XX)

The dithia compound (XX) (1.0g) in toluene (10-20 mls) was eluted down the column in the manner described. Examination of the fractions by polarimetry showed the compound to be unresolved.

(h) (3,4:5,6)-Dibenzo-(2,7)-dithia[8]metacyclophane (XXI)

A solution of the dithia compound (XXI) (1.0g) in toluene (10-20 mls) was eluted down the acetylcellulose column in the above manner; the active fractions yielded the following rotations:

Fraction	Volume ml	Rotation α_D°	Solution Strength
1	10	+0.05	m
2	"	+0.15	s
3	"	+0.25	s
4	"	+0.2	s
5	"	0.0	s
6	"	-0.15	s
7	"	-0.20	s
8	"	-0.1	s
9	"	-0.1	s
10	"	-0.05	m
11	"	-0.05	m
12	"	0.0	w

(i) (2,4)-Dithia[5]orthocyclophane (XXX; $Y=CH_2$)

A solution of the dithia-orthocyclophane (XXX; $Y=CH_2$) (0.7g) in toluene (5-10 mls) was eluted down the acetylcellulose column in the usual way. The fractions showed the following rotations:

Fraction	Volume ml	Rotation $\alpha_D{}^{\circ}$	Solution Strength
1	10	0.0	w
2	"	+0.1	m
3	"	+0.45	s
4	"	+0.4	s
5	"	+0.2	s
6	"	-0.1	s
7	"	-0.35	s
8	"	-0.35	s
9	"	-0.25	s
10	"	-0.1	m
11	"	-0.0	w

Racemisation Rate studies on optically active (1,5)-dithia-(3)-oxa[5.0]orthocyclophane (XIX; n=1)

Solutions of the optically active dithia compound (XIX; n=1) (ca 100 mg) in xylene (5 ml) were used (each solution was used for several kinetic runs). For the kinetic studies, a thermostatted water-heated 0.5 cm optical cell was used, and a period of ten minutes was allowed between filling the cell and the first optical rotation reading. The racemisation was followed by continuous measurement of the rotation at a wavelength of 370 nm. Results were obtained at five different temperatures (See Tables 8 - 12) the rate constants (See Table 13) being calculated from the half life of the reaction by the following equation. (Half life obtained by plotting log K_t against time.)

$$K_t = \frac{0.69}{t_{\frac{1}{2}}} \sec^{-1}$$

where K_t is the rate constant and $t_{\frac{1}{2}}$ is the half-life of the reaction in seconds.

The activation energy for the racemisation process was obtained from the rate constants graphically using the Arrhenius equation (See Graph)

$$\text{Log } K_t = - \frac{Ea}{2.303 \, RT} + \text{Log } K_o$$

where K_t is the rate constant, R is the gas constant, T is the temperature in degrees K and Ea is the activation energy of the process.

The enthalphy of activation ($\Delta H^{\ddagger}$) is easily obtained from the energy of activation using the relationship

$$\Delta H^{\ddagger} = \Delta Ea - RT$$

where T is the average temperature of the experiments in degrees K.

The free energy of activation ($\Delta G^{\ddagger}$) is obtained using the Eyring equation:

$$\Delta G^{\ddagger} = - 4.573 T \text{Log } \frac{K_t . h}{T \; K_B}$$

where h is Planck's constant and K_B is the Boltzmann constant.

Finally, the entropy of activation ($\Delta S^{\ddagger}$) is obtained from the equation

$$\Delta S^{\ddagger} = \frac{\Delta H^{\ddagger} - \Delta G^{\ddagger}}{T}$$

TABLE 8

Racemisation of (-) (XIX; n=1) at 65.0° ± 0.2°

Time (min)	Rotation α°_{370}
0	0.1655
33	0.1615
67	0.1560
122	0.1470
155	0.1390
186	0.1345
217	0.1295
251	0.1240
282	0.1195
315	0.1150
360	0.1090

TABLE 9

Racemisation of (+) (XIX; n=1) at 69.0° ± 0.2°

Time (min)	Rotation α°_{370}
0	0.159
48	0.1465
90	0.136
130	0.1265
170	0.118
207	0.1105
246	0.102

TABLE 10

Racemisation of (+) (XIX; n=1) at 76.0° ± 0.2°

Time (min)	Rotation α°_{370}
0	0.158
15.5	0.148
40.5	0.1335
64.5	0.121
80	0.113
90	0.1095
105	0.103
118	0.096

TABLE 11

Racemisation of (+) (XIX; n=1) at 80.8° ± 0.2°

Time (min)	Rotation α°_{370}
0	0.167
36	0.127
71	0.0985
106	0.078
141	0.062
174	0.050
208	0.0395
264	0.025
300	0.020

TABLE 12

Racemisation of (+) (XIX; n=1) at 85.0° ± 0.2°

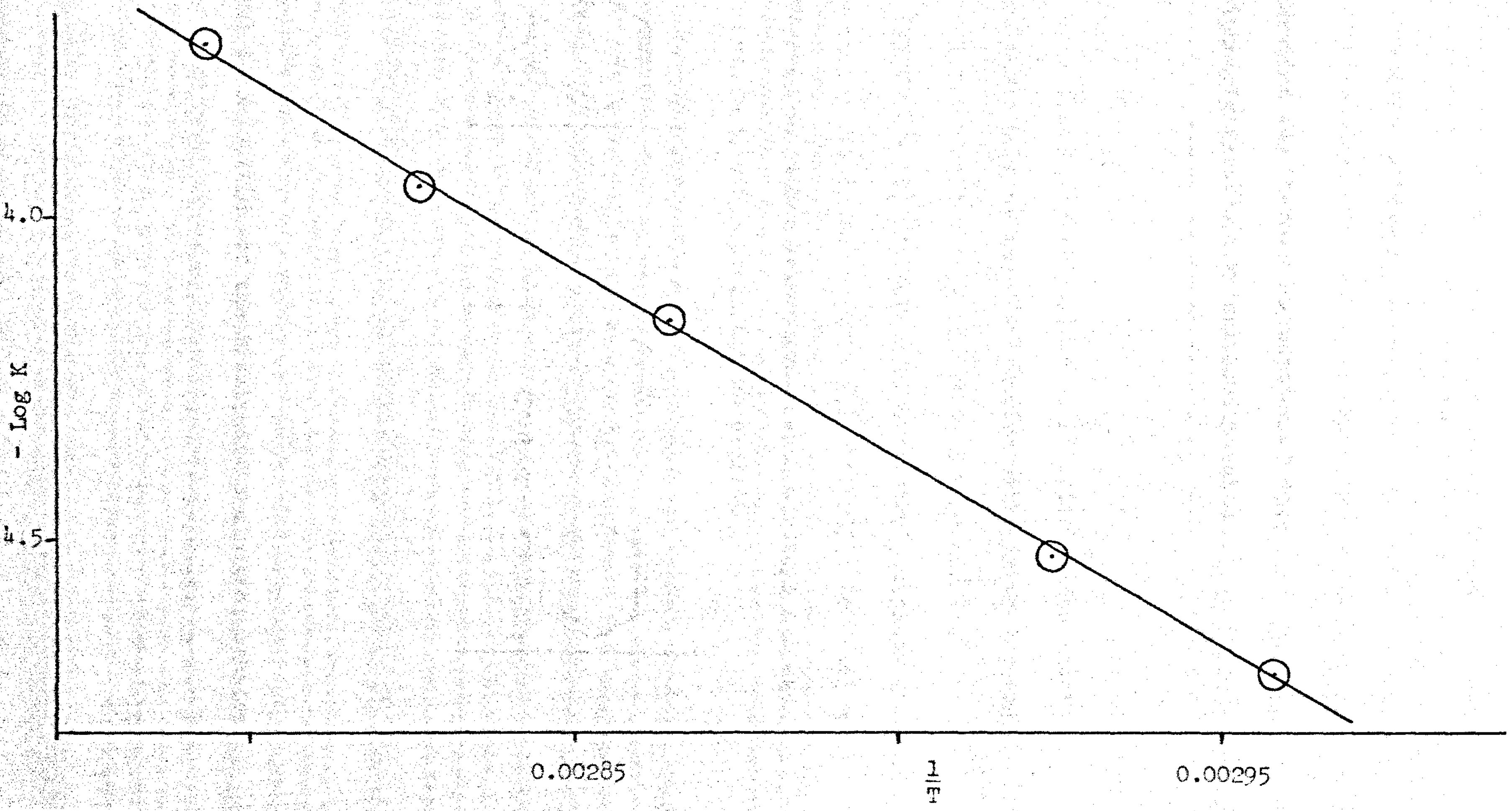
Time (min)	Rotation α°_{370}
0	0.165
14	0.140
345	0.111
52	0.0935
69	0.077
86	0.064
103	0.052

TABLE 13

Rate constants of racemisation of (XIX; n=1)

$t_{\frac{1}{2}}$(sec)x10^{-3}	K_t x 10^5 (sec^{-1})	T° ± 0.2
35.4	1.95	65.0
23.2	2.97	69.0
9.96	6.93	76.0
6.18	11.2	80.8
3.72	18.5	85.0

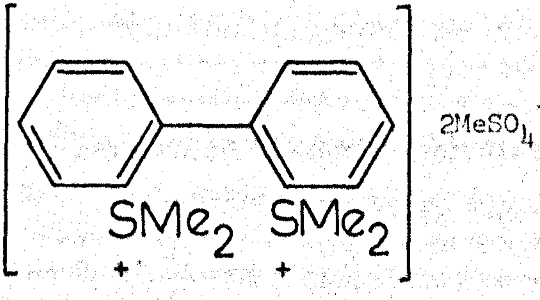
The Arrhenius Diagram for the Racemisation of the dithia compound (XVIII; n=1)



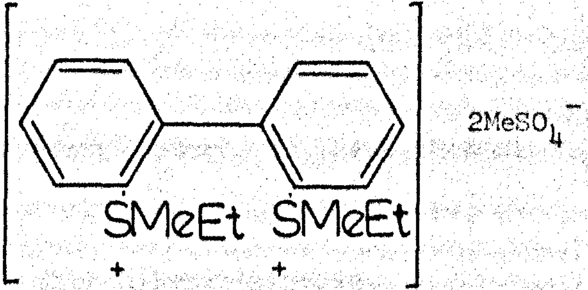
APPENDIX I

The Preparation and Thermal Degradation of Some 2,2'-Biphenylylenebisdialkylsulphonium salts

We have found that 2,2'-biphenylylenebisalkylsulphides react with dimethyl sulphate to give the disulphonium salts in good yield. Thus 2,2'-biphenylylenebismethylsulphide (XXXV; X = Me) and its ethyl analogue (XXXV; X = Et) on heating with dimethyl sulphate gave the corresponding disulphonium salts (L) and (LI). On heating some of the 2,2'-bridged dithia heterocycles with dimethyl sulphate, black tars were obtained, which could not be purified.

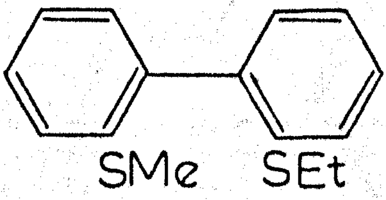


(L)



(LI)

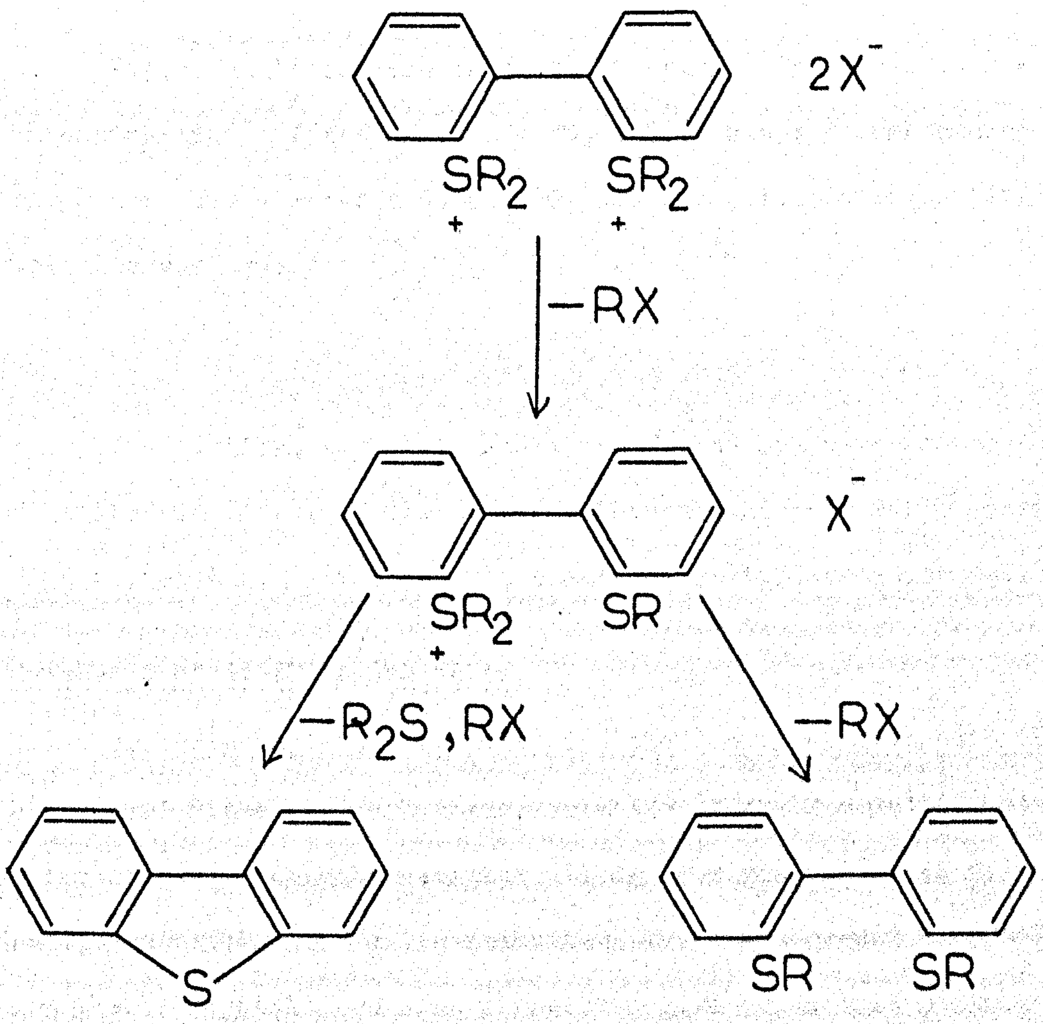
The thermal decomposition of the disulphonium dimethosulphates (L) and (LI) is of considerable interest, since it proceeds in a manner which is novel in sulphur chemistry. Thus thermal decomposition of the dimethosulphate (L) gave both the bisalkylsulphide (XXXV; X = Me) and dibenzothiophen. On the other hand the dimethosulphate (LI) on decomposition gave the two bisalkylsulphides (XXXV; X = Me and Et), the "mixed alkyl" compound (LII) and dibenzothiophen. It is significant that in the non-heterocyclic products of the last decomposition reaction, the bismethylsulphide (XXXV; X = Me) was the most abundant and the bisethylsulphide (XXXV; X = Et) the least abundant product, in accord with the greater ease with which an ethyl group is generally ejected in such reactions.



(LII)

We have found the amount of dibenzothiophen produced in these thermal decomposition reactions is dependent on the temperature, and below 200° the product is in some cases free from dibenzothiophen.

Analogous thermal decomposition reactions are known for comparable nitrogen, phosphorus and arsenic compounds,[71, 72, 73] and the thermal decompositions described here appear to be additional examples of this type of reaction. The production of dibenzothiophen is thought to take place via an internal nucleophilic reaction as follows:


$2X^-$
SR_2^+
SR_2^+
$-RX$
X^-
SR_2^+
SR
$-R_2S, RX$
$-RX$
S
SR
SR

EXPERIMENTAL

V.p.c. analysis were carried out using a Pye model 64 gas chromatograph fitted with a 6 ft. spiral glass column packed with chromosorb P coated with 5% S.E.30. silicon oil. An argon ionization detector was used.

The bisalkylsulphides (XXXV; X = Me and Et) were prepared as described in Part I of this thesis. Dibenzothiophen was prepared from biphenyl 2,2'-dithiol by the method due to Barber and Smiles.[18]

Synthesis of disulphonium salts

(a) 2,2'-Biphenylylenebisdimethylsulphonium dimethosulphate (L)

2,2'-Biphenylylenebismethylsulphide (XXXV; X = Me) (1.0g) was heated with dimethyl sulphate (1.0g) for four hours at 95°. On cooling a crystalline solid deposited, which was ground with acetone and then recrystallised from ethanol to give colourless prisms, m.p. 103-108° (1.4g., 67 %). After many recrystallisations analytical values were still unsatisfactory, and the n.m.r. spectra indicated that ethanol was present, even after drying at 60°. A dipicrate was prepared to identify the disulphonium salt. The dipicrate was prepared by mixing hot aqueous solutions of the disulphonium salt and sodium picrate. The crystalline dipicrate had m.p. 176° (Found: C, 46.2; H, 3.2; N, 11.3. $C_{28}H_{24}S_2O_{14}N_6$

requires C, 46.1; H, 3.3; N, 11.5%).

(b) 2,2'-Biphenylylenebisethylmethylsulphonium methosulphate (LI)

2,2'-Biphenylylenebisethylsulphide (XXXV; X = Et) (0.5g) and dimethyl sulphate (0.46g) were heated for four hours at 70°. After cooling and trituration with acetone a colourless solid was isolated, m.p. 160°, (0.45g., 47 %).

The yellow crystalline dipicrate was prepared to characterise the disulphonium salt, m.p. 169°, (Found: C, 46.9; H, 3.4; N, 10.9, $C_{30}H_{28}S_2O_{14}N_6$ requires C, 47.3; H, 3.7; N, 11.1%).

Thermal decomposition of disulphonium salts

(a) 2,2'-Biphenylylenebisdimethylsulphonium dimethosulphate (L)

The disulphonium salt (0.1g) was decomposed by heating in a bulb tube at 0.2 mm., in an air bath. The distillate was washed from the receiver with ether and the solution used directly for vapour phase chromatography (v.p.c.) at 200°.

(i) decomposition below 180°

V.p.c. examination of the ether extract showed one compound to be present, Rt 5.6 min; comparison with authentic material showed this to be the bismethylsulphide (XXXV; X = Me), Rt 5.6 min.

(ii) decomposition between 240-250°

V.p.c. analysis of the ether extract showed two peaks, with Rt 5.6 and 3.2 min., the 'new' peak being shown to be dibenzothiophen by comparison with authentic material. The ratio of dibenzothiophen to the bismethylsulphide was 2:8.

(b) 2,2'-Biphenylylenethylmethylsulphonium dimethylmethosulphate (LI)

The disulphonium salt (0.1g) was decomposed by heating, as above.

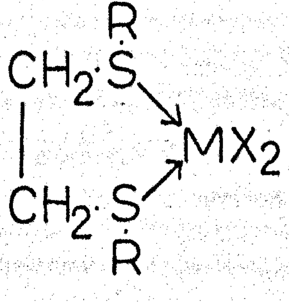
(i) decomposition at 240°

V.p.c. analysis of an ether extract of the distillate showed four peaks having Rt 3.2, 5.6, 6.3 and 7.1 min. The first two are due to the bismethylsulphide (XXXV; X = Me) and dibenzothiophen, the peak with Rt 7.1 min. was due to the bisdiethylsulphide (XXXV; X = Et), while the peak at 6.3 is probably due to the ethylmethyldisulphide (LII). The ratio of the products dibenzothiophen; bismethylsulphide (XXXV; X = Me); bisethylsulphide (XXX; X = Et); and ethylmethyldisulphide (LII) was 0.05:5:1:4. On increasing the temperature of the decomposition to 340°, the dibenzothiophen in the product increased to 9%.

APPENDIX II

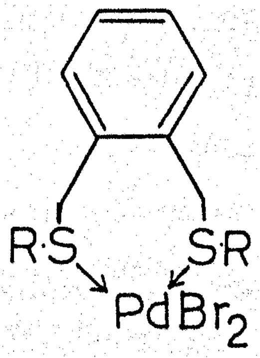
The formation of organo-metallic complexes with the dialkyl and dibenzyl derivatives of o-xylylene dithiol (V) and biphenyl 2,2'-dithiol (XVII)

Organic sulphides readily form co-ordination compounds with many transition metal cations, e.g. palladium (II), mercury (II) and platinum (II). Organic compounds containing two suitably orientated sulphide groups can act as chelate ligands with a number of (b) class metals. For example 1,2-dialkyl- and diaryl-dithioethanes form 1:1 complexes of structure (LIII) with most (b) class metals.[74]

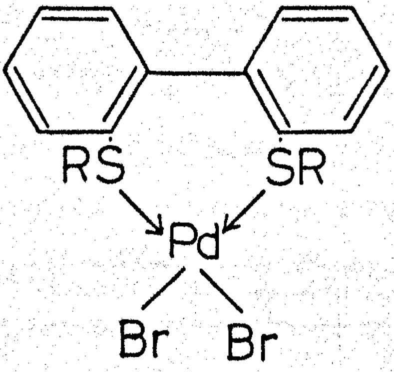


(LIII)

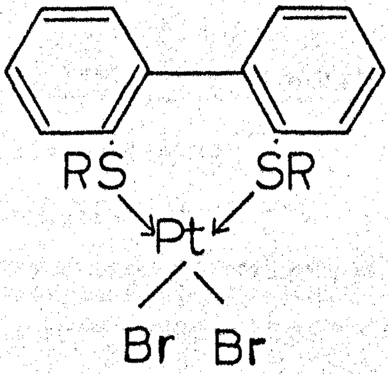
It would appear that the dialkyl and dibenzyl derivatives of o-xylylene dithiol (V) and biphenyl 2,2'-dithiol (XVII), have sulphide groups suitably disposed to act as novel chelate ligands. We have prepared a number of 1:1 co-ordination compounds, by heating the disulphides with potassium tetrabromopalladite or potassium tetrabromoplatinite in aqueous ethanol. A speciman of each type of complex was submitted for molecular weight determinations by the vapour pressure - thermistor method. The results confirmed that the complexes are at least monomeric and would appear to have the following structures:



(LIV)



(LV)



(LVI)

Whereas the dialkylsulphide compounds formed highly crystalline complexes with the platinum and palladium salts, the heterocyclic sulphur compounds formed insoluble, non-stoichiometric and amorphous substances, which were presumed to be polymeric. The preparation of the latter complexes was not pursued.

EXPERIMENTAL

The disulphides were prepared as described in Part I of this thesis.

Molecular weights were determined by the vapour pressure - thermistor method in methylene chloride. The homogeneity of the complexes was established by T.L.C.

The complexes of the o-xylylenedisulphides

(a) Dibromo(o-xylylenedimethylsulphide)palladium (II). (LIV; R = Me)

A hot saturated solution of aqueous ethanolic potassium tetrabromopalladite (104 mg) was added to a hot solution of *o*-xylylenedimethylsulphide (XXXIV; R = Me) (40 mg) in ethanol (5-10 ml). After cooling the solution fine brown crystals of the complex were deposited. The product was filtered off and washed with hot ethanol to give the pure product, m.p.-dec, (Found: C, 25.6; H, 2.95. $C_{10}H_{14}S_2PdBr_2$ requires C, 25.8; H, 3.0%).

(b) Dibromo(o-xylylenediethylsulphide)palladium (II) (LIV; R = Et)

This complex was prepared by the method (a) to give tangerine crystals, which were recrystallised from chloroform. The compound had, m.p. 218-220°C, (Found: C, 29.4; H, 3.7. $C_{12}H_{18}S_2PdBr_2$ requires C, 29.2; H, 3.7%).

(c) Dibromo(o-xylylenedibenzylsulphide)palladium (II) (LIV; R = $PhCH_2$)

The dibenzylsulphide complex (LIV; R = $PhCH_2$) was prepared under the conditions described in preparation (a), and was isolated as orange crystals, m.p. 186-188°, (Found: C, 42.7; H, 3.25. $C_{22}H_{22}S_2PdBr_2$ requires C, 42.8; H, 3.60%) (m.wt. = 452. (calc 617))

The complexes of the 2,2'-biphenylylenebis-sulphides

(a) Dibromo(2,2'-biphenylylenebismethylsulphide)palladium (II) (LV; R = Me)

This complex was made under the usual conditions, and crystallised from the hot aqueous ethanolic solution in purple crystals, m.p. 255-257°, (Found: C, 33.3; H, 2.80. $C_{14}H_{14}S_2PdBr_2$ requires C, 32.9; H, 2.75%).

(b) Dibromo(2,2'-biphenylylenebismethylsulphide)platinum (II) (LVI; R = Me)

The complex (LVI; R = Me), was prepared by the usual method and was isolated as orange crystals, m.p. 229-231°, (Found: C, 28.2; H, 2.30. $C_{14}H_{14}S_2PtBr_2$ requires C, 27.95; H, 2.35%).

(c) Dibromo(2,2'-biphenylylenebisethylsulphide)palladium (II) (LV; R = Et)

After treating the bisethylsulphide (XXXV; X=Et) with potassium tetrabromopalladite, orange-red needles of the complex were formed. The complex (LV; R = Et) had, m.p. 245°. dec (Found: C, 36.1; H, 3.1. $C_{16}H_{18}S_2PdBr_2$ requires C, 35.8; H, 3.3 %).

(d) Dibromo(2,2'-biphenylylenebisethylsulphide)platinum (II) (LVI; R = Et)

After treating the bisethylsulphide (XXXV;X=Et) with potassium tetrabromoplatinite in the usual manner, the complex crystallised from solution in fine orange prisms, m.p. 148-150°. dec ca 150°.

(Found: C, 30.7; H, 2.60. $C_{16}H_{18}S_2PtBr_2$ requires C, 30.5; H, 2.9%).

(e) Dibromo(2,2'-biphenylenebisbenzylsulphide)palladium (II) (LV; R = $PhCH_2$)

The complex (LV; R = $PhCH_2$) was prepared in the usual way, and crystallised from the aqueous ethanol in scarlet needles, m.p. 206-210°, (Found: C, 47.0; H, 3.15. $C_{26}H_{22}S_2PdBr_2$ requires C, 46.9; H, 3.3%) (m.wt = 428 (calc 665)).

(f) Dibromo(2,2'-biphenylylenebisbenzylsulphide)platinum (II) (LVI; R = $PhCH_2$)

The complex (LV; R = $PhCH_2$) was made by the usual method, and crystallised from aqueous ethanol as lemon prisms, m.p. 300°, (Found: C, 41.8; H, 2.62. $C_{26}H_{22}S_2PtBr_2$ requires C, 41.4; H, 2.95%), (m.wt. = 533 (calc 753.5)).

APPENDIX III

Results of Biological and Vulcanisation tests on some sulphur compounds carried out by Monsanto Chemicals Limited Research and Development Department, Ruabon

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RESULTS ON COMPOUNDS (14.8.69)

(a) Biphenyl 2,2'-dithiol (XVII)

Results: Some activity in fungistatic screen.

Aspergillus niger 0.02%, Pencillium expansum 0.002%.

Inactive in bacteriostatic screen and insecticidal and herbicidal screens.

No activity as vulcanisation accelerator. Marginal to moderate activity in antiozonant annulus test. Not tested as antioxidant.

(b) 2,2'-Biphenylylenebismethylsulphide (XXXV; X = Me)

Results: Some activity in herbicidal screen.

Some broadleaf selective pre-emergent activity at 10 lb/A, little activity at 1 lb/A.

Inactive in bacteriostatic and fungistatic screens and insecticidal screen.

No activity as vulcanisation accelerator. Not tested as antioxidant.

(c) 6,6'-Dimethyl dibenzo (d,f) (1,3) - dithiepin (XV; Y = CMe_2)

Results: Inactive in bacteriostatic and fungistatic screens and herbicidal and insecticidal screens.

No activity as vulcanisation accelerator.
Not tested as antioxidant.

Three other sulphur compounds,(XXII),(XXXI) and dibenzo (c,e) thiepin have also been sent for testing, but we have not yet received a report on the results.

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