# SKELETAL REARRANGEMENTS OF 9-THIABICYCLONONANES

## and RELATED SYNTHESES

a thesis

submitted to the University of Glasgow

in fulfilment of the requirements for

the degree of Doctor of Philosophy in

the Faculty of Science.

by

Catherine Mary Livingston, B.Sc.

Department of Chemistry,

April 1976.



ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

## ACKNOWLEDGEMENTS

I would like to thank Dr P.H.M$^{c}$Cabe for his helpful advice and for his patience throughout the course of this work. I am also grateful for assistance from the technical staff of the Chemistry Department, in particular Mr J.Gall and Mrs F.Lawrie for the recording of $^{1}H$ n.m.r. and infrared spectra respectively. Finally I would like to thank Dr R.K.MacKenzie for his assistance in the typing of this thesis.

CONTENTS

## SUMMARY

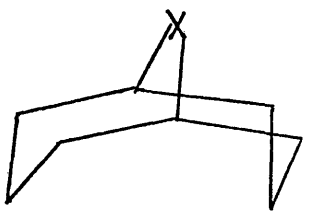
This thesis descibes two related areas of chemical investigation. In the first section pyrolytic and base-induced eliminations of 2,6-disubstituted 9-thiabicyclo[3.3.1]nonanes and 2-substituted 9-thiabicyclo [3.3.1]non-6-enes are found to occur with skeletal rearrangement. Similar rearrangement has not been observed when substituents in these positions undergo nucleophilic replacement even though assistance by the lone pairs of electrons on the bridging sulphur atom has been proposed. The rearrangement accompanying elimination is rationalised in terms of the structural and stereochemical characteristics of these compounds.

In the particular case of O-alkyl dimethyl thiocarbamate pyrolysis the expected cis elimination, yielding an alkene, is not observed. Instead a side-chain rearrangement to an S-alkyl dimethyl thiocarbamate occurs which has previously been observed only for aromatic thiocarbamates. This rearrangement in an aliphatic situation could arise by a concerted process involving the skeletal carbon-sulphur bonds and a mechanism is proposed.

The second section describes three synthetic approaches to 1,2- and 1,4-cyclooctatetraenoquinones, which are potentially pseudo-aromatic. The first method is an extention of earlier attempts to obtain the 1,2-quinone from monocyclic intermediates with protected carbonyl groups. The second and third approaches employ sulphur-bridged bicyclic compounds as synthetic intermediates to the 1,4-quinone. Appropriate functionalisation of these stable systems followed by extrusion of sulphur was proposed in order to overcome the transannular cyclisation which frustrated monocyclic routes.

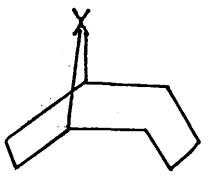
# THE SYNTHESIS AND PHOTOCHEMISTRY OF 9-HETEROBICYCLONONANES.

Bicyclic compounds have attracted the attention of chemists because their rigid skeletons make them uniquely suited to the study of certain chemical phenomena such as molecular rearrangement, neighbouring group participation and stereo-chemical features. Bicyclononanes, especially those possessing the [3.3.1] carbocyclic framework, are of particular interest in conformational analysis[1-5] and are key intermediates in the synthesis of adamantanes[6,7]. Derivatives of the bicyclo[3.3.1]nonane system have been known since the early 1900's. The parent hydrocarbon (1, X=$CH_2$) was first synthesised[8] in 1922, whereas the isomeric bicyclo-[4.2.1]nonane (2, X=$CH_2$) was prepared[9] at a much later date.




1

X= $CH_2$, O, NH or S

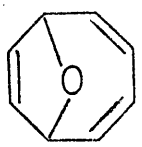



2

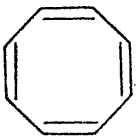
The introduction of a 9-hetero atom into the bicyclic molecule generally retains the overall geometry of the parent hydrocarbon but the reactivity is modified since the bridging hetero atom allows new functional group reactions and the possibility of neighbouring group participation. In addition the 9-aza- and 9-thiabicylononanes in particular exhibit a wide range of physiological[10] and insecticidal[11,12] activity.

9-Azabicyclononanes were discovered[13] in the last century as naturally occuring compounds; 9-azabicyclo[3.3.1]nonane (1, X=NH), also known as granatanine, is the parent compound of an important series of naturally occuring alkaloids. The 9-oxabicyclononanes have

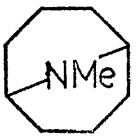
been known for a much shorter time. In 1953 9-oxabicyclo[4.2.1] nona-2,4,7,-triene (3) was suggested[14] as the oxide formed on the treatment of cyclooctatetraene (4) with perbenzoic acid. However, the first definite synthesis of a 9-oxabicyclo[4.2.1] nonane was accomplished in 1957 when the parent compound (2, X=O) and its [3.3.1] isomer (1, X=O) were prepared[15,16].




3

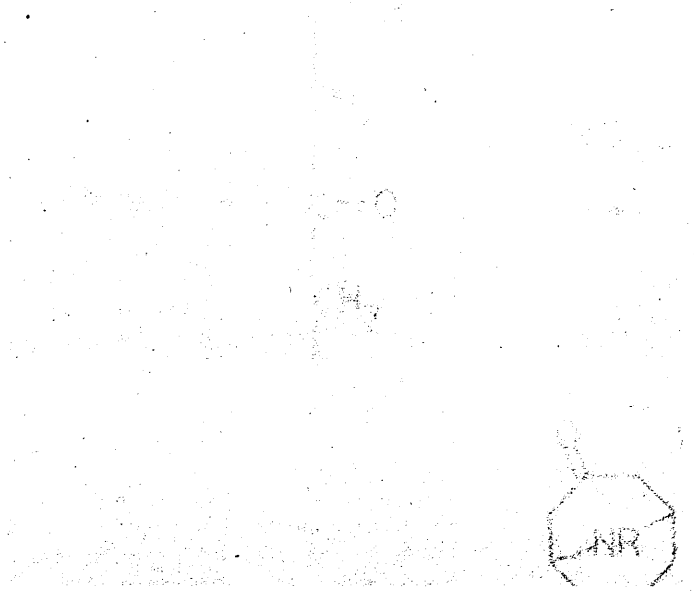


4




5

Around the same time 9-thiabicyclo[3.3.1]nonane (1, X=S) was isolated[17] from Middle East petroleum and was also synthesised in low yield, by the reaction of N-methylgranatanine (5) with hydrogen sulphide.



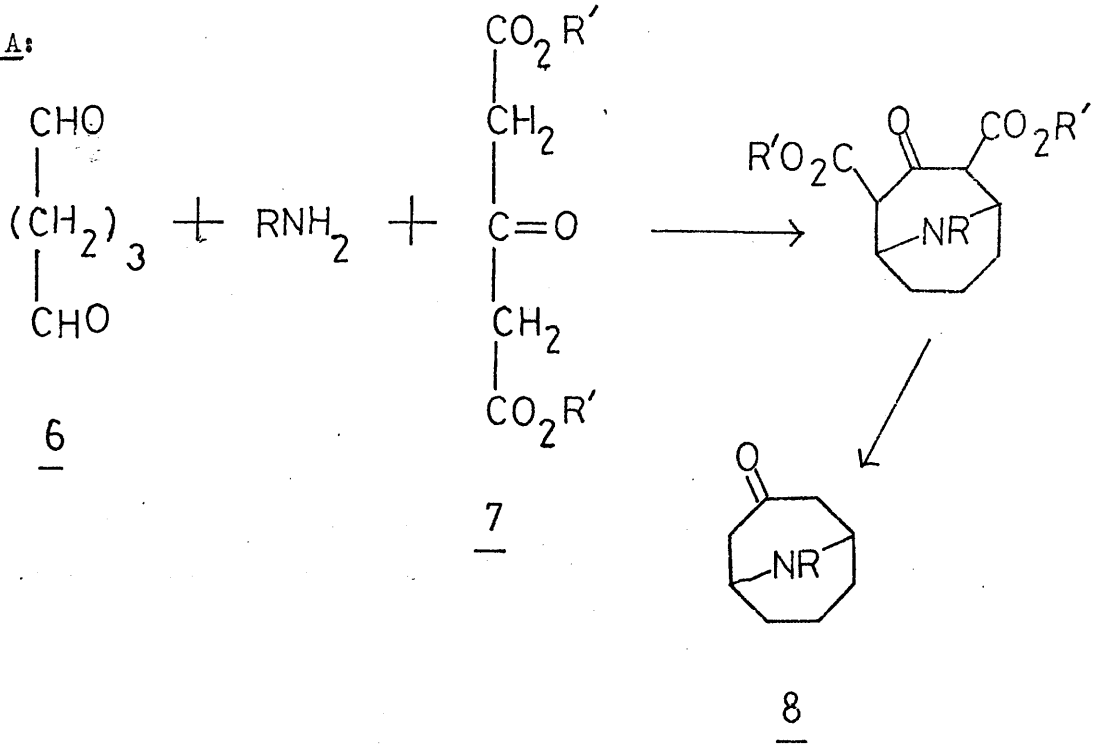
A : SYNTHESIS.

The 9-heterobicyclo[3.3.1]- and [4 .2.1] nonanes may be formally considered as consisting of an eight membered carbocyclic framework with the hetero atom bridging the ring either 1,5 (as in 1) or 1,4 (as in 2). In fact many syntheses of these compounds commence from eight membered ring substrates. However, alternative synthetic approaches have been made from condensation reactions involving smaller ring or completely acyclic precursors, or by rearrangement from other bicyclic systems.

i) Synthesis from acyclic and heterocyclic precursors:

The Robinson-Schöpf[18] synthesis of substituted pseudo pelletierines (8) is one of the earliest examples of formation of the 9-heterobicyclononane skeleton starting from acyclic precursors. Treatment of glutardialdehyde (6) with a primary amine and acetone dicarboxylic acid, or esters thereof (7) followed by decarboxylation leads to a N-substituted pseudopelletierine (Scheme A)

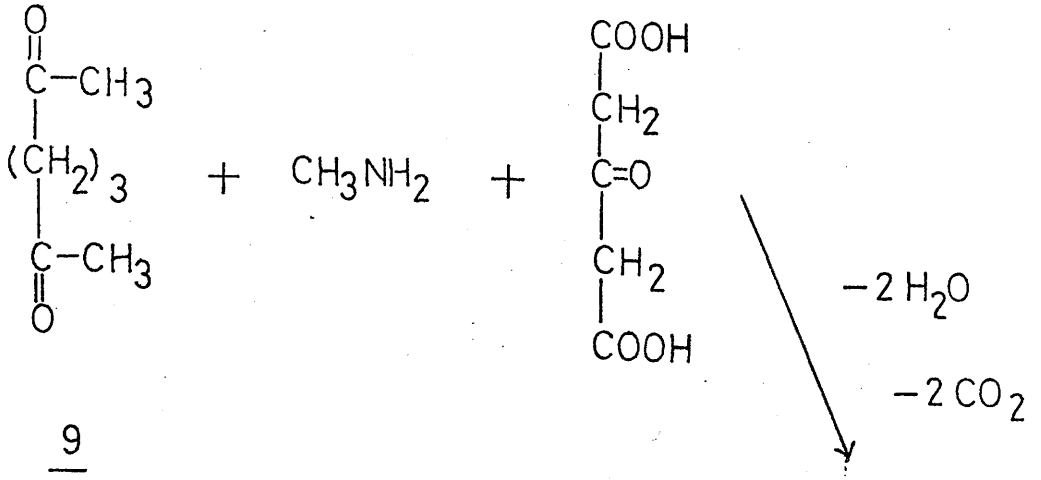
Scheme A:



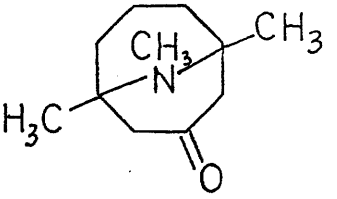

6 7 8

It is possible to vary the substituents of this reaction, for example 1,5-diketones (9) have been used[19] to give bridgehead substituted compounds (e.g. 10, Scheme B). Because of its versatility and high yield the reaction is still employed extensively[20] for the synthesis of 9-azabicyclo[3.3.1]nonanes.

Scheme B:




9

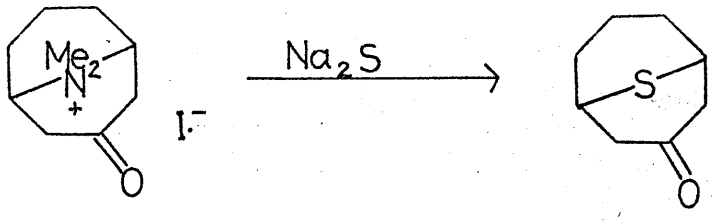



10

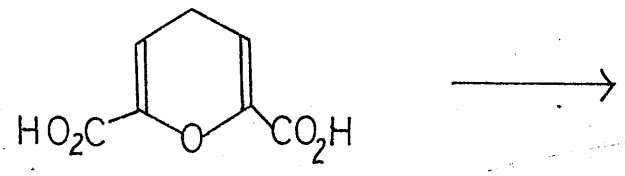
Pseudopelletierine itself (8, R=$CH_3$) played an important part in determining[21] the structure of cyclooctatetraene and is the starting material for the synthesis of the 9-thiabicyclononane system. In this approach (Scheme C) reaction[22] of the methiodide of pseudopelletierine with aqueous sodium sulphide results in the replacement of the quaternised nitrogen by a thio-ether group.

2,6-Disubstituted-4-H-pyrans (11) lead, by a series of steps (Scheme D) to a precursor (12) which on condensation with diethylmalonate yields[16] a substituted 9-oxabicyclo[3.3.1]nonane (13).

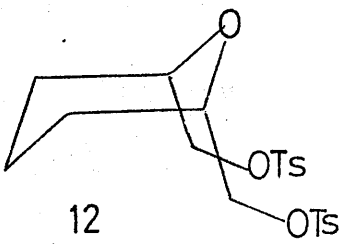
**Scheme C:**



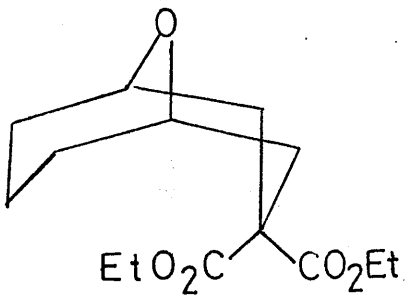

**Scheme D:**




11




12

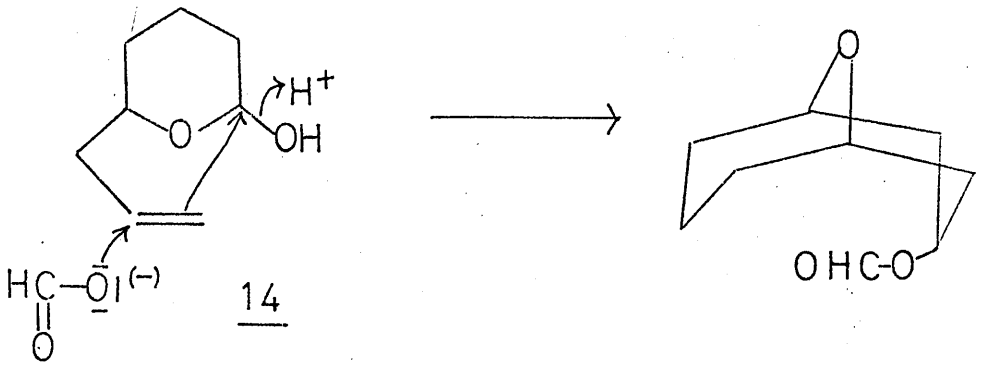



13

It is noteworthy that this is the only product isolated even though its formation requires the introduction by alkylation of a 1-carbon unit into an intermediate (12) in which the two bulky substituents occupy the sterically unfavourable axial positions.

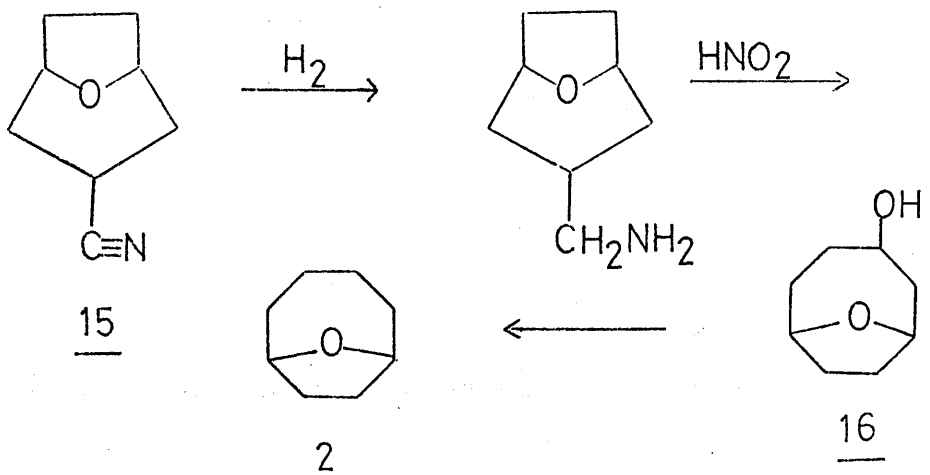
The same bicyclic skeleton was obtained[23] through the cyclisation of the hemiacetal (14) in 90% formic acid (Scheme E).

Scheme E:




The 9-oxabicyclo[4.2.1]nonane ring system has been prepared[15] by ring expansion of the 8-oxabicyclo[3.2.1]octane skeleton (Scheme F). Hydrogenation of nitrile (15) followed by treatment with nitrous acid afforded alcohol (16) which on oxidation and Wolf-Kischner reduction yielded 9-oxabicyclo[4.2.1]nonane (2, X=O).

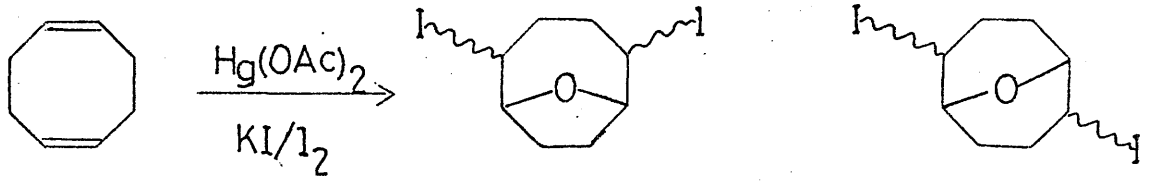
Scheme F:



ii) Synthesis by oxymercuration of cyclooctene derivatives:

This approach has been employed frequently in the synthesis of 9-oxabicyclo[3.3.1]- and [4.2.1] nonanes. The oxymercuration of cis,cis-1,5-cyclooctadiene (17) with mercuric acetate and subsequent reaction with potassium iodide and iodine (Scheme G) yields[24] a mixture of six products - the three possible stereoisomers of 2,5-diiodo-9-oxabicyclo [4.2.1]nonane (18) and those of 2,6-diiodo-9-oxabicyclo[3.3.1]nonane (19) whose proportions vary with reaction conditions.

Scheme G:



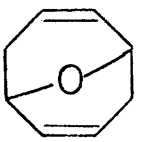

17 18 19

(a) exo,exo.

(b) exo,endo.

(c) endo,endo.

Earlier results by Stetter[25] indicated the formation of only one isomer, the exo,exo isomer of 19, which was dehydrohalogenated to diene (20), a useful reagent for the preparation of 2,6-diheteroadamantanes.

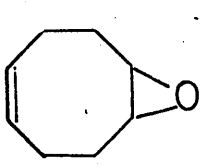



20

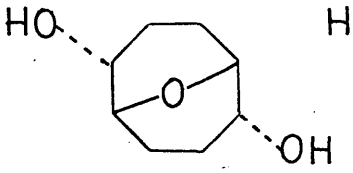
Addition of iodine to a mixture of 17 and mercuric oxide in chloroform yields[24,26] a mixture of iodides (18c and 19c). That only the endo,endo

stereoisomers of 18 and 19 are formed may be rationalised by the formation in situ of $I_2O$.

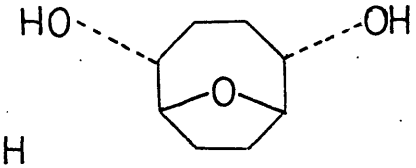
Monoepoxide (21) on oxymercuration furnishes[27] a 1:3 mixture of the endo,endo bicyclic diols (22) and (23). Treatment of cyclooocten-5-ol (24) with mercuric acetate gives[28] the 9-oxabicyclo[4.2.1]nonane (25) as the major product with formation of the [3.3.1] isomer (26a) in minor amount. However, reaction of 24 with mercuric nitrate exclusively produces the 9-oxabicyclo[3.3.1]nonane (26b).



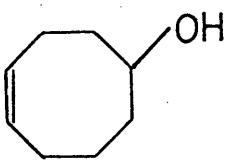

21



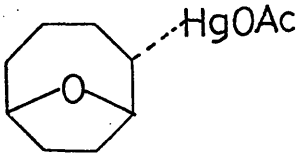

22



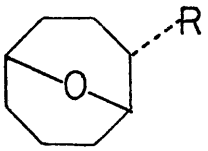

23




24

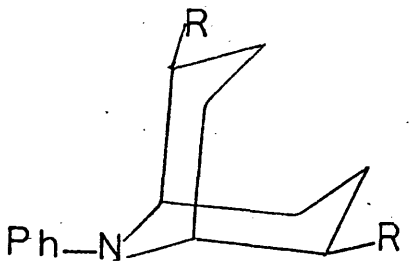



25

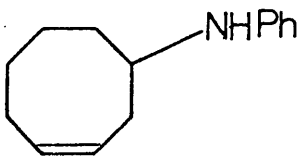



26a) R=HgOAc
b) R=$HgNO_3$

9-Azabicyclo[3.3.1]nonanes may be produced by oxymercuration of 17 performed[29] in the presence of aniline. Reduction of the mercury adduct (27a) with sodium borohydride in the presence of aniline gives N-phenyl-9-azabicyclo[3.3.1]nonane (27b). However, reduction in the absence of aniline affords a mixture of 27b and the ring opened product (28).




27a) R=HgOAc
b) R=H

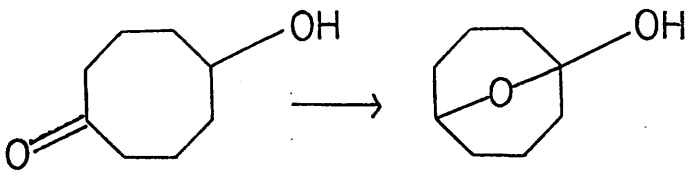



28

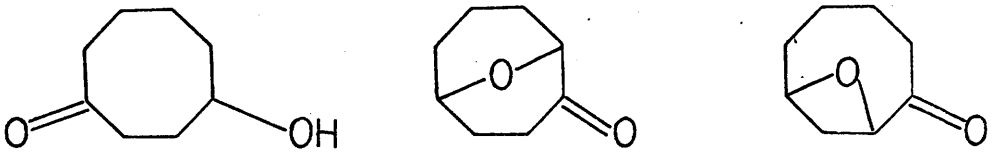
iii) Synthesis via intra molecular condensation:

Transannular processes in eight membered rings, of which there are numerous examples in the literature, have been used primarily for the formation of 9-oxabicyclononanes. Cope reports[26] that 5-hydroxy-cyclooctanone (29) exists in hemiacetal form and bromination of this compound, followed by treatment with methanolic potassium hydroxide, gives ketone (30). The isomeric [3.3.1] ketone (32) is obtained, together with some of the [5.1.1] ketone (33) by similar reaction on 4-hydroxycyclooctanone (31, Scheme H).

Scheme H:

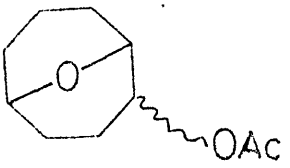


29 30

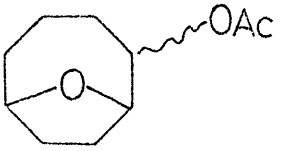


31 32 33

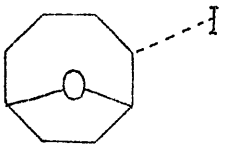
Treatment of cycloocten-5-ol (24) with lead tetraacetate gives[30] the substituted 9-oxabicyclononanes (34 and 35). Reaction of (24) with iodine gives[28] a mixture of 9-oxabicyclo[4.2.1]- and[3.3.1]nonanes (36 and 37). The stereospecific formation of endo,endo isomers may be explained by the intermediacy of the iodonium ion (38) which collapses by subsequent intramolecular attack of the free hydroxyl group to give either the [3.3.1] or[4.2.1]skeleton



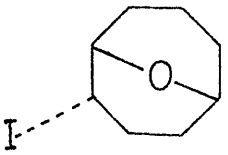
34



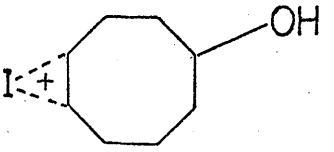
35



36

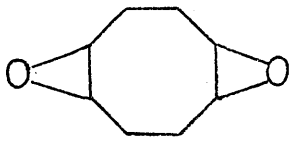


37

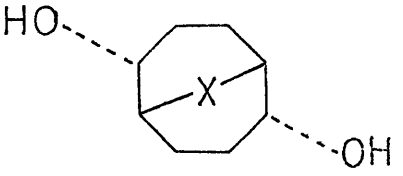


38

The action of aqueous acid on the cis,cis bisepoxide (39) gives[31] the bicyclic alcohols (22) and (23). Reaction of 39 with sodium sulphide affords the thia analogues (40a and 41), whereas treatment with ammonia yields[32] endo,endo-9-azabicyclo[3.3.1]nona-2,6-diol (40b). The reactions of 39 can be explained by initial solvolytic opening of one epoxide group. followed by transannular nucleophilic substitution on either carbon atom of the second epoxy group giving the endo,endo diols.

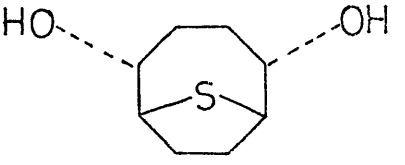


39



40 a) X=S

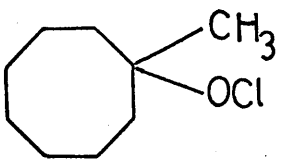
b) X=NH



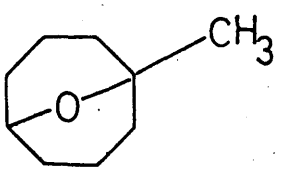
41

Photochemical rearrangement of 1-methylcyclooctyl hypochlorite (42), performed in carbon tetrachloride, produces[33] the 9-oxabicyclononanes (43 and 44) by transannular cyclisation and a similar rearrangement has been reported[34] on irradiation of N-chloroamine (45) to give N-methyl-

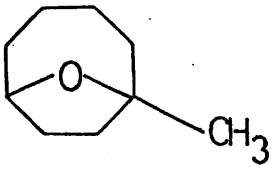
granatanine (5).



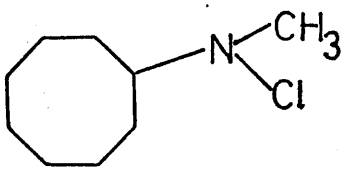
42



43



44

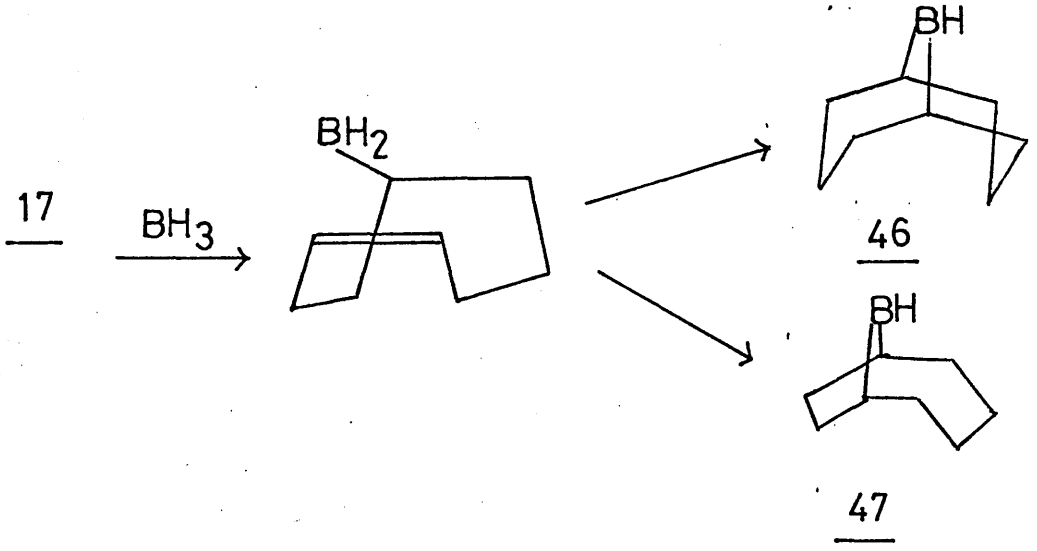


45

iv) Syntheses by intermolecular cyclisations involving cyclooctadienes:

Reaction of borane ($BH_3$) with cis,cis-1,5-cyclooctadiene (17) results[35] in the formation of 9-borabicyclo[3.3.1]nonane (46) and its [4.2.1] isomer (47) (Scheme J). Such cycloboranes have proved useful hydroborating agents, reacting rapidly and quantitatively with other alkenes and alkynes.

Scheme J:

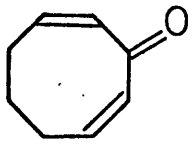



46

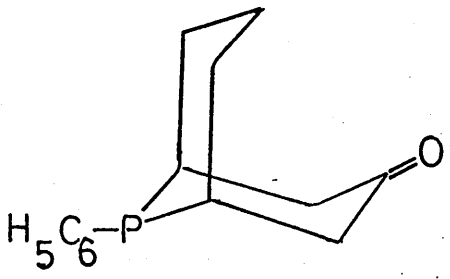
47

Cycloocta-2,7-dienone (48) has been used in the synthesis of 9-hetero-bicyclononanes. Kashman and Benary report[36] that phenylphosphine adds to 48 to give 9-phenyl-9-phosphabicyclo[3.3.1]nonan-3-one (49) and that

reaction of primary amines with 48 yields[37] 9-azabicyclononanes. The latter condensation is an extension of earlier work by Bottini and Gal[38] on the reaction of methylamine with 48 to give pseudopelletierine.

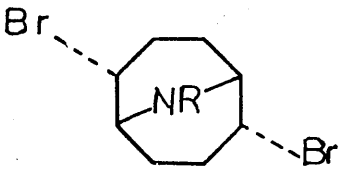


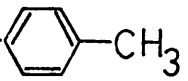

48



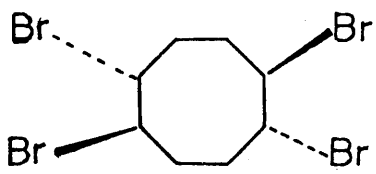

49

Alternative approaches to the 9-azabicyclononanes include the addition[32] of N,N-dibromo-p-toluene sulphonamide ($Br_2$-N-$SO_2$-$C_6H_4$-$CH_3$-p) to 17, the product being the dibromo compound 50.



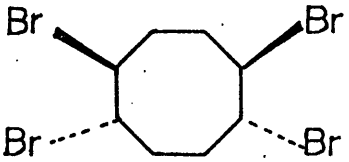

50, R = 


Reaction of tetrabromide (51) with a primary amine gives[39] a 9-azabicyclo-[3.3.1]nona-2,6-diene (52) whereas 53, a stereoisomer of 51 yields the [4.2.1] diene (54). 56, the thia analogue of 52 has been prepared[40] by treatment of dibromide[41] (55) with sodium sulphide.



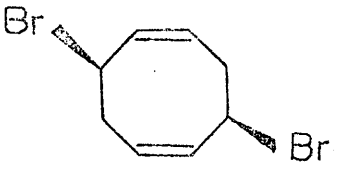

51


52




53


54

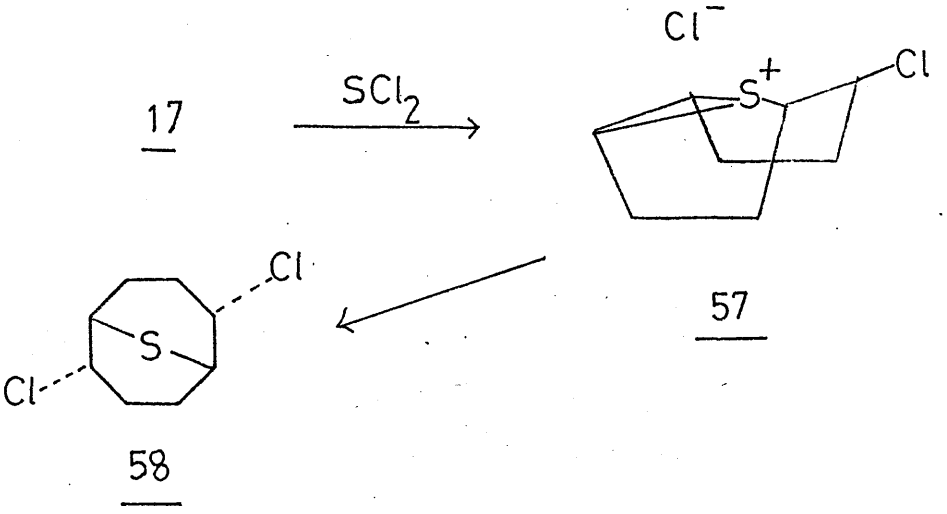



55


56

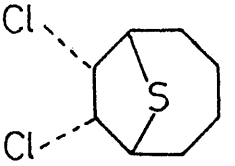
In 1966 the transannular addition of sulphur dichloride to cis,cis-cycloocta-1,5-diene (17) was described independently by three research schools[42,43,44]. This reaction gives endo,endo-2,6-dichloro-9-thiabicyclo[3.3.1]nonane (58) in high yield, thus providing the first convenient synthetic entry into the 9-thiabicyclo[3.3.1]nonane series (Scheme K).

Scheme K:




The isomeric 7,8-dichloro-9-thiabicyclo[4.2.1]nonane (60) was obtained by the analogous reaction of cycloocta-1,3-diene (59).

59



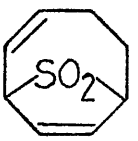

60

For both dichlorides (58 and 60) the anti configuration of the carbon-chlorine bonds relative to the sulphur bridge is the result of trans addition of a sulphenyl halide to the double bonds involved. Episulphonium

species (57) has been proposed as an intermediate in the former case; however, there is no evidence for formation of 2,5-dichloro-9-thiabicyclo [4.2.1] nonane in this reaction. It is expected here that thermodynamic control is operative, the resulting molecular framework comprising two six-membered rings in the chair-chair conformation which allows the most favourable staggering of the carbon-hydrogen bonds.

Treatment of 1,3,5-cyclooctatriene (61) with sulphur dioxide produces[45] 9-thiabicyclo [4.2.1] nona-2,7-diene-9,9-dioxide (62) whereas reaction of

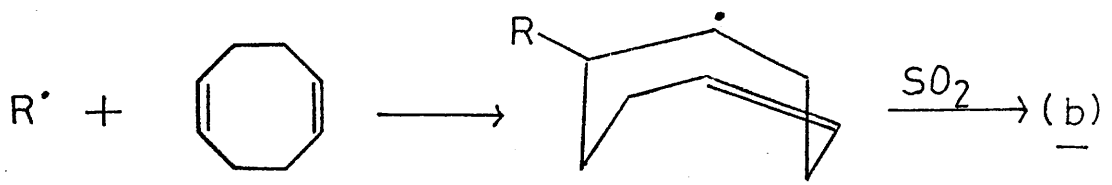
61



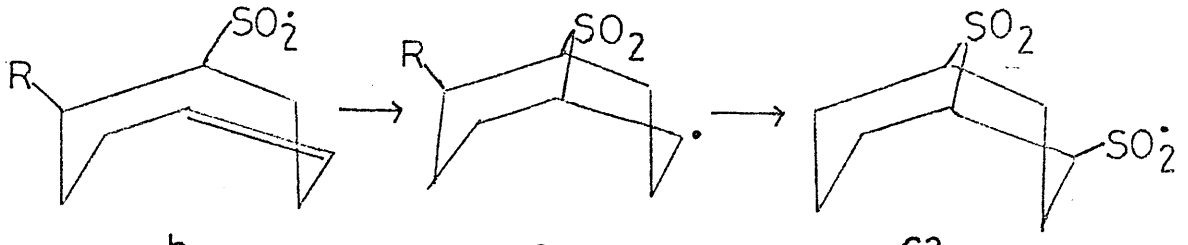

62

1,5-cyclooctadiene (17) with sulphur dioxide in the presence of radical initiators results[46] in a polymer, the structural unit of which is a bicyclic sulphone (63). The formation (Scheme L) of this polymer may be considered as involving attack of the growing radical chain ($R^{\bullet}$) on the diene to give the hydrocarbon radical (a) which reacts with sulphur dioxide. The resulting radical (b) cyclises intramolecularly to give (c) which reacts with sulphur dioxide and so the chain is propagated.

Scheme L:



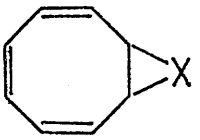

17 (a)




b c 63

v) Synthesis by addition to cyclooctatetraene:

Reactions involving addition to cyclooctatetraene (4) generally result in a 1,2 adduct (64) or a 1,4 adduct (65). Reaction[47] of dichlorophenylphosphine (67) with the dianion of cyclooctatetraene (66)

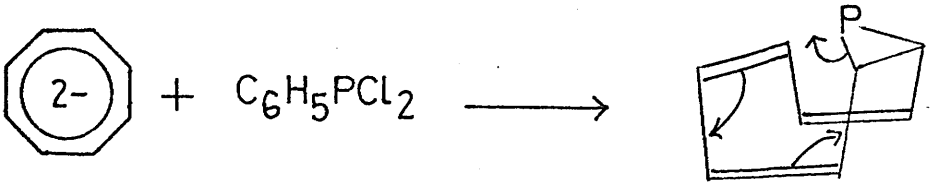



64

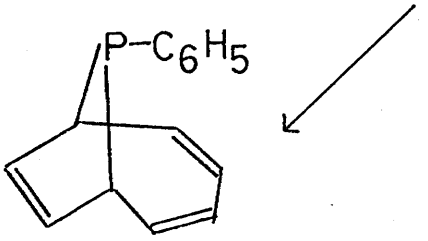

65

(Scheme M) gives intitially the 1,2 adduct (68) but this isomerises at 70° to 9-phenyl-9-phosphabicyclo[4.2.1]nona-2,4,7-triene (69).

Scheme M:

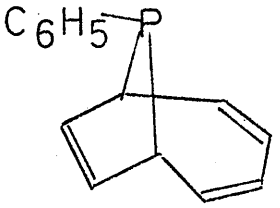



66 67 68



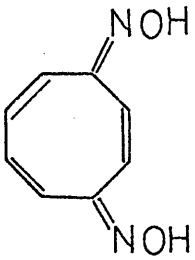

69

A n.m.r. comparison of 69 with the derived methiodide and P-oxide suggests that only one of the two possible epimers (69 and 70) is formed, viz. that which has the phenyl substituent lying towards the four membered bridge. However, isomerisation to the more stable epimer (70) occurs readily on heating. The stereospecificity and the ease with which 68 rearranges to 69, although 69 is the less stable epimer, suggests an intramolecular process.

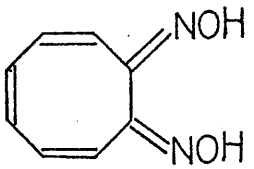



70

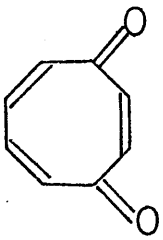
Using the known reaction of alkyl nitrites with carbanions to produce oximes, Okamura and coworkers reacted[48] the dianion of cyclooctatetraene with isoamylnitrite in an attempt to prepare 71 or 72 which are the bisoxime derivatives of cyclooctatetraenoquinones 73 and 74 respectively. However, the product obtained was a 9-azabicyclo[4.2.1]nonatriene (75) the result of formal 1,4 bridging of the cyclooctatetraene ring.



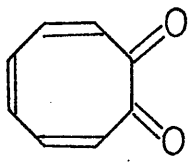

71



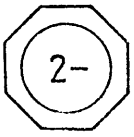

72




73



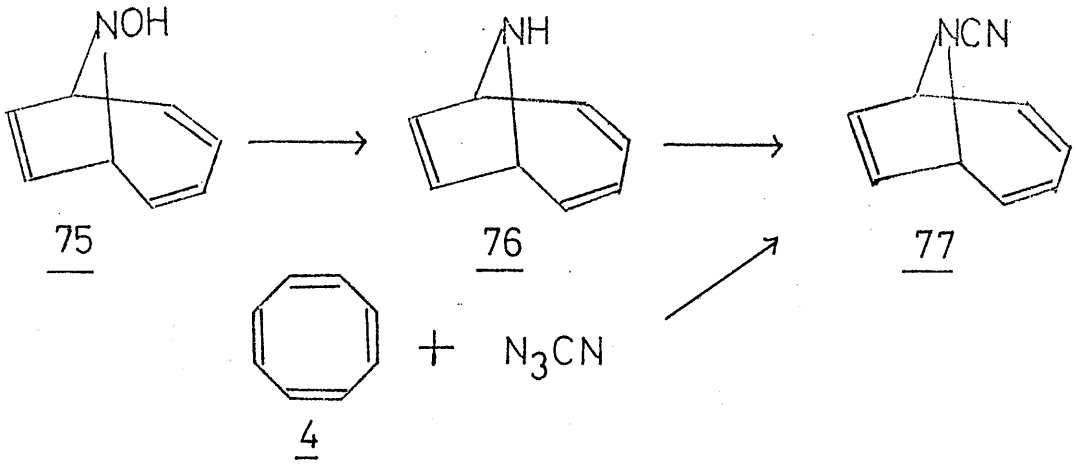

74



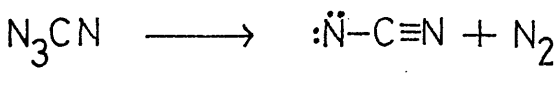


75

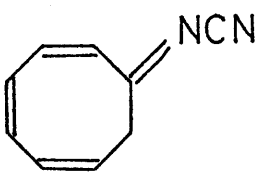
Scheme N:



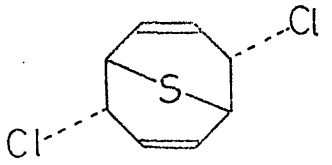

Reduction of 75 with zinc in acetic acid gave parent amine (76) which formed the N-cyano derivative (77) on reaction with cyanogen bromide (Scheme N). 77 had already been isolated[49,50] as a minor product of the reaction of cyanogen azide ($N_3CN$) (78) with cycloocta-tetraene (4) at 78°. At this temperature it is expected that cyanogen azide fragments to nitrogen and cyano nitrene (NCN) (79) and hence 77 is probably the result of 1,4 addition of 79 to 4. This proposal is supported by the observation that reaction of 4 with cyanogen azide at room temperature furnishes N-cyanoimine (80) which does not isomerise to 77 at 78°.




78 79

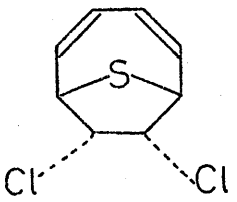



80

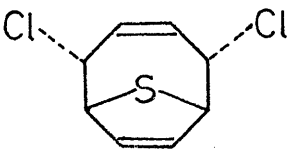


81

A one-to-one adduct assigned the structure 81 was obtained[51] from the reaction of sulphur dichloride and cyclooctatetraene (4). The endo,endo configuration is proposed since oxidation produces a single sulphoxide which remains unchanged on attempted inversion with triethyloxonium fluoroborate ($Et_3O^+$ $BF_4^-$). Alternative structures (82 and 83) for this product have been ruled out on n.m.r. evidence.

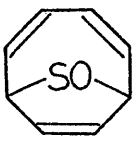


82

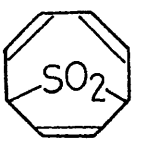


83

Sulphur monoxide, generated in situ from the thermolysis of thiiran-1-oxide has been found[52] to add in a 1,4 fashion to 4 to give 84 in about 30% yield. Oxidation of 84 with m-chloroperbenzoic acid gave the correspond-



84

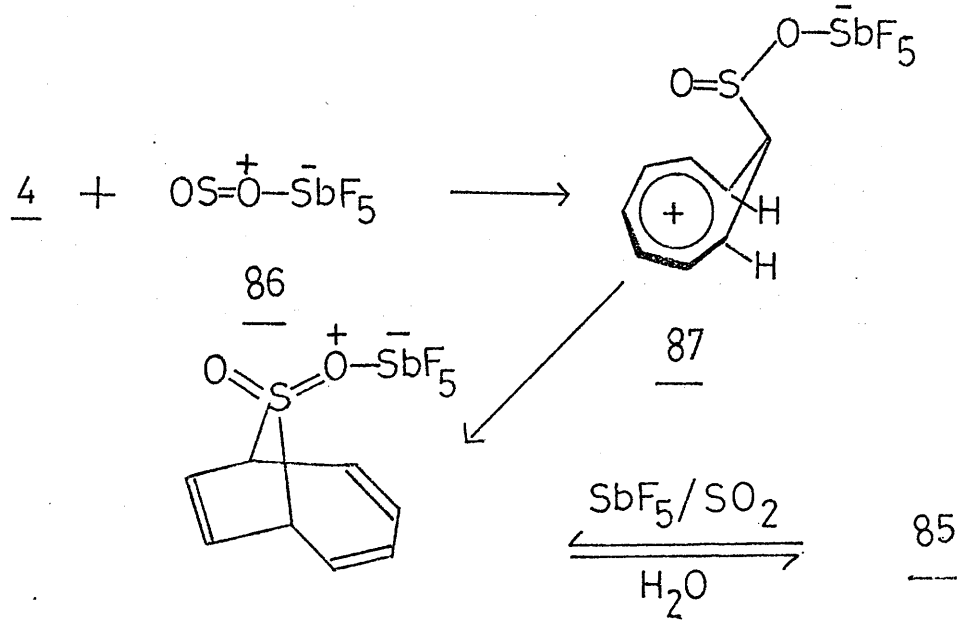


85

ing sulphone (85) which has also been directly prepared[53] from 4 in 95% yield by treatment with liquid sulphur dioxide in the presence of antimony pentafluoride. Decoupling experiments excluded the possibility

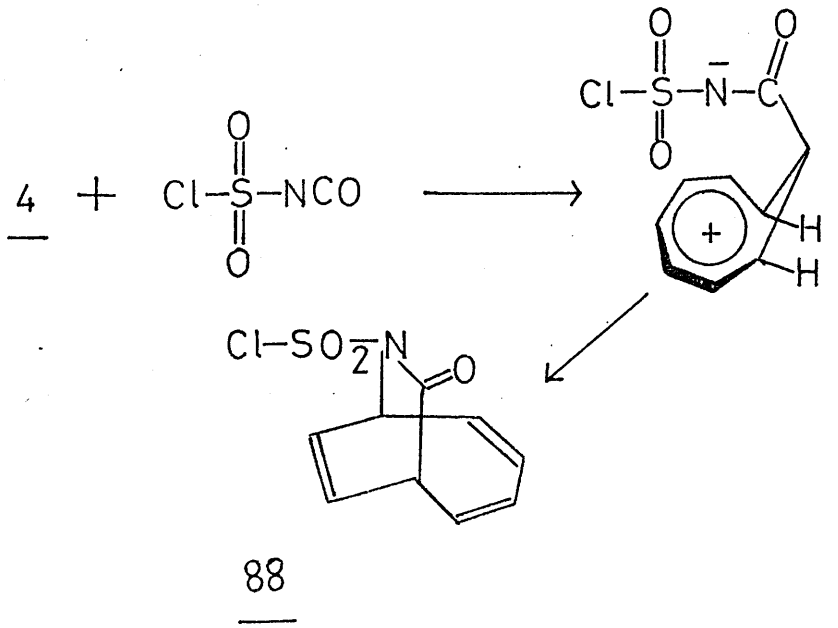
of the 1,2 adduct. The addition of sulphur dioxide to 1,3 dienes can take a concerted pathway as a chelotropic reaction. However, the lack of a planar diene system in 4 probably prevents concerted sulphur dioxide addition. The mechanism suggested (Scheme P) involves formation of an

Scheme P:




electrophilic 1:1 complex of sulphur dioxide and antimony pentafluoride (86) which attacks 4 from the endo side to form a homotropylium species (87) which undergoes ring closure. An analagous process is the treatment[54] of 4 with chlorosulphonyl isocyanate to give the 1,4 adduct (88) through a homotropylium zwitterion species (Scheme Q).

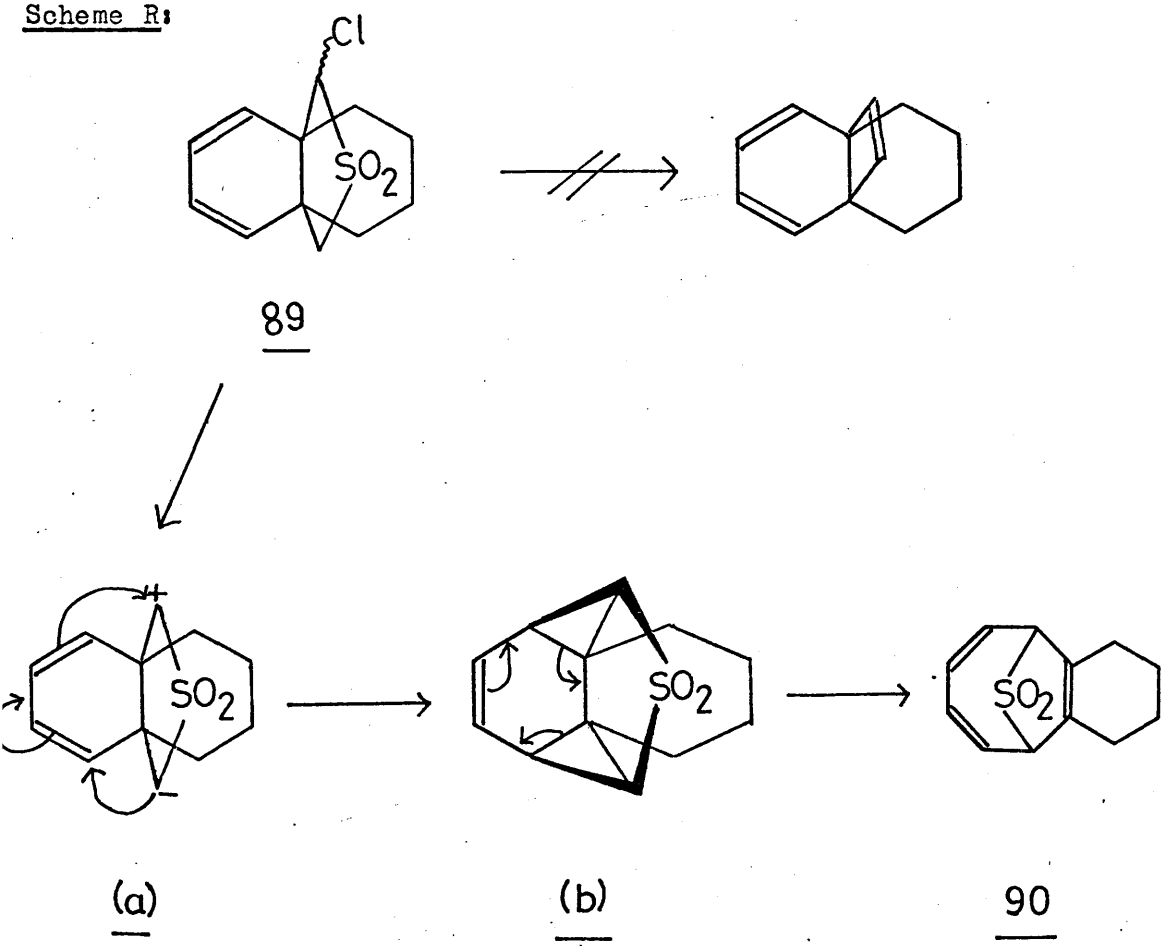
Scheme Q:



vi) Rearrangement from other bicyclic systems:

9-Thiabicyclo[4.2.1]nonanes have been reported[55] as products of the attempted Ramberg-Bäcklund[56] rearrangement of unsaturated $\alpha$-halo sulphones such as 89. The alkaline reaction conditions probably cause initial removal of the $\alpha$-sulphonyl proton (Scheme R). It is postulated that subsequent heterolysis of the C-Cl bond yields a zwitterion (a) which rearranges to a dicyclopropyl sulphone (b). Such a compound would be under steric strain and therefore be expected to rearrange to 90. The proximity of the diene function both to the developing $\alpha$-sulphonyl carbanion centre and to the site of ultimate nucleophilic displacement may explain why this rearrangement is favoured over the competing 1,3 elimination process normally observed for $\alpha$-halosulphones.

Scheme R:




89

(a) (b) 90

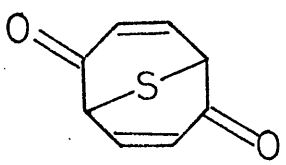
B : PHOTOCHEMISTRY.

Photochemically induced isomerisations of the 9-heterobicyclo nonanes have been investigated by several different groups[57,58,59]

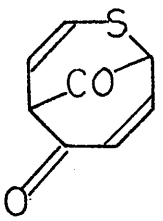
Photochemically induced isomerisations of the 9-heterobicyclo-nonanes have been investigated by several different groups[57,58,59].

The ultra-violet characteristics of ketothioethers have been shown to be substantially different from those of other saturated ketones and this has been attributed to interaction of a lone pair of electrons on the sulphur atom with the carbonyl group, the coupling being strongly dependent on the orientation of the two groups[60]. Not suprisingly therefore all the 9-thiabicyclononanes photolysed contain a carbonyl group in a position $\beta$ to the 9-sulphur atom. When comparison of the irradiation products of the 9-oxa- and the 9-thiabicyclo compounds under study has been made the results indicate that two photochemical processes are operative - one of which is seen in both 9-oxa- and 9-thia- compounds, the other exclusive to 9-thiabicyclo compounds.

Mellor and Webb studied the irradiation of dione (91) in benzene and in ether and reported formation of only one monomeric product (92), probably the result of a (1,3) shift by a concerted sigmatropic rearrangement because the reaction does not appear to be influenced by solvent.



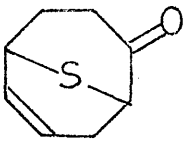

91



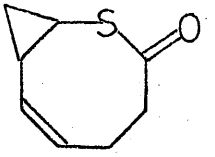

92

The $\beta$-keto sulphide (93) is found[58] to rearrange on irradiation in pentane solution to the $\alpha$-ketosulphide (94). Using methanol as solvent irradiation of 93 yields 95 as the major product, together with

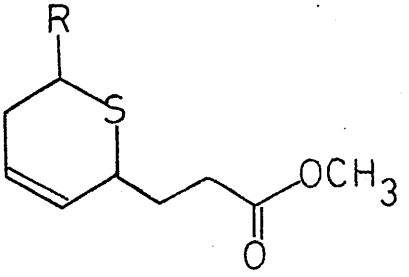
small amounts of 94.



93



94

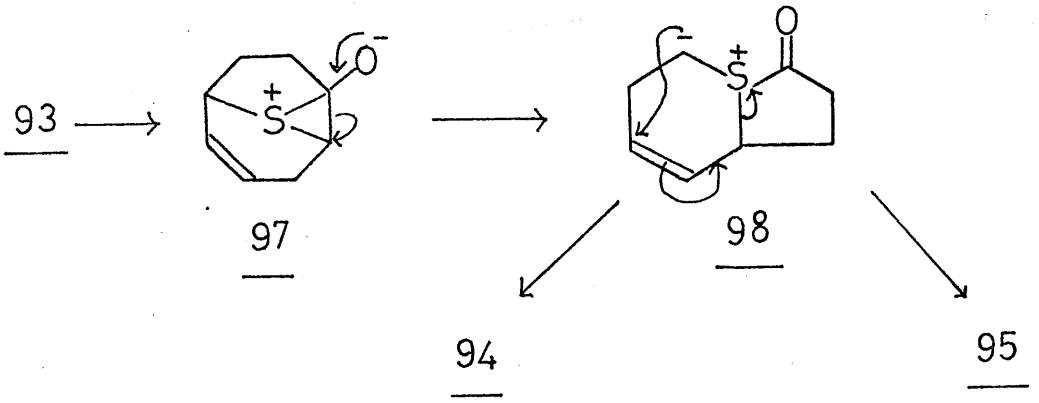


95, R=H

96, R=D

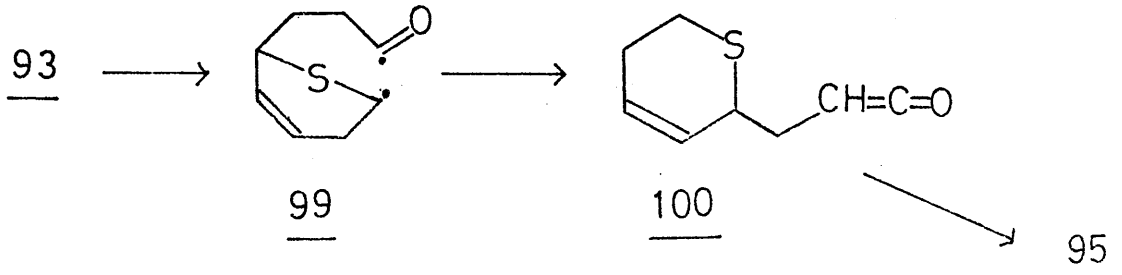
Two different mechanisms may be proposed for the rearrangement of 93. The first involves formation of a charge-transfer complex (97) which may undergo bond reorganisation to the observed products via an ylide intermediate (98) (Scheme S).

Scheme S:

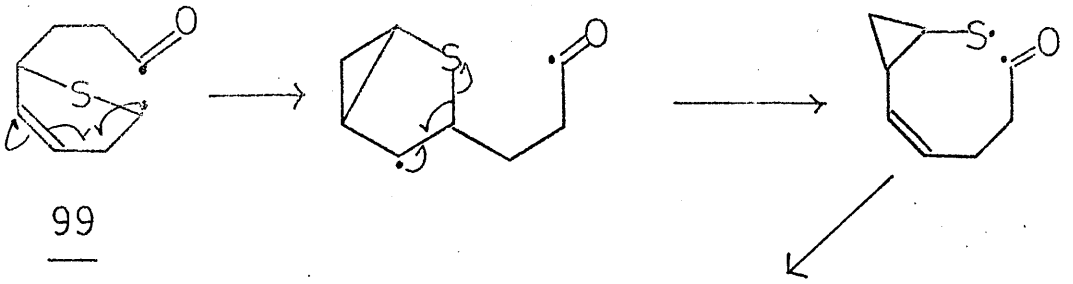


Alternatively, Norrish type I homolysis may be followed by diradical reorganisation (Scheme T).

Scheme T:



Scheme T (contd.):



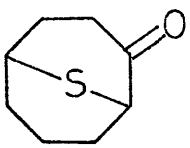
99

94

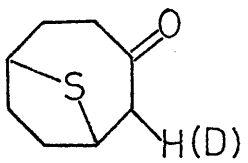
Irradiation of 93 performed in deuteriomethanol gave 96, the position of the deuterium atom being ascertained from the mass spectral fragmentation pattern of the molecule. The intermediacy of ketene (100) formed via Norrish type I cleavage followed by internal hydrogen abstraction should result in the deuterium atom being positioned $\alpha$ to the carbonyl group, and for this reason the authors rule out Scheme T. However, the results are in accord with formation of the charge-transfer complex in Scheme S.

Nevertheless, 96 could conceivably be formed by reaction of deuteriomethanol with 99 in Scheme T; in addition these results do not indicate which mechanism is operative in pentane solution.

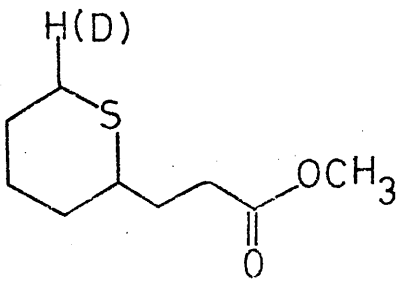
The photochemistry of $\beta$-ketosulphide (101) was examined in methanol and in deuteriomethanol, the two products (102 and 103) being formed in approximately equal proportions. The formation of 102 may be envisaged



101



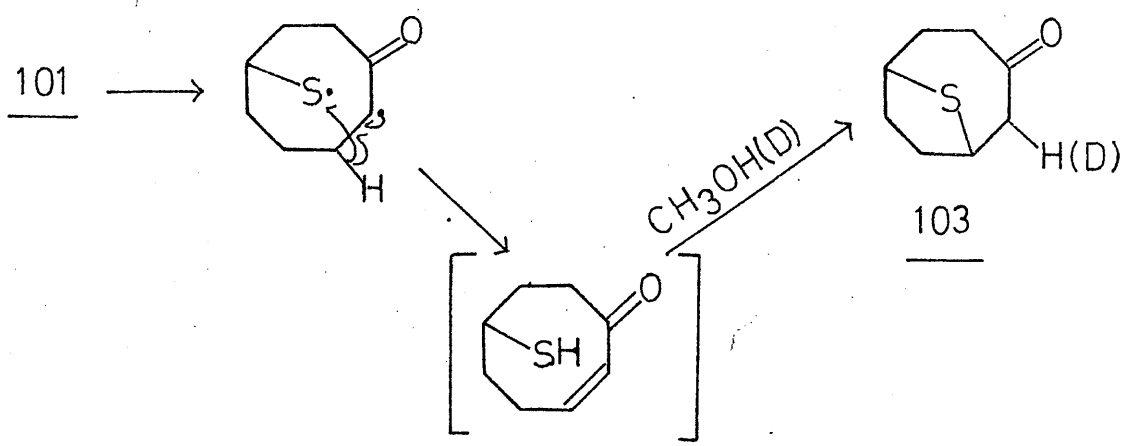
103



102

as proceeding via a charge-transfer complex analagous to 97 above. Compound 103 may arise by cleavage of the bond between the sulphur atom and the carbon atom $\alpha$ to the carbonyl group ($C_\alpha$-S fission), followed by internal hydrogen abstraction and subsequent intramolecular cyclisation of the transient intermediate (104) (Scheme U). This accounts for the incorporation of deuterium and is in agreement with the results of Ganter and Moser on the photolysis of 110.

Scheme U:

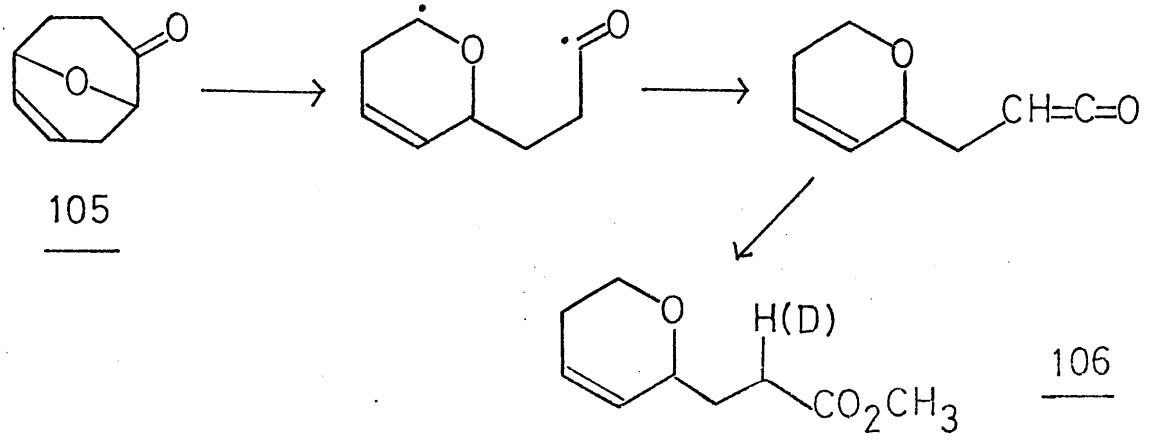



103

104

The 9-oxa compounds (105) and (107), analogues of 93 and 101, do not show an excited state interaction between the oxygen lone pairs and the carbonyl group. The products of the irradiation (106) and (108) can be explained simply by Norrish type I cleavage and internal disproportionation (Schemes V and W).

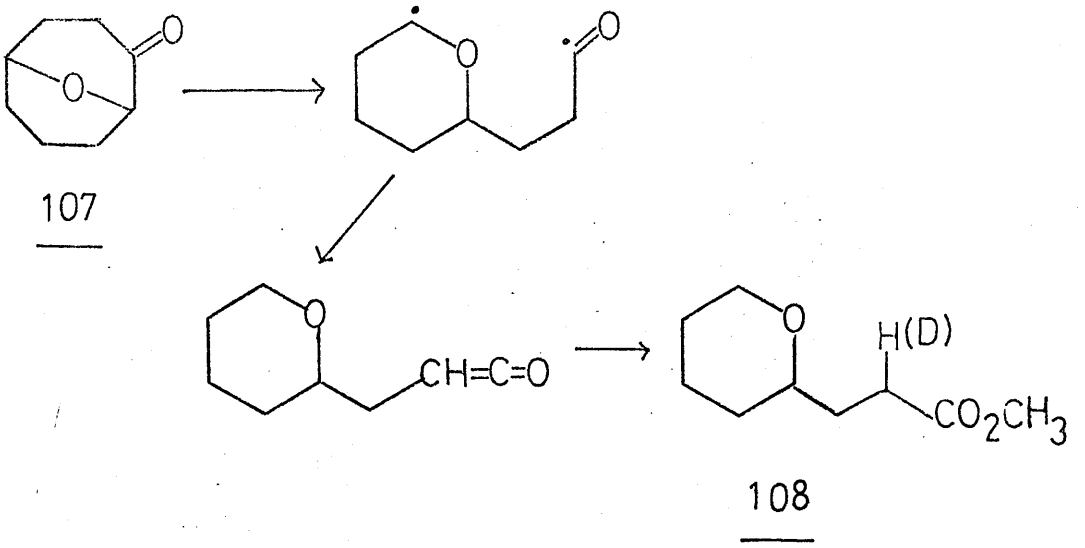
Scheme V:




105

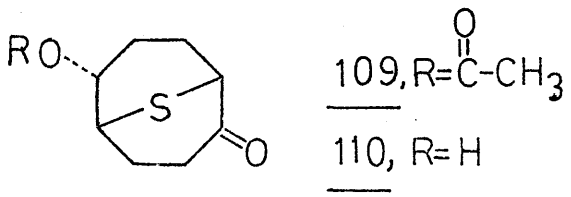
106

Scheme II:



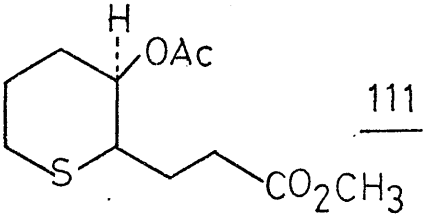
107

108



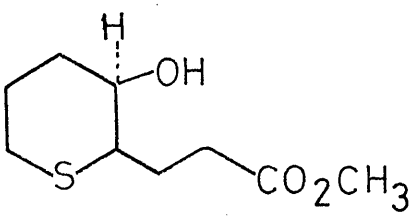
109, R = $C(=O)-CH_3$

110, R = H

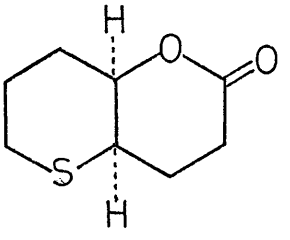


111

The irradiation of 109 and 110 has been examined[59] both in benzene and methanol solution. The initial step postulated is cleavage of the bond between the carbonyl carbon and the carbon alpha to sulphur ($\alpha$-cleavage). In this way 109 reacts to give 111, and 110 to give 112 and 113.

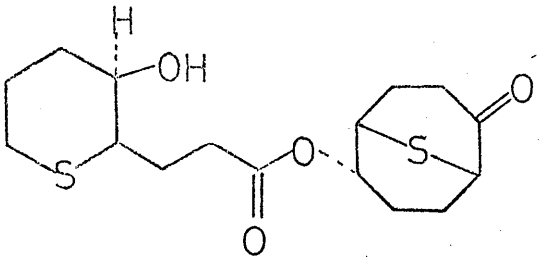


112

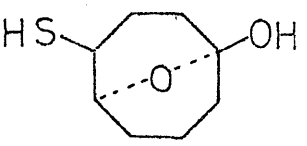


113

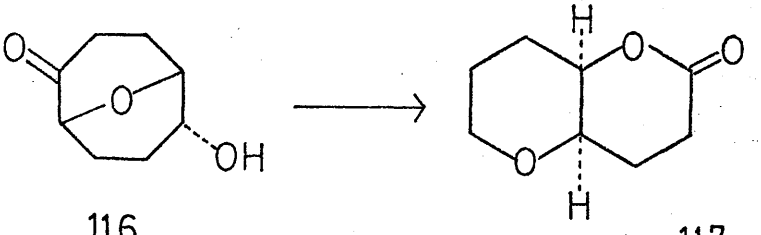
Two other compounds are also produced on irradiation of 110, intermolecular reaction resulting in 114, and $C_\alpha$-S fission with intramolecular hemiacetal formation to give 115. The oxa analogue of 110 (116)



114

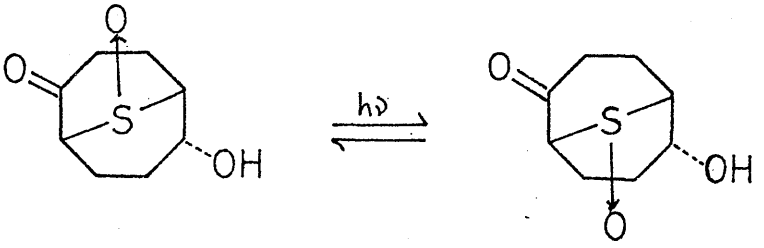


115



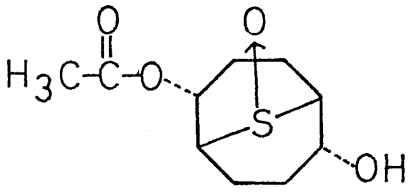
116 117

yields 117 by straightforward $\alpha$ cleavage.



118 119

Photolysis of the bicyclic sulphoxides (118) and (119) results in photostereomutation which involves an inversion of the sulphoxide sulphur stereochemical configuration as a result of an internal energy transfer from the excited carbonyl to the sulphoxide group on direct irradiation. Further evidence for this explanation was gained from the

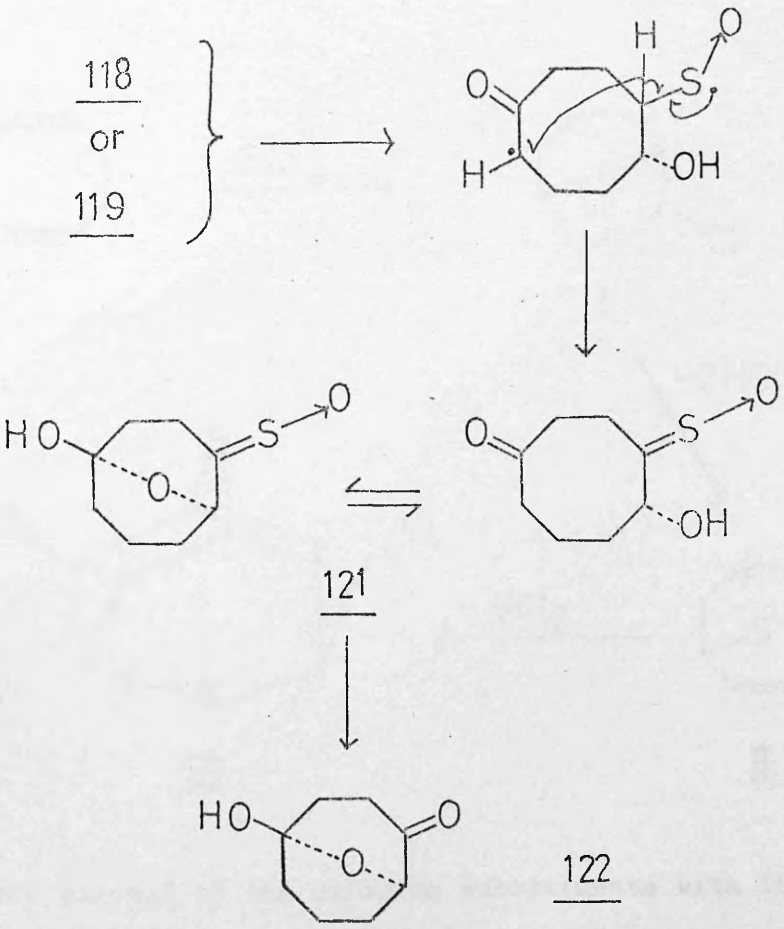


120

irradiation of 120 and its epimer which are no longer $\beta$-ketosulphoxides, in which no stereomutation was observed.

Photostereomutation is invariably accompanied by formation of decomposition products which can be derived from a radical pair by scission of the $C_\alpha$-S bond. Hence epimerisation on sulphur may operate by recombination of such radical primary photoproducts. For 118 and 119 a reformation of the $C_\alpha$-S bond should be highly favoured because of the conformational rigidity of the bicyclic skeleton. Prolonged irradiation, however, leads to a desulphurised ketone (122) which may result from trans annular shift of hydrogen after $C_\alpha$-S cleavage. The resulting sulphine (121) would be expected[62] to decompose by loss of sulphur to ketone (122) (Scheme X ).

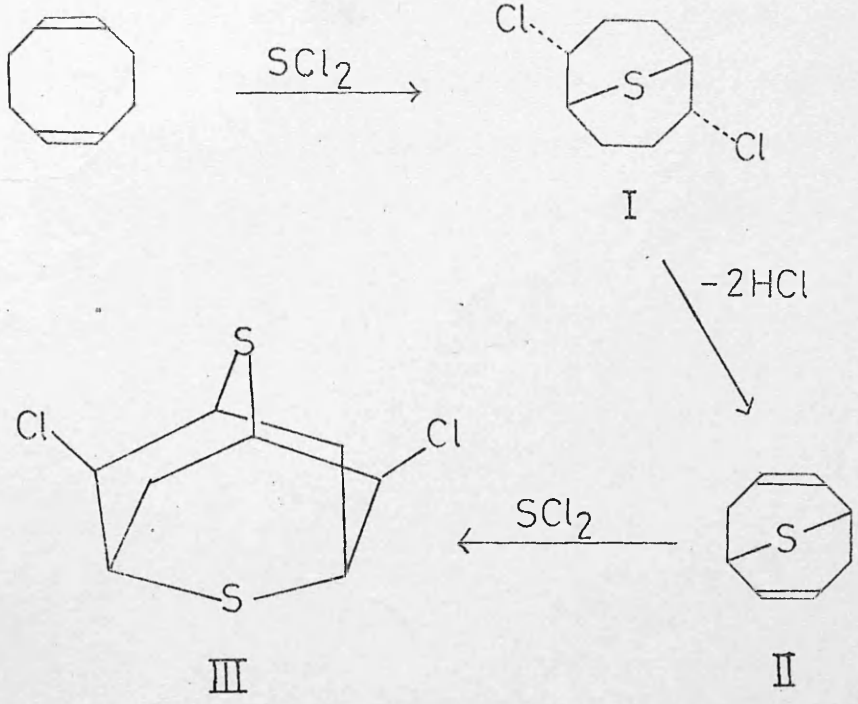
Scheme X:



## RESULTS AND DISCUSSION.

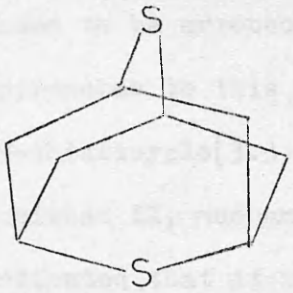
In continuation of our studies[63] of 9-thiabicyclo[3.3.1]nonane chemistry a three-step sequence (Scheme 1) was devised for the synthesis of 4,8-dichloro-2,6-dithiaadamantane (III). It was proposed that 2,6-dichloro-9-thiabicyclo[3.3.1]nonane (I), prepared by cycloaddition of cis,cis-1,5-cyclooctadiene with sulphur dichloride would dehydrochlorinate readily to the diene (II) which would condense with sulphur dichloride to give the dithiaadamantane (III).

Scheme 1:




Reductive removal of the chlorine substituents with lithium aluminium hydride would be expected to yield 2,6-dithiaadamantane (IV) itself. In addition, functional group modification of III would produce a series of 2,6-dithiaadamantane derivatives which it was hoped would be of synthetic and spectroscopic interest or furnish a series of compounds for pharmacological testing. The synthesis of the dithiaadamantane skeleton has been briefly reported in the literature[51] using cyclooctatetraene as

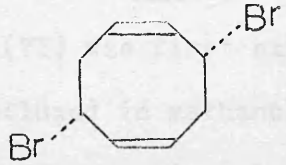
starting material but resulting in very small overall yield (ca. 6%). However, attempts to reproduce these results have always proved unsuccessful.




IV

The first stage of Scheme 1 is a reaction known[42,43] to proceed in high yield and the third stage, being analagous to this, was not envisaged to give much difficulty. Hence the key stage in the synthesis was the preparation of 9-thiabicyclo[3.3.1]nona-2,6-diene (II).

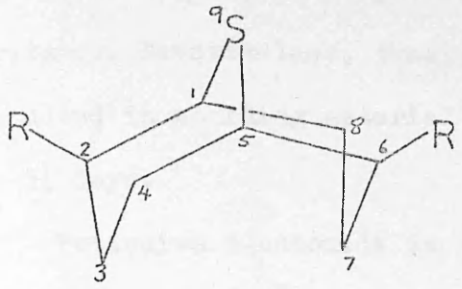
Although II would appear to have been reported[12] its structural assignment has been shown to be erroneous (*vide infra*). This chapter describes synthetic approaches to this diene *via* elimination reactions of 2,6-disubstituted 9-thiabicyclo[3.3.1]nonanes. While this method has not, in the event, furnished II, mechanistic rationalisation of the products formed has indicated that it may not, after all, be possible to prepare diene (II) by elimination from a bicyclic precursor. However, a successful preparation of II has subsequently been effected[40] by addition of sodium sulphide to *cis*-3,7-dibromocycloocta-1,5-diene (V). This is possible because of the *cis* orientation of the bromine atoms which allows addition of the sulphide dianion with concomitant expulsion of the two bromide ions.




V

Base Treatments of Dihalides (VI) and (VII):

Dihalides (VI) and (VII) were expected to undergo a facile dehydrohalogenation. The reason for this expectation was two-fold: firstly the relief of the interaction between the endo hydrogen atoms at C-3 and C-7[43], which Dreiding models indicate to be about 1 Å apart, and secondly because of the halides in the 2 and 6 positions which have already been shown[43] to be extremely labile. Thus at first the dehydrochlorination conditions employed were extremely mild.



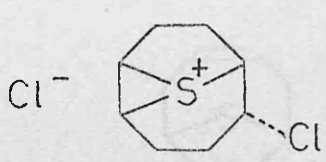

VI, R=Cl

VII, R=I

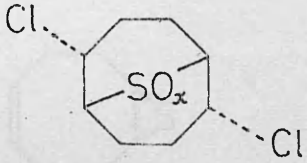
VIII, R=$OC_2H_5$

IX, R=$OCH_3$

Treatment of a chloroform solution of diiodide (VII) with basic alumina at $60^0$ resulted in formation of the diethoxy compound (VIII) presumably by nucleophilic attack on the diiodide by the ethanol stabiliser present in analar chloroform. Similarly, reaction of VII with potassium carbonate in refluxing methanol yielded dimethoxide (IX), whereas pyrolysis of an intimate mixture of the dichloride (VI) and anhydrous potassium carbonate resulted in an intractable tarry mixture. In order to overcome the facility of nucleophilic displacement of the halogen atoms of VI and VII which is probably occuring[43] via a sulphonium ion intermediate such as X, the dichlorosulphide (VI) was first oxidised to the corresponding sulphone (XIa) before being refluxed in methanolic potassium hydroxide. However, in this case the halogen atoms were inert to elimination. Sulphoxide (XIb), which has only one lone pair of electrons available, was also found to be inert to base treatment both when refluxed in methanolic potassium hydroxide and in 2,4,6-collidine.




X




XI a, x = 2

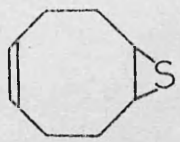
b, x = 1

1,5-Diazabicyclo[4.3.0]non-5-ene (DBN) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) are reported[64] to dehydrochalogenate readily at low temperatures. Nevertheless, treatment of dichloride (VI) with either DBN or DBU resulted in starting material only, even when refluxed in benzene for as long as $5\frac{1}{2}$ days.

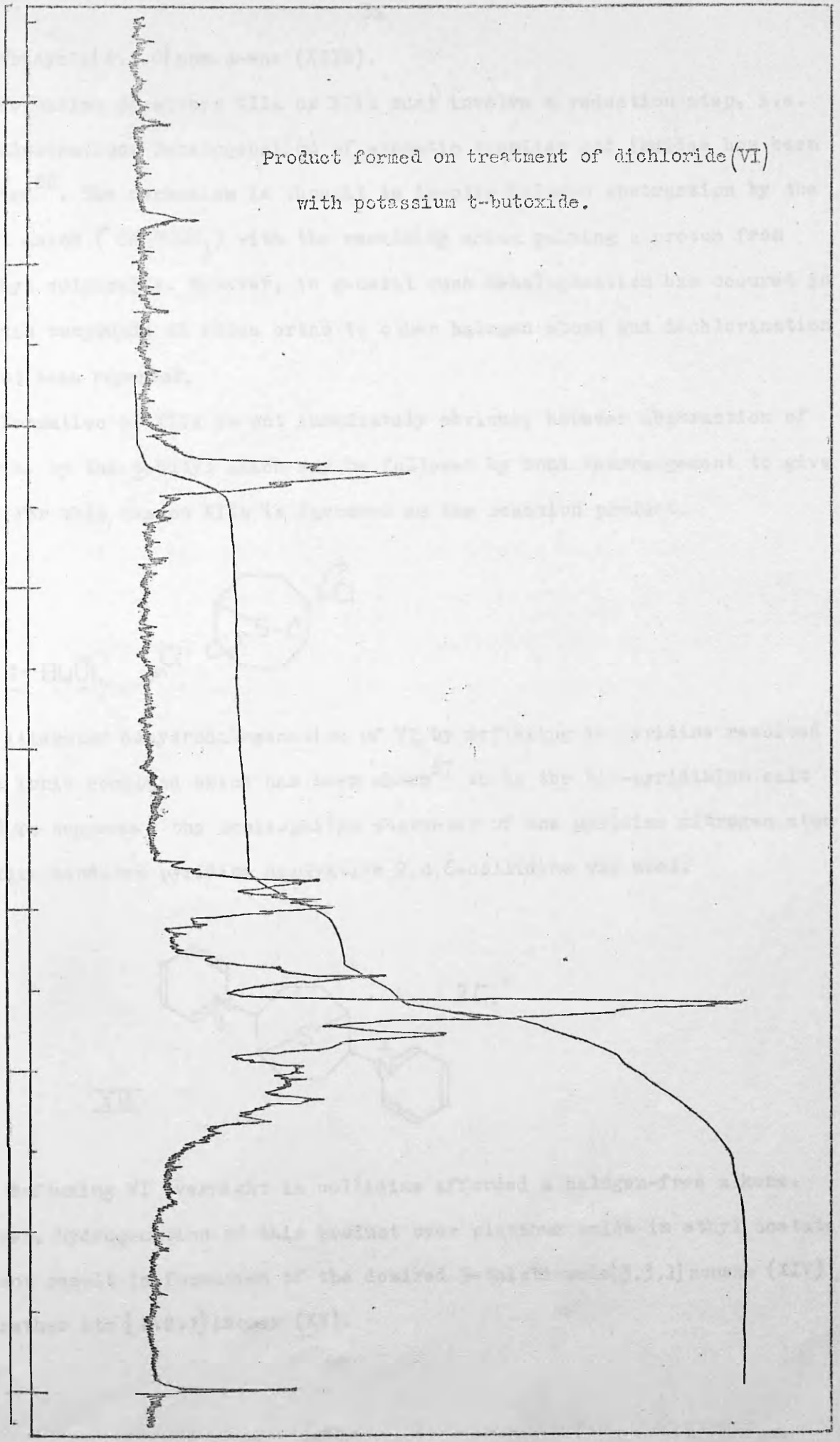
Potassium t-butoxide is rapidly becoming a popular base. Its base strength is variable and dependent upon the solvent employed, being greatest in dimethyl sulphoxide (DMSO) and least in benzene and other non-polar solvents[65]. In addition, the steric requirement of the t-butoxide anion makes it a poor nucleophile. Hence a solution of the base in DMSO was added to a solution of dichloride (VI) in DMSO at room temperature. The major product isolated was an alkene as indicated by the presence of vinyl protons (τ4.17-4.51) in the n.m.r. spectrum. However, the vinyl signal was due to two protons as shown by integration of the spectrum, and a molecular ion of m/e 140 in the mass spectrum confirmed that this was indeed a monoene. N.m.d.r. experiments showed that decoupling of the bridgehead protons (τ6.79-7.10: 2H) affected all the methylene protons (τ7.33-8.36:8H) but had no effect on the vinyl protons. Decoupling of the allylic methylenes sharpened the bridgehead protons and collapsed the vinyl protons; irradiation of the vinyl protons sharpened the allylic methylenes only, leaving the bridgehead and other methylene protons unaffected.

This evidence rules out the possibility of 9-thiabicyclo[3.3.1]non-2-ene or 9-thiabicyclo[4.2.1]non-2-ene as the product of this reaction but does not distinguish adequately between 9-thiabicyclo[4.2.1]non-3-ene (XIIa) or


XIIa




XIIb

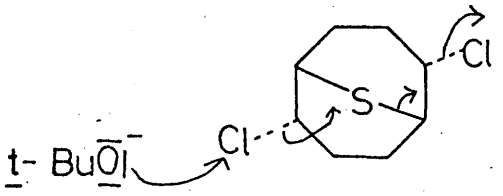



Product formed on treatment of dichloride (VI) with potassium t-butoxide.

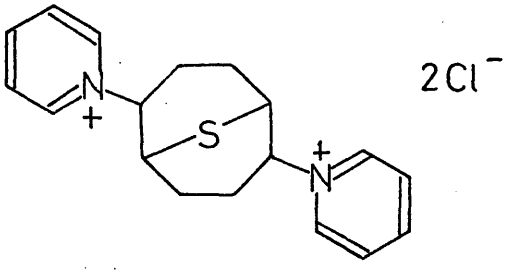
9-thiabicyclo[6.1.0]non-4-ene (XIIb).

Formation of either XIIa or XIIb must involve a reduction step, i.e. a dechlorination. Dehalogenation of aromatic bromides and iodides has been reported[66]. The mechanism is thought to involve halogen abstraction by the dimsyl anion ($^{-}CH_2SOCH_3$) with the resulting anion gaining a proton from dimethyl sulphoxide. However, in general such dehalogenation has occured in aromatic compounds at sites ortho to other halogen atoms and dechlorination has not been reported.

Formation of XIIa is not immediately obvious, however abstraction of chlorine by the t-butyl anion may be followed by bond rearrangement to give XIIb. For this reason XIIb is favoured as the reaction product.



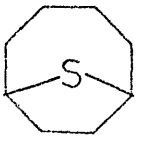

Attempted dehydrohalogenation of VI by refluxing in pyridine resulted in an ionic compound which has been shown[67] to be the bis-pyridinium salt (XIII). To suppress the nucleophilic character of the pyridine nitrogen atom the more hindered pyridine derivative 2,4,6-collidine was used.




XIII

Refluxing VI overnight in collidine afforded a halogen-free alkene. However, hydrogenation of this product over platinum oxide in ethyl acetate did not result in formation of the desired 9-thiabicyclo[3.3.1]nonane (XIV) but rather its [4.2.1]isomer (XV).

XIV

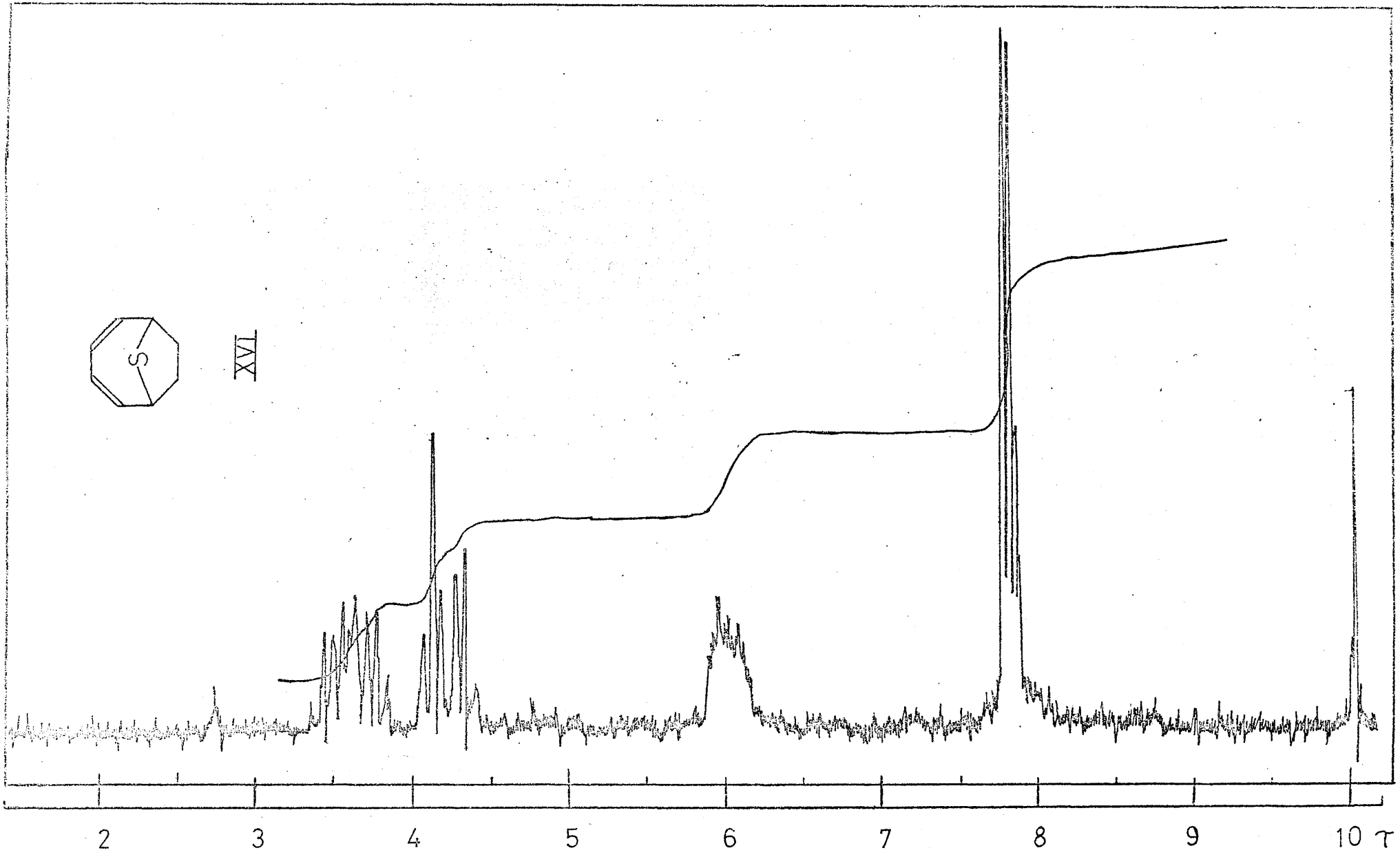


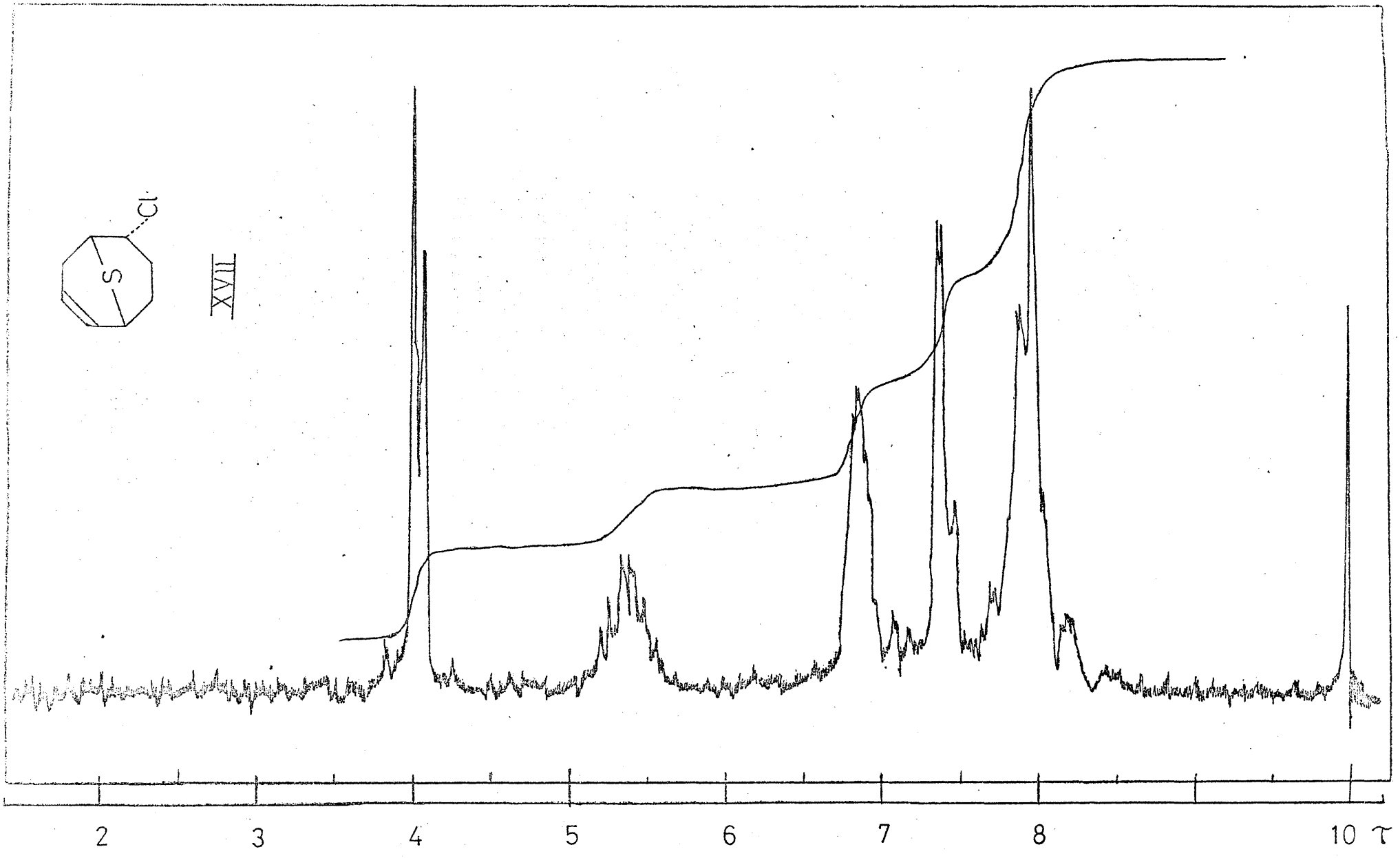
XV

The collidine reaction product exhibits spectroscopic characteristics closely similar to those reported for 9-heterobicyclo[4.2.1]nonadienes[31] and trienes[52]. The diene exhibits an intense absorption in the u.v. spectrum (see experimental p.75) characteristic of conjugated double bonds. The n.m.r. spectrum of the diene shows a complex four spin (AA'BB') system[68] in the vinyl region, $\tau$3.50-3.82 (2H) and $\tau$4.13-4.40 (2H) and possesses a H-C-S multiplet (2H) at $\tau$6.00. Double irradiation of the latter signal simplified the lower-field vinyl envelope and the methylene multiplet ($\tau$7.80) but double irradiation at $\tau$7.80 sharpened only the H-C-S resonance. Thus, a vinylic hydrogen and a methylene group cannot be adjacent as in II but must be separated by a bridgehead hydrogen atom, as in XVI.

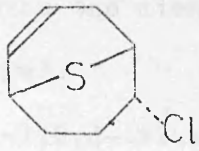
XVI

In contrast chloroalkene (XVII) and hydroxyalkene (XVIII) which have one double bond in a situation identical to the alkene groups of II each exhibit a narrow vinyl multiplet ($\tau$4.00 and $\tau$4.10 respectively) and have an allylic bridgehead signal at considerably higher field ($\tau$6.90

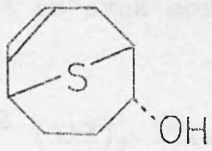

S
XVI
2
3
4
5
6
7
8
9
10 τ


Cl
S
XVII
2
3
4
5
6
7
8
10 τ

and τ 7.00)[69]. As expected, double irradiation of the allylic methylene multiplet of XVII collapses both the vinyl and the bridgehead resonances.



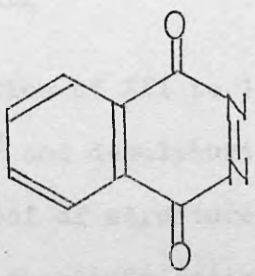

XVII



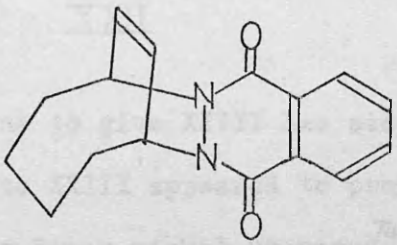

XVIII

It is concluded, on spectroscopic evidence that the product of reaction of collidine with dichloride (VI) has structure XVI.

If this structural assignment is correct then XVI as a conjugated diene should be expected to undergo a (4+2) cycloaddition reaction with a dienophile. However, attempted addition of maleic anhydride to this diene failed, not only in refluxing benzene, but also when the two reactants were mixed together in the absence of solvent and heated to 140° in a sealed tube. In both cases only the two starting materials were obtained. Phthalazine-1,4-dione (XIX) has been described[70] as a very potent dienophile, adding to 1,3-cyclooctadiene at ice-bath temperature to give Diels Alder adduct (XX) in good yield when previous attempts to form an adduct with maleic anhydride had resulted[71] only in polymeric material.



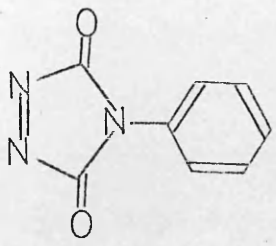

XIX



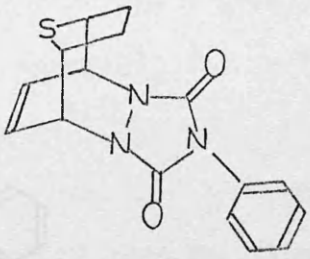

XX

Nevertheless, when diene (XVI) was treated with XIX only the two starting materials were recovered from the reaction mixture. It appears therefore that the dienophile may be hindered, perhaps by the sulphur atom, as it approaches the diene system and that an even more potent dienophile must be employed.

4-Phenyl-1,2,4-triazoline-3,5-dione[72] (XXI), like XIX has a nitrogen-nitrogen double bond constrained to a cis configuration and it is this which greatly enhances their dienophilic activity over such compounds as dimethyl azodicarboxylate in which the N=N bond can adopt the trans configuration. In addition XXI is inherently more strained than XIX having this double bond in a five membered ring and the relief of this strain renders it an even more potent dienophile than XIX. For this reason the diene and XXI were refluxed together in dry benzene. The course of the reaction could be observed by the gradual discharge of the deep-red colour of XXI to give a yellow solution. Evaporation of solvent afforded crystals of a 1:1 adduct assigned structure XXII.



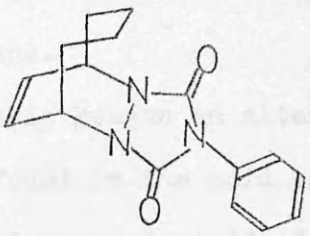
XXI



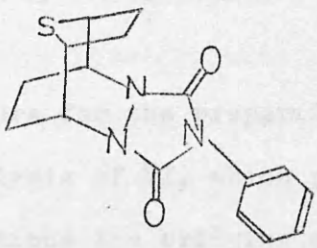
XXII

Addition of XXI to 1,3-cyclooctadiene to give XXIII has since been reported[73] and desulphurisation of XXII to XXIII appeared to provide a simple proof of structure. However, using Raney nickel prepared[74] for selective desulphurisation in the presence of double bonds, reaction with XXII yielded a product which still exhibited H–C–S protons but no vinylic protons in the n.m.r. spectrum, and was assigned structure XXIV. $\omega$-2

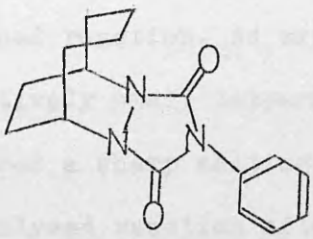
Raney nickel, deactivated by refluxing in acetone[75] before addition of substrate gave no reaction. However, using ω-2 Raney nickel without deactivation, a product showing neither H–C–S protons nor vinylic protons was obtained. This product, which was identical to the hydrogenation product of XXIII in all spectroscopic and chromatographic details, in melting point and in mixed melting point was assigned structure XXV. This proves that XXII is in fact the correct structural assignment for the 1:1 adduct of the diene and XXI and that this diene is in fact the conjugated diene 9-thiabicyclo[4.2.1]nona-2,4-diene (XVI).



XXIII



XXIV



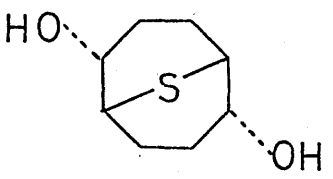
XXV

Dehydration of Diol (XXVI):

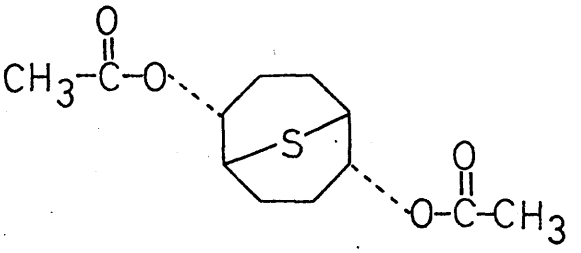
An alternative synthesis of diene (II) was sought by dehydration of diol (XXVI) or by elimination reactions of derivatives of this diol. XXVI has previously been obtained[43] from the base catalysed hydrolysis of the corresponding dichloride (VI). However, the melting point of the crude reaction product was found to occur over such a wide temperature range that some formation of the diol with the isomeric [ 4.2.1 ] skeleton was suspected. Attempts to determine whether indeed this was a mixture by a g.l.c. analysis of the dibenzoate or of the bistrimethylsilyl ether derivative met with no success when conditions for distinct retention times of derivatives of the pure [ 3.3.1] and [ 4.2.1 ] compounds could not be found.

For this reason an alternative procedure for the preparation of the diol was found in the acid catalysed hydrolysis of VI, which proceeded readily and in good yield. In acidic conditions the bridging sulphur would be expected to protonate and hence be unable to utilise its lone pairs to form an episulphonium intermediate. A species such as X, which permits but does not require rearrangement, is a probable intermediate in the base catalysed reaction. As expected, the crude reaction product melted over a relatively small temperature range (ca. $5^{0}$) and on recrystallisation afforded a sharp melting product identical to that obtained from the base catalysed reaction after many recrystallisations.

Unfortunately, attempted dehydration of the diol with phosphorus oxychloride met with little success, resulting in a variety of products all present in too small a quantity to allow isolation and identification. However, the compound is still a useful starting material for the corresponding esters whose pyrolyses could provide an alternative method to the dehydrohalogenation of VI or VII.



XXVI



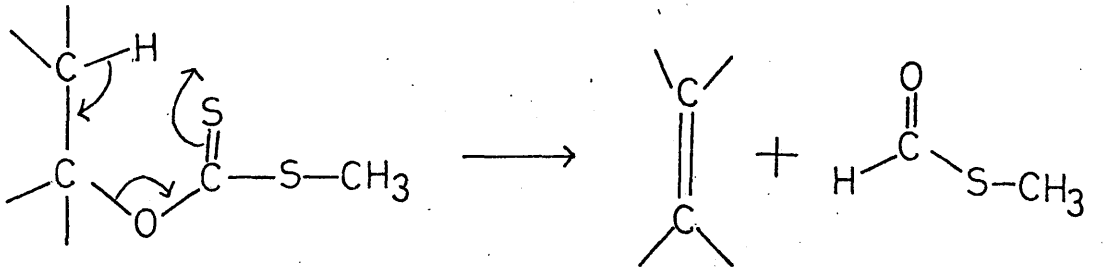
XXVII

Pyrolytic Eliminations:

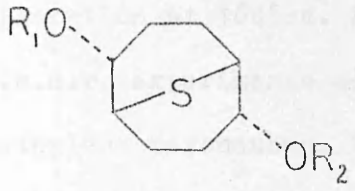
The readily available diacetate (XXVII) did not readily eliminate on pyrolysis, requiring a high temperature and resulting in a mixture of an alkene and black decomposition products. However, this alkene was identical in all respects to the product of the reaction of VI with collidine and hence was assigned structure XVI. It may be argued that the initial product of pyrolysis was the desired [ 3.3.1] diene (II) which isomerises at the high reaction temperature and hence a milder method of pyrolysis was sought.

The Chugaev reaction[76] involves the thermal decomposition of the xanthate esters of an alcohol, containing a $\beta$ hydrogen atom, to produce an alkene. Because the reaction goes via a cis elimination process (Scheme 2) and at a lower temperature than the corresponding acetates it appeared ideally suited to the formation of diene (II).

Scheme 2:



However, attempts to synthesise the bis S-methylxanthate (XXVIII) furnished a mixture containing mainly the mono S-methylxanthate (XXIX) although the latter was never isolated in a pure state.



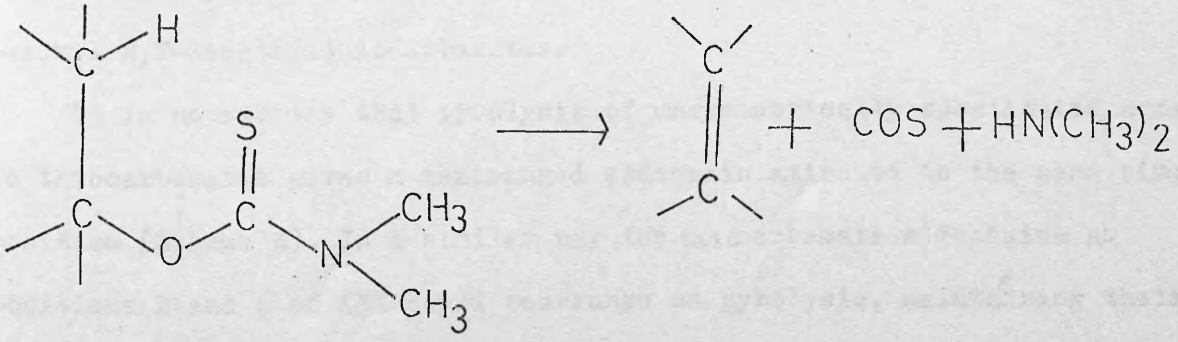
XXVIII, $R_1 = R_2 = -C(=S)-S-CH_3$

XXIX, $R_1 = H$, $R_2 = -C(=S)-S-CH_3$

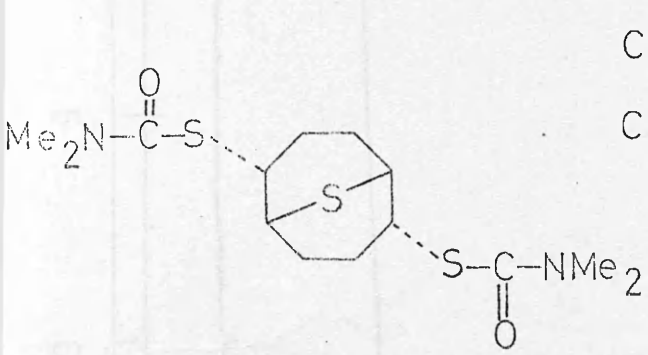
XXX, $R_1 = R_2 = -C(=S)-N(CH_3)_2$

A report by Newman[77] indicated that O-alkyl N,N-dimethylthiocarbamates were easily prepared in high yield from the corresponding alcohols and more readily purified than xanthates. Pyrolysis of those with a $\beta$ hydrogen atom are reported to give alkenes in high yield (Scheme 3). Moreover, the temperature required for the pyrolysis is somewhat lower than that needed for the corresponding xanthates. Presumably, this is because of the electron donating effect of the nitrogen atom which increases, through resonance, the electron density on the sulphur atom.

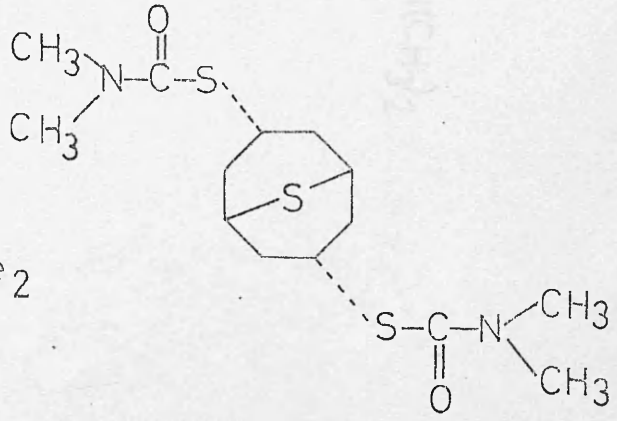
Scheme 3:




Treatment of diol XXVI with sodium hydride gave the corresponding alkoxide salt which on reaction with N,N-dimethylthiocarbamoyl chloride ($(CH_3)_2N.CS.Cl$) gave XXX directly. Pyrolysis of XXX did not yield the desired diene but furnished a rearranged product which exhibits a carbonyl absorption at 1645cm.$^{-1}$ Double irradiation of the bridgehead protons in n.m.d.r. experiments collapsed the other $\underline{H}-\overset{|}{C}-S$ signal and sharpened the methylene resonances. This suggests that the product of rearrangement was XXXI rather than XXXII in which decoupling of the bridgehead position would produce an effect at the methylenes with little or no effect on the other $\underline{H}-\overset{|}{C}-S$ signal.



XXXI

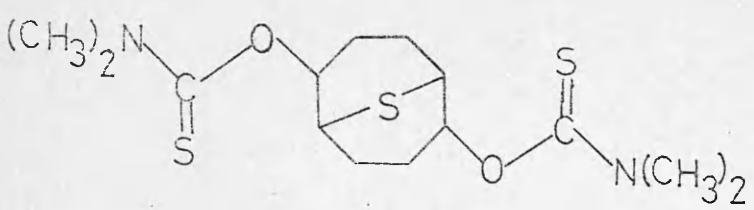


XXXII

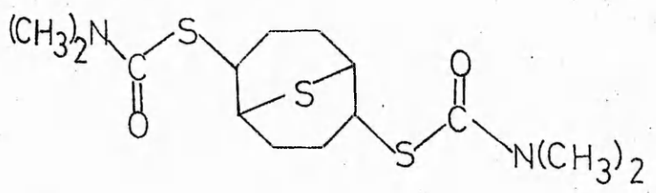
Although there are analogies for such a rearrangement in the literature[78] these occur mainly for aromatic N,N-dimethylthiocarbamates and with certain protected sugars[77] which give low yields of the corresponding S-alkyl N,N-dimethylthiocarbamates.

It is noteworthy that pyrolysis of unsymmetrically substituted aromatic thiocarbamates gives a rearranged sidechain attached to the same ring position (Scheme 4). In a similar way the thiocarbamate sidechains at positions 2 and 6 of XXX could rearrange on pyrolysis, maintaining their site of attachment.

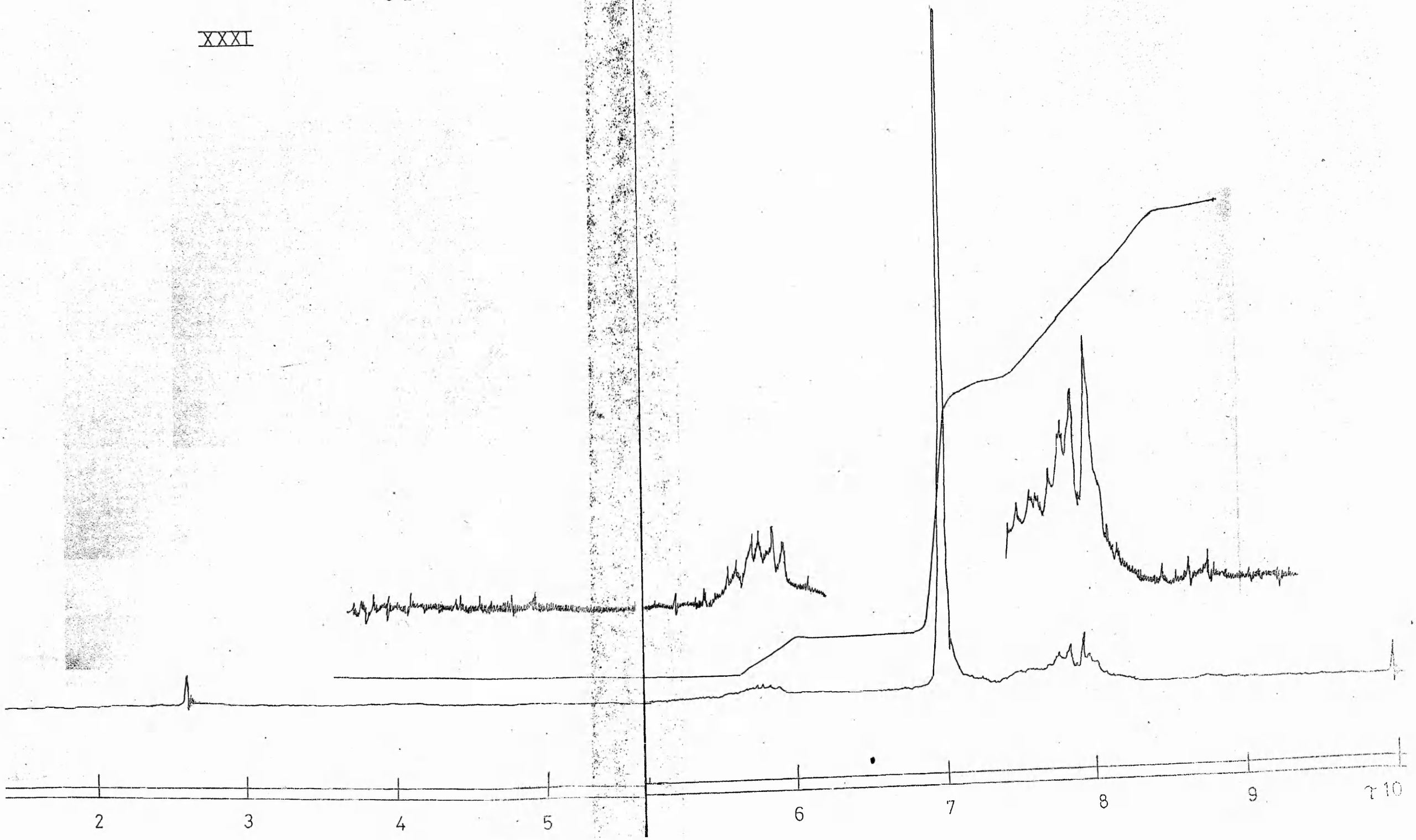
However, since this facile sidechain inversion is uncharacteristic of an alkylthiocarbamate the rearrangement could be anchimerically assisted



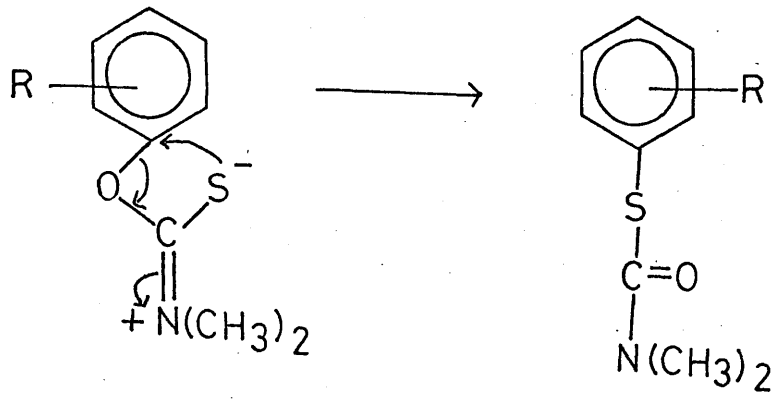

XXX



XXXI

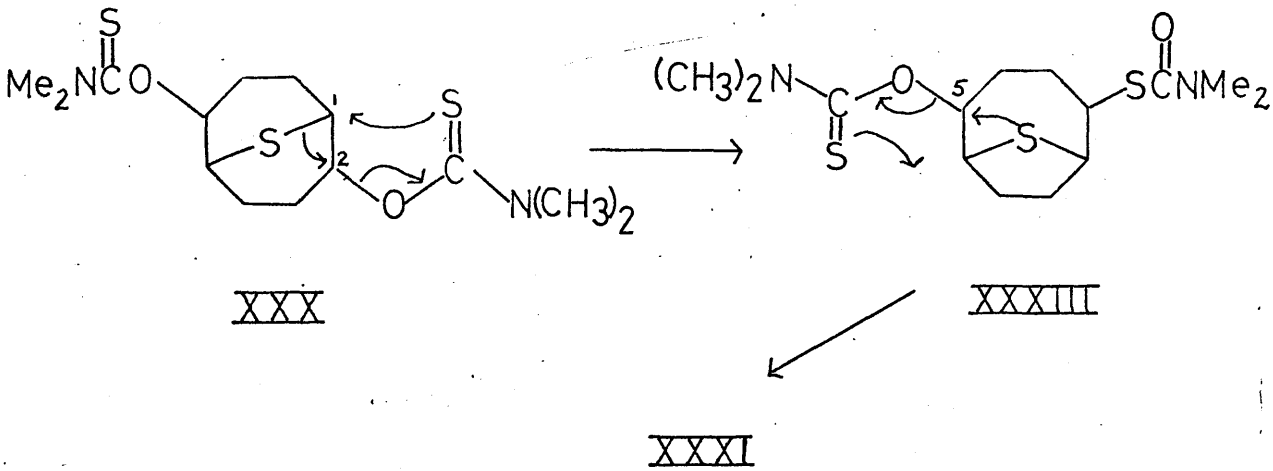


Scheme 4:




by the sulphur bridge (Scheme 5). Backside attack on a bridgehead position by the thione sulphur and fission of the C-2-O bond can be accompanied by C-1 to C-2 migration of the bridge. The thiocarbamate substituent at C-5 of the resulting 9-thiabicyclo[4.2.1]nonane (XXXIII) could undergo rearrangement in a similar manner restoring the bicyclo[3.3.1]skeleton. The feasibility of this mechanism is at present under investigation.

Scheme 5:

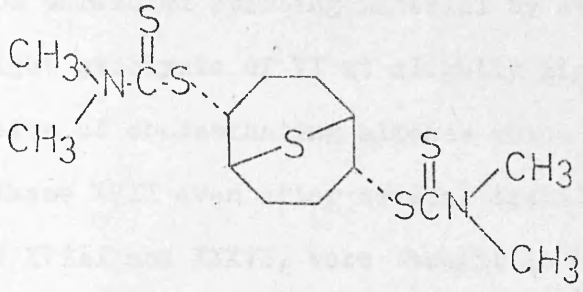



XXX XXXIII

XXXI

N,N-dimethyldithiocarbamate (XXXIV) should either undergo pyrolytic elimination by a method analogous to that of Scheme 3 or undergo a rearrangement similar to that already observed for XXX to give only starting material. Thus XXXIV was prepared[43] by the reaction of dichloride (VI) with sodium dimethyldithiocarbamate and pyrolysed. Pyrolysis around 200° gave a quantitative yield of starting material and higher temper-

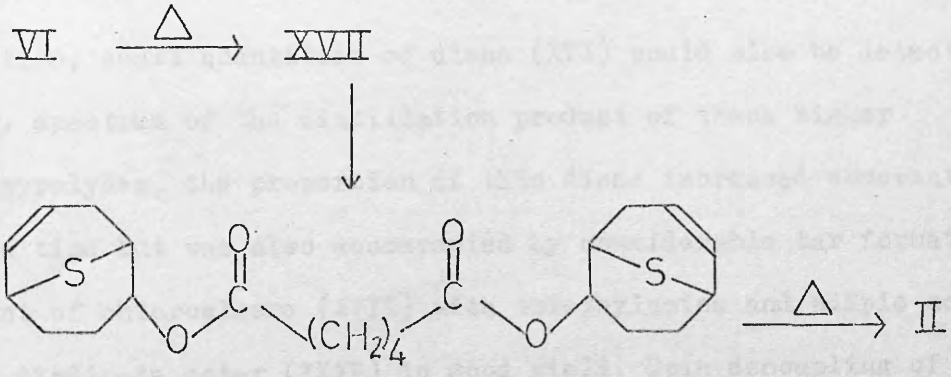
atures afforded a mixture of starting material and tarry decomposition products. Presence of a small amount of [4.2.1] diene XVI was observed in the n.m.r. spectra of these higher temperature pyrolysis products but no evidence of any other alkene could be detected.



XXXIV

A previously reported[12] method for the preparation of diene (II) involves pyrolysis of the diadipate ester (XXXV). This had not been attempted because of the initial difficulty experienced in preparing the intermediate chloroalkene (XVII) by the reported pyrolytic dehydrohalogenation of VI and because this preparation involved several steps (Scheme 6).

Scheme 6:

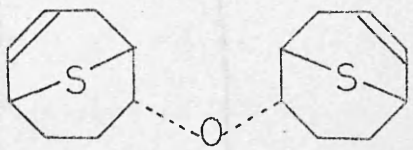


XXXV

Pyrolysis of VI in a cylindrical heated glass tube through which a slow stream of nitrogen was passed, was found to be ineffective because of

the ready sublimation of VI from the pyrolysis boat. A more efficient procedure was found to be overnight heating of VI in a partially evacuated sealed tube totally enclosed in a pyrolysis oven at ca. 165°.

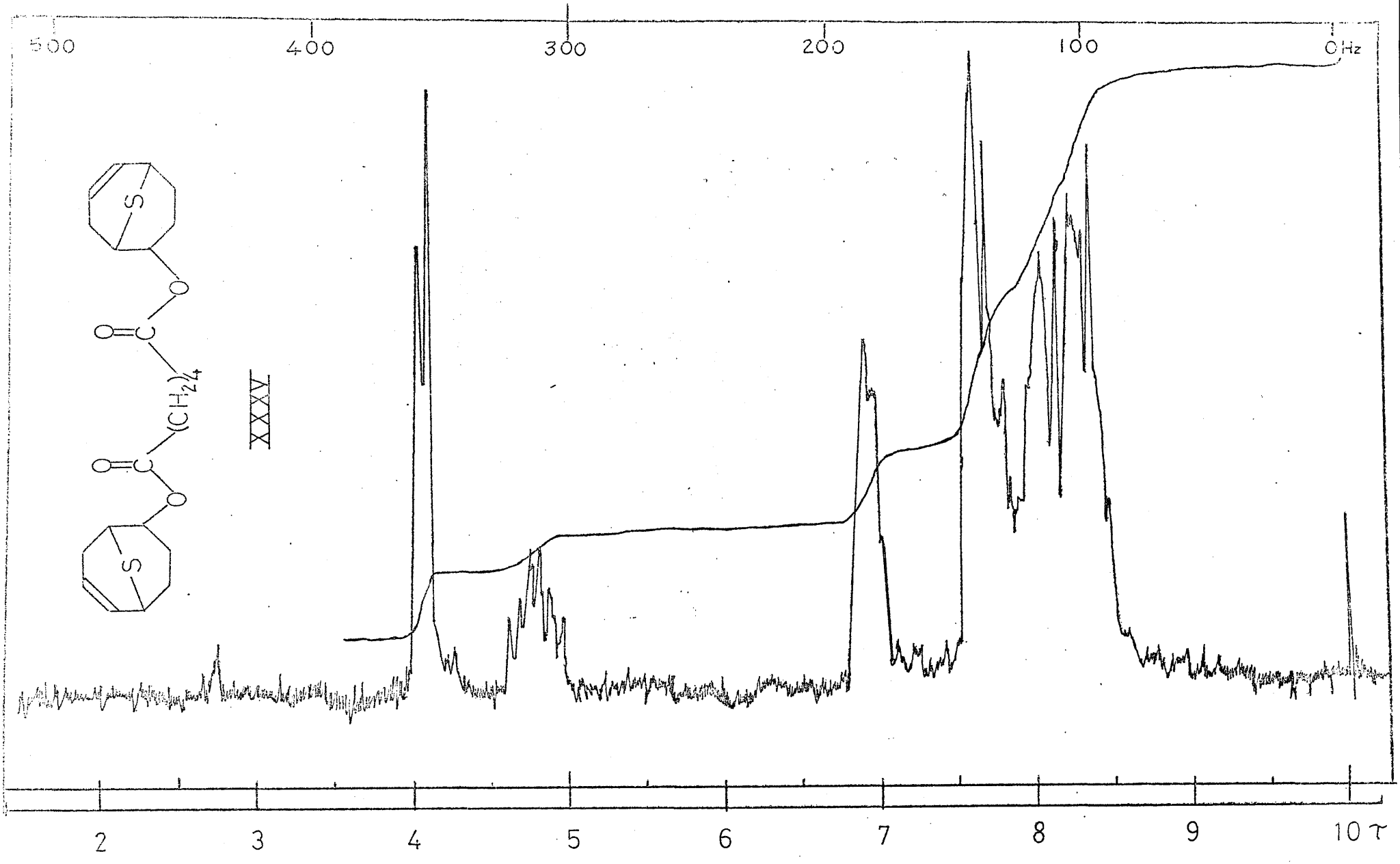
These conditions did not give complete reaction but XVII was easily separable from unreacted starting material by ether extraction and distillation. Overnight pyrolysis of VI at slightly higher temperatures resulted in the formation of contaminating alkenes which were not readily separable from chloroalkene XVII even after several distillations. These alkenes identified as XVIII and XXXVI, were thought to be the result of reaction of XVII at these elevated temperatures with water adsorbed on the surface of the glass tube and were formed to some extent even when the tube had been rigorously flame-dried before reaction.




XXXVI

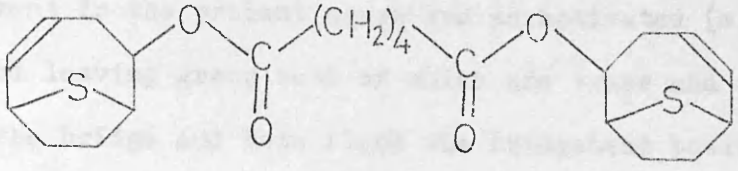
In addition, small quantities of diene (XVI) could also be detected in the n.m.r. spectrum of the distillation product of these higher temperature pyrolyses, the proportion of this diene increased somewhat with reaction time but was also accompanied by considerable tar formation.

Treatment of chloroalkene (XVII) with triethylamine and adipic acid afforded the diadipate ester (XXXV) in good yield. Spin decoupling of the bridgehead proton (τ6.90;4H) of XXXV collapsed both the allylic methylene (τ7.60;4H) and the H–C–O signals (τ4.80;2H) whereas double irradiation at the H–C–O affected the bridgehead proton and part of the methylene envelope (τ7.60–8.50) but left the allylic methylene signal unchanged. This indicates that the H–C–O must be separated from the allylic methylene




XXXV

by the bridgehead proton as in XXXV and that rearrangement to the isomeric [4.2.1] skeleton of XXXVII has not occurred during this reaction.



XXXVII

Nevertheless, although pyrolysis of XXXV occurredsmoothly the product was not 9-thiabicyclo[3.3.1]nona-2,6-diene (II) as reported but was the isomeric 9-thiabicyclo[4.2.1]nona-2,4-diene (XVI).

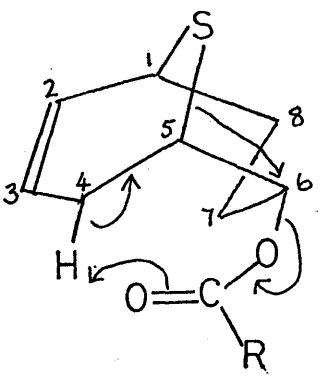
Mechanism of Rearrangement:

In replacement reactions at C-2 and C-6 of 9-thiabicyclo[3.3.1]nonane derivatives, the observation that skeletal rearrangement to 9-thiabicyclo [4.2.1]nonane products does not occur has been rationalised in terms of the favourable thermodynamic stability of the twin-chair conformation of the former and the increased angle strain in the latter. It is the more suprising that 9-thiabicyclo[4.2.1]nonane products are not observed, even as the products of kinetic control when episulphonium ions such as X have been proposed as reaction intermediates.

For the intermediacy of a fully developed episulphonium ion, elimination of a good leaving group must precede interaction with a nucleophile. In the absence of a nucleophile an episulphonium ion such as X must eliminate a positively charged grouping (e.g. $H^+$) to proceed to a neutral product. As for replacement reactions this elimination can conceivably occur with retention of the [3.3.1] skeleton or with rearrangement to the [4.2.1] structure.

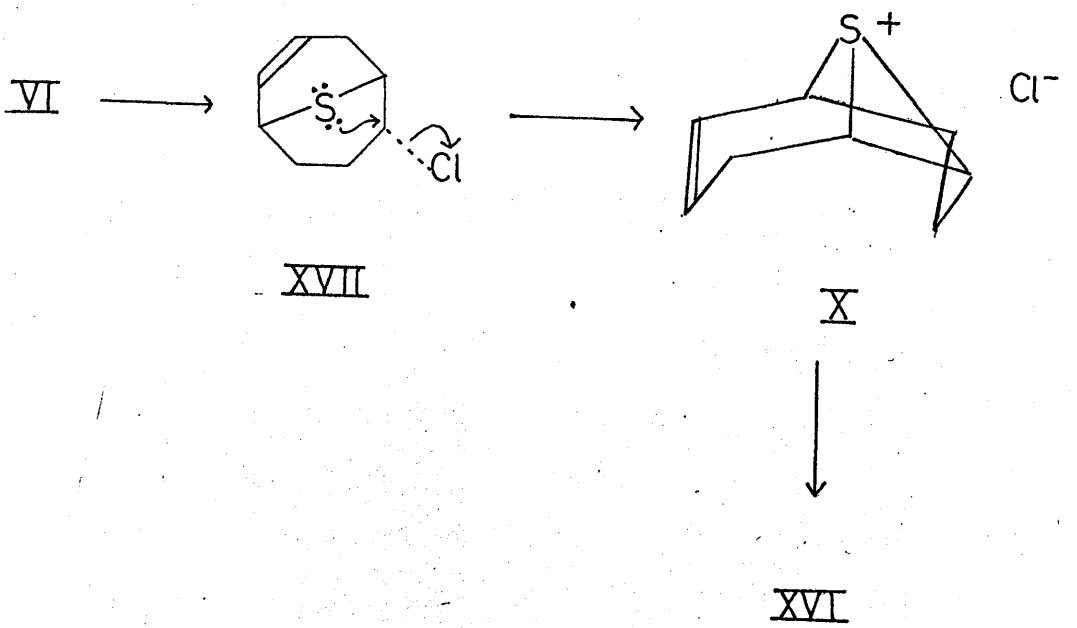
It now appears that both the pyrolytic and base induced eliminations of 2-substituted or 2,6-disubstituted 9-thiabicyclo[3.3.1]nonanes can indeed occur with skeletal rearrangement. The structural features which promote rearrangement in the present cases are an activated (e.g. allylic) C-H bond and a good leaving group both of which are trans and anti-periplanar to a C-S bond of the bridge and both flank the bridgehead position. (see Scheme 7). The pyrolytic and solvolytic eliminations of these bicyclic compounds differ only in sequence of events. In the former case (Scheme 7) an electron rich site on the leaving group induces elimination of the quasi equitorial hydrogen atom at C-4. A $\Delta^{4,5}$ double bond is formed with C-5 to C-6 migration of the C-S bond and expulsion of the leaving group.

Scheme 7:




In the latter case (Scheme 8) the polar solvent promotes ionisation of the C-Cl bond, this cleavage being anchimerically assisted by a sulphur bridge lone pair. The resulting episulphonium ion collapses by elimination of the anti C-4 hydrogen atom. It now seems clear that the synthesis of diene (II) by stepwise elimination reactions of 2- and/or 6-substituted 9-thiabicyclo[3.3.1]nonanes will not succeed because of the activating influence of the first formed double bond and the alignment of the leaving groups.

Scheme 8:

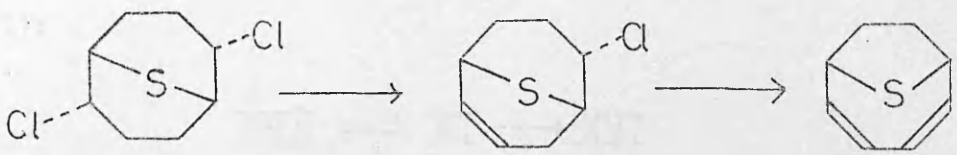


Investigations into the mechanism of rearrangement:

To further our understanding of the skeletal rearrangement involved in the transformation of 2,6-dichloro-9-thiabicyclo[3.3.1]nonane (VI) to 9-thiabicyclo[4.2.1] nona-2,4-diene(XVI), reaction of dichloride (VI) with 2,4,6-collidine was studied as a function of reaction time. N.m.r. spectra (pp56-59) of aliquots taken as the reaction progressed indicated that chloroalkene (XVII) is produced before formation of diene (XVI). Hence it appears that rearrangement to the bicyclo[4.2.1] skeleton does not occur until after formation of the double bond.

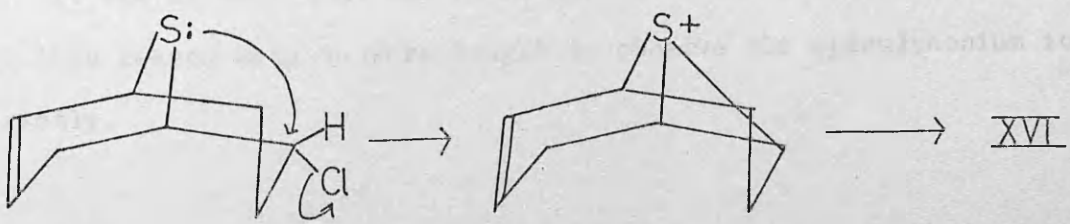
The reaction of chloroalkene (XVII) with 2,4,6-collidine was studied in a similar manner. In this case the only product detectable by n.m.r. was diene (XVI). Thus chloroalkene (XVII) is a definite precursor of XVI.

The possible pathways for the rearrangement of dichloride (VI) to XVI were considered. The most direct route would involve monodehydrochlorination of VI yielding XVII with subsequent rearrangement to diene XVI, viz:



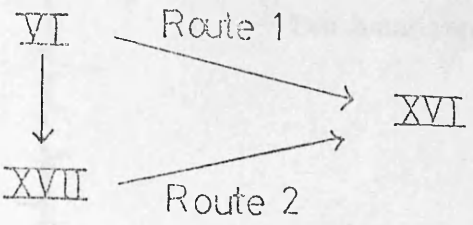

VI XVII XVI

This route, in which sulphonium species X, arising by sulphur assisted elimination of chloride, would probably participate was considered to be the most likely:

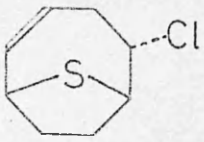



XVII X

However, other pathways may be envisaged. For example, the dichloride (VI) may initially form chloroalkene (XVII) and each may yield diene (XVI) by separate reaction pathways:

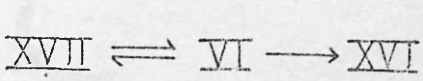



VI may conceivably go to diene XVI via an intermediate such as:



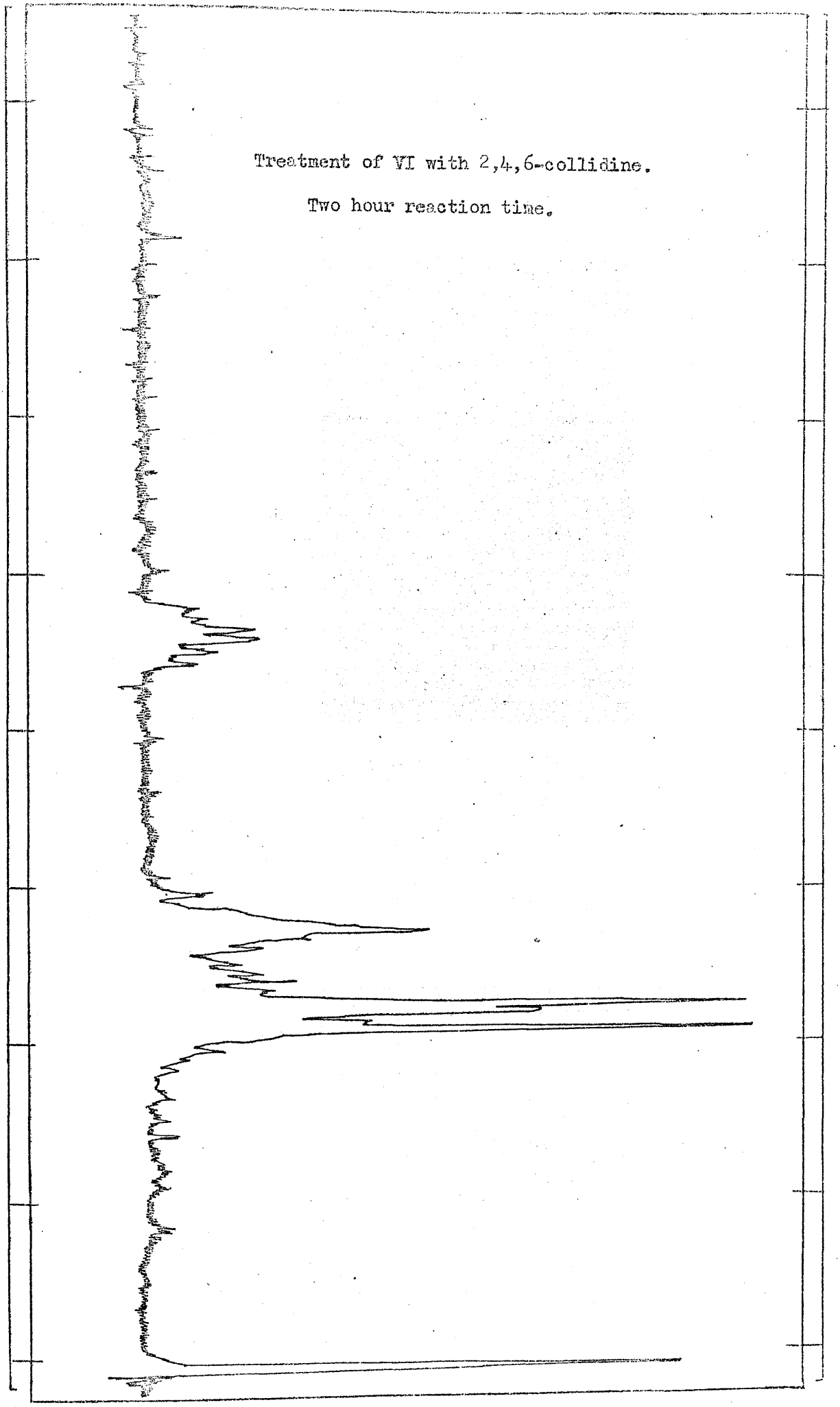

That there is no n.m.r. evidence for such a species could be explained if it were reactive and hence short-lived. Nevertheless such a route was considered to be unlikely.

A third possibility involves a reversible reaction between the dichloride and chloroalkene with subsequent rearrangement of the dichloride to diene (XVI):



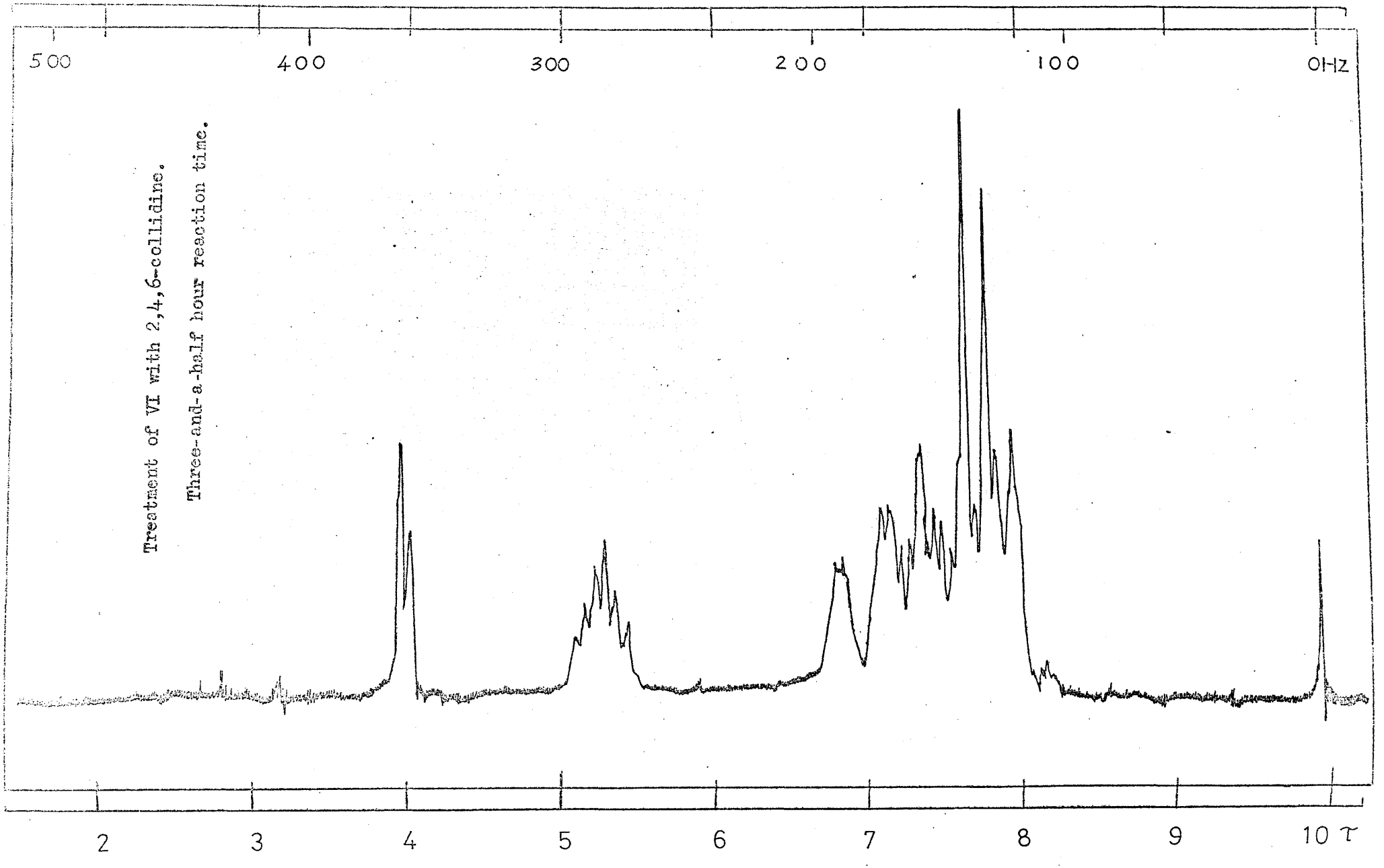

However, this possibility was excluded when XVII was found to rearrange to XVI with no appearance of VI in the n.m.r. spectrum. Therefore the first mechanism was considered to be the most probable.

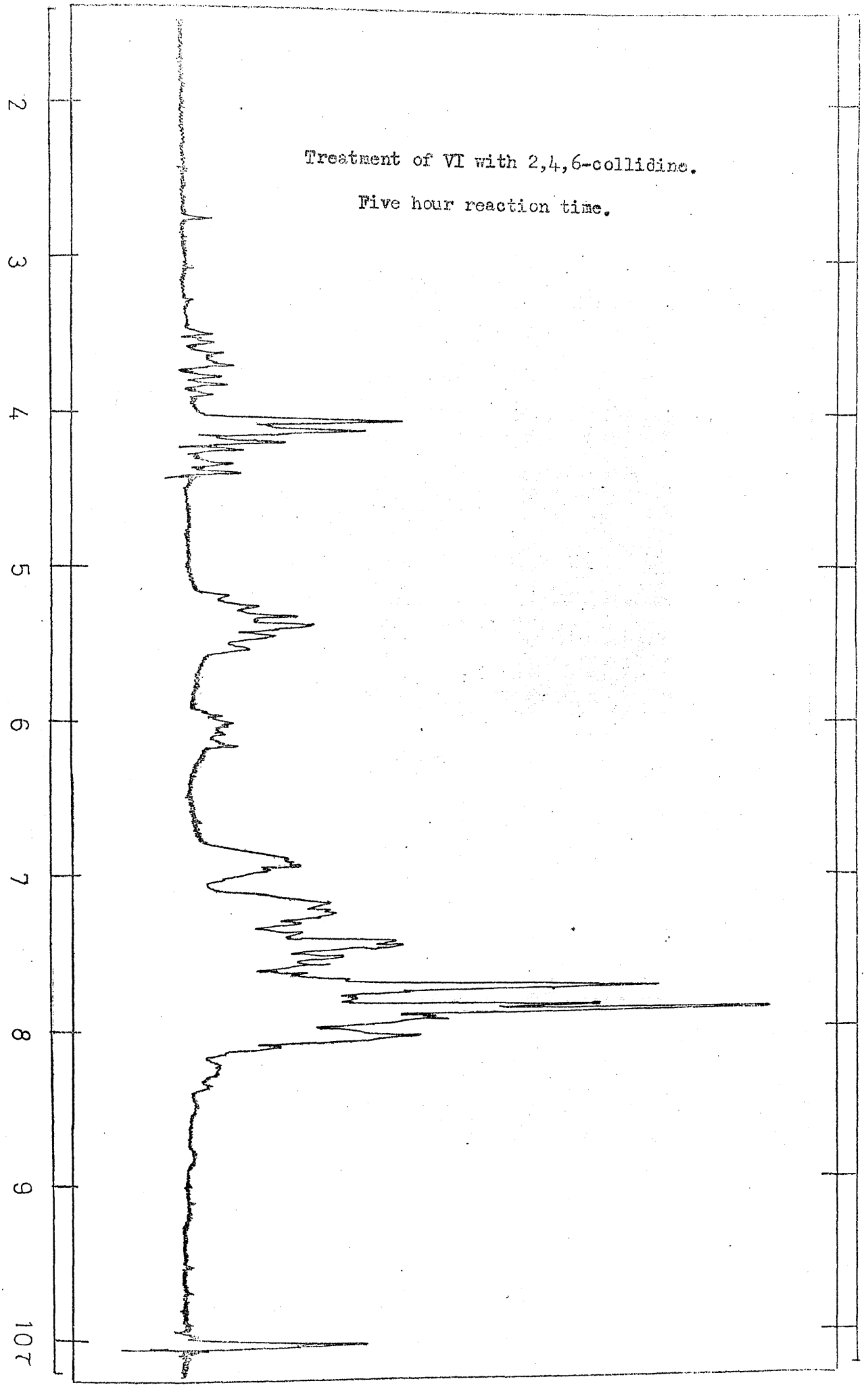
It was assumed that the rearrangement involved sulphur-participation. For this reason methods were sought to observe the episulphonium ion species X directly.




Treatment of VI with 2,4,6-collidine.

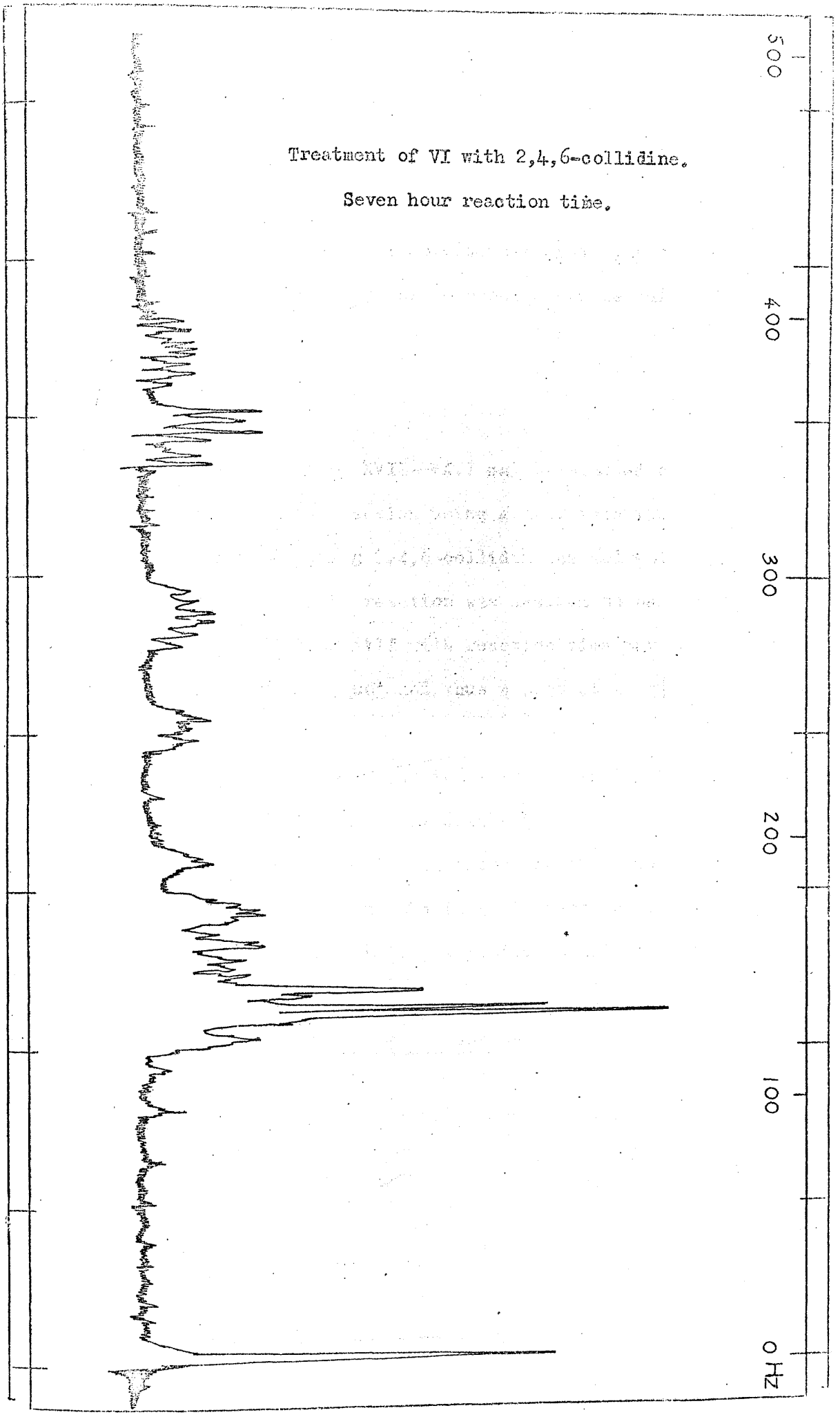
Two hour reaction time.


500
400
300
200
100
0 Hz
Treatment of VI with 2,4,6-collidine.
Three-and-a-half hour reaction time.
2
3
4
5
6
7
8
9
10 τ




Treatment of VI with 2,4,6-collidine.

Five hour reaction time.




Treatment of VI with 2,4,6-collidine.

Seven hour reaction time.

A) Ultra-Violet-Method:

A study of the rearrangement using a u.v. method would be complicated by the presence of 2,4,6-collidine in the spectrum.
To eliminate this by "working up" aliquots before examining spectra would reduce the possibility of observing the sulphonium species directly.

B) G.L.C.-Kinetic Method:

The kinetics of the reaction XVII $\longrightarrow$ XVI may be studied conveniently by analysing aliquots from the reaction using g.l.c. techniques. Because the reaction was carried out using 2,4,6-collidine as solvent as well as the dehydrochlorinating agent the reaction was assumed to be first-order. The decrease in concentration of XVII with reaction time may be determined from the g.l.c. trace of the aliquot and thus a plot of $-\log[\text{XVII}]_t$ against time (t) can be obtained.

A typical plot of a first order reaction is given in figure 1. However, if episulphonium species (X) is an intermediate it is reasonable to suppose that as the concentration of chloride ion increases then the back reaction, $X + Cl^- \longrightarrow$ XVII, is favoured, causing the forward reaction to slow down. The plot of $-\log[\text{XVII}]_t$ against time (t) expected in this case is given in figure 2.

Figure 1. Normal First-Order Reaction

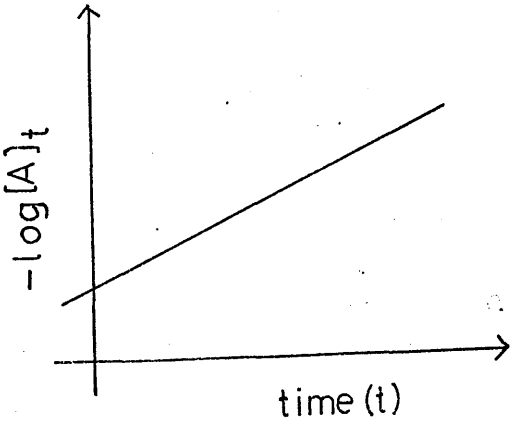
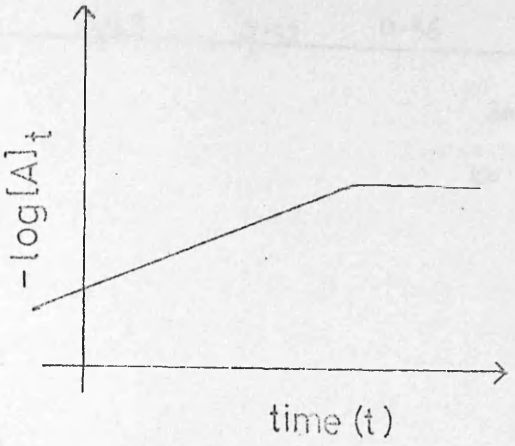
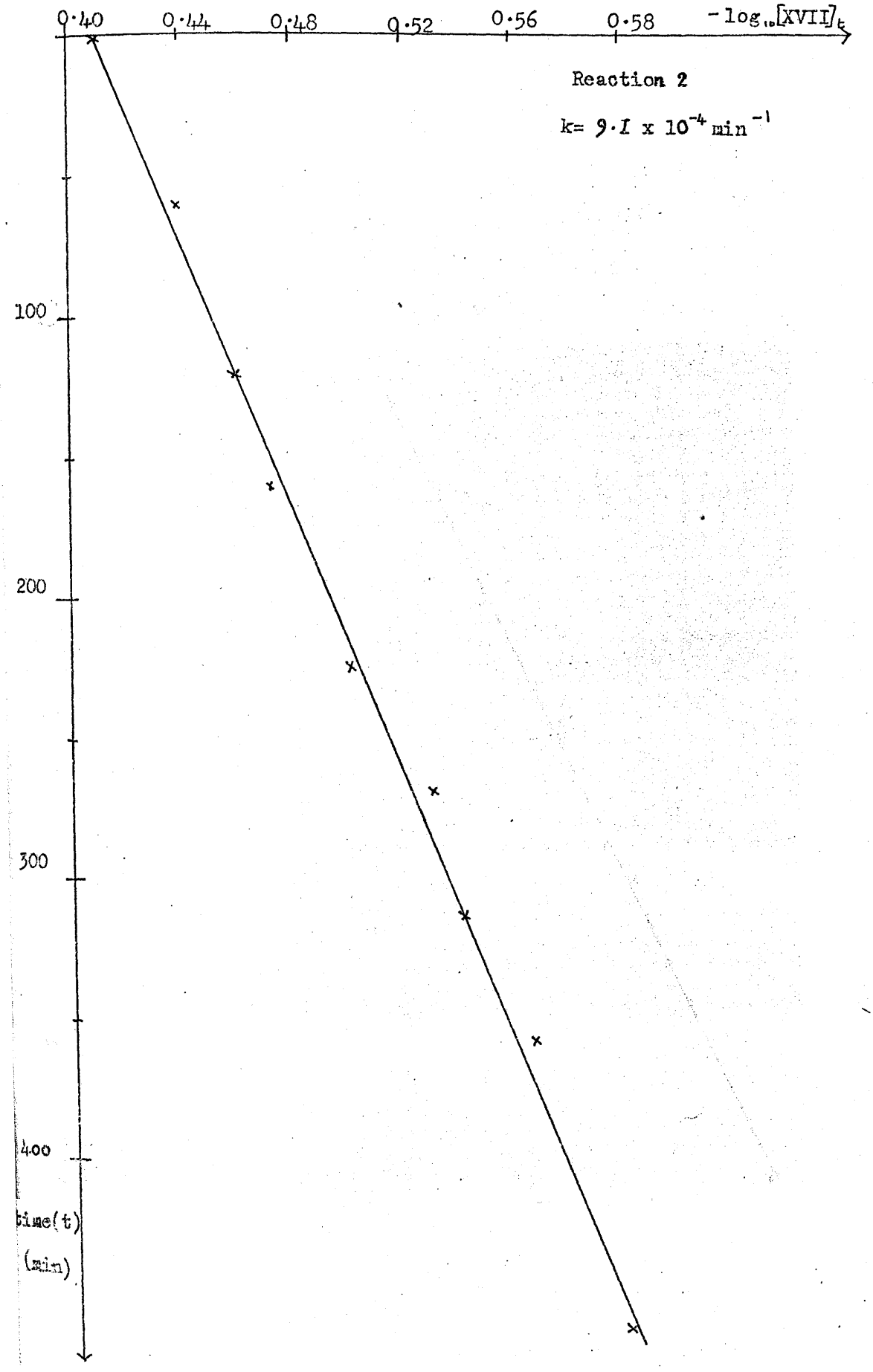


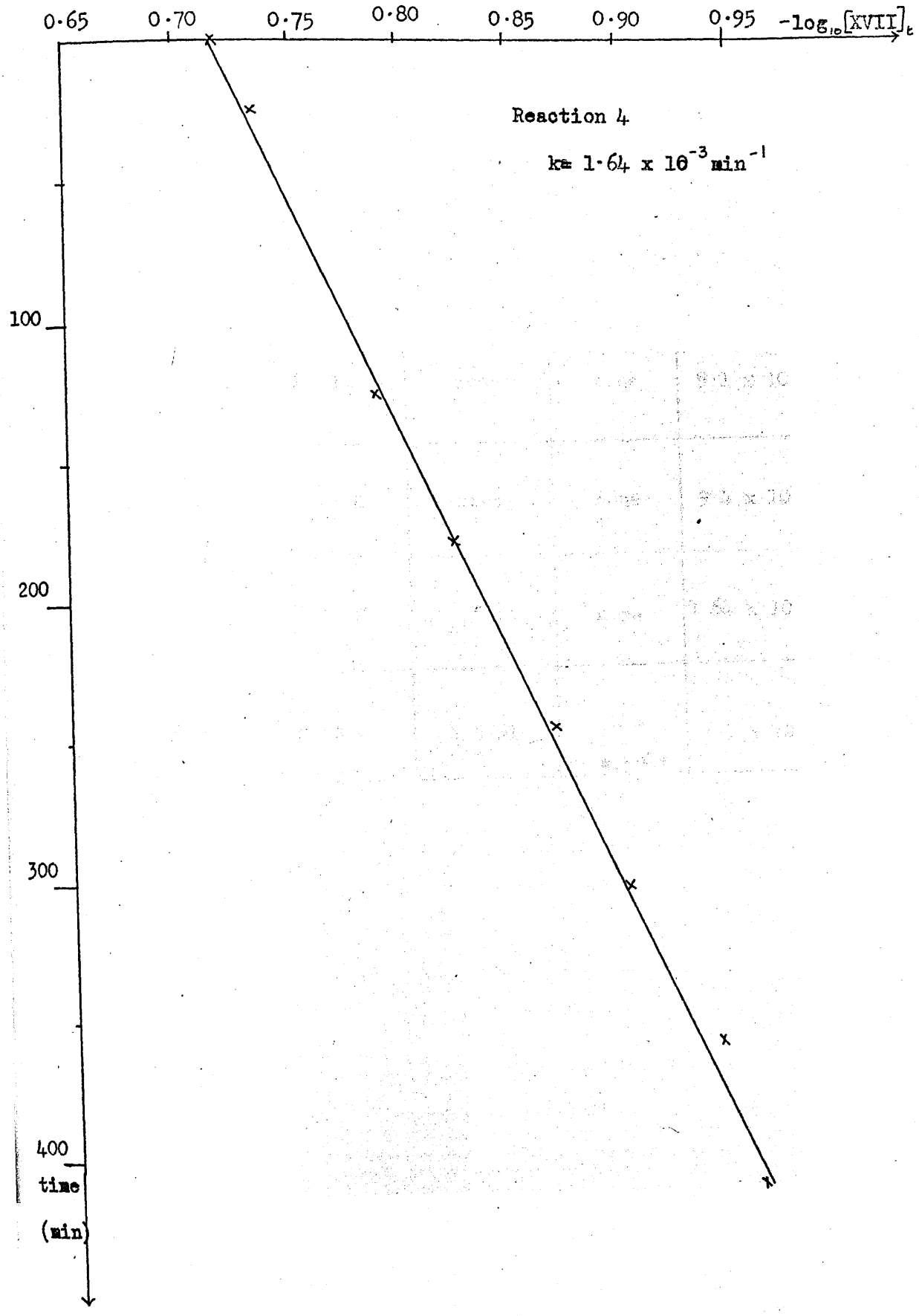
Figure 2.




Initially, experiments were carried out using a known initial concentration of XVII in excess 2,4,6-collidine (b.p. 175-178°). Nevertheless, as the reaction proceeded no flattening of the straight-line obtained could be observed (e.g. p 62 ). However, during the course of the reaction a precipitate of collidine hydrochloride was seen to collect and hence no build up of chloride ion was able to occur. For this reason a solvent, nitrobenzene, was added to the reaction mixture, 2,4,6-collidine still being present in excess (b.p. of solution 195°). Nitrobenzene was used because it is a good solvent for collidine hydrochloride, it is inert to the reactants and it did not interfere with the g.l.c. trace of the "worked up" aliquots. However, a plot of $-\log_{10}[XVII]_t$ against time (p.63) again gave a straight line without any decrease in rate constant with time. Indeed an enhancement in rate was observed, which is probably due to an increase in the reaction temperature. The reaction was repeated a further time with added collidine hydrochloride as a source of excess chloride ion, and additional nitrobenzene. However, once again no decrease in rate constant with time was observed

Unfortunately, these results are inconclusive. Although they do not prove the existence of sulphonium species X, neither do they disprove it. Perhaps, under reaction conditions which allow the build-up of chloride ion concentration without an increase in reaction temperature, a decrease in rate constant with time would have been observed. On the other hand it may be that


0·40
0·44
0·48
0·52
0·56
0·58
$-\log_{10}[XVII]_t$
Reaction 2
$k = 9 \cdot 1 \times 10^{-4}\ min^{-1}$
100
200
300
400
time(t)
(min)

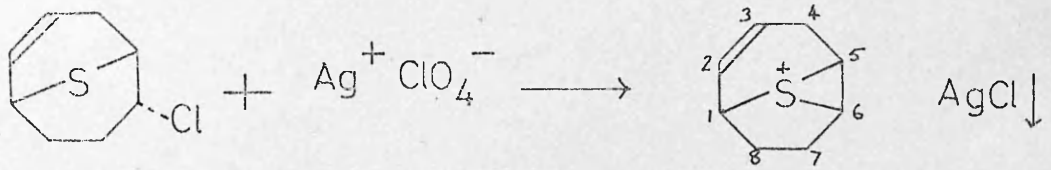

0·65
0·70
0·75
0·80
0·85
0·90
0·95
$-\log_{10}[XVII]_t$
Reaction 4
$k = 1{\cdot}64 \times 10^{-3}\,min^{-1}$
100
200
300
400
time
(min)

| REACTION | INITIAL CONC. | ADDED NITROBENZENE | ADDED $Cl^-$ | RATE CONSTANT ($min^{-1}$) |
|---|---|---|---|---|
| 1 | 0·22 M | none | none | $8{\cdot}8 \times 10^{-4}$ |
| 2 | 0·39 M | none | none | $9{\cdot}1 \times 10^{-4}$ |
| 3 | 0·23 M | none | none | $9{\cdot}4 \times 10^{-4}$ |
| 4 | 0·19 M | 3 ml | none | $1{\cdot}64 \times 10^{-3}$ |
| 5 | 0·13 M | 4·5 ml | 0·8 m.mole | $1{\cdot}7 \times 10^{-3}$ |

X is very short-lived and so the reverse reaction will not be favoured giving no change in the kinetics of the reaction as it proceeds.

Other Methods of Obtaining X:

Addition of an acetone solution of silver perchlorate to an acetone solution of monochloride XVII was found to give a dense colourless precipitate, assumed to be silver chloride. Performing this reaction in $d_6$-acetone and filtering off the precipitate allowed a n.m.r. spectrum of the bright yellow filtrate to be obtained. The spectrum recorded when silver perchlorate was added to XVII in a molar ratio of 1:1 is shown on p.67. Although this spectrum contains intense methyl resonances, arising by hydrogen-deuterium exchange in solvent, it could be reasonably explained by formation of sulphonium ion X in this reaction:




XVII

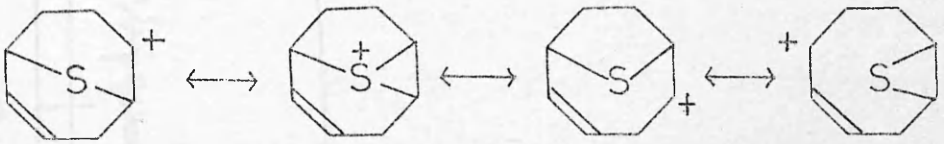
Vinylic resonances at τ3.9 and 4.0 (2H) may be attributed to protons on C-2 and C-3. Similarly the resonances between τ5.6 and 6.0 (1H) and τ6.2 to 6.7 (2H) may be assigned to protons on C-1 and C-5,6 respectively. Allylic methylenes on C-4 resonate between τ 7.3 and 7.5 (2H) with the remaining methylene protons on C-7 and C-8 occuring between τ7.8 and 8.5 (>4H). The presence of the intense methyl signals, showing deuterium coupling, is to be expected since an ion such as X would readily exchange hydrogen atoms with deuterium from the solvent.

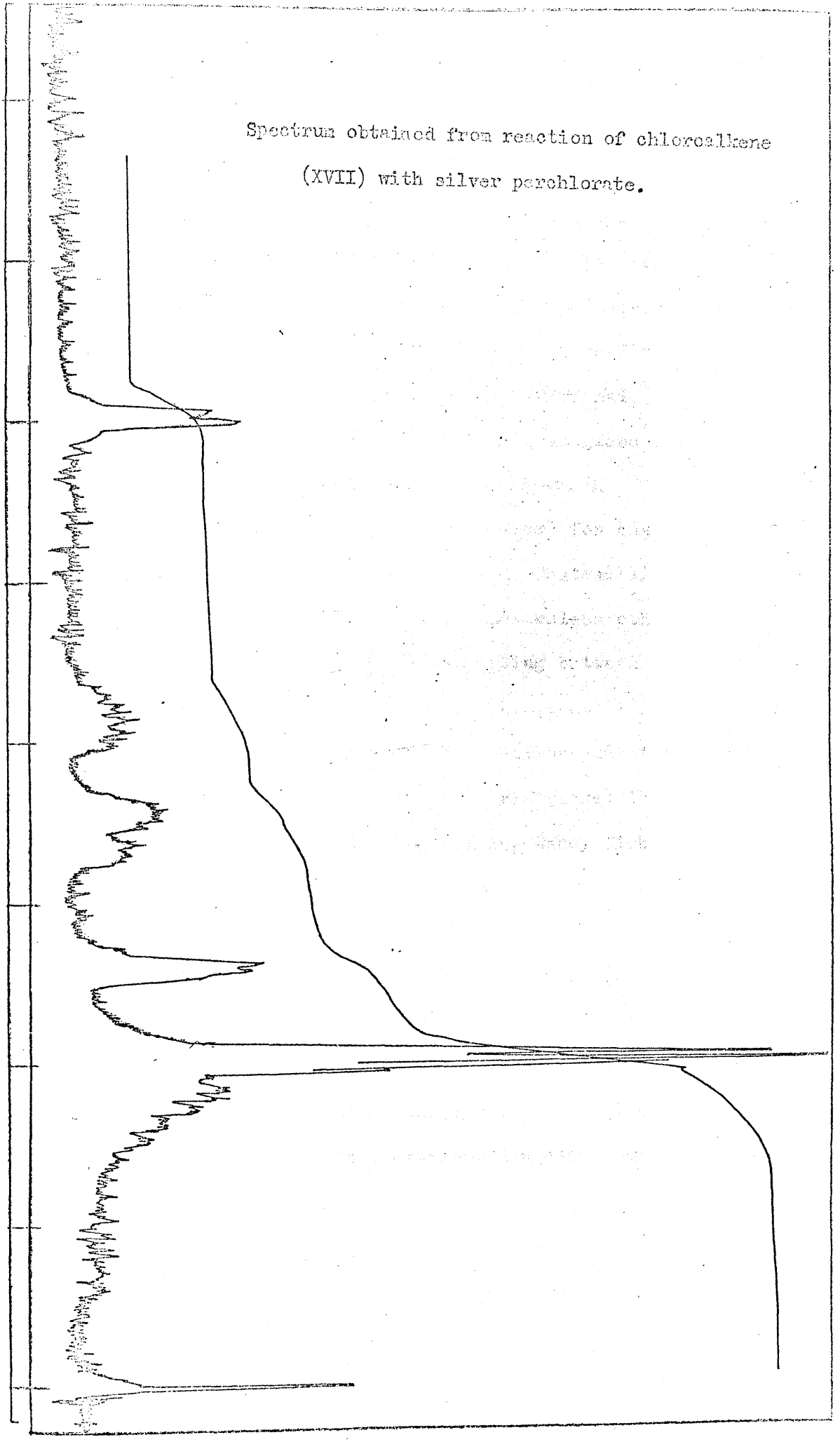
When $d_8$-toluene was added as solvent no spectrum was obtained after filtration. In a qualitative experiment water was added to the precipitate

producing a yellow aqueous solution together with undissolved silver chloride. Thus this product is obviously polar and hence insoluble in a hydrocarbon solvent.

An acetone solution of the product darkened considerably within an hour, even when stored in a refrigerator, the final product being hydroxyalkene (XVIII), presumably formed by reaction with water from the solvent.

That chloroalkene (XVII) reacts to form hydroxyalkene (XVIII) at room temperature with precipitation of chloride ion, is strongly indicative of a resonance-stabilised ionic reaction in which episulphonium species (X) has a finite but limited existence.






Spectrum obtained from reaction of chlorocalkene (XVII) with silver perchlorate.

## EXPERIMENTAL.

$^1$H n.m.r. spectra were recorded on Varian T-60 and HA-100 instruments with $CDCl_3$ as solvent and tetramethylsilane as internal reference standard. Ultra-violet spectra (in ethanol) and mass spectra were measured on Unicam SP800A and A.E.I.-G.E.C. MS12 spectrometers respectively. Infra-red spectra were recorded on pressed discs or on solutions in chloroform or carbon tetrachloride on Perkin-Elmer 225 and Unicam SP1000 instruments. G.l.c. measurements were made on a Perkin-Elmer F11 chromatograph using a 12 foot helical glass column containing OV-1 (1%) or SE-30(1%) adsorbed on Gaschrom. Q.

T.l.c. was carried out using Kieselgel G (Merck) for analytical purposes and Kieselgel $HF_{254}$ for preparative work. Neutral alumina (Woelm) grade I was used for column chromatography unless otherwise stated.

Petroleum spirit refers to the fraction boiling between 60 and 80°, unless otherwise stated. Special solvents, e.g. 2,4,6-collidine, pyridine and dimethyl sulphoxide, were purified by distillation and stored over potassium hydroxide pellets. Methylene chloride was passed through basic alumina and stored over 4Å molecular sieves. Raney Nickel for desulphurisation was prepared by the method described in Fieser and Fieser[74].

Pyrolyses were performed in flame-dried glass tubes (43cm long; internal diameter 22mm; wall thickness 4mm), flushed out with nitrogen and sealed under vacuum (ca. 0.1mm). The tubes were heated in steel inserts in a Gallenkamp pyrolysis oven. Small-scale pyrolyses in glass tubes of 17cm length, internal diameter of 7mm, external diameter 10mm, were heated in a Gallenkamp sublimation block.

Organic solutions were dried over anhydrous sodium sulphate or magnesium sulphate. Solvents were removed on a rotary evaporator under reduced pressure.

Melting points were determined on a Kofler hot-stage apparatus, using microscope slides with cover slips, and are uncorrected.

Abbreviations:

| | |
|---|---|
| b. | broad |
| d. | doublet |
| m. | multiplet |
| q. | quartet |
| s. | singlet (in n.m.r.) |
| s. | strong intensity absorption (in i.r.) |
| vs. | very strong intensity absorption |
| sh. | shoulder |
| t. | triplet |
| w. | weak intensity absorption |

Treatment of (VII) with basic aluminium oxide:

2,6-Diiodo-9-thiabicyclo[3.3.1]nonane (VII) (293mg; 0.74m.mole) and alumina (Woelm; basic; 3.5g) were refluxed in analar chloroform (10ml) for 3½ hr. and stirred at room temperature for a further 16 hr. Filtration and evaporation of solvent yielded a yellow oil (200mg). T.l.c. investigation indicated formation of one product and a considerable proportion of starting material.

Refluxing the diiodide (VII) (578mg; 1.47m.mole) overnight in chloroform (50ml) with alumina (Woelm; basic; 20g) followed by filtration and evaporation of solvent again afforded a yellow oil. Purification by prep. t.l.c. (solvent - 1:1 ether/petroleum spirit) yielded a pale yellow oil (271mg; 1.18m.mole; 80%).

n.m.r. ($CDCl_3$) : $\tau$ 5.9-6.7 (complex m., 6H); 7.2 (m., 2H); 7.3-8.3 (complex m., 8H) and 8.8 (t.; 6H) indicates this product to be 2,6-diethoxy-9-thiabicyclo[3.3.1]nonane (VIII).

Treatment of (VII) with potassium carbonate in methanol solution:

2,6-Diiodo-9-thiabicyclo[3.3.1]nonane (VII) (296 mg; 0.75m.mole) and potassium carbonate (654 mg; 4.73 m.mole) were refluxed in methanol (18ml) for 19 hr. After filtration the solvent was removed *in vacuo*. The crude reaction product was extracted with ether and the washings passed through a short plug of acid alumina. Examination of the product on t.l.c. indicated the presence of one product which was identified by n.m.r. as the dimethoxy compound (IX).

Reaction of (VI) with potassium carbonate:

2,6-Dichloro-9-thiabicyclo[3.3.1]nonane (VI) (195mg; 0.9m.mole) and anhydrous potassium carbonate (292mg; 2.11m.mole) were intimately mixed using a mortar and pestle and then heated at 120° for two hours, and at 300° for 30 min., in a sublimation tube. The black residue was extracted with chloroform, the solvent evaporated off and the residue was tested for solubility in both boiling petroleum spirit and boiling ether, and was found to be insoluble in both.

2,6-Dichloro-9-thiabicyclo[3.3.1]nonan-9,9-dioxide (XI):

m-Chloroperbenzoic acid (9.5g; 55m.mole) in dichloromethane (50ml) was added dropwise over 30 min. to a solution of 2,6-dichloro-9-thiabicyclo [3.3.1] nonane (VI) (5.27g; 25m.mole) in dichloromethane (20ml). The reaction mixture was left to stir at room temperature for a further 4 hr., during which a heavy colourless precipitate was observed. After filtering, the filtrate was washed with sodium sulphite (1M, 1x50ml), with sodium carbonate (3x70ml, 1M) and dried. Evaporation of solvent afforded a colourless solid (5.59g; 23m.mole; 92%). Recrystallisation from chloroform/ether gave sulphone (XI) m.p. 176-177° (lit. 175-176°),

m/e 242, 244, 246 ($M^+$)

n.m.r. ($CDCl_3$) : $\tau$ 4.96-5.43 (2H, m.); 6.63-6.96 (2H,m.); 7.20-8.06 (8H,m.);

i.r. ($CCl_4$) : $\nu$ 3000, 2981, 2952, 2939, 2894, 2861, 1484(s), 1448, 1439, 1323(s), 1261, 1183(s), 1123(vs), 1072 $cm^{-1}$.

Treatment of sulphone (XI) with methanolic potassium hydroxide:

2,6-Dichloro-9-thiabicyclo[3.3.1]nonan-9,9-dioxide (XI) (248mg; 1m.mole

in 10% (w/v) methanolic potassium hydroxide (15ml) was refluxed for 4hr. The reaction mixture was cooled by addition of ice/water and extracted with dichloromethane (4x50ml) to give a quantitative yield of starting material (XI) from n.m.r. and t.l.c. comparison.

Treatment of sulphone (XI) with potassium t-butoxide in D.M.S.O.:

A suspension of potassium t-butoxide (1.07g; 9.5m.mole) in dimethylsulphoxide (10ml) was cautiously added over 30min. to a stirred solution of sulphone (XI) (460mg; 1.9m.mole) in DMSO (10ml) and stirring continued at room temperature for 18hr. The brown reaction mixture was poured onto ice, extracted with dichloromethane, dried and evaporated. The residue was shown by t.l.c. and n.m.r. data to be the starting sulphone (XI).

2,6-Dichloro-9-thiabicyclo[3.3.1]nonan-9-oxide:

m-Chloroperbenzoic acid (1.90g; 11m.mole) in dichloromethane (20ml) was added dropwise over 15min. to an ice cooled, stirred solution of dichloride (VI) (2.11g; 10m.mole) in dichloromethane (25ml). After stirring at room temperature for 30min. the thick colourless precipitate was filtered off. The residue was washed with sodium sulphite (1M, 1x30ml), with sodium carbonate (1M, 3x50ml) and dried. Removal of solvent *in vacuo* afforded colourless plates (2.23g; 9.8m.mole; 98%) m.p. 119-121$^{0}$ (chloroform/petroleum spirit) (lit. m.p. 121-122$^{0}$); m/e 226, 228, 230 ($M^{+}$);

n.m.r. ($CDCl_3$) : $\tau$ 4.73-5.23 (1H,m.); 5.36-5.80 (1H,m.); 6.46-6.83 (2H,m.); 7.10-8.20 (8H,m.);

i.r. ($CCl_4$) : $\nu$ 3000, 2978, 2952, 2929, 2893, 2878, 2852, 1487(s), 1448, 1436, 1338, 1283, 1277, 1248, 1082(vs), 1063(vs) cm-1

Treatment of 2,6-dichloro-9-thiabicyclo[3.3.1]nonan-9-oxide with 2,4,6-collidine:

A solution of 2,6-dichloro-9-thiabicyclo[3.3.1] nonan-9-oxide(500mg; 2.2m.mole) in 2,4,6-collidine (12ml) was refluxed in a nitrogen atmosphere for 24hr. After filtration, the filtrate was taken up in ethyl acetate (30ml), washed with aqueous copper sulphate (4x30ml) and dried. Evaporation of solvent afforded a crude product (450mg) which appeared to be predominantly starting material from n.m.r. and t.l.c. data. Similar treatment of the sulphoxide with collidine for 1 week gave starting material only.

Treatment of 2,6-dichloro-9-thiabicyclo[3.3.1]nonane (VI) with DBN:

DBN (620mg; 5m.mole) in benzene (5ml; sodium dried) was added to a stirred solution of (VI) (238mg; 1.13m.mole) in benzene (3ml). After stirring at room temperature in a nitrogen atmosphere for 17hr. the reaction mixture was poured onto an ice/dilute sulphuric acid mixture (5ml. 1M $H_2SO_4$ and 2g. ice) and extracted with ether-petroleum spirit (1:9). The extract was washed with brine to neutrality, dried and evaporated to yield a colourless crystalline solid (235mg). The n.m.r. of this solid was found to be identical to that of starting material (VI).

Treatment of (VI) with DBU:

DBU (675mg; 4.38m.mole) in sodium dried benzene (5ml) was added to a stirred solution of (VI) (220mg; 1.04m.mole) in benzene (3ml). The solution turned light brown and was left stirring under nitrogen at room temperature for $4\frac{1}{2}$ days. Work-up as in the treatment of (VI) with DBN yielded a

colourless crystalline solid (210mg) whose n.m.r. was found to be identical to that of (VI). The reaction was repeated, using refluxing benzene as solvent, for 24 hr. and for 5½ days. In both cases starting material was returned unchanged.

Treatment of (VI) with potassium t-butoxide in dimethyl sulphoxide:

A solution of potassium t-butoxide (6.2g; 55m.mole) in dimethyl sulphoxide (50ml) was added to a stirred solution of 2,6-dichloro-9-thiabicyclo[3.3.1]nonane (VI) (5.8g; 27m.mole) in dimethyl sulphoxide (70 ml) over 25 min during which the solution turned dark brown. After stirring at room temperature for 2 hr. the reaction mixture was poured on to ice and extracted with ether (2x250 ml). Excess dimethyl sulphoxide was removed by washing with saturated brine (4x200ml). The ether layer was dried and solvent removed *in vacuo* to afford a viscous red oil (3.25g) which was chromatographed over alumina (neutral, 30g). Elution with ether-petroleum spirit (1:9) yielded a colourless oil (470mg; 13%). Found: C,68.82; H,8.48. $C_8H_{12}S$ requires: C,68.54; H,8.63%.

n.m.r. ($CDCl_3$) : $\tau$ 4.17-4.51 (2H,m); 6.79-7.10 (2H,m); 7.33-8.36 (8H,m)

(see spectrum page 33 ).

i.r. ($CCl_4$) : ν 3017,2972 (2984sh),2940,2896,1653(w) and 1648(w),1478, 1465,1442,1431 $cm^{-1}$.

mass spec. : m/e 140 ($M^+$),107 ($M^+$ - HS).

9-Thiabicyclo[4.2.1]nona-2,4-diene (XVI):

A solution of 2,6-dichloro-9-thiabicyclo[3.3.1]nonane (VI) (10.72g; 51m.mole) in 2,4,6-collidine (23ml) was refluxed for 14 hr. The reaction mixture was filtered to remove precipitated collidine hydrochloride and the filtrate was taken up in ethyl acetate (50ml), washed with aqueous copper sulphate (5x60ml) and dried. Evaporation of solvent afforded a brown oil which was chromatographed over alumina (acidic, 250g). Elution with ether-petroleum spirit (40-60$^0$) (1:19) gave diene (XVI) as a clear colourless oil (4.2g; 30.4m.mole; 60%). Alternatively, excess collidine may be removed by washing with 0.1M sulphuric acid (2x50ml), with water until neutral, and dried.

$\lambda$max(Ethanol): 257n.m.(log$\varepsilon$=3.56);262n.m.(3.57);273n.m.(sh.,3.45);297n.m.(3.04)

m/e 138 ($M^+$); Found : C,69.38; H,7.22. $C_8H_{10}S$ requires : C,69.53; H,7.29%.

n.m.r. ($CDCl_3$) : $\tau$ 3.50-3.82 (2H,m); 4.13-4.40 (2H,m); 5.94-6.17 (2H,m); 7.70-7.98 (4H,m) (see spectrum page 36 ).

i.r. ($CCl_4$) : $\nu$ 3024(sh),3015,2962(sh),2940,2894,2850,1610(w),1470,1450, 1400,1325(sh),1310 cm$^{-1}$.

Hydrogenation of 9-thiabicyclo[4.2.1]non-2,4-diene (XVI)

9-Thiabicyclo[4.2.1]nona-2,4-diene (XVI) (180mg; 1.3m.mole) and Adam's catalyst (19mg) in ethyl acetate (10ml) were stirred in a hydrogen atmosphere for 24hr. The reaction mixture was filtered and removal of solvent afforded 75mg. of a yellow oil which comprised two products (t.l.c) Purification by prep. t.l.c. (1:19 ether/petroleum spirit) yielded a crystalline product (17mg) and starting material (50mg). The crystalline product was redissolved in ether and filtered through a small cotton wool plug. Evaporation of solvent affored 9-thiabicyclo[4.2.1]nonane (XV) as

colourless plates (m.p. 125-127$^0$: lit. m.p. 127-128$^0$ ); m/e 142 ($M^+$);
n.m.r. ($CDCl_3$) :$\tau$ 6.16-6.53(2H,m); 7.73-8.70(12H,m);
i.r. ($CCl_4$) :$\nu$ 2912(s),2895(sh),2858,2844,1463,1442,1434 $cm^{-1}$.

Treatment of diene (XVI) with phthalazine-1,4-dione (XIX):

To an ice-cooled, stirred solution of N,N' phthaloyl hydrazine (810mg; 5m.mole) and 9-thiabicyclo[4.2.1]nona-2,4-diene (XVI) (650mg; 4.7m.mole) in dichloromethane (50ml) was added lead tetraacetate (2.08g; 6m.mole) in one portion. The light green reaction mixture was left to stir for 16hr. in the dark before being filtered. Evaporation of the filtrate yielded a crude solid smelling strongly of acetic acid. This was purged with benzene under vacuum and passed through a small plug of basic alumina. N.m.r. and t.l.c. data on the reaction product (980mg) indicated only the two starting materials.

Treatment of diene (XVI) with N-phenyl maleimide:

A. N-phenylmaleimide (346mg; 2m.mole) in benzene (30ml) was added to a solution of the diene (XVI) (235mg; 1.7m.mole) in benzene (15ml) and refluxed for 48 hr. N.m.r. and t.l.c. data on the yellow oily solid obtained after evaporation of solvent showed it to be a mixture of the two starting materials.

B. Diene (XVI) (200mg; 1.45m.mole) and N-phenylmaleimide (495mg; 2.83m.mole) were mixed in the absence of solvent and heated in a sealed tube at 140$^0$ for two hours. The product was taken up in chloroform and t.l.c. and n.m.r. data showed the presence of the two starting materials only.

Adduct (XXII):

4-Phenyl-1,2,4-triazoline-3,5-dione (370mg; 2.1m.mole) was added to a stirred solution of the diene (XVI) (220mg; 1.6m.mole) in benzene (20ml). The solution was stirred at room temperature overnight during which the red colouration was discharged. Evaporation and crystallisation (chloroform/ether) afforded colourless needles (350mg; 1.12m.mole;70%) m.p. 241-243°.

Found : C,61.58; H,4.80; N,13.64. $C_{16}H_{15}N_3O_2S$ requires : C,61.33; H,4.83; N,13.41%.

n.m.r. ($CDCl_3$) : τ 2.45-2.72(5H,m); 3.77-3.85(2H,d.d.,J=3Hz); 4.58-4.82 (2H,m); 6.04-6.24(2H,m); 7.28-7.51 and 7.56-7.94(4H).

i.r. ($CCl_4$) : ν 3020,2995(sh),2980,2950,2865,1763(s),1703(s),1598,1501, 1410 $cm^{-1}$.

mass spec. : m/e 313 ($M^+$), further peaks at m/e 280 (M-HS), 236 ($M-C_6H_5$) and 136 ($M-C_8H_7N_3O_2$).

Adduct (XXIII):

4-phenyl-1,2,4-triazoline-3,5-dione (280mg; 1.6m.mole) was added to a solution of 1,3-cycloctadiene (137mg; 1.3m.mole) in benzene (20ml) with stirring, and the original red colour of the solution faded over 3 hr. Removal of solvent in vacuo gave a yellow residue which was washed with a little ethyl acetate and crystallised from chloroform/ether to yield XXIII as colourless needles (270mg; 0.95m.mole;75%) m.p. 204-206° (lit. m.p. 203.5-206.5°).

n.m.r. ($CDCl_3$) : τ 2.36-2.73 (5H,m); 3.83-3.89(2H,d.d.,J=2Hz.);4.89-5.10 (2H,m); 7.58-8.0 and 8.06-8.48(8H,m);

i.r. ($CCl_4$) : ν 3045,2930,1765(s),1704(vs),1500,1415 $cm^{-1}$.

mass spec. : m/e 283 ($M^+$), further peaks at 206 ($M-C_6H_5$) and 106 ($M-C_8H_7N_3O_2$).

Treatment of adduct (XXII) with Raney Nickel:

A. Adduct (XXII) (60mg; 0.19m.mole) in acetone (40ml) was added to a stirred suspension of Raney nickel (~200mg) in refluxing ethanol (10ml). After 3 hr. the supernatant liquid was decanted, the nickel washed with boiling acetone (5x25ml) and solvent removed under suction. The grey residue was taken up in chloroform, filtered through a celite plug and evaporated. The product (XXIV) crystallised from chloroform/ether as colourless needles (52mg; 0.17m.mole;89%) m.p. 264-265°.
Found : C,61. 12;H,5.27. $C_{16}H_{17}N_3O_2S$ requires:C,60.94; H,5.43%.
n.m.r. ($CDCl_3$) : τ 2.28-2.75(5H,m); 4.90-5.22(2H,m); 5.85-6.20(2H,m); 7.20-8.06(8H,m);
i.r. ($CCl_4$) : ν 2970,2950,1775(sh),1761(s),1707(vs),1598,1500,1409 $cm^{-1}$.
mass spec. : m/e 315 ($M^+$), further peaks at m/e 282(M-HS), 238 ($M-C_6H_5$) and 138 ($M-C_8H_7N_3O_2$).

B. Adduct (XXII) (40mg; 0.13m.mole) in ethanol (40ml) was added to a suspension of Raney nickel (~200mg) in reluxing ethanol (10ml). After 20 hr. at reflux the reaction mixture was worked up as in method A. to yield (XXV) as colourless needles (26mg; 0.09m.mole; 71%) m.p. 177-179° (chloroform/ether). All spectral data were identical to the product formed on hydrogenation of adduct (XXIII).

Hydrogenation of (XXIII):

Adduct (XXIII) (190mg; 0.67m.mole) in ethyl acetate (15ml) was hydrogenated over 10% palladium-charcoal for 1 hr at atmospheric pressure.

Filtration and removal of solvent gave a colourless solid (180mg; 0.63m.mole; 94%) which crystallised from chloroform/petroleum spirit as plates. m.p. 179-180°.

Found: C,67.34; H,6.71; N,14.73. $C_{16}H_{19}N_3O_2$ requires: C,67.17; H,6.72; N,14.52%.

n.m.r. ($CDCl_3$) : τ 2.16-2.63(5H,m); 5.03-5.40(2H,m); 7.47-8.53(12H,m);

i.r. ($CCl_4$) : ν 2965(sh),2930,2862,2850,1761(s),1700(vs),1599,1501,1412 $cm^{-1}$.

mass spec. : m/e 285 ($M^+$), further peaks at 208 ($M-C_6H_5$) and 108 ($M-C_8H_7N_3O_2$).

Acid hydrolysis of 2,6-dichloro-9-thiabicyclo[3.3.1]nonane(VI):

Hydrochloric acid (6M, 1.2l) was added over 30 min to a solution of 2,6-dichloro-9-thiabicyclo[3.3.1]nonane (VI) (350g; 1.66mole) in acetone (2l) and the reaction mixture was refluxed for 2 hr. On cooling a saturated solution of sodium carbonate was added until neutrality was obtained. The reaction mixture was reduced in volume under suction until the organic material precipitated out. After filtration 2,6-dihydroxy-9-thiabicyclo[3.3.1]nonane (XXVI) (218 g; 1.25 mole;75%) was crystallised from methanol/ethyl acetate as colourless plates (m.p. 234-239°, lit. 249-250°). Recrystallisation from methanol/ethyl acetate increased the m.p. to 247-249°.

n.m.r. ($d_6$-DMSO): τ 5.05 and 5.15 (2H,d., exchangable with $D_2O$); 5.80-6.26(2H,t. with further splitting,J=6Hz);6.70-6.85 (2H,t.,J=8Hz); 7.36-7.80 (4H,m) and 7.86-8.46(4H,m);

i.r. (KBr disc) : ν 3370(vs),2990,2942,2915,2890(sh),2848,1485,1455,1433, 1350,1035(sh),1023(vs) $cm^{-1}$.

mass spec. : m/e 174 ($M^+$) also 141 (M-HS).

Attempted dehydration of diol (XXVI):

Phosphorous oxychloride (6ml) was added to 2,6-dihydroxy-9-thia-bicyclo[3.3.1]nonane (XXVI) (224mg; 1.29m.mole) in pyridine (25ml). The reaction mixture was refluxed for $5\frac{1}{2}$ hr., allowed to cool and then added dropwise to ice. The aqueous layer was extracted first with ether (3x75ml) and then with ethyl acetate (2x100ml). Each extract was washed with a saturated solution of copper sulphate, dried and evaporated to afford a brown oil (37mg, in total). T.l.c. investigation of this oil indicated the presence of many compounds, and separation was not attempted.

2,6-Diacetoxy-9-thiabicyclo[3.3.1]nonane (XXVII):

Acetyl chloride (3.16g; 40m.mole) was added dropwise to a stirred solution of 2,6-dihydroxy-9-thiabicyclo[3.3.1]nonane (1.75g; 10m.mole) in pyridine (20ml). A considerable heating effect was observed and the reaction mixture turned light brown. After stirring at room temperature for 14 hr. the precipitated pyridine hydrochloride was filtered off and excess pyridine removed by evaporation in vacuo to give 2.98g of an orange semi-solid. Purification by prep. t.l.c. (1:1 ether/petroleum spirit) yielded 2,6-diacetoxy-9-thiabicyclo[3.3.1]nonane (2.17g; 8.4m.mole; 84%) as colourless needles m.p. 101-102$^0$ (lit. 100-101$^0$); m/e 258 ($M^+$);

n.m.r. ($CDCl_3$) : $\tau$ 4.66 (2H, t.J=10Hz, with further splitting, J=4Hz);
7.06-7.33 (2H,m); 7.46-8.16 (m); 7.93 (s)(14H);

i.r. (KBr disc) : $\nu$ 2985,2950(sh),2920,2843,1724(vs),1485,1450,1430,1380,
1355,1240,1225(d;v.s.),1022 $cm^{-1}$.

Pyrolysis of 2,6-diacetoxy-9-thiabicyclo[3.3.1]nonane (XXVII):

2,6-Diacetoxy-9-thiabicyclo[3.3.1]nonane (XXVII) (200mg; 0.78m.mole) was pyrolysed ($210^0$) for 19 hr in a glass tube sealed at 1 atmosphere. After cooling, the contents of the tube were extracted with chloroform and found to be starting material only, obtained in quantitative yield.

The experiment was repeated at $240^0$ for 24 hr. The slightly blackened product was extracted with chloroform and filtered through a small plug of cotton wool to yield a brown oil (180mg) which was chromatographed over alumina (basic; 10g). Elution with ether/petroleum spirit (1:5) gave 9-thiabicyclo[4.2.1]nona-2,4-diene (XVI) (21mg) in the earlier fractions, followed by starting material (XXVII) (132mg).

Attempted preparation of bis xanthate (XXVIII) of 9-thiabicyclo[3.3.1]-nona-2,6-diol:

Dimethyl sulphoxide (23ml) was added to sodium hydride (1.44g of a 60% dispersion in benzene; 36m.mole) and the solution was stirred at $75^0$ (bath temp.) for 45 min. Diol (XXVI) (1.65g; 9.48m.mole) in DMSO (5ml) was added at room temperature and stirring continued for 1 hr. Carbon disulphide (4g; 52.6m.mole) was added dropwise with external cooling (ice). While stirring for 1hr. the reaction mixture gradually became homogeneous and a red colouration developed which was dispelled on addition of methyl iodide (3.41g; 24m.mole). The pale yellow solution was stirred for a further hour before being poured onto ice and extracted with ether (3x200ml). The ether extracts were washed with water (4x200ml), with brine (1x250ml), dried and solvent was removed to yield a crude product (3.2g) of which 1.5g was found to be soluble in petroleum spirit. This fraction was placed on alumina (neutral; 75g) and eluted with ether/

petroleum spirit (1:9). A yellow oil (1.3g) was obtained, which appeared, on n.m.r. data, to be the mono xanthate (XXIX).

N,N-dimethylthiocarbamate (XXX):

Sodium hydride (480mg; 20m.mole) was added over 30 min to a stirred, cooled solution of the diol (XXVI) (870mg; 5m.mole) in dry dimethyl formamide (7ml) and the reaction mixture was heated at 60° for 2hr. N,N-dimethylthiocarbamoyl chloride (1.5g; 13m.mole) was added to the cooled solution over 30 min and the reaction mixture was stirred overnight. After heating at 60° for 2 hr it was cooled, poured on to ice and extracted several times with chloroform. The combined extracts were dried and evaporated affording a colourless solid (1.14g; 3.27 m.mole; 66%). Crystallisation from chloroform/ether gave (XXX) as colourless needles (m.p. 148-150°); m/e 348 ($M^+$). Found : C,48.02; H,7.06; N,8.11. $C_{14}H_{24}N_2O_2S_3$ requires : C,48.27; H,6.94; N,8.04%.

n.m.r. ($CDCl_3$) : $\tau$ 3.90-4.33(2H,m); 6.62 (6H,s); 6.85 (6H,s); 6.93 - 7.15 (2H,m); 7.43-8.10 (8H,m);

i.r. (KBr disc) : $\nu$ 2983(sh),2930,2888,2872,2848,1510,1490,1311,1292,1180(s), 1152(sh) $cm^{-1}$.

Pyrolysis of (XXX):

N,N-dimethylthiocarbamate (XXX) (300mg; 0.86m.mole) was pyrolysed at 200° for 2½ days in a glass tube sealed under vacuum. After extraction with chloroform and filtration the two main components of the crude reaction products were separated by prep. t.l.c. (1:1 chloroform/petroleum spirit). The more mobile band contained starting material (194mg). The less mobile

band (42mg; 0.12m.mole;14%) crystallised from chloroform/ether as colourless needles (m.p. 133-134$^0$; m/e 348 ($M^+$)). Found : C,48.52; H,7.09; N,8.24. $C_{14}H_{24}N_2O_2S_3$ requires C,48.27; H,6.94; N,8.04%.

n.m.r. ($CDCl_3$) : $\tau$ 5.36-5.83 (2H,m); 5.83-6.23 (2H,m); 7.0 (12H,s); 7.40-8.36 (8H,m);

i.r. ($CCl_4$) : $\nu$ 2995(sh),2918,2880(sh),2838,1645(vs),1475,1430,1400,1360(s), 1253(s),1090(s) $cm^{-1}$.

N,N-dimethyldithiocarbamate (XXXIV):

N,N-dimethyldithiocarbamate (XXXIV) was prepared by the reaction of dichloride (VI) with an aqueous solution of sodium dimethyldithiocarbamate as reported[43]. The product (XXXIV) crystallised from benzene/heptane as colourless needles, m.p. 211-212$^0$ (lit. 210-211$^0$); m/e 380 ($M^+$).

n.m.r. ($CDCl_3$) : $\tau$ 5.05-5.50 (2H,m); 6.50 and 6.60 (12H,d); 6.73 (2H,m); 7.30-8.0 (8H,m);

i.r. ($CCl_4$) : $\nu$ 2920,2841,1486,1477(sh),1442,1430,1369,1252,1138,978 $cm^{-1}$.

Pyrolysis of (XXXIV):

N,N-dimethyldithiocarbamate (XXXIV) (200mg; 0.53m.mole) was heated at 217-220$^0$ for 18 hr. in a glass tube sealed under reduced pressure. On cooling, the opened tubes were washed out with chloroform and the extract was filtered through a small plug of alumina. Evaporation of solvent gave a slightly blackened product which was purified by prep. t.l.c. (1:1 chloroform/petroleum spirit). N.m.r., t.l.c. and mixed melting point determination showed the product to be starting material.

6-Chloro-9-thiabicyclo[3.3.1]non-2-ene (XVII):

2,6-dichloro-9-thiabicyclo[3.3.1]nonane (VI) (13g; 61.6m.mole) was pyrolysed at 173-175$^0$ for 24 hr in 4 sealed tubes. The tubes were cooled to -70$^0$ before being opened and the tarry reaction mixture was extracted with ether. Filtration and removal of solvent afforded a dark brown oil from which unreacted dichloride (VI) (3g) precipitated out. The residue was distilled (69-72$^0$; 0.15mm) to give chloroalkene (XVII) (5.8g; 33.2m.mole; 70% from reacted dichloride).

Found C,55.18; H,6.40, $C_8H_{11}SCl$ requires: C,54.99; H,6.35%.m/e 176,174 ($M^+$).

n.m.r. ($CDCl_3$) : $\tau$ 3.98 and 4.06 (2H,d.,J=4Hz); 5.36 (1H,t.with further splitting, J=4Hz); 6.70-7.0 (2H,m); 7.23-7.50 (2H,d. with further spitting, J=2Hz); 7.66-8.12 (4H,m);

i.r. ($CCl_4$) : $\nu$ 3027,2963,2937,2908,2846,2821,1651 (w) $cm^{-1}$.

Adipate (XXXV):

To a refluxing solution of adipic acid (2.48g;17m.mole) in acetone (30ml) was added a solution of triethylamine (3.99g;40m.mole) in acetone (15ml) and of chloroalkene (XXVI) (5.92g;34m.mole) in acetone (50ml) and refluxing was continued for a further 16hr. After cooling the colourless precipitate was filtered off and the residue was evaporated to dryness to furnish a colourless oily solid which was chromatographed over alumina (neutral, 42g). Elution with ether/petroleum spirit (2:3) gave adipate (XXXV) (4.2g;10m.mole; 60%) as colourless plates from chloroform/petroleum spirit, m.p. 112-114$^0$ (lit. m.p. 109-111$^0$); m/e 422 ($M^+$).

Found C,62.21; H,7.26. $C_{22}H_{30}O_4S_2$ requires C,62.54; H,7.16%.

n.m.r. ($CDCl_3$) : $\tau$ 4.0 and 4.06 (4H,d.,J=4Hz); 4.57-5.0 (2H,t,J=7Hz, with further splitting, J=3Hz); 6.76-7.10 (4H,m); 7.46-8.23 (20H,m);

i.r. ($CCl_4$) :) 3026,2940,2909,2894(sh),2875(sh),2850,2820,1736(vs), 1650(w),1448,1430,1415,1160,1132 $cm^{-1}$.

Pyrolysis of adipate (XXXV):

Adipate (109mg; 0.26m.mole) in a glass tube, sealed under vacuum, was heated at 247-255$^0$ for 2 hr. The contents of the tube were extracted with ether and filtered to yield diene (XVI) (42mg; 0.31m.mole;66%). Unreacted starting material (XXXV) (10mg) was also obtained.

## REFERENCES


1). W.A.C.Brown , G.Eglinton , J.Martin, W.Parker and G.A.Sim, Proc.Chem. Soc., 1964, 57; G.Eglinton, J.Martin, and W.Parker, J.Chem. Soc., 1965, 1243.

2). P.D.Cradwick and G.A.Sim, J.Chem.Soc.(B), 1971, 2218; G.A.Sim and C.Tamura, J.Chem.Soc. (B), 1968,1241.

3). R.Lygoe, J.M$^{c}$Kenna and I.O.Sutherland, Chem. Comm., 1965, 356.

4). R.A.Appleton, S.C.Egan,J.M.Evans,S.H.Graham and J.R.Dixon, J.Chem.Soc. (C) , 1968, 1110.

5). I.Fleming,S.W.Hanson and J.K.M.Saunders, Tett.Lett., 1971, 3733.

6). H.Stetter,O.Bander and W.Neumann, Ber., 1956, 89, 1922.

7). S.Landa and Z.Kamycek, Coll. Czeck. Chem. Comm., 1959,24, 4004.

8). H.Meerwein, J.Prakt. Chem., 1922, 104, 161.

9). W.Sanne, Chem.Abs., 1962, 56, 9996 (a).

10). For example: M.Kojima, T.Nose, K.Shintomi and N.Yoneda, Jap. J. Pharmacol. , 1971, 21, 276.

11). S.Greenbaum,U.S.Patent: 3,365,465(1968); E.D.Weil and K.J.Smith, Ger. Patent 1,297,111 (1969).

12). E.D.Weil, U.S.Patent 3,574,233 (1971).

13). G.Clamician and R.Silber, Ber., 1894, 27, 2854.

14). O.H.Wheeler, J. Amer. Chem. Soc., 1953, 75, 4858.

15). A.C.Cope and B.C.Anderson, J. Amer. Chem. Soc., 1957, 79, 3892.

16). A.C.Cope and A.Fournier, J.Amer.Chem. Soc., 1957, 79, 3896 ,3900.

17). S.F.Birch, T.V.Cullum and R.A.Dean, Ind. Eng. Chem., 1958, 3, 359.

18). R.C.Menzies and R.Robinson, J. Chem. Soc., 1924, 125, 2163; C.Schöpf and G.Lehmann, Ann., 1935, 518, 26.

19). P.Agocs, K.Koczka, I.Weisz and K.Kovács, Monatsh, 1971, 102, 591.

20). For example: A.C.Cope, H.L.Dryden and C.F.Howell, Org. Synth., (coll. vol. IV), 1963,816; E.Jucker and A.J.Lindemann,Chem.Abs.,1968,69,96514; K.Alder and H.A.Dortmann,Chem.Ber.,1953,86,1545; O.Dold, K.Stach and W.Schaumann, Chem.Abs., 1964, 61, 12053.

21). R.Willstätter and E.Waser, Ber.,1911, 44, 3423; R.Willstätter and M. Heidelberger, Ber.,1913, 46, 517.

22). V.Horák, J.Závada and A.Pískala, Chem. Ind., 1958, 1113; V.Horák, J Závada and A.Pískala,Acta Chim. Acad. Sci. Hung., 1959, 21, 97.

23). F.Bohlmann, H.J.Schulz and J.Riemann, Tet. Lett., 1964, 1705.

24). C.Ganter,K.Wicker, W.Zwahlen and K.Schaffer- Sabba, Helv. Chim. Acta, 1970,53, 1618.

25). H.Stetter and H.-J.Meissner, Tet Lett.1966, 4599; H.Stetter, H.-J. Meissner and W.D.Last, Chem. Ber.,1968, 101, 2889.

26). A.C.Cope,M.A.McKervey and N.M.Weinshenker, J. Org. Chem., 1969, 34, 2229.

27). J.L.Jernow, D.Gray and W.D.Clossen, J. Org. Chem., 1971, 36,3511.

28). C.Ganter, R.O.Duthaler and W.Zwahlen, Helv. Chim. Acta, 1971, 54, 578.

29). V.Gomez Aranda, J.Barluenga Mur, G.Ascensio and M.Yus,Tet. Lett.,1972, 3621.

30). S.Moon and L.Haynes, J.Org. Chem.,1966, 31, 3067.

31). A.C.Cope, B.S.Fisher, W.Funke, J.M.McIntosh and M.A.McKervey, J.Org.Chem., 1969, 34, 2231.

32). H.Stetter and K.Heckel, Tet. Lett.,1972, 801;Chem. Ber.,1973, 106, 339.

33). A.C.Cope, R.S.Bly, M.M.Martin and R.C.Peterson, J. Amer. Chem. Soc., 1965, 87, 3111.

34). S.Wawzonek and P.J.Thelan, J.Amer.Chem.Soc., 1950,72, 2118.

35). E.F.Knights and H.C.Brown, J.Amer.Chem.Soc., 1968, 90, 5280; H.C.Brown, E.Negishi and P.L.Burke, J.Amer.Chem.Soc., 1972, 94, 3561.

36). Y.Kashman and E.Benary, Tet., 1972, 28, 4091.

37). Y.Kashman and E.Benary,J.Org.Chem.,1972, 37, 3778.

38). A.T.Bottini and J.Gal, J.Org.Chem.,1971, 36, 1718.

39). C.Ganter and R.E.Portmann, Helv. Chim.Acta, 1971, 54, 2069.

40). D.D.MacNicol and E.Cuthbertson, J.Chem.Soc.,(Perkin I), 1974, 1893.

41). R.K.MacKenzie, D.D.MacNicol, H.H.Mills,R.A.Raphael, F.B.Wilson and J.A. Zabkiewicz, J.Chem.Soc., (Perkin II), 1972, 1632.

42). E.J.Corey and E.Block, J.Org. Chem., 1966, 31, 1663.

43). E.D.Weil,K.J.Smith and R.J.Gruber, J.Org. Chem.,1966, 31, 1669.

44). F.Lautenschlaeger, Can. J.Chem., 1966, 44, 2813.

45). W.L.Mock, J.Amer. Chem. Soc.,1970, 92, 3807.

46). A.H.Frazer and W.P.O'Neill,J.Amer. Chem. Soc.,1963, 85, 2613.

47). T.J.Katz, C.R.Nicholson and C.A.Reilly, J. Amer. Chem. Soc.,1966, 88, 3832.

48). G.C.Tustin, C.E.Monken and W.H.Okamura, J. Amer. Chem. Soc.,1972, 94, 5112.

49). A.G.Anastassiou, J. Amer. Chem. Soc., 1965, 87, 5512.

50). A.G.Anastassiou, J.Amer. Chem. Soc., 1968, 90, 1527; A.G.Anastassiou and R.P.Cellura, J.Org. Chem.,1972, 37, 3126.

51). F.Lautenschlaeger, J. Org. Chem.,1968, 33, 2627.

52). A.G.Anastassiou and B.Y.-H. Chao, Chem. Comm.,1971, 979.

53). J.Gasteiger andR.Huisgen, J.Amer. Chem. Soc.,1972, 94, 6541.

54). L.A.Paquette, J.R.Malpass and T.R.Barton, J.Amer. Chem. Soc.,1969, 91, 4714.

55). L.A.Paquette, R.E.Wingard and R.H.Meisinger, J.Amer. Chem. Soc., 1971, 93, 1047; J.Amer. Chem. Soc.,1973, 95,2230.

56). L. Ramberg and K.Bäcklund, Chem. Abs., 1940, 34, 4725; L.A.Paquette, Accounts Chem. Res., 1968, 1, 209.

57). J.M.Mellor and C.F.Webb, J. Chem. Soc.,(Perkin I), 1972, 211.

58). A.Padwa and A.Battisti, J. Amer. Chem. Soc., 1969, 91, 4000; J. Amer. Chem. Soc., 1971, 93, 1304; J. Amer. Chem. Soc., 1972, 94, 521.

59). C.Ganter and J.-F.Moser, Helv. Chim. Acta, 1969, 52, 725; Helv. Chim. Acta, 1971, 54, 300.

60). L.A.Paquette and L.D.Wise, J.Amer. Chem. Soc.,1967, 89, 6659.

61). C.Ganter and J.-F. Moser, Helv. Chim. Acta, 1971, 54, 2228.

62). A.G.Schulz and R.H.Schlessinger, Chem. Comm.,1970, 1051.

63). D.D.MacNicol, P.H.McCabe and R.A.Raphael, Synth. Comm.,1972, 2, 185.

64). H.Oediger, F.Möller and K.Eiter, Synthesis,1972, 591.

65). D.E.Pearson and C.A.Buehler, Chem. Rev., 1974, 74, 45.

66). J.F.Bunnett and R.R.Victor, J. Amer. Chem. Soc.,1968, 90, 810.

67). A.Reid, B.Sc. Thesis, University of Glasgow, 1975.

68). K.B.Wiberg and B.J.Nist, "The Interpretation of N.M.R. Spectra," W.A. Benjamin Inc., New York, 1962, ch.5; L.M.Jackman and S.Sternell, "Applications of N.M.R. Spectroscopy in Organic Chemistry," Pergamon Press, Oxford,1969, p. 134 and references cited therein.

69). H.J.Franz, W.Höbold, R.Höhn, G.Müller-Hagen, R.Müller, W.Pritzkow and H.Schmidt, J.Prakt. Chem.,1970, 312, 622.

70). R.A.Clement, J.Org. Chem., 1960, 25, 1724; J.Org. Chem.,1962, 27, 1115; T.J.Kealy, J.Amer. Chem.Soc.,1962, 84, 966.

71). O.L.Chapman and S.J.Dominianni, J.Org. Chem.,1966, 31, 3862.

72). R.C.Cookson, S.S.Gupte, I.D.R.Stevens and C.C.Watts,Org. Synth. vol.51, p.121.

73). C.Y.-J.Chung, D.MacKay and T.D.Sauer, Can. J. Chem.,1972, 50, 3315.

74). For preparation see: Fieser and Fieser, "Reagents for Organic Synthesis," Vol I, 729.

75). R.Mozingo, Org. Synth. (Coll. Vol III), 1955, 181.

76). R.Nace, Organic Reactions, 1962, 12, 57.

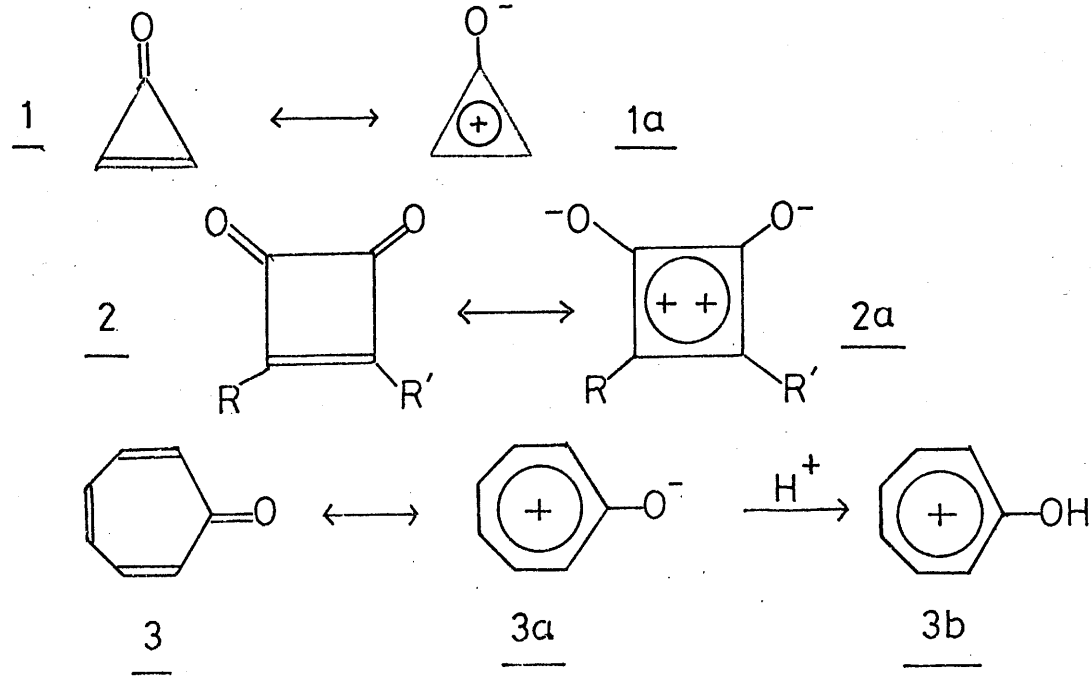
77). M.S.Newman and F.W.Hetzel, J. Org. Chem., 1969, 34, 3604.

78). M.S.Newman and H.A.Karnes, J.Org. Chem., 1966, 31, 3980.

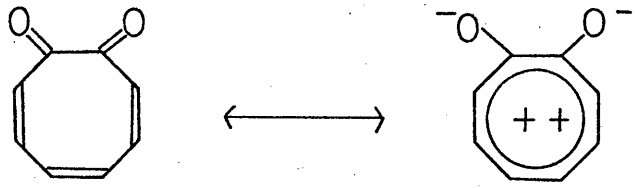
## CYCLOOCTATETRAENOQUINONES.

The advent of Hückel's rule[1], which relates the aromaticity of a planar cyclic compound to the number (4n+2) of π-electrons in the system, and its empirical extension[1] to polycyclic compounds, has brought about widespread interest[2] in the synthesis and properties of various cyclic π-electron species.

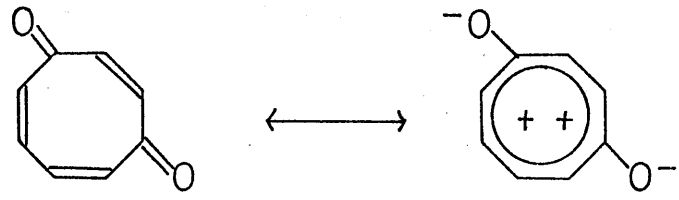
Systems in which a carbonyl group is in conjugation with double bonds have frequently been used in designing potentially aromatic molecules. In compounds suchas 1,2,3,4 and 5 the function of the carbonyl group is to attain the requisite number of π-electrons while maintaining complete conjugation. If molecules of this type are to exhibit pseudo aromaticity the polarised canonical forms (1a to 5a) must contribute appreciably to the resonance hybrid. Moreover, the stability achieved in becoming (4n+2) π-electron systems must more than compensate for the increase in energy due to the assumption of a planar conformation and to the separation of charge required by these structures. Thus the ultimate properties of these compounds are controlled by the gain in resonance energy set against the various energy requirements of the polarised forms.



For the small-ring compounds cyclopropanone (1) and cyclobutadienoquinone (2) the canonical forms (1a) and (2a) involve no increase in angle strain and indeed these molecules are found[3] to exhibit unusual stability. Conversely, tropone (3) has only a minor contribution from its resonance form (3a)[4] presumably because of the high angle strain and charge separation involved in 3a. However, in this case, charge separation has been eliminated by protonation and the resulting hydroxytropylium ion (3b) shows[5] appreciable aromatic character.

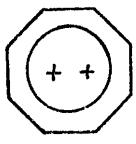


4 4a

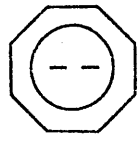


5 5a

The cyclooctatetraenoquinones (4) and (5) are of considerable interest because their canonical forms (4a and 5a) embody the cyclooctatetraene dication (6) (4n+2,n=1) which has not been observed directly[6]. By comparison, cyclooctatetraene dianion (7) is well known and exists as a planar aromatic molecule indicating that the angle strain involved in this planar configuration is more than compensated for by the stability conferred by the 10π-electron system (4n+2,n=2).

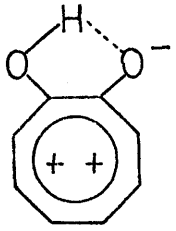


6

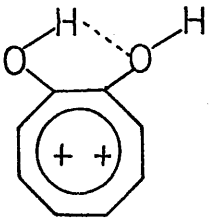


7

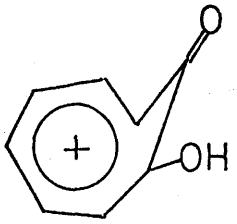
However, as in tropone, there is a separation of charge implied in species 4a and 5a; in 4a there is an additional coulombic interaction between the negative charges on the oxygens of the adjacent carbonyls. These factors will tend to raise the energy of 4a and 5a and hence decrease their resonance contribution. Thus it is not known whether the cyclooctatetraenoquinones are likely to exhibit pseudoaromatic character or exist as non-planar and therefore non-aromatic molecules. Again, as for tropone, there exists the possibility that if 4 and 5 are not aromatic then their protonated forms could be. Such protonated species may still embody dication (6) (e.g. 8 and 9) or involve a homotropylium ion such as 10 analogous to that observed[8] (by n.m.r.) on protonation of 2,4,6-cyclooctatrienone at low temperature.



8

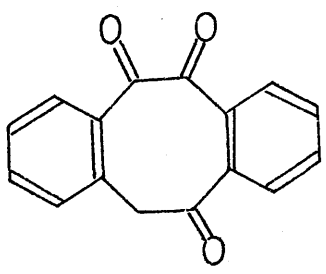


9

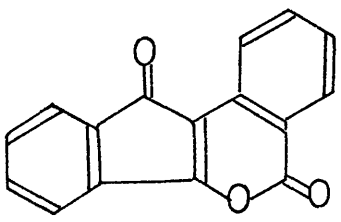


10

The first derivative of a cyclooctatetraenoquinone to be mentioned in the literature was a compound assigned[9] structure 11 in 1940. However, this assignment has since been revised[10] and this product is now believed to be the tetracyclicpyrone (12). Attempts to obtain the



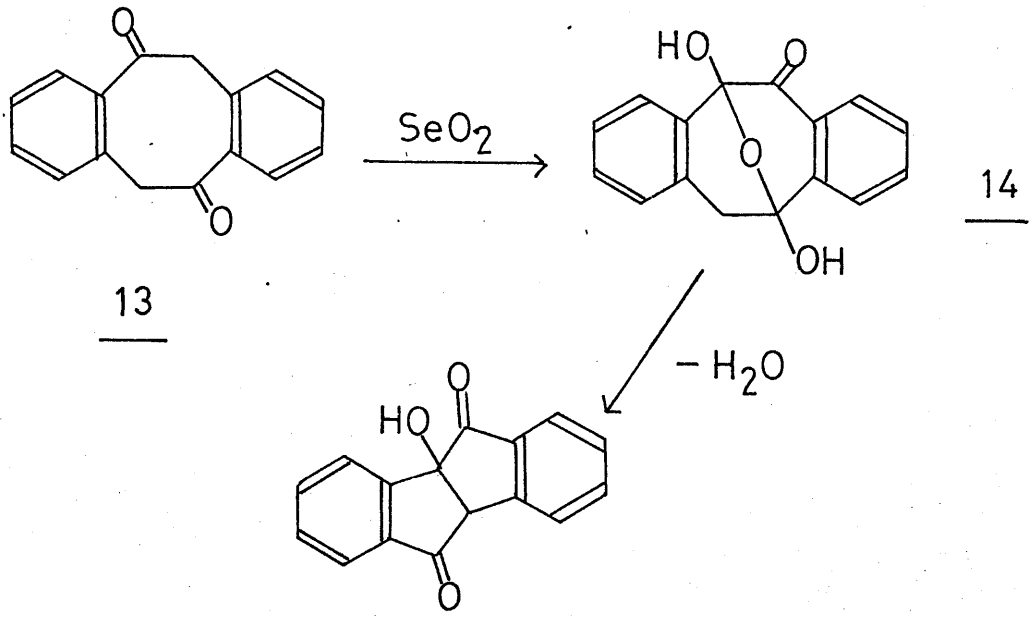
11



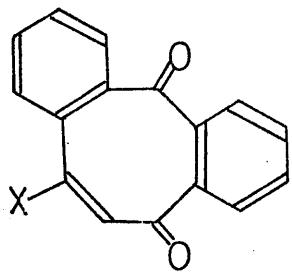
12

trione (11) were made[11] by selenium dioxide oxidation of the dione (13) (Scheme A). Compound 14, a hydrate of 11, was obtained but attempts to dehydrate 14 gave only 15, an intramolecular condensation product of the elusive trione.

Scheme A:

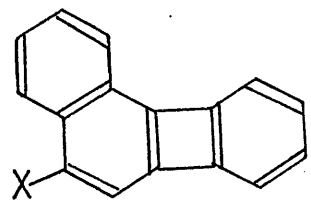



In 1962 the formation of the halodibenzo-1,4-cyclooctatetraenoquinones (16 and 17) from the sodium dichromate-acetic acid oxidation of the corresponding biphenylene derivatives (18 and 19) was described[12]. However, this was a reinvestigation of the oxidation of these biphenylenes and no mention was made of the possible aromatic nature of the quinone derivatives.




16, X=Br

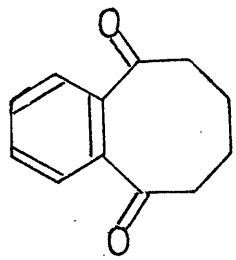
17, X=I



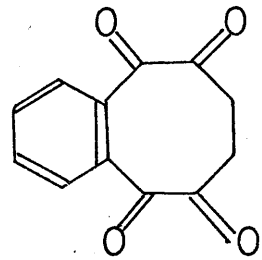

18, X=Br

19, X=I

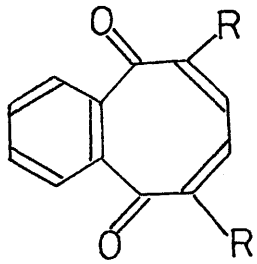
The first deliberate attempts to obtain cyclooctatetraenoquinone derivatives reported in the literature were made by Proctor and coworkers in 1966, who attempted[13] to oxidise diketone (20) to the tetraketone (21 or 22) with a view to obtaining the quinone derivative (23). However, attempts to obtain the tetraketone failed and the several methods used (selenium dioxide or sodium methoxide with or without ethyl formate) led only to transannular aldol condensation products of the type 24.



20

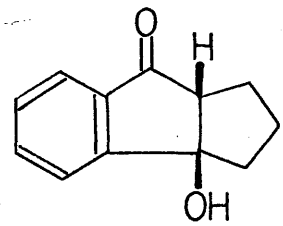


21



22, R=OH

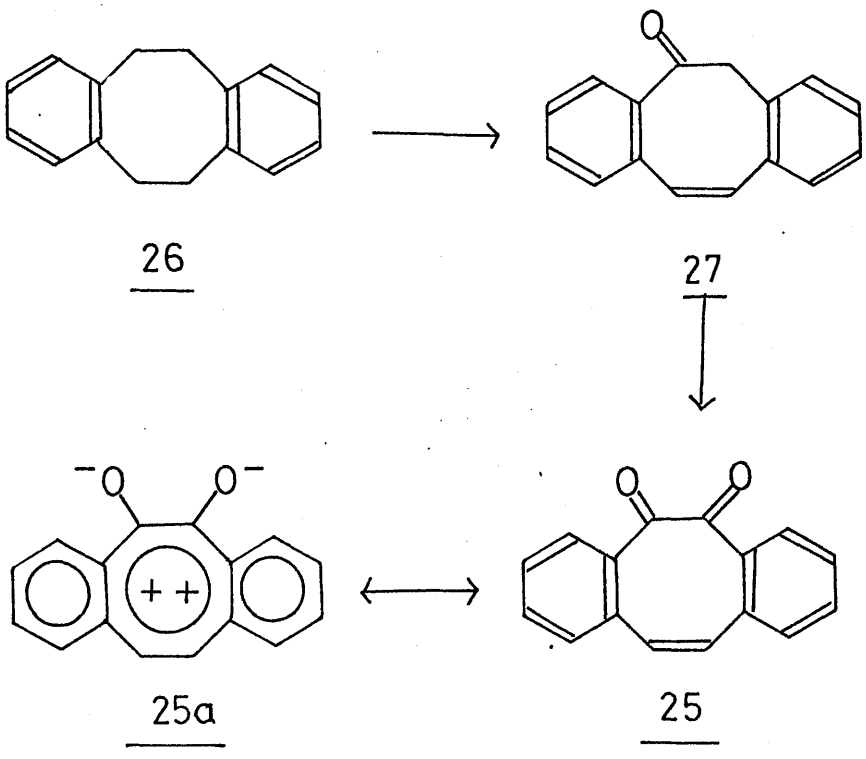
23, R=H



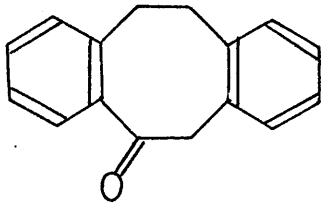
24

The first successful synthesis of a cyclooctatetraenoquinone derivative was described[14] by Yates, Lewars and McCabe who prepared dibenzo (a,e)cyclooctene-5,6-dione (25). The hydrocarbon (26) on bromination with N-bromosuccinimide followed by oxidation gave enone (27) as one of the products, formed in 20% yield (Scheme B). Subsequent oxidation of 27 with selenium dioxide furnished quinone (25). A study of the infra-red and n.m.r. spectra of 25 indicates that any participation by the canonical form 25a must be very small indeed. A large contribution

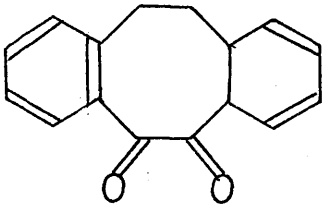
Scheme B:



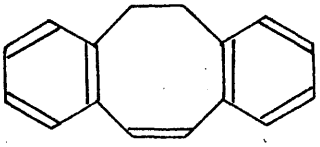

from this structure should cause the carbonyl stretching frequency to occur at an appreciably longer wavelength than the corresponding bands in enone (27) or ketones (28 and 29). That the carbonyl adsorption occurs at shorter wavelength than these compounds may be accounted for by dipole-dipole interaction between the adjacent carbonyls in 25 which may be accentuated by the relatively small dihedral angle between them. Models indicate that in structure 25 this angle would be of the order of $0^{0}$-$40^{0}$. In addition the two protons on the eight-membered ring resonate at $\tau$ 3.17 in the n.m.r. spectrum. The corresponding protons in enone (27) and hydrocarbon (30) occur at $\tau$ 3.12 and $\tau$ 3.30 respectively. If 25 were indeed aromatic the $\pi$-electron system should be capable of sustaining a diamagnetic ring current which would significantly deshield these protons. The n.m.r. spectrum of 25 recorded in trifluoroacetic acid is essentially the same as that obtained in deuteriochloroform and hence there is no evidence of special stability in the mono- or di- protonated forms of 25 analagous to structures 8, 9 and 10.



28



29

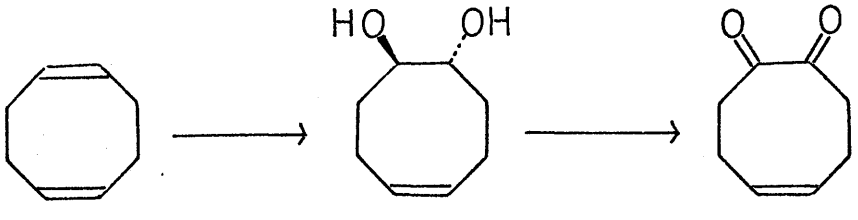


30

However, aromaticity in the monocyclic systems 4 and 5 or their protonated derivatives is not excluded by the absence of aromaticity from 25. The two benzene rings fused to the eight-membered ring may tend to appropriate π-electrons for their individual aromatic systems and hence suppress aromaticity in the eight-membered ring[15].

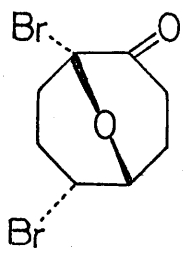
Synthetic approaches to the monocyclic system (4) were made[16] starting from cis,cis-1,5-cyclooctadiene (31). The trans diol (32), obtained from the diene by performic acid oxidation followed by hydrolysis, was oxidised to the corresponding dione (33) (Scheme C). However, attempted allylic bromination of this compound was unsuccessful. Treatment of 33

Scheme C:

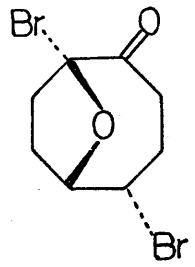



31 32 33

with N-bromosuccinimide led to intractable tarry mixtures and bromination with bromine in carbon tetrachloride was accompanied by transannular bond formation to give keto ether (34 or 35). The formation of this



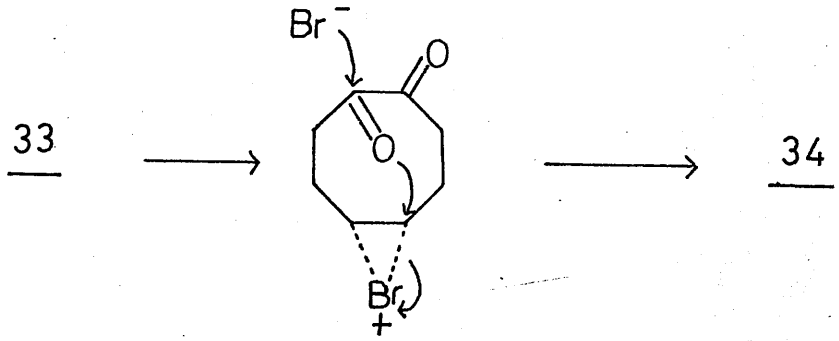

34



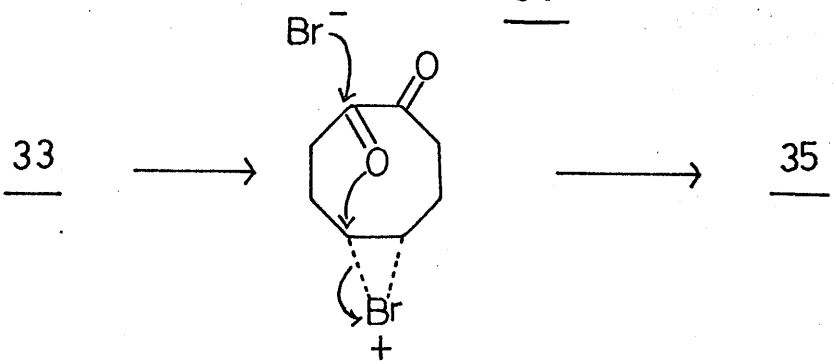

35

bicyclic compound is thought to occur via the bromonium ion (36) (Scheme D).

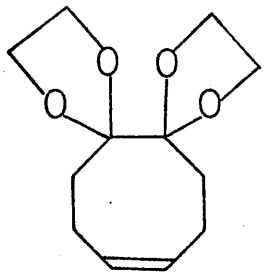
Scheme D:



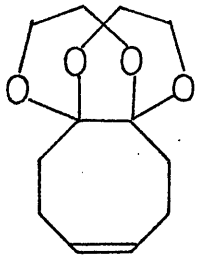

36



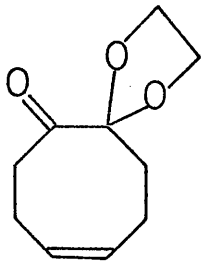

To protect the carbonyl functions 33 was treated with ethylene glycol and p-toluene sulphonic acid. Three ketals were produced, diketal (37), monoketal (38) and the crossed ketal (39). The proportions of these products varied with reaction time and a two-week reaction optimised the yield of 37 at the expense of the other two products. Bromination of diketal



37



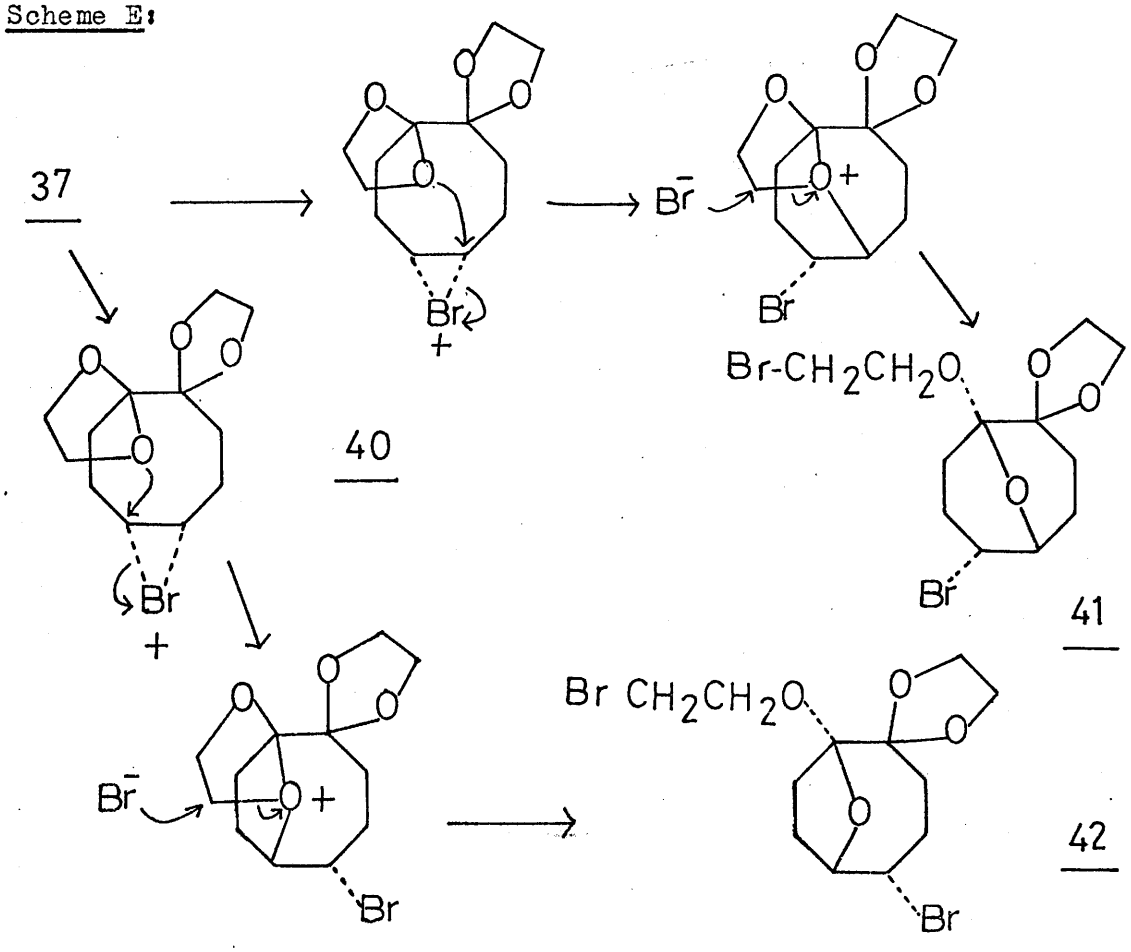
39



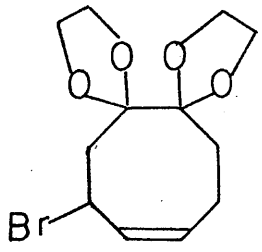
38

(37) with bromine or with pyridinium bromide perbromide resulted in transannular cyclisation producing 9-oxabicyclo[3.3.1]- or[4.2.1]nonane derivatives (41 or 42). The postulated mechanism (Scheme E) again involves formation of a bromonium ion (40) followed by nucleophilic attack by the ketal oxygen.

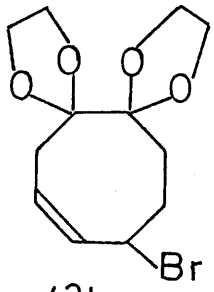
Scheme E:



Small-scale bromination of diketal (37) with N-bromosuccinimide or 1,3-dibromo-5,5-dimethylhydantoin gave an allylic bromide (43a or 43b). The yield of this reaction was very variable and large scale bromination was found to give low yields of 43 as well as the two bicyclic dibromides (41 and 42). The low yield of the bromination step has so far prevented the accumulation of sufficient bromide (43) for this synthesis of 1,2-cyclooctatetraenoquinone to be completed.

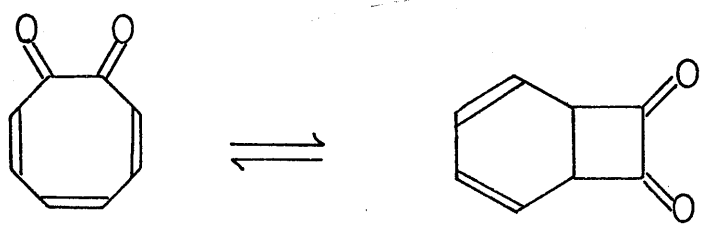



43a

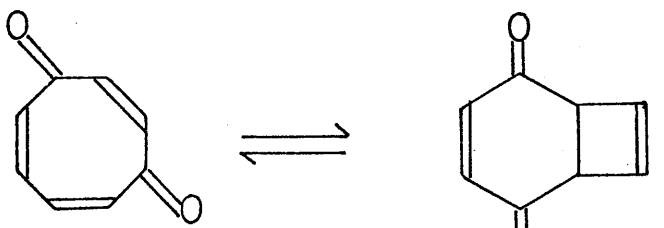



43b

Alternative routes to quinones 4 and 5 through the valence tautomers (44 and 45) have been investigated by several groups. Attempts to obtain



4 44

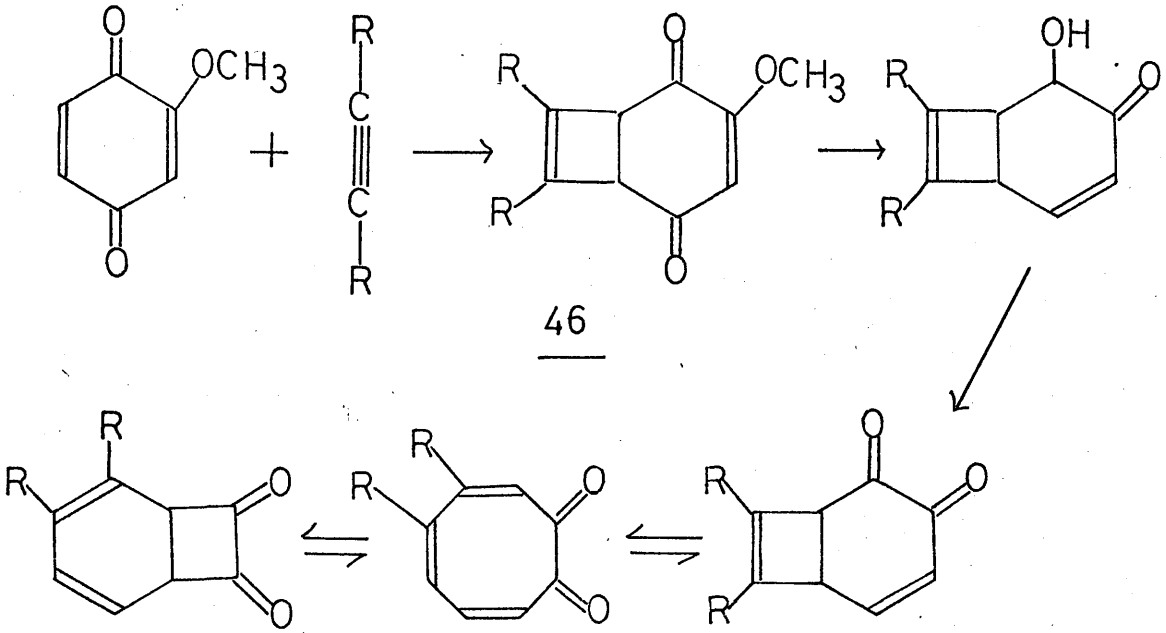


5 45

a substituted derivative of 44 were reported[17] by Pappas and coworkers. The proposed reaction sequence (Scheme F) involved photo-addition of an alkyne to methoxy-p-benzoquinone to give a substituted bicyclo[4.2.0]octene

(46) which could be converted to a derivative of 1,2-cyclooctatetraeno-quinone (47) by a series of steps. The only previous reports[18] of alkyne

Scheme F:



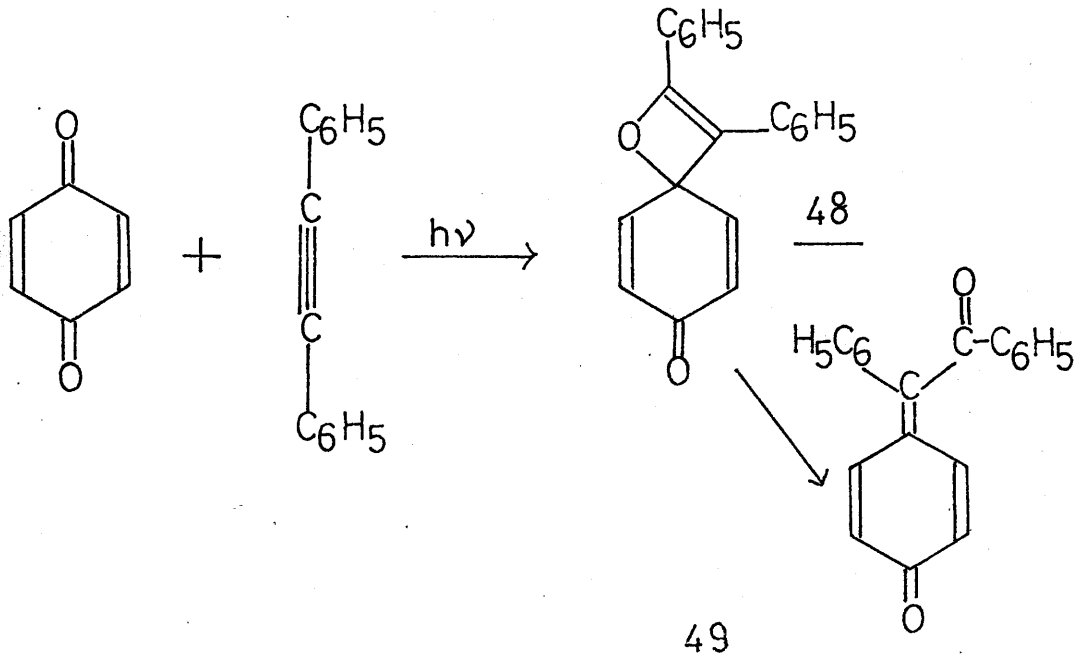
46



47

addition to a p-benzoquinone had given (Scheme G) an adduct (49) formed by addition to the carbonyl group presumably occuring via the oxetane intermediate (48). However, although Pappas found that addition of an

Scheme G:

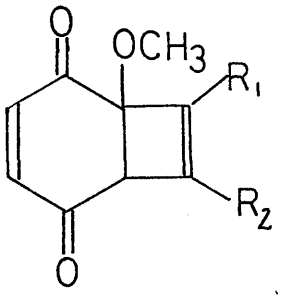


48

49

alkyne to methoxy-p-benzoquinone did not occur at the carbonyl group; the addition invariable took place at the methoxyl side of the quinone to give 50 and hence the reaction sequence given in Scheme F was inapplicable.

50



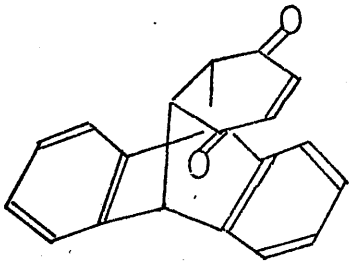
a) $R_1=R_2=CH_3$

b) $R_1=R_2=C_6H_5$

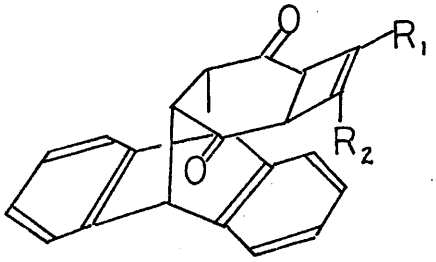
c) $R_1=CH_3$, $R_2=C_6H_5$

d) $R_1=C_6H_5$, $R_2=CH_3$

In 1973 Yates also reported[19] on the photoaddition of an alkyne to p-benzoquinone and to 2,5-dimethyl-p-benzoquinone. Addition to the carbonyl group was again found to occur. In order to overcome this problem Yates sought to modify the quinone chromophore to favour reaction at an ethylenic bond. He found that reaction[20] of p-benzoquinone with anthracene gave enedione (51) which underwent photoaddition at the ethylenic bond to give adducts (52, 53 and 54), in good yield, with but-2-yne, with phenylacetylene and with dimethylacetylenedicarboxylate respectively. The stereochemical assignment of these molecules was based on the assumption that addition occurs at the less hindered side of the double bond. Adducts (52 and 53)



51

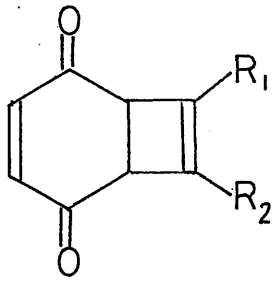


52, $R_1=R_2=CH_3$

53, $R_1=C_6H_5$, $R_2=H$

54, $R_1=R_2=CO_2CH_3$

fragmented thermally by a retro-Diels Alder reaction to give 55 and 56 in good yield, but the valence tautomerism of these products was not discussed.

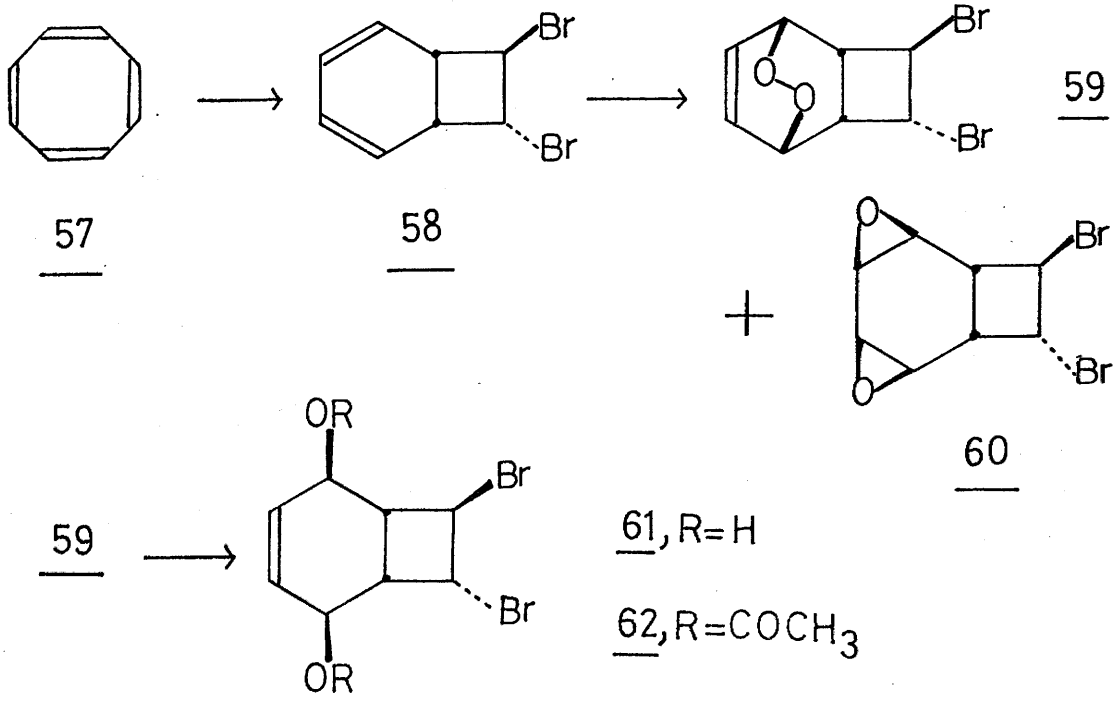


55, $R_1 = R_2 = CH_3$

56, $R_1 = C_6H_5$, $R_2 = H$

Very recently, the preparation of 45 itself has been described[21] (Scheme H). Photooxygenation of trans-7,8-dibromobicyclo[4.2.0]octa-2,4-diene[22] (58), a bromination product of cyclooctatetraene (57), gave mainly epidioxide (59) accompanied by small amounts of diepoxide (60). Reduction of 59 with lithium aluminium hydride yielded diol (61) which was converted to diacetate (62). Debromination of 62 with zinc dust to give 63 with subsequent reductive deacetylation afforded diene diol (64). Oxidation with Jones reagent led to bicyclo[4.2.0]octa-3,7-diene-2,5-dione (45) in 41% overall yield from cyclooctatetraene. Valence tautomerism of 45 to quinone (5) is now under active investigation by this group.

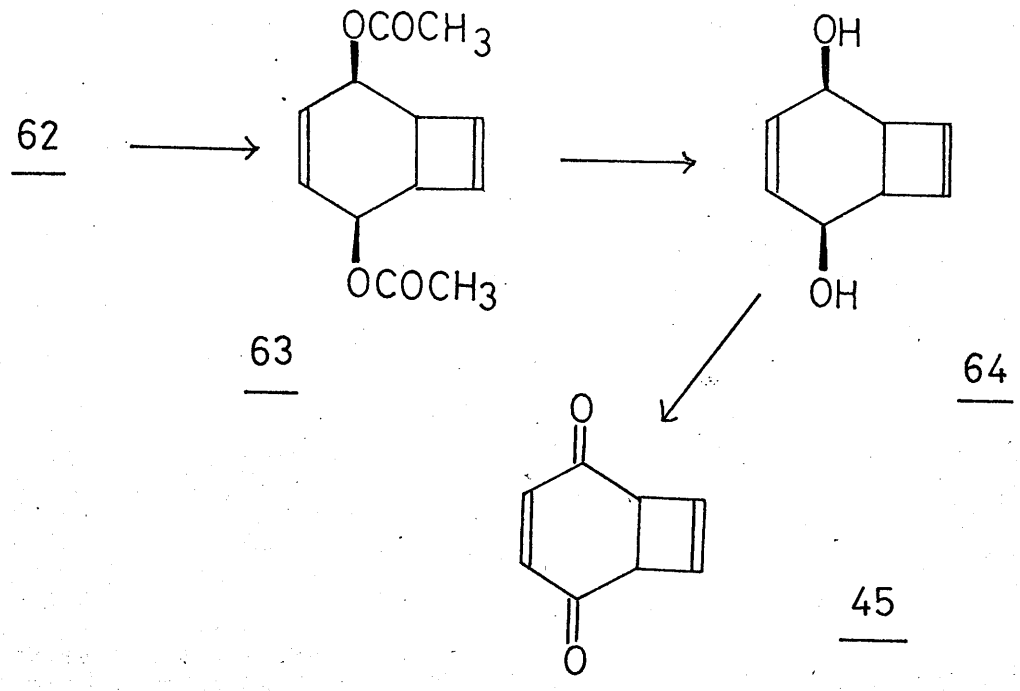
Scheme H:




57 58 59 60

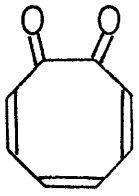
59 → 61, R = H; 62, R = $COCH_3$

Scheme H (cont):

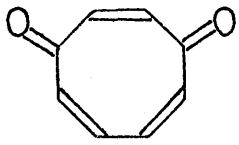


## RESULTS AND DISCUSSION.

Because of the considerable interest in the cyclooctatetraeneoquinones, as detailed in the introduction, we sought to synthesise either cycloocta-3,5,7-triene-1,2-dione (I) or cycloocta-2,5,7-triene-1,4-dione (II).



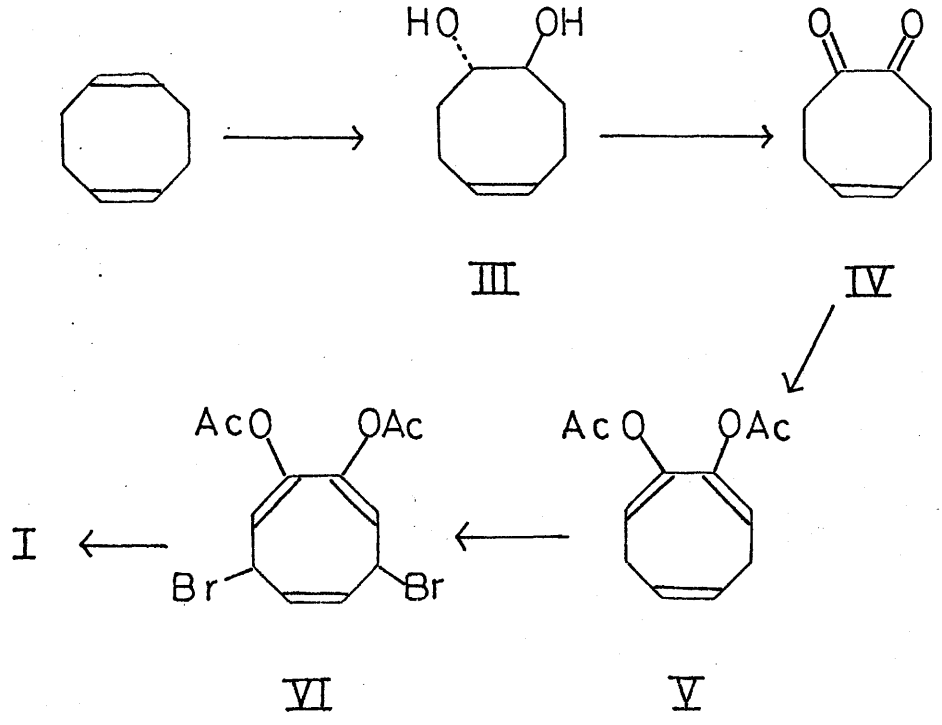
I



II

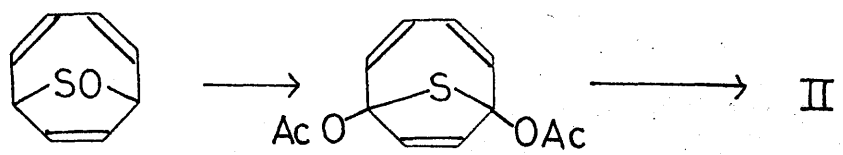
Three synthetic approaches were undertaken. The first (Scheme 1), an adaptation of the route to (I) attempted by Yates et al[16], involves the formation of enone moieties by the established[23] allylic bromination of enol acetates. It was felt that the bromination step should be particularly facile since both methylene groups of V are doubly allylic.

Scheme I:



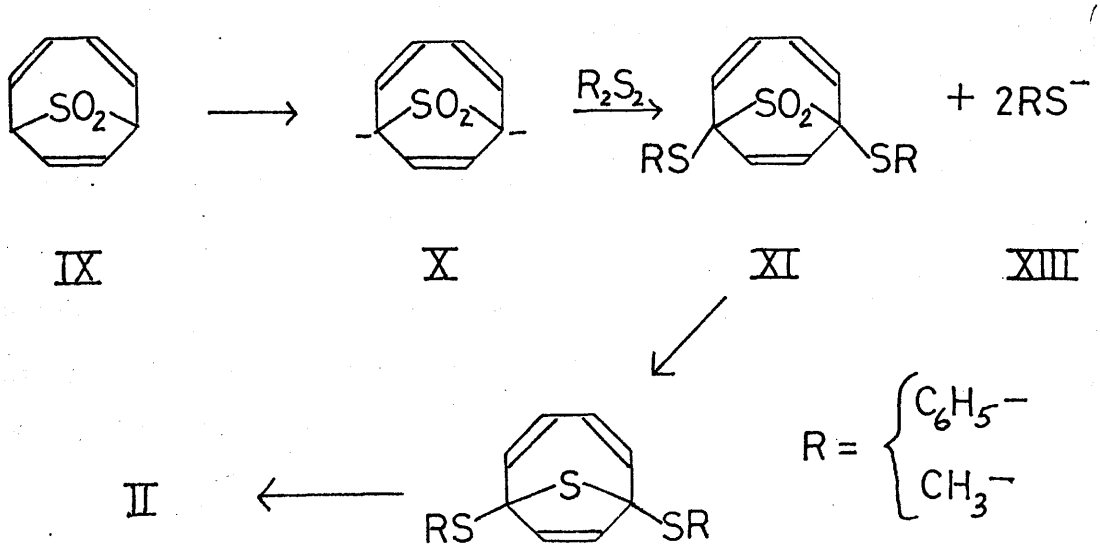
The other two routes utilise bicyclic precursors (Schemes 2 and 3) for the synthesis of II. It was expected that these bicyclic compounds would allow 1,4-difunctionalisation of the 8-membered carbon skeleton while their conformational rigidity would prevent the transannular cyclisation reactions which have impeded the monocyclic routes already attempted. The Pummerer reaction of VII (Scheme 2) or the electrophilic attack of disulphides on the α-sulphonyl anions of IX (Scheme 3) represent two possible methods of introducing substituents at the bridgehead positions.

Scheme 2:




VII VIII

Scheme 3:




IX X XI XIII

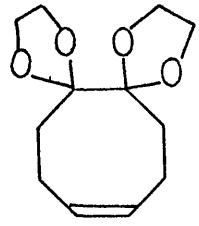
XII

The Monocyclic Route:

This route involves formation of transdiol (III) from the performic hydroxylation[24] of 1,5-cyclooctadiene. Although this was reported[16,25] to go smoothly, in our hands the mono- and di-formate esters of III were formed as by-products. Steam distillation of the crude reaction mixture afforded diol (III) but in greatly reduced yield. However, reduction of the formate ester mixture with lithium aluminium hydride gave III in an overall yield of 52%.

Because of the known tendency of 1,2-diols to undergo ready oxidative cleavage the mild oxidising system dimethyl sulphoxide-acetic anhydride[26] was used to effect the oxidation of III to ene-dione (IV).

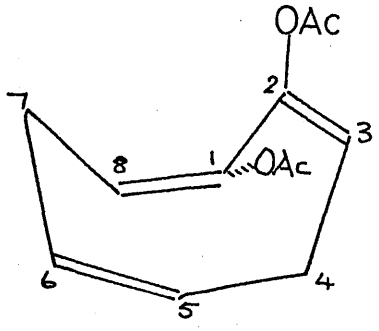
As discussed earlier, attempts to introduce double bonds into 8-membered carbocyles by the technique of bromination and dehydrobromination had resulted either in tarry mixtures or in transannular condensation products, both with ene-dione (IV) and the corresponding diketal (XIII).



XIII

An alternative intermediate is the bisenol acetate derivative (V) which has two advantages over the dione and diketal. Firstly, the conformation of this bisenol acetate is such that the acetate oxygen ($-\underline{O}-\overset{O}{\overset{\|}{C}}-CH_3$) cannot interact with the $\Delta 5,6$ double bond (see diagram) and in any case the $-\overset{O}{\overset{\|}{C}}-CH_3$ group will have an electron withdrawing effect and therefore this acetate oxygen will not have such good nucleophilicity as either the carbonyl or ketal oxygens in IV and XIII respectively. Secondly, positions 4 and 7 are doubly allylic in V and therefore allylic bromination with N-bromo-succinimide may reasonably be expected to be more facile than bromination of

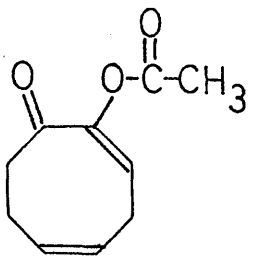
IV and XIII and to compete in rate with any transannular reactions (c.f. allylic bromination was previously very sluggish[16]). Decomposition of dibromide (VI) either spontaneously or by mild base treatment should give the desired 1,2-quinone (I).




V

Formation of bisenol acetate (V) proved more difficult than at first expected. Isopropenyl acetate, with p-toluene sulphonic acid as catalyst reacted sluggishly with dione (IV) and only starting material could be isolated from the reaction mixture. Again, using acetic anhydride with sodium acetate, mainly starting material was isolated although the n.m.r. spectrum obtained on the reaction product showed some change in the vinyl region, and the appearance of an acetate methyl signal indicated some formation of at least monoenol acetate.

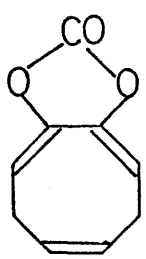
Using acetic anhydride with a catalytic amount of concentrated sulphuric acid gave the most hopeful results with definite changes in the n.m.r. spectrum of the reactionproducts which appeared to be a mixture of starting material and monoenol acetate (XIV). A broadening in the vinylic resonances from $\tau$4.43 to $\tau$4.56 was clearly visible and may be accounted for by the new vinyl proton present in XIV. In addition, a multiplet observed between $\tau$6.73- 7.06 may be due to protons which are doubly allylic and hence resonating downfield of the allylic methylene protons in IV. A sharp singlet at $\tau$7.86 indicated the presence of the acetate methyl group.



XIV

However, attempts to improve the reaction either by using more acid catalyst, or by longer reaction time resulted only in intractable tarry mixtures.

Attempts to form XV by treatment of IV with sodium hydride in dimethyl sulphoxide and subsequent reaction with diethyl carbonate did not result in XV but gave only starting material.



XV

From the above discussion it appeared that protection of dione IV as bisenol acetate (V) or carbonate (XV) was more difficult than anticipated. In consequence, this synthetic approach was not further investigated.

The Bicylic Routes:

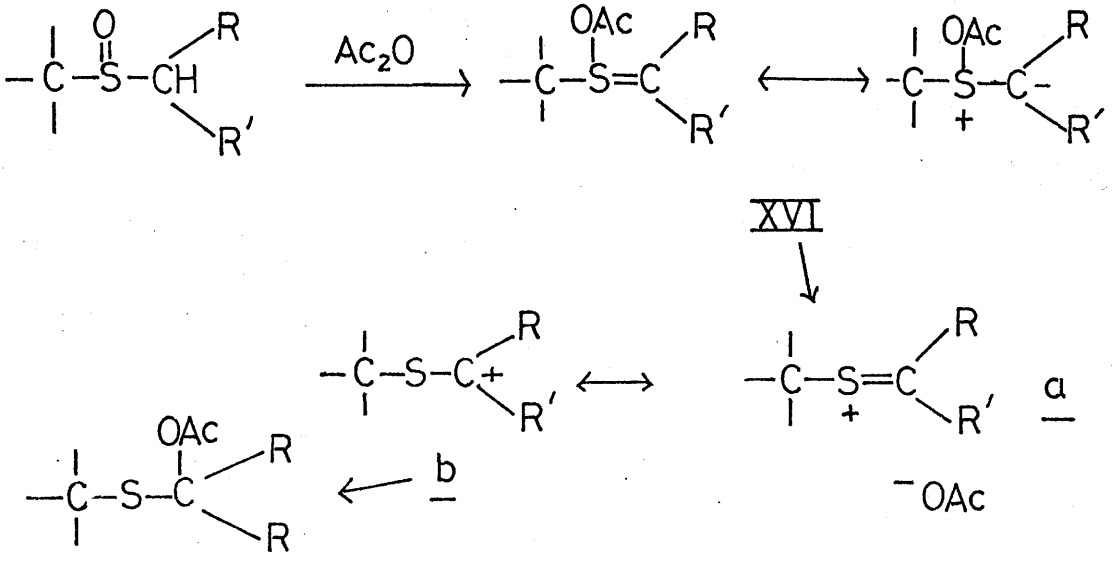
a) The Pummerer Reaction:

Transformations of sulphoxides to α-acetoxy sulphides using acetic anhydride were observed by Pummerer as early as 1909[27]. Thus it was proposed to react acetic anhydride with sulphoxide VII[28], prepared by the reaction of cyclooctatetraene and sulphur monoxide, generated *in situ* by the thermolysis of ethylene sulphoxide[29]. The desired product VIII (Scheme 2) would be a key intermediate in the formation of 1,4-quinone (II).

Reaction of VII with excess acetic anhydride lead to a non-polar product, the n.m.r. spectrum of which showed resonances only in the $\tau$ 2.6-2.8 region. This indicated that the product contained neither a sulphide bridge nor an acetoxyl function. Repeating this reaction for a shorter time led to a complex mixture of products. The least polar compound in this mixture showed spectroscopic characteristics identical to those of the previous single product. The several products of intermediate polarity observed on t.l.c. were present in quantities too small to allow identification but the major, and most polar, component was unreacted starting material. Varying the amount of acetic anhydride employed again gave only a non-polar product or starting material and using sulphuric acid as a catalyst in the reaction resulted in a black oil from which no products could be isolated. Reaction of VII with a mixture of acetic anhydride and acetyl chloride gave a product with two bridgehead signals in the n.m.r. spectrum, attributed to a mixture of starting material and hydrogen on carbon bearing sulphur. However, no incorporation of acetate was observed.

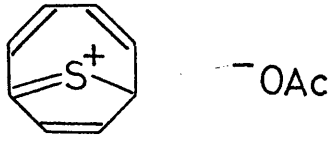
There have been several mechanisms proposed[30] for the Pummerer rearrangement but the one most generally accepted involves formation of an ylid intermediate (Scheme 4). Loss of acetate from such an ylid would give a sulphide salt such as a.

Scheme 4:



The transformation of a to b was suggested by Johnson and Phillips[31] who found that when more than one reaction pathway was available then substituents (R) which favour a carbonium ion favour the production of Pummerer products, and also that highly polar solvents capable of stabilising carbonium ions facilitate the reaction. The possible intramolecular rearrangement of XVI was excluded[32] on studying the reaction using $^{18}O$-labelled acetic anhydride.

However, formation of an intermediate such as a would involve structure XVII which contains a strained double bond (c.f. Bredt's Rule). Although the formation of certain bridgehead double bonds has been observed[33] in the 9-thiabicyclo[3.3.1]nonane series, it may be that the energy of formation of a sulphur-free product is lower than that of XVII and hence reaction of VII with acetic anhydride will be expected to give this product rather than the normal Pummerer product.




XVII

b) Bridgehead Anion Method:

In view of the fact that functionalisation of the bridghead positions did not appear to be possible by the Pummerer reaction, the feasibility of introducing bridgehead $\alpha$-sulphonyl carbanions was examined. Dianion (X), on reaction with a disulphide and subsequent reduction should give XII, a bisthioketal of 1,4-quinone (II). (Scheme 3).

Formation of compounds such as XI, by the addition of carbanions to disulphides, has an analogy[34] in the addition of $\alpha$-carbonyl carbanions to dialkyldisulphides and to diphenyldisulphide. Evidence that the sulphonyl group is capable of stabilising an adjacent bridgehead carbanion was gained

some years ago[35] in the bicyclo[2.2.2]octane series and more recently in the 9-thiabicyclo[3.3.1]nonane[36,37], and the 8-thiabicyclo[3.2.1]octane[36] series. In addition, the electronic interactions of bridgehead α-sulphonyl carbanions in the 9-thiabicyclo[4.2.1]nonane series have been studied[38] as a function of the unsaturation in the carbon framework.

Addition of excess n-butyl lithium to a solution of the sulphone (IX) in anhydrous tetrahydrofuran at $-70^{\circ}$ in a dry nitrogen atmosphere resulted in formation of dianion (X), exhibited by an intense purple colouration. Because XIII (R=Ph) was expected to be a good leaving group the solution of the dianion X was quenched with an excess of diphenyl disulphide dissolved in tetrahydrofuran. However, this resulted in a mixture of the starting sulphone (IX) and n-butylphenyl sulphide, even after varying reaction time and temperature.

Possibly the very bulky anion experiences too much steric hindrance in its approach to the large molecule of diphenyldisulphide and for this reason dimethyldisulphide was employed. Unfortunately, preliminary attempts with dimethyldisulphide appear to be unsuccessful, t.l.c. data indicating the formation of a large number of compounds.

## EXPERIMENTAL.

For general experimental detail, see page 68

### Trans-5-cyclocten-1,2-diol (III):

To 1,5-cyclooctadiene (114 ml; 100g; 0.92moles), stirred in an ice bath, was added a mixture of hydrogen peroxide (33% solution; 100ml; 110g; 1.0moles) and 99% formic acid (620ml) over 1hr., maintaining the temperature at 40-45°. The ice-bath was removed, and the temperature rose to 55° when the mixture became homogenous. The reaction was stirred for a further 5min. and then heated at 65° on the steam bath for 2hr. after which no peracid was observed (starch-iodide). On removal of formic acid and water under vacuum the residue was stirred and cooled in an ice bath while a solution of sodium hydroxide (56g; 1.2mole) in water (240ml) was cautiously added. The aqueous mixture was extracted with chloroform. After drying and evaporation of solvent, the crude product was distilled through a simple stillhead collecting the product (74g) between 116 and 140° (0.8-1.0mm).

Because the n.m.r. spectrum indicated the presence of formate esters, this product was treated with lithium aluminium hydride (LAH). A slurry of LAH (4.8g; 0.13mole) in ether (300ml) was added carefully to a stirred solution of this mixture (27.5g) in ether (300ml). Stirring was continued at room temperature for 50min. after which an aliquot indicated the presence of only one product by t.l.c. Excess LAH was destroyed by cautious addition of saturated sodium sulphate solution. Filtration and evaporation of solvent afforded trans-5-cycloocten-1,2-diol (III) as a colourless mobile oil in 90% yield, b.p. 86°/0.35mm (lit.[39] 153-155°/16mm); m/e 142 ($M^+$);

n.m.r. ($CDCl_3$) : $\tau$ 4.10-4.56 (2H,m); 6.13 (2H,s,exchangeable with $D_2O$); 6.20-6.48 (2H,m); 7.46-8.47 (8H,m);

i.r. ($CCl_4$) : $\nu$ 3400(b),3018,2976 (sh),2932,2860,1650,1045(sh),1036(s) $cm^{-1}$.

5-Cycloocten-1,2-dione (IV):

Diol (III) (7.5g; 52.8mmole), dimethyl sulphoxide (75ml) and acetic anhydride (38ml) were allowed to stand at room temperature for 24hr. in a stoppered flask. The light-green reaction mixture was poured into dilute hydrochloric acid (18ml of conc. hydrochloric acid in 200ml of water) while cooling with an ice bath, in order to hydrolyse acetic anhydride and acetoxy methyl methyl sulphide[32] to water soluble compounds. The mixture was stirred at room temperature for 30min. before being extracted with dichloromethane (4x50ml), washed with water and dilute sodium bicarbonate and dried. Evaporation of solvent furnished a yellow-green liquid (10.5g) which was distilled through a simple stillhead to give enedione (IV) (3.65g; 26.5mmole; 50%) as a light yellow liquid (b.p. 40-56°/0.2mm). Redistillation (45-56°/0.25mm) furnished IV as a light yellow oil (2.85g) which crystallised from pentane at -20° as pale yellow crystals (m.p. 32-34°). (lit. 35-36°; m/e 138 ($M^+$));

n.m.r. ($CDCl_3$) : $\tau$ 3.97-4.33 (2H,m); 7.20-7.93 (8H,m);

i.r. ($CCl_4$) : $\nu$ 3024,2965,2946,2911,2870,1719(v.s),1708(vs),1463,1429, 1413,1330,1317,1300 $cm^{-1}$.

$\lambda_{max}$(hexane) : 281nm ($\log\varepsilon$=3.5); 290nm (sh., 3.1); 346nm (1.7).

Attempted bisenol acetylation of (IV):

Method A:

Diketone (IV) (158mg; 0.15mmole) in isopropenyl acetate (6ml) was heated in the presence of p-toluene sulphonic acid (9mg) for 18hr. at 118° (bath temperature) allowing acetone to distil off . After removal of excess isopropenyl acetate by distillation, the dark brown residue was taken up in ethyl acetate and washed with saturated sodium bicarbonate

solution. On drying and evaporation of solvent, the crude product was treated with boiling petroleum spirit. The extract contained a single compound (t.l.c.) which was shown by n.m.r. and i.r. to be the starting material.

The reaction was repeated at a bath temperature of 107° for 1 week. In this case, the p-toluene sulphonic acid was neutralised by the addition of solid potassium carbonate and the reaction mixture extracted with boiling petroleum spirit. The extract again furnished starting material.

Method B:

A solution of diketone (IV) (138mg; 1mmole) in acetic anhydride (1ml) with anhydrous sodium acetate (6mg) as catalyst was refluxed for 3hr. at 148° (bath temperature). Excess acetic anhydride was removed by azeotropic distillation with benzene and the dark brown residue was extracted with boiling petroleum spirit. On evaporation the extract gave mainly starting material. However, mono-enolacetate characteristics were evident in the n.m.r. spectrum, e.g. a definite broadening of the vinylic resonances from $\tau$4.33-4.55; a multiplet at $\tau$6.73-7.06 and a sharp singlet at $\tau$7.86.

Method C:

Diketone (IV) (400mg; 2.94mmole) was dissolved in acetic anhydride (30ml) and concentrated sulphuric acid (2 drops) was added cautiously, when the solution was seen to turn dark brown. The solution was heated at 140-150° (bath temperature) for 5 hr. allowing acetic acid to distil over. After azeotropic distillation with benzene the black residue was extracted with boiling petroleum spirit furnishing 250mg. of a product which consisted of at least two compounds (t.l.c.). Attempted separation by prep. t.l.c. (solvent, 1:1 chloroform/petroleum spirit) afforded pure starting material (IV) as the major compound (200mg) and 12mg. of a mixture of starting

material and monoenol acetate (XIV).

On repeating this reaction procedure for longer reaction time (44hr) similar results were obtained, with no noticeable increase in acetate formation.

Attempted preparation of bisenol carbonate (XV):

a). Chloromethyl formate (1ml) was added dropwise at room temperature to a solution of dione (IV) (450mg; 3.26mmole) in pyridine (1ml). The colourless solid which first formed redissolved on addition of pyridine (5ml). The reaction mixture was heated overnight at 110° (bath temperature) allowing methanol to distil over. Excess pyridine was ditilled out and final traces removed by washing with aqueous copper sulphate, after the residue had been taken up in ethyl acetate. Drying and evaporation of solvent yielded mainly starting material as shown by t.l.c., i.r. and n.m.r. spectra.

b). Sodium hydride (186mg. of 60% dispersion in benzene; 4.65mmole) was placed in a 50ml. round bottomed two necked flask equipped with a drying tube and septum cap. Dimethyl sulphoxide (5ml) was added by syringe and some effervescence was observed. After stirring for 1hr. at 75° (bath temperature) a solution of dione (IV) (302mg ; 2.19mmole) in dimethyl sulphoxide (3ml) was added by syringe. Stirring was continued for 2hr. at room temperature. The flask was fitted with a stillhead and heated to 90° (bath temperature) allowing ethanol to distil over. After 20hr. the reaction mixture was poured on to ice, extracted with chloroform and washed with brine, to remove excess dimethyl sulphoxide. After evaporation of the chloroform extracts the crystalline product was shown to be starting material from i.r. and n.m.r. spectra.

Preparation of Thiiran-1-oxide:

A solution of sodium periodate (23.5g; 0.11 mole) in water (240ml) in a 500ml conical flask was cooled in an ice bath. A suspension of ethylene sulphide (6g; 0.10mole) in methanol (60ml) was added dropwise with stirring. After 1hr. at ice bath temperature the solution was filtered and extracted with dichloromethane (3x200ml). Evaporation of solvent under suction afforded thiiran-1-oxide (3.8g;0.05mole; 50%) as a colourless oil: m/e 76 ($M^+$);
n.m.r. ($CDCl_3$) : $\tau$ 7.23-7.56(2H, complex m); 7.63-8.10 (2H, complex m);
i.r. (liquid film): $\nu$ 3092,2995,1110,1050(v.s.),1012(sh) $cm^{-1}$.

Preparation of 9-thiabicyclo[4.2.1] nona-2,4,7-triene-9-oxide (VII):

Cyclooctatetraene (4.6g; 44.2mmole) and thiiran-1-oxide (3.56g, 46.8mmole) were refluxed in xylene (130ml) for 30min. After cooling, the light-brown reaction mixture was passed through a filtration column (20g of neutral alumina), eluting first with petroleum spirit to remove most of the xylene, then with ether and finally with chloroform. Those fractions containing polar material (t.l.c) were recombined and purified by chromatographing on an alumina column (80g) made up in chloroform/ether (1:4) and eluting with chloroform/ether (1:3). 9-Thiabicyclo[4.2.1]nona-2,4,7-triene-9-oxide (VII) (2.02g,13.27mmole,30%) was obtained as colourless needles from chloroform/petroleum spirit (m.p. 122-123°; lit.120-121°); m/e 152 ($M^+$).
Found:C,63.05; H,5.43. $C_8H_8SO$ requires : C,63.15; H,5.30%.
n.m.r. ($CDCl_3$) : $\tau$ 3.2-3.4 (2H,m. protons on $C_3$ and $C_4$);
3.83-4.26 (2H,m. protons on $C_2$ and $C_5$);
4.46 and 4.52 (2H,d. J=4Hz , protons on $C_7$ and $C_8$);
5.75 (2H, d.d., J=4Hz, J=8Hz, bridgehead protons);
i.r. (KBr disc) : $\nu$ 3024(w),3016,3010,3000(w),2968(w),2943,1487,1078(vs), 1065 $cm^{-1}$.
$\lambda$ max (ethanol) : 223nm (log$\varepsilon$ =3.6); 281 (3.39).

Attempted Pummerer reaction on 9-thiabicyclo[4.2.1]nona-2,4,7-triene-9-oxide:

9-Thiabicyclo[4.2.1]nona-2,4,7-triene-9-oxide (VII) (65mg; 0.41mmole) and acetic anhydride (2.5ml) were refluxed for 5hr., after which time excess acetic anhydride was removed by azeotropic distillation with benzene. T.l.c. performed on the product indicated that it was much less polar than starting material. Purification by prep. t.l.c. (ether/petroleum spirit, 1:4) afforded a pale yellow oil (11.4mg.) as the main product. Its i.r. spectrum indicated that neither sulphoxide nor carbonyl adsorptions were present.

Preparation of 9-Thiabicyclo[4.2.1]nona-2,4,7-triene-9,9-dioxide (IX):

To a solution of 9-thiabicyclo[4.2.1]nona-2,4,7-triene-9-oxide (VII) (458 mg.; 3.01mmole) in chloroform (20ml) stirred in an ice bath was added a solution of m-chloroperbenzoic acid (570mg, 3.3mmole) in chloroform (30ml). After stirring at room temperature in the dark for 24hr. the reaction mixture was washed with sodium sulphite (50ml), sodium carbonate (4x50ml) and dried. Evaporation to dryness yielded 9-thiabicyclo[4.2.1]nona-2,4,7-triene-9,9-dioxide(IX) (500mg; 2.98mmole; 99%), colourless needles from chloroform/ether, m.p. 188-190° (lit. 192-193° (dec));

m/e 168($M^+$);

n.m.r. ($CDCl_3$) : $\tau$ 4.35-4.55 (2H, d.t, J=5Hz, J=10Hz. protons on $C_3$ and $C_4$);
4.61-5.11 (4H, m. protons on $C_2$,$C_5$,$C_7$and $C_8$);
6.85-6.98 (2H, d. J=8Hz, with further splitting, bridgehead protons);

i.r. (KBr disc) : $\nu$ 3030(w),3021,3010,3000(w),2975,1481,1302(v.s.),1118(v.s.) $cm^{-1}$.

Preparation of the dianion (X) of 9-thiabicyclo[4.2.1]nona-2,4,7-triene-9,9-dioxide:

n-Butyl lithium (0.7ml, approx. 1mmole) was added by syringe through a septum cap into a flask containing 9-thiabicyclo[4.2.1]nona-2,4,7-triene-9,9-dioxide (IX) (63mg; 0.375mmole) in dry tetrahydrofuran (7.5ml) stirred in a dry nitrogen atmosphere at -70°. The solution turned red instantaneously, and on complete addition had become a deep purple colour.

a). Quenching of the dianion with diphenyl disulphide:

After formation of the dianion, as detailed above, a solution of diphenyl disulphide (175mg; 0.8mmole) in tetrahydrofuran (3ml) was added over 3 min. and left to stir for 45 min., during which time the reaction mixture was allowed to warm at room temperature. Excess n-butyl lithium was destroyed by cautious addition of a little water until no more effervescence could be seen and excess tetrahydrofuran was reduced in volume by evaporation under suction. The resulting solution was extracted with chloroform (4x50ml) and dried. Removal of solvent afforded a crude product (195mg) which consisted of three compounds (t.l.c.). Isolation by prep. t.l.c. (1:9 chloroform/petroleum spirit) gave, in order of polarity: n-butylphenyl sulphide, diphenyl disulphide and the starting sulphone (IX).

b). Quenching of the dianion with dimethyl disulphide:

The deep purple solution formed by addition on n-butyl lithium to 9-thiabicyclo[4.2.1]nona-2,4,7-triene-9,9-dioxide (IX) and assumed to be a solution of the dianion (X) of the sulphone was quenched by addition of dimethyl disulphide (140mg; 1.3mmole) in tetrahydrofuran (2ml) over 30sec. at -70°. The reaction mixture was then left to stir for 20hr. and worked up

as in a) above.

Alternatively, a solution of the dianion (formed as above) in dimethyl formamide (7ml) at -70° was quenched by addition of a vast excess of dimethyl disulphide (1.3g; 13.8mmole) in tetrahydrofuran (10ml). After warming to room temperature the reaction mixture was stirred for 1hr. and again worked up as in a) above.

In both cases t.l.c. analyses of the crude reaction mixture indicated the formation of a large number of products.

REFERENCES.


1) E.Hückel, Z.Phys., 1931, 70, 204; Z.Elektrochem., 1937, 43, 751; Grundzüge der Theorie unsättiger und aromatischer Verbindungen, Verlag Chemie, Berlin, 1938.

2) see for example: a) D.Ginsburg (editor), Non-benzenoid Aromatic Compounds. Interscience Publishers, Inc., New York, 1959; b) D.M.G.Lloyd, Carbocyclic Non-Benzenoid Aromatic Compounds. Elsevier, New York, 1966.

3) E.J.Smutny, M.C.Caserio and J.D.Roberts, J.Amer.Chem.Soc., 1960, 82, 1793; M.P.Cava and M.J.Mitchell, Cyclobutadiene and Related Compounds. Acad.Press Inc., New York, 1962, Ch. 7.

4) G.L.Buchanan and D.R.Lockhart, J.Chem.Soc., 1959, 3586; Ch.6. in 2(b); D.J.Bertelli and T.G.Andrews Jr., Tet.Lett., 1967, 4467; D.J.Bertelli and T.G.Andrews Jr., J.Amer.Chem.Soc., 1969, 91, 5280; D.J.Bertelli, T.G.Andrews Jr. and P.O.Crews, J.Amer.Chem.Soc., 1969, 91, 5286

5). Ch. 5 in 2(b).

6). D.Bryce-Smith and W.A.Perkins, J.Chem.Soc., 1962, 1339.

7). T.J.Katz, J.Amer.Chem.Soc., 1960, 82, 3784, 3785; T.J.Katz and H.L. Strauss, J.Chem.Phys., 1960, 32, 1973; T.J.Katz, W.H.Reinmuth and D.E. Smith, J.Amer.Chem.Soc., 1962, 84, 802; H.L.Strauss, T.J.Katz and G.K.Fraenkel, J.Amer.Chem.Soc., 1963, 85, 2360.

8). M.Brookhart, M.Oligiaruso and S.Winstein, J.Amer.Chem.Soc., 1967, 89, 1965.

9). S.Wawzonek, J.Amer.Chem.Soc., 1940, 62, 745.

10). S.Wawzonek and J.K.Stowell, J.Org.Chem., 1968, 33, 896; E.G.Lewars, J.K.Stowell, S.Wawzonek and P.Yates, Chem.Ind., 344, 1968; P.Yates and E.G.Lewars, Chem.Comm, 1967, 622.

11). P.Yates and E.G.Lewars, Can.J.Chem., 1970, 48, 796.

12). M.P.Cava and K.W.Ratts, J.Org.Chem., 1962, 27, 752.

13). D.M$^{c}$Intyre, G.R.Proctor and L.Rees, J.Chem.Soc. (C), 1966, 985.

14). P.Yates, E.G.Lewars and P.H.M$^{c}$Cabe, Can.J.Chem., 1970, 48, 780.

15). M.Stiles and A.J.Libbey, J.Org.Chem., 1957, 22, 1243.

16). P.Yates, E.G.Lewars and P.H.M$^{c}$Cabe, Can.J.Chem., 1972, 50, 1548.

17). S.P.Pappas and B.C.Pappas, Tet.Lett., 1967, 1597; S.P.Pappas, B.C.Pappas and N.A.Portnoy, J.Org.Chem., 1969, 34, 520.

18). H.E.Zimmerman and L.Craft, Tet.Lett., 1964, 2131; D.Bryce-Smith, G.I.Fray and A.Gilbert, Tet.Lett., 1964, 2137.

19). P.Yates and G.V.Nair, Synth.Comm., 1973, 3, 337.

20). E.Clar, Chem.Ber., 1931, 64, 1676; P.Yates and P.Eaton, J.Amer.Chem.Soc., 1960, 82, 4436.

21). M.Oda, Y.Kayama and Y.Kitahara, Tet.Lett.,1974, 2019.

22). V.Georgian, L.Georgian and A.V.Robertson, Tet., 1963, 19, 1219.

23). C.Djerassi, Chem.Rev., 1948, 43, 271; C.Djerassi and C.R.Scholz, J.Org. Chem., 1949, 14, 660.

24). See for example: D.Swern, "Organic Reactions" vol VII, Chapter 7, R.Adams, ed., Wiley, New York, 1953.

25). E.G.Lewars, Ph.D. Thesis, University of Toronto, 1969.

26). J.D.Albright and L.Goldman, J.Amer.Chem.Soc., 1967, 89, 2416.

27). R.Pummerer, Chem.Ber., 1909, 42, 2282; R.Pummerer, Chem.Ber., 1910, 43, 1401.

28). A.G.Anastassiou and B.Y-H.Chao, Chem.Comm., 1971, 979.

29). R.M.Dodson and F.F.Sauers, Chem.Comm., 1967, 1189.

30). L.Horner and P.Kaiser, Leibigs Ann., 1959, 626, 19; W.J.Kenney, J.A. Walsh and D.A.Davenport, J.Amer.Chem.Soc., 1961, 83, 4019; F.G.Bordwell and B.M.Pitt, J.Amer.Chem.Soc., 1955, 77, 572.

31). C.R.Johnson and W.G.Phillips, Tet.Lett., 1965, 2101; J.Org.Chem., 1967, 32, 1926.

32). S.Oae, T.Kitao, J.Kawamura and Y.Kitaoka Tet., 1963, 19, 817.

33). C.B.Quinn and J.R.Wiseman, J.Amer.Chem.Soc., 1973, 95, 6120.

34). B.M.Trost and T.N.Salzmann, J.Amer.Chem.Soc., 1973, 95, 6840; D.Seebach and M.Tescher, Tet.Lett., 1973, 5113.

35). W.von E.Doering and L.K.Levy, J.Amer.Chem.Soc., 1955, 77, 509.

36). L.A.Paquette and R.W.Houser, J.Amer.Chem.Soc., 1969, 91, 3870.

37). C.B.Quinn, J.R.Wiseman and J.C.Calabrese, J.Amer.Chem.Soc., 1973, 95, 6121.

38). L.A.Paquette, R.H.Meisinger and R.Gleiter, J.Amer.Chem.Soc., 1973, 95, 5414.

39). Fr. Patent: 1, 294, 313 (1962); Chem. Abs., 1962, 57, 16437.