Novel Syntheses and Rearrangements of Cyclic Thioethers

A thesis submitted to the University of Glasgow for the degree of Doctor of Philosophy in the Faculty of Science

by

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Summary

Part 1: A novel synthesis is described in which potassium t-butoxide dehalogenation of β,β'-dihaloalkyl sulphides is used to prepare unsaturated episulphides and limitations of the method are discussed. For example, 31 undergoes monodehydrochlorination to 32, while 50 and 51 fail to react. The intermediacy of sulphonium ions is supported by the conversion of isomeric dihalides, 35 and 40, to the same episulphide, viz 44.

Part 2: Treatment of diene monoepisulphides with halogens yielded sulphur-bridged compounds. Halogenolysis of 57 furnished disulphides which could be converted to bicyclic thioethers with excess chlorine or bromine. In contrast, halogen additions to 11 and 44 did not produce disulphides but gave bicyclic β,β'-dihalosulphides. The electrophilic ring opening process was extended to provide a new synthesis of the 1,2-dithiolane (120) through condensation of sulphur dichloride with 57.

Part 3: Reactions of alkyl halides with meta-chloroperbenzoic acid and photolyses of 2,6-dihalo-9-thiabicyclo (3.3.1) nonanes were investigated. High yield synthesis of 149 and 164 from m-CPBA treatments of 10 have been achieved and provide a most convenient preparative method for these compounds. The observed formation of an ether (173) from peracid reaction with an alkyl iodide (171) has not been previously reported. Carbonium ions are

postulated as intermediates in the dehydroiodination and photoelimination reactions observed. Considerable photoreduction occurred in the photolysis of dibromide (166).

Part 1

Dehalogenation of β, β'-Dihalosulphides with Potassium tert-Butoxide - A Novel Route to Thiiranes.

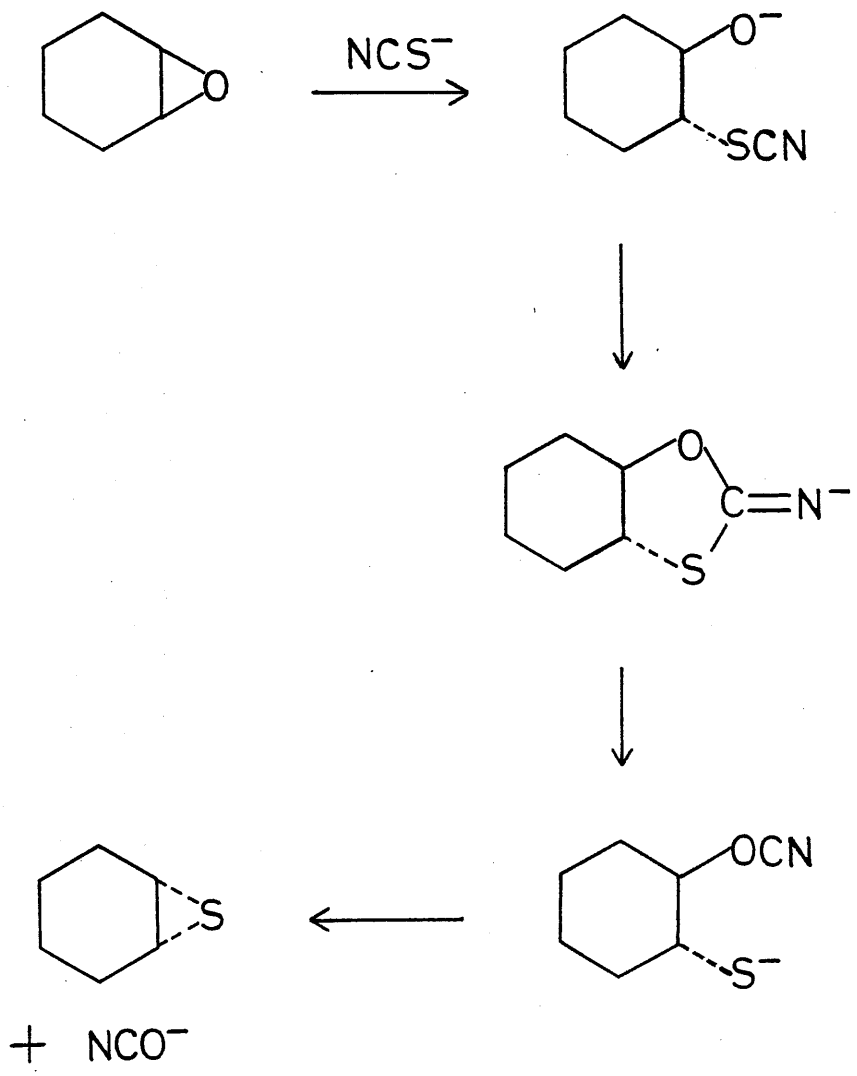
Introduction

For many years, episulphides were believed to be of principally theoretical interest, their chemistry being investigated to elucidate the nature of three-membered ring compounds. However, the information accumulated on their properties has now made[1-4] a significant contributic to theoretical and synthetic organic chemistry, particularly in the field c polymers, physiologically active compounds, detergents and oil additives.

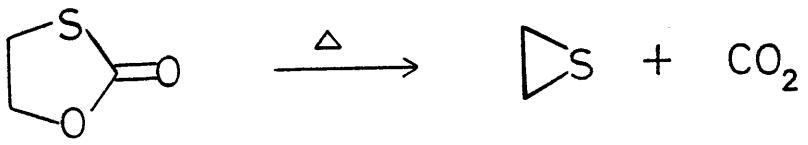
Although considerable advances in the chemistry of episulphides have been achieved in the last decade, synthetic approaches to this ring system are still somewhat limited in scope.[3,5]

The synthesis of episulphides by the reaction of their oxygen analogues with alkali metal thiocyanates or thiourea, which has been known since 1934,[6] remains the most important method of preparation. A review by Weissberger[7] adequately describes the historical development of this method. The mechanism, depicted in Scheme 1 for cyclohexene oxide as substrate, is thought to involve two Walden inversions.[8] Nucleophilic opening of the epoxide three-membered ring by thiocyanate is followed by isomerisation of the resulting alkoxide, *via* an intermediate cyclic state, to a thiolate anion, and the conversion of the latter to the episulphide with elimination of cyanate. According to this mechanism, only epoxides derived from acyclic and unstrained cycloalkenes can be expected to give rise to episulphides. Those derived from strained cycloalkenes should not react, because of the inaccessibility of a highly strained intermediate. In support of the mechanism the synthesis fails with cyclopentene oxide.[8] A similar pathway has been proposed for the reaction of epoxides with thiourea.[9]

Scheme 1



Scheme 2



Another important synthesis of thiiranes involves pyrolysis of cyclic monothiol carbonates (e.g. Scheme 2).[10] The substrates are readily prepared by heating open-chain β-mercaptoethyl carbonates in the presence of sulphonic acids.[11] An advantage of this method is that cyclic carbonates can be stored for extended periods and the thiirane generated simply by heating.

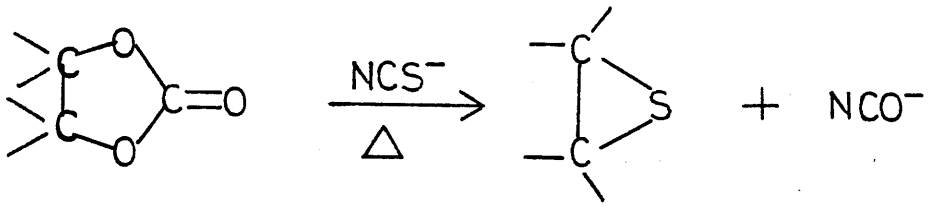
Reaction of cyclic carbonates of 1,2-diols with alkali thiocyanates at 100-200° also furnishes [12] corresponding thiiranes (Scheme 3). A four-step mechanism, which includes two Walden inversions, analogous to the reaction with alkene oxides, is proposed.[12]

Lautenschlaeger and Schwartz have reported[13] a method of episulphide synthesis which involves addition of sulphur monochloride to an olefin followed by reduction and dehydrohalogenation of the resulting mixture of chloroalkylmono-,di-, and trisulphides (Scheme 4). However, a major disadvantage of this method is that a large excess of the alkene must be used and therefore such a procedure is unsuitable for expensive or nonvolatile olefinic starting materials.

Hinshaw described[5] a synthesis in which olefins are reacted with iodine thiocyanate to yield β-iodothiocyanates which undergo conversion to episulphides on base treatment (Scheme 5). This route gives moderate yields (26-57%) of cyclic episulphides and cannot be employed for acyclic alkenes.

Other synthetic approaches to episulphides include the reaction[14] of ketohydrazones with sulphur, the reduction[15] of β-hydroxyethyl

Scheme 3



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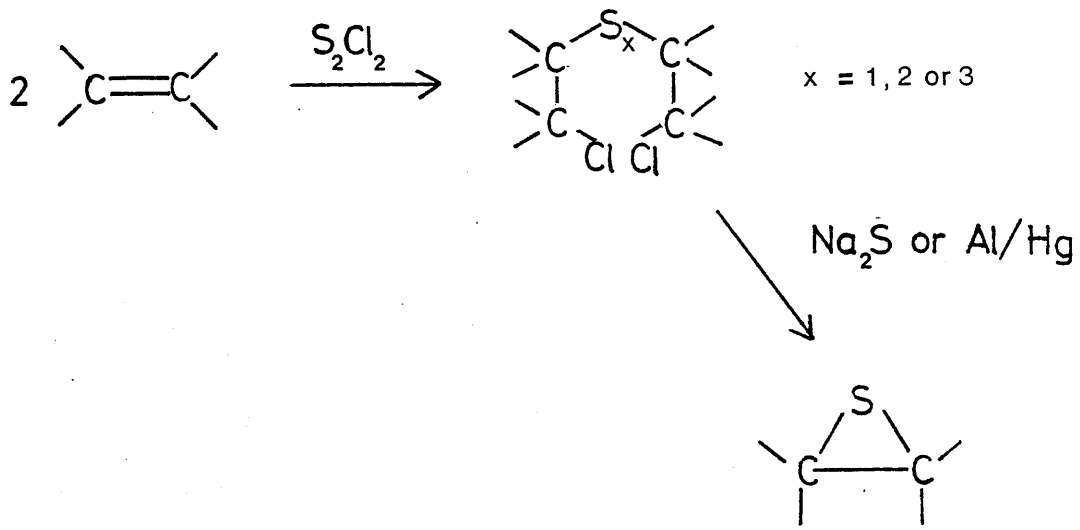
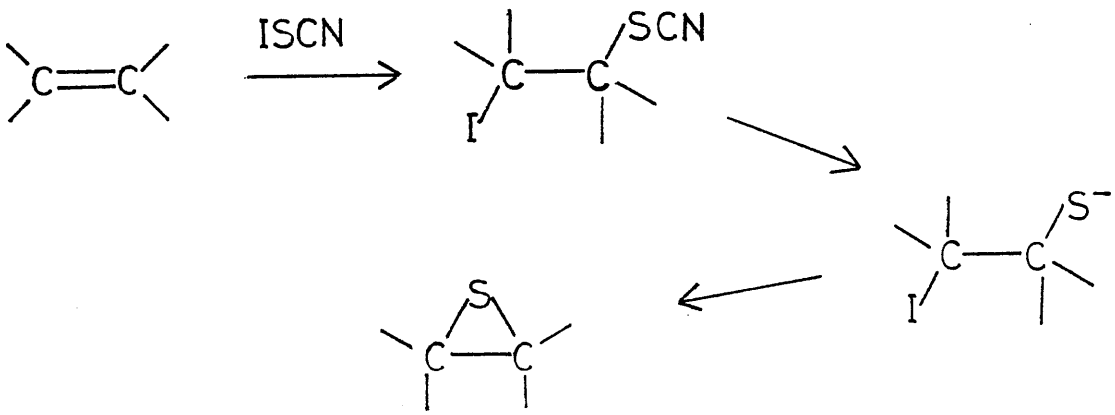


Scheme 5

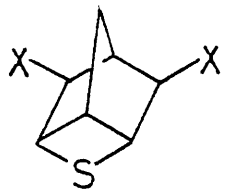


disulphides with phosphines, the pyrolysis [16] of aryl- or alkyl-2-hydroxyethyl thiolcarbonates, and the reaction[17] of carbonyl compounds with 2-(alkylthio)-2-oxazolines (e.g. Scheme 6).

Particularly relevant to the present study was the reported reaction between 3,5-bis-exo-dichloro-8-thiatricyclo ($2.2.1.1^{2,6}$) octane (1) and potassium cyanide in aqueous ethanol which gave a 30% yield of an elimination product, 2,3-endo-epithio-norborn-5-ene(3) (Scheme 7).[18] This result contrasts with the substitution products normally obtained[19] by cyanide treatment of cyclic β,β'-dichlorosulphides. To account for the formation of 3 it was suggested[18] that the reaction proceeds *via* a sulphonium ion (4) which undergoes elimination of chloronium ion, Cl^+ . The cyanide anion was considered to initiate formation of 4 and act as a scavenger for eliminated chlorine.

Lautenschlaeger attempted[18] to extend this reaction type to other β,β'-dichloroalkyl sulphides with little success. Thus, treatment of 5 with potassium cyanide in glycerol led to both 2,5-dihydrothiophene (6) and 3,4-epithio-but-1-ene (7) in a yield of less than 5%. Furthermore, attempts to isolate olefinic episulphide (11) from 2,6-dichloro-9-thiabicyclo (3.3.1)nonane (8) and potassium cyanide failed. It was thus concluded that the formation of an episulphide by the dechlorination of β,β'-dichloroalkyl sulphides is not a general reaction.

Recently, Ziman and Trost reported[20] that reduction of 2 with aluminium hydride gave 3 in a yield of 17% while reaction with sodium cyanide furnished the same product in high yield. The mechanism of



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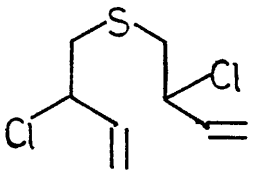
2 X = Br



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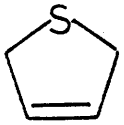

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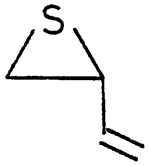

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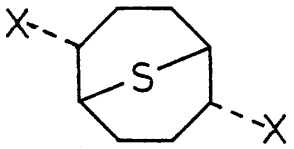
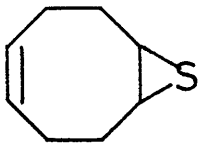


8 X = Cl
9 X = Br
10 X = I



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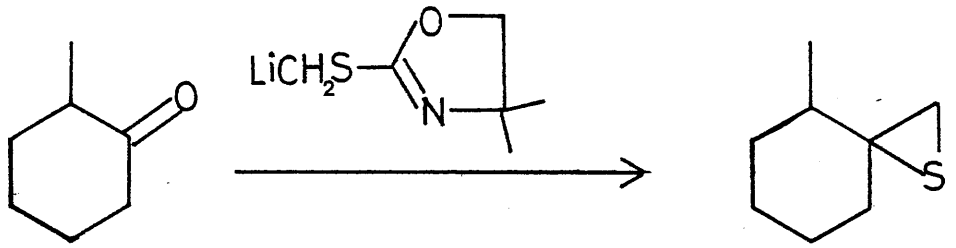
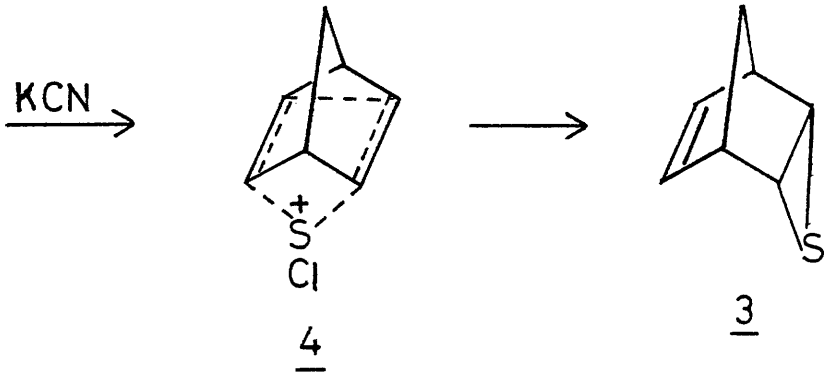
Scheme 6



Scheme 7



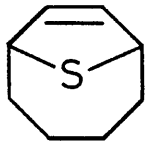
the former was considered to proceed *via* episulphonium ion (12) which gives 3 by hydride attack on sulphur followed by loss of hydrogen bromide (Scheme 8). Cyanide reaction with 2 was thought to proceed by a different mechanism, involving abstraction of bromonium ion, Br^+, in a manner similar to the proposed dechlorination mechanism (*vide supra*).

An apparently related dehalogenation was encountered[21] during attempts to effect simple dehydrochlorination of 8 which would give 9-thiabicyclo (3.3.1) nona-2,6-diene (13), a potential precursor to 2,6-dithiaadamantanes. Treatment of 8 with potassium t-butoxide ($KOBu^t$) in dimethyl sulphoxide yielded, as the principal product, a liquid alkene whose spectra were consistent with 9-thiabicyclo(6.1.0) non-4-ene (11). Proton decoupling results clearly ruled out structures 14 and 15 but did not adequately distinguish between 11 and 16. However, 11 was favoured[21] by comparison with the previously described dehalogenations and from mechanistic considerations. Formation of 11 was rationalised as involving the sulphur-assisted expulsion of chloride followed by nucleophilic attack of t-butoxide (or dimsyl) anion on chlorine (Scheme 9). It is noteworthy that $KOBu^t$ treatment of 17 gave[22,23] substitution product (19) *via* the bridgehead alkene (18) (Scheme 10) while 20 was inert[21] to $KOBu^t$. Thus, sulphur participation is required to facilitate the dechlorination process.

The elimination-rearrangement contrasts with the reaction of 8 with strong bases such as sodium hydroxide or sodium ethoxide which furnish[19,21] substitution products 21 or 22. Moreover, pyridine reacts with 8 to give a bis-pyridinium salt (23)[21] while the hindered bases

13

14



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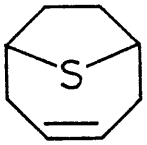

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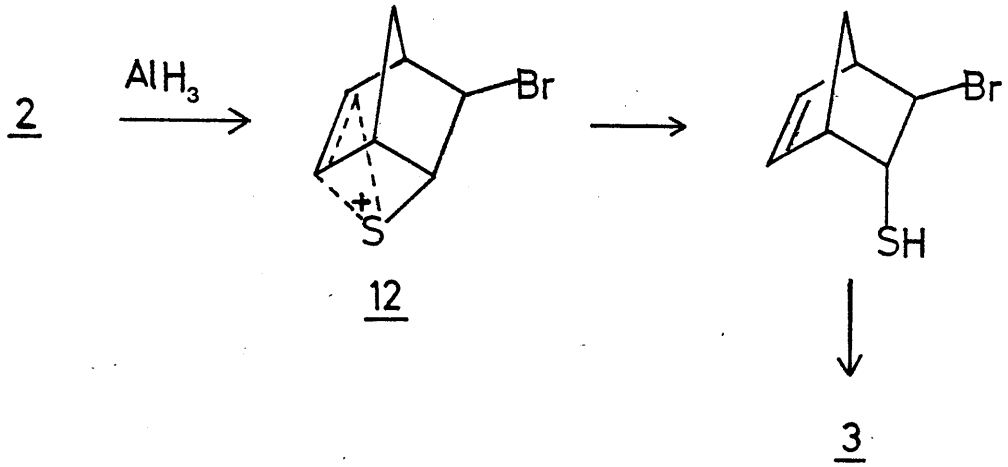
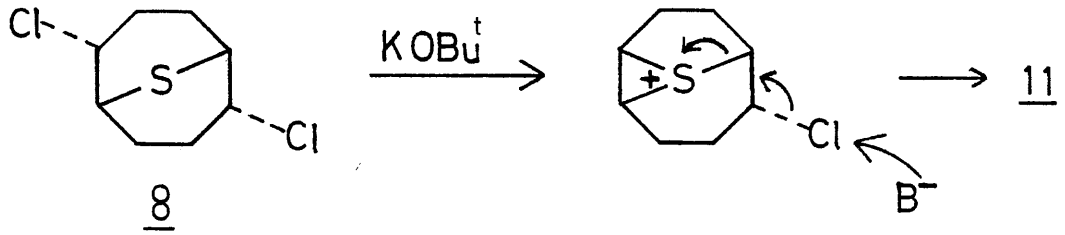
Scheme 8

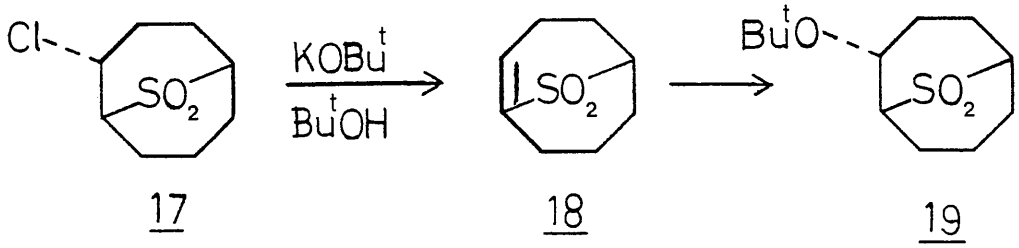


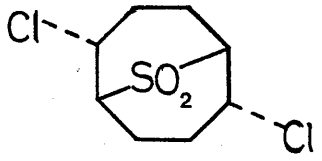
Scheme 9



$B^- = (CH_3)_3CO^-$ or $CH_3SOCH_2^-$

Scheme 10





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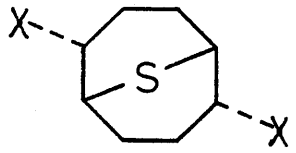
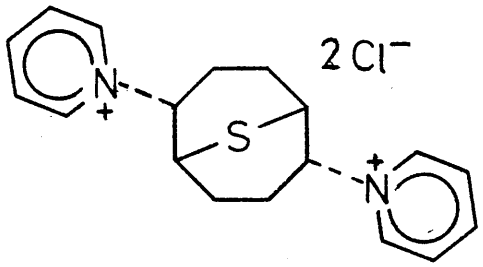


21 X = OH

22 X = OC_2H_5



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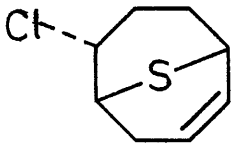

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1,5-diazabicyclo (4.3.0) non-5-ene and 1,8-diazabicyclo (5.4.0) undec-7-ene fail[21] to react. Although dehydrochlorination of 8 was effected[21] with 2,4,6-collidine, the product was the rearranged diene (24), formed via chloroalkene (25), a known substance obtained[19] by Weil and co-workers on pyrolysis of 8.

The results of investigations of $KOBu^t$ treatments of β, β'-dihaloalkyl sulphides are described in the following discussion. Further examples of dehalogenation - rearrangements to olefinic episulphides have been found.

Discussion

$KOBu^t$ treatment of 2,6-dihalo-9-thiabicyclo (3.3.1) nonanes (8, 9 and 10)

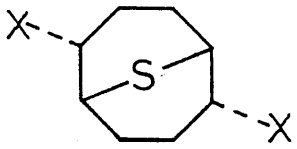
Potassium t-butoxide, which is widely used to dehydrohalogenate alkyl halides because of its strong basicity combined with poor nucleophilicity, has been reported[24] to debrominate and deiodinate aromatic halides. However, in general such dehalogenations occur at sites ortho to other halogen atoms and are most facile for tri-substituted halo-benzenes. Although debromination of 5α, 6β-dibromo steroids with $KOBu^t$ has been accomplished[25] it is believed that dichlorocarbene, formed by reaction with solvent ($CHCl_3$), is the active dehalogenating agent. Conversion of 8 to 11 represents the first example of dechlorination with $KOBu^t$.[26,27] The novelty of this reaction, the difficulty of selective preparation[5] of unsaturated episulphides and the availability of the substrates by the facile sulphur dichloride addition[19,28-30] to cyclic dienes provided incentive for the following study.

The most immediate aim of the research was to confirm the identity of the product (11). That this indeed was the correct structure was shown by comparison (spectra, mixed t.l.c. and g.l.c.) with an authentic sample, prepared by the addition of iodine thiocyanate[5,31] to cycloocta-1,5-diene (see Part 2). The yield of 11 was considerably increased by replacing dimethyl sulphoxide by t-butanol and on raising the reaction temperature from 20° to 80°. Both these changes are known[26,32] to reduce the basicity of $KOBu^t$. The crude reaction product (ca. 68%), substantially pure by t.l.c. and p.m.r., was obtained as a slightly yellow oil and was purified by column chromatography (neutral alumina, ether-petroleum spirit, 1:9) or by vacuum

distillation (b.p. 65°, 1·2mmHg; lit.[13] b.p. 44°, 0·3mmHg). These purification techniques caused losses of ca. 50% as a result of the sensitivity of 11 which polymerises as a neat liquid but is stable in solution.

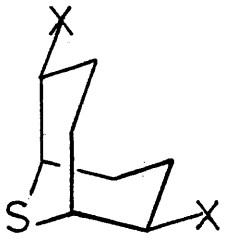
During a large-scale reaction the initial fractions collected from a column purification of crude reaction mixture contained, on removal of eluent, a small amount of a colourless liquid which distilled at 65-70° (0·1mmHg) to give a waxy solid (m.p. 65-75°). A microanalysis of this indicated a molecular formula, $C_{16}H_{30}O_2S$, which was supported by a mass spectral molecular ion at m/e 286. The p.m.r. spectrum exhibited a strong singlet at δ1·16 (18H), consistent with t-butoxy groups, a H-C-S absorption at δ2·48 (m,2H) and a multiplet at δ3·72-4·00 (2H), attributed to H-C-O. In addition, a broad methylenic envelope was present at δ1·51-2·20 (8H). The infra-red spectrum possessed strong C-O stretching bands at 1197 and 1055cm^{-1} while there were no absorptions (ca. 1030 and 645cm^{-1})[18] attributable to a thiirane grouping. In support, desulphurisation[33] with triphenyl phosphine failed. This minor product was therefore the di-t-butyl ether (26) (ca. 1%). 26 is likely to arise by a sulphur-assisted S_N1 mechanism[19] involving episulphonium intermediates, although the bis-endo stereochemistry of the t-butoxy substituents was not established. The broadness of the H-C-O multiplet prevented the assignment of configuration of these groups from coupling constant analysis.[22]

That dehalogenation-rearrangement was not restricted to the dichloride (8) was shown by reaction of $KOBu^t$ with the bromo- and



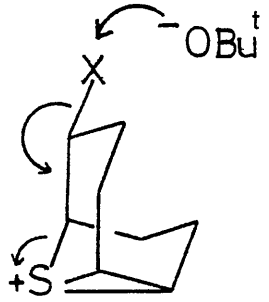
9 X = Br
10 X = I
26 X = OBu^t
30 X = CN

Scheme 11



X = Cl, Br, I

$KOBu^t$ / Bu^tOH

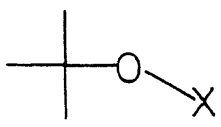


27

+ Bu^tOX

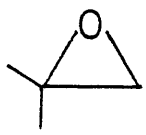
11

Scheme 12



X = Cl, Br, I

$KOBu^t$



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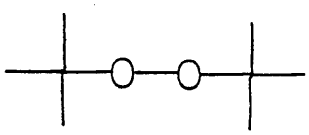
or



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iodo- analogues (i.e. 9 and 10), prepared from 8 by hydrogen bromide and sodium iodide treatments[19] respectively. Unsaturated episulphide (11) was obtained in both reactions, the yields being 51% for 9 and 41% for 10. It is considered then that an episulphonium ion (27) is an intermediate in these reactions. 27 can undergo loss of positive halogen by attack of t-butoxide anion, rearrangement being facilitated by the approximate antiperiplanar alignment of the bonds which are to be cleaved (Scheme 11). The lower yield for deiodination may reflect some difficulty in the formation of t-butyl hypoiodite which, unlike t-butyl hypochlorite, has never[34] been isolated but can be generated *in situ* by the reaction[35] of t-butyl hypochlorite or t-butoxide with iodine. The fate of the t-butyl halites is unknown, although it is likely that under the reaction conditions considerable decomposition of these heat sensitive[34,36] compounds occurs. Conversion to epoxide (28)[34] or di-t-butyl peroxide (29) are possible (Scheme 12). A low intensity singlet at $\delta 1{\cdot}17$ in the p.m.r. spectrum of the reaction product mixture may indicate the formation of 29. However, on purification no peroxide could be isolated.

It is noteworthy that the reaction of 8 with $KOBu^t$ gives very little substitution while with sodium cyanide[18] the dicyanosulphide (30) is the only product.[19] Thus, the bulky t-butoxide anion is likely to be a more versatile agent than cyanide in effecting dehalogenation-rearrangements of dihalosulphides.

Reaction of 31 with $KOBu^t$

The ability to form an episulphonium ion (see Scheme 11) is considered crucial to the $KOBu^t$ dehalogenation of a dihaloalkyl sulphide.

Compounds unable to form these ions should not undergo such an elimination. To test this prediction 7,8-bis-endo-dichloro-9-thiabicyclo (4.2.1) nonane (31), which was prepared by SCl_2 condensation[19] with cycloocta -1,3-diene, was treated with $KOBu^t$ in t-butanol. The chlorine atoms in 31 are extremely unreactive[19] compared to typical β-chlorosulphides, this unreactivity being explained on the basis of the excessive bond-angle distortion required for the sulphur to participate in chloride release. Hence, dechlorination of 31 with $KOBu^t$ was not expected to occur. After a prolonged period (71 hr), a mixture of starting material and a single product was present as indicated by analytical t.l.c. and p.m.r. spectroscopy. On distillation, a colourless oil (b.p. 35-37°, 0·01mmHg) was obtained whose 60MHz p.m.r. spectrum (Figure 1) consisted of a methylenic envelope at δ1·43-2·33 (8H), two distinct bridgehead multiplets centred at δ3·80 (1H) and 3·94 (1H), and a one-proton olefinic doublet at δ5·90 with J=4Hz. An absorption at 1634cm^{-1} in the infra-red spectrum confirmed the presence of a double bond. The mass spectrum possessed parent ions at m/e 174 and 176 in the ratio 3:1 which was in accord with the molecular formula, $C_8H_{11}ClS$. From the spectroscopic evidence it was deduced that the product was 7-chloro-9-thiabicyclo (4.2.1) non-7-ene (32). This deduction was supported by comparing the p.m.r. spectrum with that of 9-thiabicyclo (4.2.1) non-7-ene (15) which was prepared by zinc promoted[19] dechlorination of 31. Both spectra were similar in appearance. However, the bridgehead resonance of 15 consisted of a two-proton multiplet and the olefinic doublet appeared at δ5·81 with J=2Hz.

Scheme13

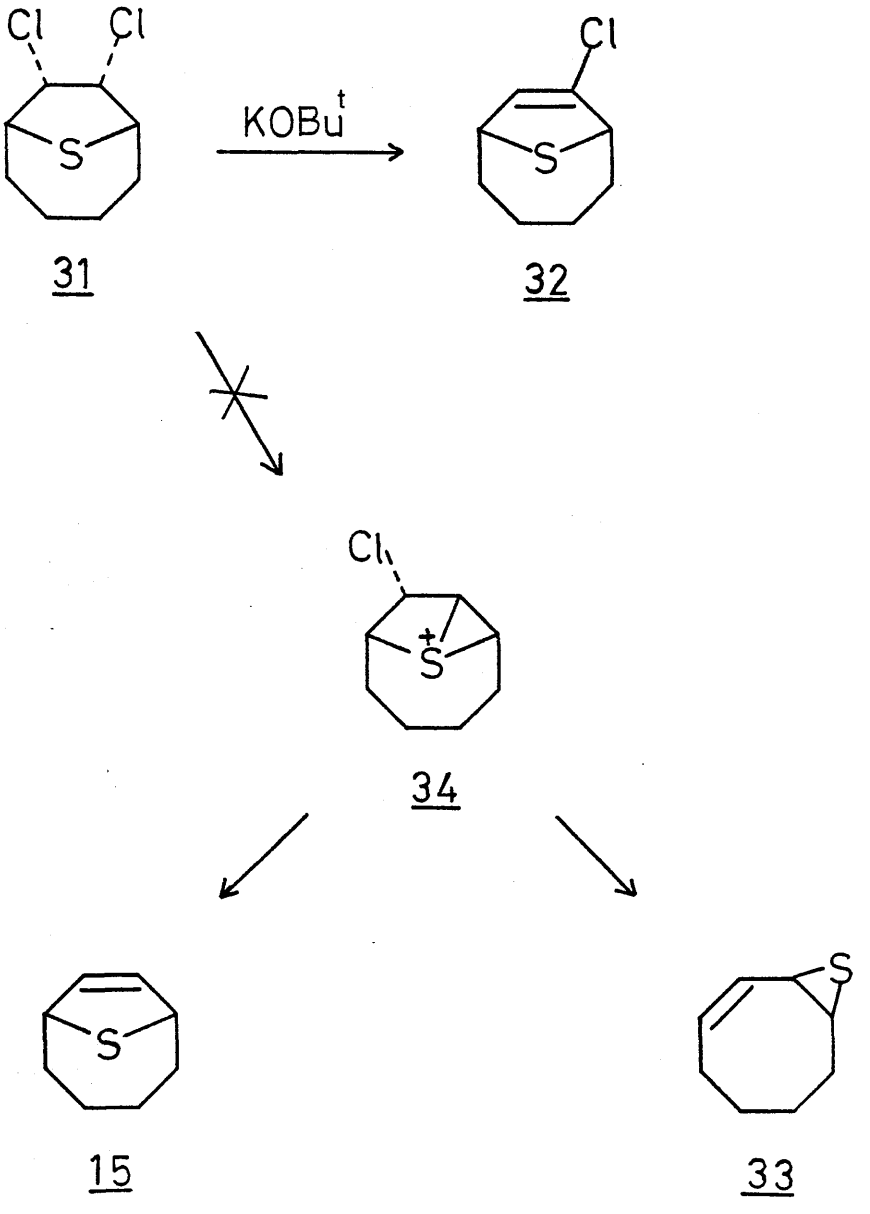
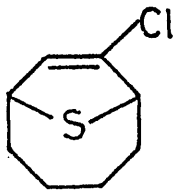


Figure 1



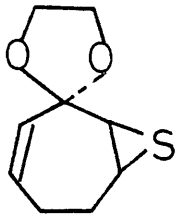
32

That 32 was the sole product from t-butoxide treatment of 31, with no evidence for either 15 or 33 (Scheme 13), lends indirect support to an episulphonium ion pathway for the $KOBu^t$ dehalogenation reactions since formation of a strained intermediate such as 34 is unfavourable.

Reactions of dihalo-8-thiabicyclo (3.2.1) octanes with $KOBu^t$

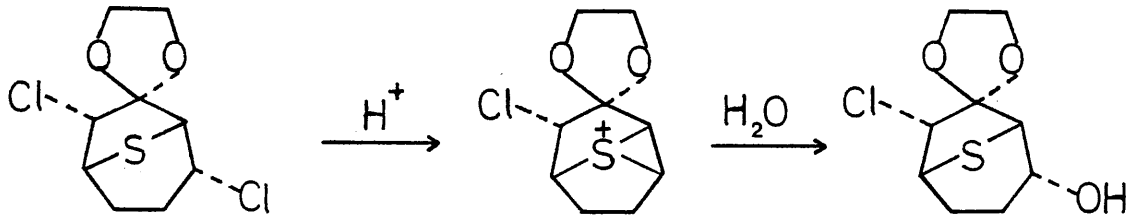
It has been proposed[37] that an episulphonium ion (43) is an intermediate in the acid hydrolysis of dichloro ketal (35) to 38 (Scheme 14).[37] This led us to investigate the reaction of 35 with $KOBu^t$, which was expected to give rise to unsaturated episulphide (44) via 43.

35, prepared by SCl_2 condensation[37] with 46 which was obtained from cycloheptanone (45)(Scheme 15),[37,42] on reaction with $KOBu^t$ gave a mixture of two products. Purification was achieved by preparative t.l.c. The uppermost band furnished a colourless oil, b.p. 60-62° (0·1mmHg), identified spectroscopically as 44 (31%). Its p.m.r. spectrum (Figure 2) exhibited a narrow olefinic two-proton multiplet at δ5·71 while the H-C-S resonance at δ3·27, which was a doublet with J=7Hz, was clearly due to the proton adjacent to the dioxolane moiety, viz H-C(7). An absorption at δ2·71-3·13 (m) was assigned to the other H-C-S and the four-proton multiplet at δ2·30 to the methylenic protons of the seven-membered ring. The dioxolane protons appeared as a narrow multiplet at δ4·02. In the infra-red spectrum, the double bond absorption was present at 1650cm^{-1} and the episulphide structure was indicated[18] by strong peaks at 1044 and 637cm^{-1}. The mass spectrum showed the parent ion at m/e 184 and a daughter ion at m/e 152, due to loss of sulphur. Further support for structure 44 was obtained from



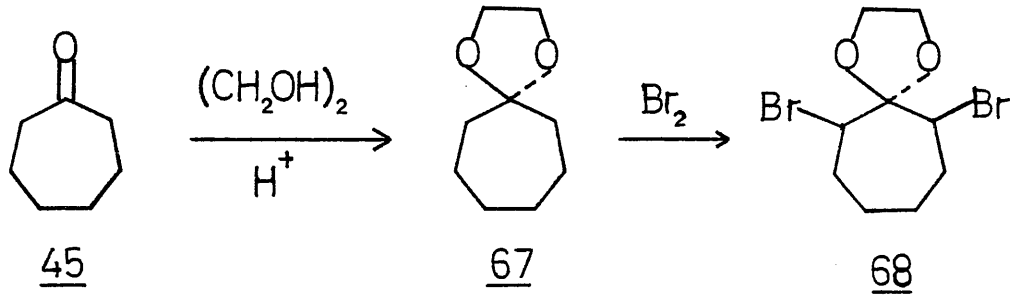
44

Scheme 14

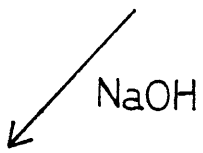


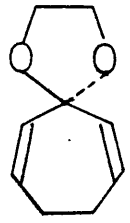
35 43 38

Scheme 15

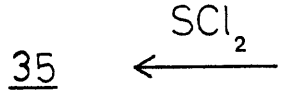


45 67 68



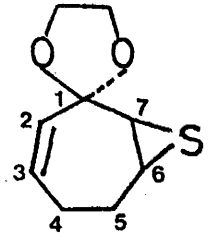


46



35

Figure 2



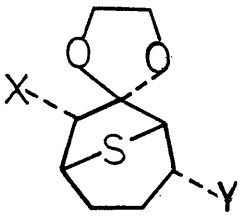
44

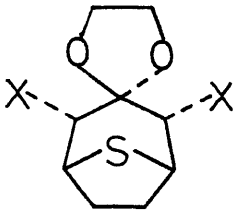
proton decoupling. Double irradiation at δ2·30, *viz* H-C(4) and H-C(5), simplified vinyl and H-C(6) resonances while irradiation at the vinyl absorption did not affect the H-C(6) signal but simplified the methylenic multiplet. Decoupling the H-C(6) proton collapsed the H-C(7) doublet and removed splitting in the multiplet at δ2·30 but decoupling of the H-C(7) proton only simplified the H-C(6) multiplet.

The other band on the preparative plate gave a yellow oil. That this consisted largely of 38 (ca. 25% yield) was shown by comparing spectra with those of an authentic sample.[37] 38 may arise partly from hydrolysis of 35 by potassium hydroxide impurity in the $KOBu^t$ and partly from hydrolysis of unreacted dichloride (35) on the silica of the t.l.c. plate (*vide infra*). Examination of p.m.r. spectra before and after purification of the crude reaction mixture indicated that some 38 is actually formed during the reaction.

43 is a likely intermediate in the reaction of 35 with $KOBu^t$. Loss of chloronium ion from 43, on attack by t-butoxide anion, and rearrangement would yield 44 (Scheme 16). In support of this mechanism, the symmetrical dichloride (40) (*vide infra*) on reaction with $KOBu^t$ also furnished 44 (41%), indicating the intermediacy of 43. The absence of hydrolysis product (38) from the latter reaction suggests that, in the conversion of 35 to 44, the relatively large amount of 38 found was mainly a result of hydrolysis of substrate (35) on preparative t.l.c.

Analogously, a 1:2 mixture of isomeric dibromides 36 and 41,

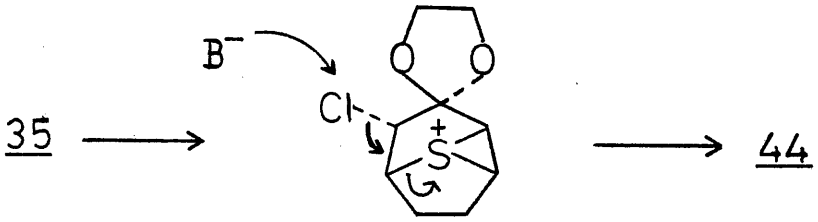




36 X = Y = Br
37 X = Y = I
38 X = Cl, Y = OH
39 X = I , Y = OH

40 X = Cl
41 X = Br
42 X = I

Scheme 16



43

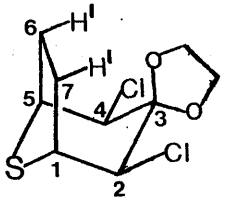
$B^- = (CH_3)_3CO^-$

prepared from bromine addition to 44 (see Part 2), also yielded 44 (59%) on $KOBu^t$ treatment. Although a shortage of substrates prevented separate base treatments of 36 and 41, the high yield of 44 obtained indicated that both isomers underwent debromination-rearrangement.

Hydrolysis and isomerisation of 35

35, prepared by SCl_2 reaction with 46 (Scheme 15), was crystallised from ethyl acetate. However, analytical t.l.c. showed three spots. That the sample of 35 was indeed pure was shown by microanalysis, p.m.r. and mass spectroscopy. Preparative t.l.c. (silica) of a sample of 35 (100mg) gave three bands. The uppermost, on extraction, yielded colourless prisms (10·6mg) m.p. 110-112°. Microanalysis indicated a molecular formula of $C_9H_{12}Cl_2O_2S$, which was in accord with the mass spectral ions at m/e 254, 256 and 258 (9:6:1, dichloride). In the 60MHz p.m.r. spectrum (Figure 3) the methylene protons of the dioxolane moiety gave rise to a broad four-proton envelope at δ4·01-4·47. The presence of a single bridgehead multiplet at δ3·71, integrating for two-protons, favoured a symmetrical structure such as 40. This was supported by the appearance of a two-proton H-C-Cl doublet (J=2Hz) centred at δ4·54, which contrasts with two distinct bridgehead multiplets and two separate H-C-Cl signals in the p.m.r. spectrum of 35. A notable feature was the presence of two separate two-proton envelopes at δ 1·72-2·44 and 2·60-3·03 in accord with symmetrical bicyclic dichloride (40) since, in the conformation shown, two protons (H') attached to C-6 and C-7 are orientated towards the ketal function and would therefore be deshielded relative to the other two methylene protons. In contrast,

Figure 3



40

the p.m.r. spectrum of 35 exhibits a single four-proton methylene envelope at δ1·90-2·83.

Extraction of the middle band furnished colourless needles of 35 (27mg), with identical spectra and melting point to that applied to the t.l.c. plate. The lowest band afforded colourless prisms of 38 (22·6mg), whose structure was firmly established from spectra. A strong hydroxyl stretching absorption appeared at 3540cm^{-1} in the infra-red spectrum. The mass spectrum showed molecular ions at m/e 236 and 238 (3:1), and microanalysis indicated a molecular formula, $C_9H_{13}ClO_3S$, confirming one chlorine atom. In the 60MHz p.m.r. spectrum (Figure 4), similar to that of 35, the H-C-Cl resonance of 35 at δ4·49 had been replaced by a one-proton H-C-O multiplet at δ3·94 and a deuterium oxide exchangeable OH doublet (1H, J=12Hz) at δ2·86. Retention of a one-proton H-C-Cl doublet (J=6Hz) at δ4·59 showed that hydrolysis had not occurred at C-6. Column chromatography of 35 gave a similar result to t.l.c., the initial fractions collected containing 40 while later fractions contained 38.

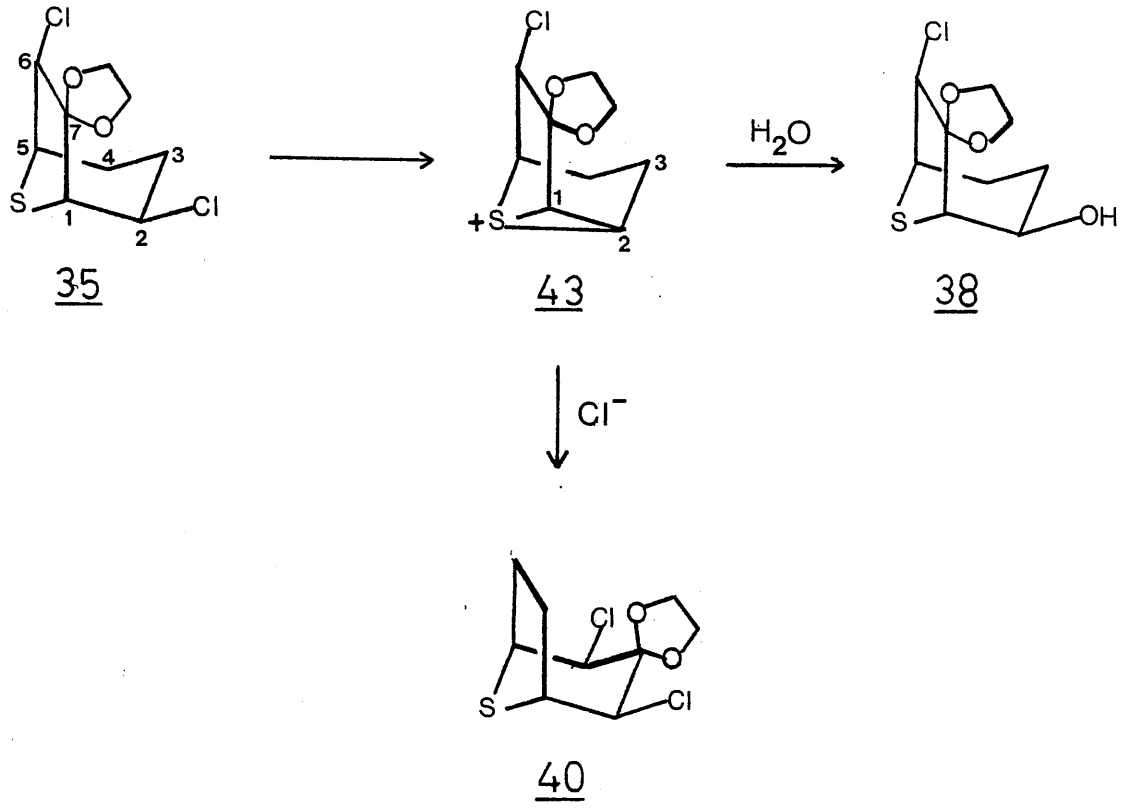
Thus, hydrolysis and isomerisation of 35 is extremely facile implying that the proposed intermediate episulphonium ion (43), formed by sulphur lone-pair displacement of chloride at C-2 of 35, is easily formed (Scheme 17). 43 can be attacked by a water molecule at C-2 to give 38 or converted to 40 by attack of chloride ion at C-1.

In view of these findings it is surprising that SCl_2 addition to 46 does not produce a mixture of isomeric dichlorides (35 and 40) but yields exclusively the less symmetrical adduct (35). To explain this

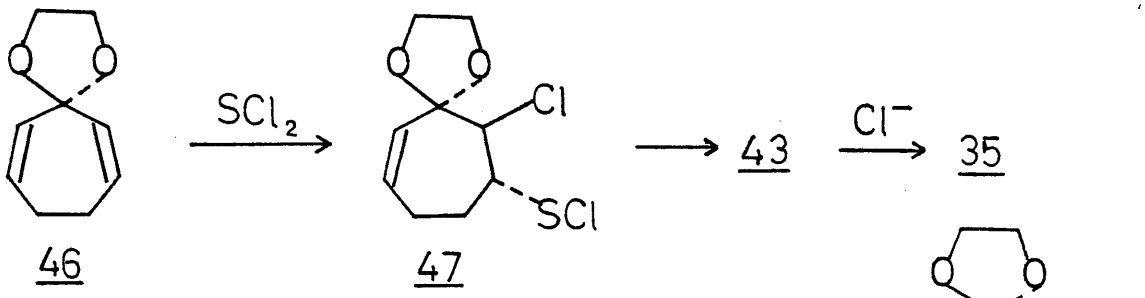
38

Figure 4

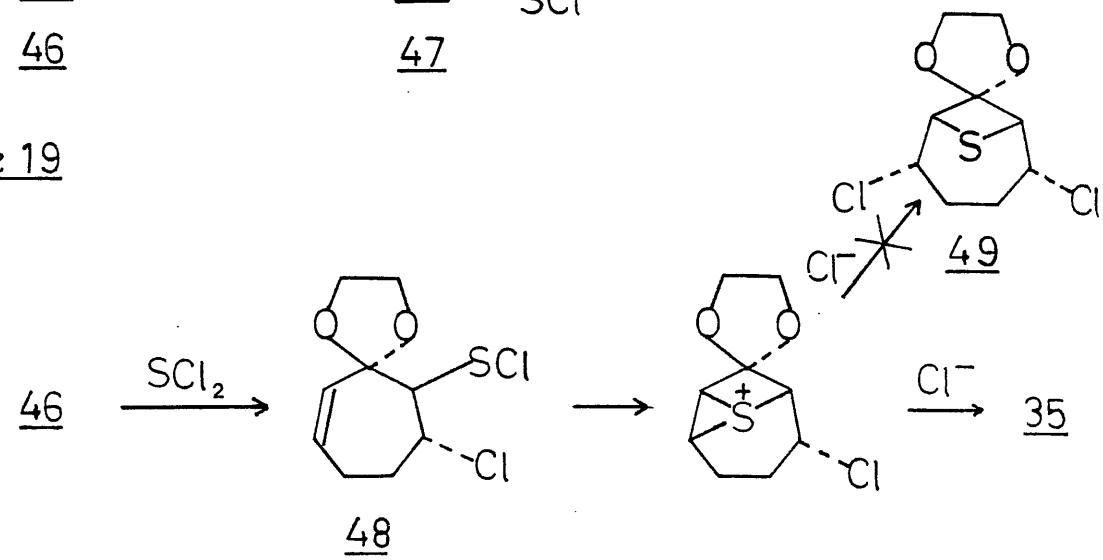
Scheme 17



Scheme 18



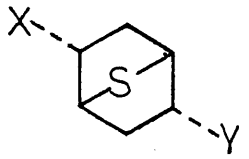
Scheme 19



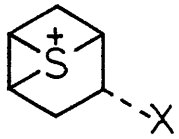
the initial formation of 47 was proposed[37] and rearrangement to 35 was considered to take place in a thermodynamically controlled process (Scheme 18). This argument, however, was based on the assumption that 35 was more stable than 40 which was supported from an examination of molecular models. These apparently showed greater steric interactions between bulky groups in the symmetrical dichloride (40). The present results and a re-examination of molecular models suggest that this explanation is unsatisfactory. It is proposed that 35 and 40 do not have sufficiently different thermodynamic stabilities that allows exclusive formation of 35 from 47. Postulation of an alternative chlorosulphenyl chloride intermediate (48)best rationalises the formation of the less symmetrical adduct (35) (Scheme 19). Intramolecular addition of the sulphenyl chloride moiety of 48 to the double bond would yield 35 rather than the highly strained (4.1.1) isomer (49).

$KOBu^t$ treatment of 2,5- dihalo-7-thiabicyclo (2.2.1) heptanes (50 and 51)

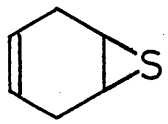
The observation by Corey and Block[28] that the acetolysis of 50 proceeds with retention of bis-endo stereochemistry at C-2 and C-5 was taken to imply the intermediacy of sulphonium ion (54). If this were the case, 54 could also, in principle, be generated by the $KOBu^t$ treatment of 50. However, on prolonged heating of 50 (prepared by SCl_2 condensation[28] with cyclohexa-1,4-diene) with $KOBu^t$ (5 days), only starting material was recovered. Dibromosulphide (51), obtained from bromine addition to 57 (see Part 2), also failed to react with $KOBu^t$. These results may indicate that episulphonium ions (54 and 55) are not readily generated from 50 and 51, due to their high degree of angle strain. Kinetic studies by Tabushi,[38] however, show the acetolysis of 2-endo-chloro-7-thiabicyclo (2.2.1) heptane (58) to exhibit second-order kinetics, implying that sulphonium ion (59) is formed quickly, and attack on it by solvent constitutes the rate-determining step. If 54 and 55 are formed in the t-butoxide reactions, their inability to form unsaturated episulphide (57) may suggest that they are distorted, to relieve ring strain, in such a way that the carbon-halogen bond is no longer anti-periplanar to the adjacent carbon-sulphur bond, a reasonable requirement for elimination of positive halogen. However, Tabushi[38] also found that chloride ions did not retard the solvolysis of 58 which suggested that the chloride ion might be tightly bound in the intermediate. A plausible structure postulated[38] was that of a covalently bound chlorosulphurane (60). It thus appears that β-halo-7-thiabicyclo (2.2.1) heptanes display a novel type of sulphur participation.



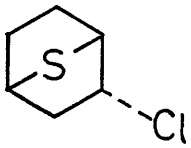
50 X=Y=Cl
51 X=Y=Br
52 X=Y=I
53 X=Br, Y=I



54 X=Cl
55 X=Br
56 X=I

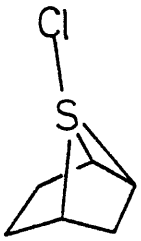


57



58

59



60

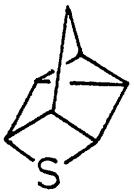
The postulate that the potassium t-butoxide dehalogenations of dihaloalkyl sulphides proceed *via* sulphonium species was reinforced by studying the t-butoxide treatment of a tricyclic dihalosulphide (1).

Reaction of 3,5-bis-exo-dichloro-8-thiatricyclo (2.2.1.$1^{2,6}$) octane (1) with $KOBu^t$

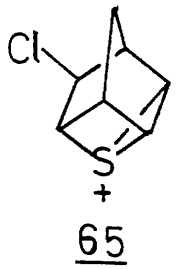
In view of Lautenschlaeger's dechlorination of 1 with potassium cyanide, it was deduced that a similar elimination-rearrangement would take place on $KOBu^t$ treatment. This was borne out by experiment. Dichloride (1) (prepared by SCl_2 condensation[39] with norbornadiene), on reaction, gave olefinic episulphide (3) as the principal product. The yield of this compound (ca. 32%), from distillation of the crude product mixture, was similar to that in the potassium cyanide route. However, in the present reaction, substantial losses of 3 were encountered due to its high volatility. 3 was obtained as a colourless oil since a residual amount of t-butanol prevented solidification. That the isolated compound had structure 3, rather than the alternative structure 61, was evident from the spectral data. The infra-red spectrum showed bands at 3034 and 1642cm^{-1} attributable to a norbornene double bond. Strong absorptions at 1040 and 655cm^{-1} are compatible with an episulphide group. In the 60MHz p.m.r. spectrum (Figure 5), the olefinic protons appear as a two-proton multiplet at δ5.73. The exo-hydrogens attached to the three-membered ring (*viz* H-C-S) are found as a multiplet at δ3.20 (2H), the allylic hydrogens at δ3·07 (m, 2H) and the methylenic protons as a broad singlet at δ2·10 (2H). The mass spectrum possessed

Figure 5

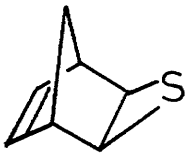
3



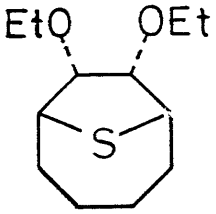
61



65

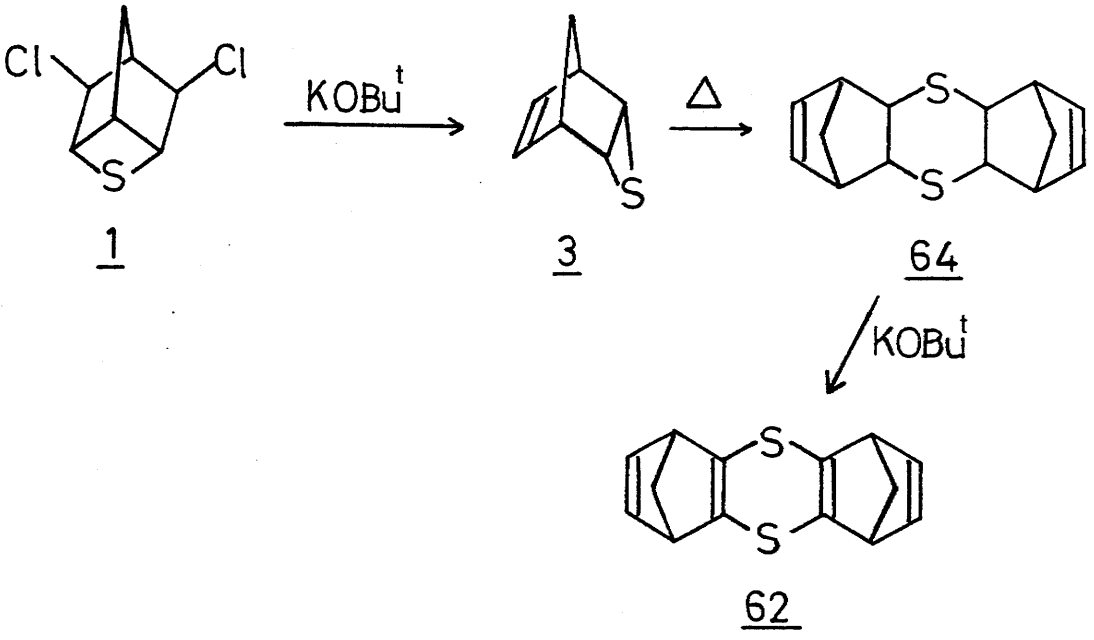


63



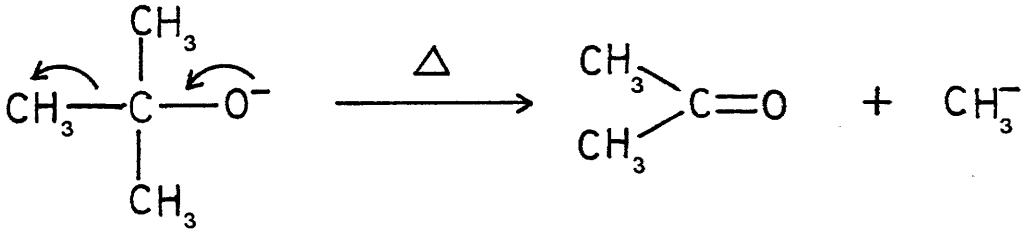
66

Scheme 20

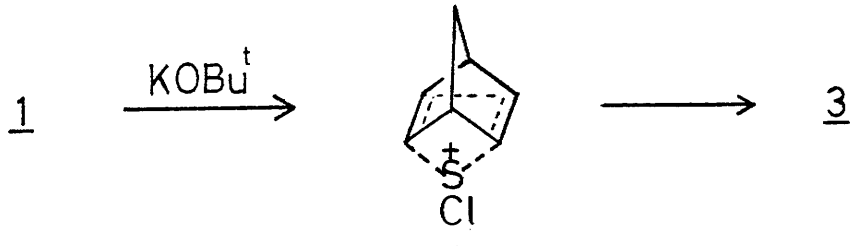


1 3 64 62

Scheme 21



Scheme 22



4

a parent ion at m/e 124 together with daughter ions at m/e 192 (M^+-S) and 66 (loss of sulphur and acetylene), which can readily be interpreted on the basis of structure 3.

Preparative t.l.c. of the distillation residue gave a minor product, as yellow crystals, m.p. 152-153°. The p.m.r. spectrum of this compound showed four regions of absorption. Significantly, the position of the lowest field absorption, δ6·79 (m, 4H), was similar to that of the norbornadiene olefinic resonance (δ6·75)[40]. An allylic-bridgehead multiplet was present at δ3·20 (4H) and two different types of methylene hydrogen were indicated by separate resonances at δ2·04 (m, 2H) and 1·97 (m, 2H). The infra-red spectrum bore a close resemblance to that of norbornadiene; in particular, the olefinic peak appearing at low frequency (1570cm^{-1}). A mass spectral ion at m/e 244 was in accord with the molecular formula, $C_{14}H_{12}S_2$. Major fragment ions were present at m/e 218 (loss of acetylene), 211 (M^+-HS) and 185 (loss of two acetylene groups and HS). On the basis of such evidence this product, which was isolated in low yield (ca. 2%), was identified as 62. This new compound may have been generated from 3, via a radical process, since it has been reported[41] that thermolysis of exo-2,3-epithionorborn-5-ene (63) gives 64 as a minor product, a radical pathway being favoured. It is conceivable that, during the reaction, a small amount of initial product (3) (or an intermediate leading to 3) is converted, under the influence of heat, to 64 (Scheme 20). The latter may then be dehydrogenated to 62 by KOBu^t (present in excess), whichhas been reported[43] to bring about loss of hydrogen from monocyclic terpenes in the absence of oxygen. The active dehydrogenating agent is considered[43] to be the methide ion (CH_3^-), generated from t-butoxide

anion on strong heating (Scheme 21).

For the mechanistic interpretation of the formation of 3, it is proposed that 1 initially gives rise to 4 which, on attack by t-butoxide, rearranges to 3 with loss of chloronium ion (Scheme 22). An alternative episulphonium intermediate (65) is considered too highly strained and lacking in appropriate alignment of the bonds to be cleaved (vide supra).

Conclusions

The results from this study clearly show that potassium t-butoxide is more versatile than potassium cyanide[18] in effecting the conversion of dihalosulphides to unsaturated thiiranes. In general, t-butoxide reactions with cyclic β,β'-dihaloalkyl sulphides, in which sulphur-participation in the displacement of the halogens readily occurs, is a potentially useful source of olefinic episulphides (or rearranged isomers). The method cannot be applied to compounds in which facile 1,2-elimination of hydrogen halide can take place.

EXPERIMENTAL

General

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Qualitative infra-red spectra were obtained on ca. 1-2mg samples dispersed in pressed potassium bromide discs (300mg) on a Perkin-Elmer 257 spectrometer. Quantitative infra-red spectra were obtained in carbon tetrachloride on a Perkin-Elmer 225 instrument. Proton magnetic resonance (p.m.r.) spectra were recorded in deuteriochloroform solution (unless otherwise stated) on a Varian T.60 (60 MHz) or Perkin-Elmer R.32 (90 MHz) instrument. Band positions are reported in parts per million (p.p.m.) downfield from tetramethylsilane as internal reference (δscale). Ultraviolet spectra were recorded on a Unicam SP800 grating spectrophotometer. Routine mass spectra were obtained on an AEI MS12 spectrometer while high resolution mass determinations were carried out on an AEI MS902 instrument.

For reactions that required heat, the temperature quoted refers to the temperature of the oil bath. The progress of reactions was monitored by analytical thin layer chromatography (t.l.c.), performed using layers of Merck Kieselgel G (0·25mm) on microscope slides. Chromatograms were visualised by spraying either with ceric sulphate solution followed by heating to 120°, or with iodine vapour. Preparative t.l.c. was carried out using 1mm layers of Merck Kiesegel HF_{254} silica (unless otherwise stated) on 20cm x 20cm or 20cm x 100cm plates and were viewed under ultraviolet light (λ 254mm). Alumina employed in column chromatography was Woelm Grade 1 (neutral), unless otherwise stated.

Petroleum spirit used was previously distilled and was of boiling range 60-80°. Methylene chloride was distilled and stored over 4A molecular sieves. Tert-butanol was refluxed with a small amount of sodium, distilled and stored over 4A molecular sieves.[44,45] Other solvents employed in preparative work were either of AnalaR grade or were distilled prior to use.

Sodium bicarbonate and sodium chloride solutions used were saturated. Solutions in organic solvents were dried over anhydrous magnesium sulphate before being stripped of solvent using a Buchi rotary evaporator in conjunction with a water aspirator.

Sulphur dichloride was freshly distilled, prior to use, from a small amount of phosphorous trichloride, the fraction boiling between 58° and 61° being retained.[45] Potassium t-butoxide used was of commercial grade or was freshly prepared[44,46] from potassium and dry t-butanol. All reactions using $KOBu^t$ were carried out in an atmosphere of nitrogen, which had been passed through conc. H_2SO_4 and silica gel. Iodine was sublimed before use.

Photolyses were carried out in sodium-dried benzene solutions through which nitrogen was bubbled by means of a fritted inlet. A Hanovia medium-pressure mercury-vapour lamp was used as ultraviolet source in a quartz immersion-well photolysis apparatus with a water-cooling jacket.

Treatment of 2,6-dichloro-9-thiabicyclo (3.3.1) nonane (8)[19] with $KOBu^t$

A solution of $KOBu^t$ (7·05g, 63mmol) in t-butanol (200ml) was added to a stirred solution of 8 (6·33g, 30mmol) in t-butanol (200ml) over 30 min, during which a precipitate formed. After stirring at 80° for 3 hr the pale yellow reaction mixture was poured into ice-cold water (100ml) and extracted with ether (2 x 450ml). The combined ether extracts were washed with brine (6 x 200ml), water (2 x 200ml) and dried. Removal of solvent afforded a viscous yellow oil (3.21g) which was chromatographed over alumina (30g). Elution with ether-petroleum spirit (1:9) yielded 11 (1·53g, 36%) as a colourless oil, b.p. 65°, 1·2mmHg (lit.[13] b.p. 44°, 0·3mmHg); $\nu_{max}^{CCl_4}$ 3018, 2984, 2940, 2896, 2855, 1653, 1479, 1466, 1432, 1246, 1217 and 1057 cm^{-1}; $\delta(CDCl_3)$ 1·38-2·62 (br m, 8H, $C\underline{H}_2$), 2·80-3·24 (m, 2H, $\underline{H}$-C-S) and 5·75 (m, 2H, olefinic $\underline{H}$); m/e 140 (M^+), 107 (M^+-HS), 93 and 91; t_R=168 sec (1% OV-1 on gas chrom Q at 100°). Identical spectral data were obtained from an authentic sample of 11. In a larger scale reaction, the initial fractions collected from column purification contained a colourless oil (26, 300mg, 0·9%) which distilled at 65-70°, 0·1mmHg to give 26 as a waxy solid, m.p. 65-75°. Anal. calc. for $C_{16}H_{30}O_2S$: C 67·07, H 10·56%. Found: C 67·20, H 10·60%; $\nu_{max}^{CCl_4}$ 2983, 2938, 2882, 1391, 1366, 1197, 1055, 1024 and 916cm^{-1}; $\delta(CDCl_3)$ 1·16 (s, 18H, $C\underline{H}_3$), 1·51-2·20 (m, 8H, $C\underline{H}_2$), 2·48 (m, 2H, $\underline{H}$-C-S) and 3·72-4·00 (m, 2H, $\underline{H}$-C-O); m/e 286 (M^+) 229, 213, 173 and 155.

Attempted desulphurisation of 26 with triphenyl phosphine[33]

To a solution of triphenyl phosphine (17·5mg, 0·066mmol) in

chloroform (2ml) was added a solution of 26 (18mg, 0·063mmol) in chloroform (2ml). The reaction mixture was refluxed for 12 hr then solvent removed by distillation. Analysis by p.m.r. showed only starting material present.

2,6-Dibromo-9-thiabicyclo (3.3.1) nonane (9)[19]

A solution of dichloride (8) (10·5g, 50mmol) in glacial acetic acid (300ml) at 50° was saturated with hydrogen bromide gas, obtained by the slow addition of conc. H_2SO_4 to hydrobromic acid. After standing for 12 hr in a stoppered flask, the colourless crystalline precipitate which had collected was filtered, washed with water and brine until the washings were neutral to litmus and vacuum dried. The crude product (11·3g) on recrystallisation from heptane-benzene furnished colourless prisms of 9 (9·0g, 60%), m.p. 133-135° (lit.[19] m.p. 134-135°); $\nu_{max}^{CCl_4}$ 2920, 1435, 1145, 662 and 605 cm^{-1}; $\delta(CDCl_3)$ 2·10-2·75 (m, 8H, $C\underline{H}_2$), 2·79-3·15 (m, 2H, H-C-S) and 4·70-5·19 (m, 2H, H-C-Br); m/e (302, 300 and 298) (M^+), (221 and 219) (M^+-Br) and 140 (M^+- 2Br).

2,6-Diiodo-9-thiabicyclo (3.3.1) nonane (10)[19]

A mixture of dichloride (8) (10·5g, 50mmol) and sodium iodide (30g, 200mmol) in acetone (300ml) was stirred at room temperature, in the absence of light, for 15 hr. After filtration, to remove salt, the yellow filtrate was evaporated to dryness and the green resicue

heated in n-heptane to extract diiodide (10). Filtration and evaporation of the filtrate gave yellow crystals which recrystallised from heptane-benzene as colourless prisms (3·2g, 16·2%), m.p. 144-146° (lit.[19] m.p. 145-146°); δ($CDCl_3$) 1·70-2·85 (m, 8H, CH_2), 3·10 (m, 2H, H-C-S) and 4·91-5·42 (m, 2H, H-C-I).

Reaction of 9 with $KOBu^t$

A solution of $KOBu^t$ (700mg, 6·25mmol) in t-butanol (15ml) was added to a stirred solution of 9 (500mg, 1·66mmol) in t-butanol (15ml) over 10 min. After stirring at 60° for 2 hr, the yellow reaction mixture was poured into ice-cold water (15ml), which dissolved precipitate, and extracted with ether (2 x 60ml). The combined extracts were washed with brine (4 x 30ml), water (2 x 30ml) and dried. Removal of solvent afforded 11 (120mg, 51%) as a slightly yellow oil, substantially pure by t.l.c. (ether-petroleum spirit, 1:9) and p.m.r. with only a trace amount of 26 present. Passage through a column of alumina (2g, ether-petroleum spirit, 1:1) gave 11 (75mg, 32%) as a colourless oil.

Reaction of 10 with $KOBu^t$

A solution of $KOBu^t$ (300mg, 2.68mmol) in t-butanol (15ml) was added to a stirred solution of 10 (500mg, 1·27mmol) in t-butanol (15ml) over 10 min. After stirring at 80° for 3 hr, the reaction mixture was worked up as for the previous reaction. Removal of solvent afforded 11 (160mg) as a yellow oil. A minor contaminant present was t-butanol

which was removed by chromatographing over alumina (2g, benzene) to give 11 (73mg, 41%) as a colourless oil.

7,8-Dichloro-9-thiabicyclo (4.2.1) nonane (31)[19]

From separate funnels cycloocta -1,3-diene (10·8g, 0·1mol) and SCl_2 (10·3g, 0·1mol) were added with stirring to dry benzene (500ml) at 20-25° (water-bath cooling) over 5 hr. The yellow reaction mixture was allowed to stand for 12 hr, then benzene was removed by distillation leaving a brown oil (23·2g) which distilled *in vacuo* to give, as distillate, a viscous brown oil (7·1g) which, from p.m.r. and t.l.c., was a mixture of cycloocta -1,3-diene and 31. Purification was achieved by chromatographing over alumina (70g, ether-petroleum spirit, 1:19). Initial fractions collected contained cycloocta -1,3-diene (1·9g), while later fractions gave 31 (3·9g, 22%) as colourless prisms, m.p. 182-186° (lit.[19] m.p. 185·5-186·5°); δ($CDCl_3$) 1·35-2·70 (br m, 8H, CH_2), 3·51-4·00 (m, 2H, H-C-S) and 4·84 (sh m, 2H, H-C-Cl); m/e (214, 212 and 210) (M^+), (177 and 175) (M^+-Cl), 141, 140, 139, 105 and 97.

Reaction of 31 with $KOBu^t$

To a stirred solution of 31 (88mg, 0·417mmol) in t-butanol (30ml) was added a solution of $KOBu^t$ (98·2mg, 0·876mmol) in t-butanol (5ml) over 5 min at 40°. The reaction mixture was heated at 50° for 68 hr. A further amount of $KOBu^t$ (30mg, 0·268mmol) in t-butanol (2ml) was

added since t.l.c. indicated incomplete reaction. After 3 hr the reaction mixture was worked up as for the reaction of 9 with $KOBu^t$. Solvent removal left a yellow oil (70mg), which on distillation gave, as first fraction, a colourless oil, 7-chloro-9-thiabicyclo (4.2.1) non-7-ene (32) (25mg, 42%), b.p. 35-37°, 0·01mmHg; $\nu_{max}^{CCl_4}$ 2940, 2856, 1634, 1448, 1440, 1340, 1036, 976, 960, 912, 845, 840 and 683 cm^{-1}; $\delta(CDCl_3)$ 1·43-2·33 (br env, 8H, CH_2), 3·69-4·09 (m, 2H, H-C-S) and 5·86-6·00 (d, J=4Hz, 1H, olefinic H); m/e (176 and 174) (M^+), 139, 131 and 97. A second fraction, collected at 60-70°, 0·05mmHg, was identified as starting material (31) (10mg, 11·4%) from its p.m.r. spectrum. The residue consisted of impure 31 (6mg, 6·8%).

9-Thiabicyclo (4.2.1) non-7-ene (15)

A mixture of dichlorosulphide (31) (422mg, 2mmol), zinc dust (392mg, 6mmol), and anhydrous ethanol (5ml) was vigorously refluxed for 4 days. The mixture was then filtered (after employing a small amount of magnesia and fullers' earth to remove zinc chloride, a tenacious impurity[19]), the filtrate was stripped free of ethanol and the residual oil (600mg) purified by preparative t.l.c. (ether-petroleum spirit, 1:9). The uppermost band provided 15 (26mg, 9·3%) as a colourless oil; $\delta(CDCl_3)$ 1·70 (br m, 8H, CH_2), 3·95 (m, 2H, H-C-S) and 5·81 (d, J=2Hz, 2H, olefinic H); m/e 140 (M^+), 111, 97 and 84. The lower band furnished a colourless oil (150mg), tentatively assigned structure 66 on the basis of its p.m.r. and mass spectra. Since this oil was not completely pure, and further purification was not attempted,

the p.m.r. spectrum could not be interpreted unambiguously. However, the mass spectrum shows a parent molecular ion at m/e 230 (M^+) and a daughter ion at m/e 184 ($M^+ - C_2H_5OH$), consistent with the presence of an ethyl ether.

Cycloheptanone ethylene ketal (67)[37]

A mixture of cycloheptanone (56·8g, 0·51mol), ethylene glycol (54·2g, 0·88mol), benzene (75ml) and toluene-p-sulphonic acid (40mg) was refluxed for 20 hr using a Dean and Stark trap containing silica gel as drying agent. The mixture was allowed to cool, poured into ether (250ml), washed with sodium bicarbonate solution (80ml), and brine (3 x 100ml), dried over anhydrous sodium sulphate and stripped of solvent. The crude product was purified by distillation giving 67 (71·3g, 0·46mol, 90%) b.p. 56-60°, 0·12mmHg; $\nu_{max}^{liq.\ film}$ 2928, 2862, 1459, 1371, 1216, 1121, 1098, 1073, 1032, 1011, 947, 885 and 783 cm^{-1}; $\delta(CDCl_3)$ 1·30-2·07 (complex m, 12H, cycloheptane CH_2) and 3·86 (s, 4H, dioxolane CH_2).

Cyclohepta-2,6-dienone ethylene ketal (46)[37,42]

Bromine (128g, 0·8mol) was added to a solution of 67 (62·4g, 0·4mol) in ether (500ml) at such a rate as to maintain a gentle reflux. Further bromine was added dropwise until the brown colour persisted. A solution of monosodium ethylene glycolate, prepared from sodium (20g, 0·87mol) and ethylene glycol (300ml), was added slowly with vigorous stirring

and the resultant mixture poured into water. The ether layer was separated, washed with brine and dried over anhydrous sodium sulphate. Evaporation of solvent gave, as a yellow oil (127g), crude dibromo-ketal (68). The unpurified product was added to a mixture of sodium hydroxide (88g, 2·2mol) and methanol (400ml), and was refluxed for a further 48 hr. The reaction mixture was poured into brine and extracted with pentane (2 x 400ml). The extracts were combined and dried, and solvent evaporated at atmospheric pressure. Distillation of the residue at reduced pressure gave 46 (42·3g, 0·28mol, 70%), b.p. 65-70°, 1·0mmHg (lit.[42] b.p. 58°, 0·75mmHg); $\nu_{max}^{liq.\ film}$ 3020, 2935, 2872, 1661, 1399, 1211, 1090, 1006, 963, 820 and 791 cm^{-1}; $\delta(CDCl_3)$ 2·29 (m, 4H, allylic CH_2), 3·88 (s, 4H, dioxolane CH_2), 5·60 (d, J=12Hz, 2H, C(2,7) H) and 5·91 (m, 2H, C(3,6) H).

Addition of sulphur dichloride to ketal (46)[37]

Cyclohepta-2,6-dienone ethylene ketal (46) (3·8g, 25mmol) and SCl_2 (2·58g, 25mmol), each dissolved in methylene chloride (25ml), were added simultaneously over 10 min to methylene chloride (100ml) which was vigorously stirred at -70°. The stirred mixture was maintained at -70° for 60 min and was allowed to come to room temperature. The solution was washed in turn with sodium bicarbonate and brine, dried and solvent removed to give a yellow crystalline solid (6·08g). Recrystallisation from ethyl acetate furnished 35 (4·1g, 16·1mmol, 65%) as colourless needles, m.p. 113-115°. Anal. calc. for $C_9H_{12}Cl_2O_2S$: C42·36, H4·74%. Found: C42·12, H5·01%; ν_{max}^{KBr} 2975, 2928, 1462,

1334, 1301, 1251, 1205, 1156, 1129, 1098, 1038, 997, 953, 885, 822, 749, 728 and 635 cm^{-1}; $\delta(CDCl_3)$ 1·90-2·83 (br env, 4H, C(3,4) $\underline{H}_2$), 3·26 (m, 1H, C(1)$\underline{H}$), 3·40 (m, 1H, C(5) $\underline{H}$), 3·80-4·32 (m, 4H, dioxolane $C\underline{H}_2$), 4·49 (m, 1H, C(2)$\underline{H}$) and 4·68 (d, J=6Hz, 1H, C(6)$\underline{H}$); m/e (258, 256 and 254) (M^+), 221, 219, 183, 146, 120 and 99.

Reaction of 35 with $KOBu^t$

(a) Addition of $KOBu^t$ to 35

To a stirred solution of 35 (255mg, 1mmol) in t-butanol (15ml) was added a solution of $KOBu^t$ (235mg, 2·1mmol) in t-butanol (15ml) over 15 min at 30°. The yellow reaction mixture was heated at 50° for 12 hr then worked up as for the reaction of 9 with $KOBu^t$. Solvent removal afforded a viscous yellow oil (193mg). Preparative t.l.c. (ethyl acetate-hexane, 1:9) gave two bands. The uppermost band on extraction furnished 44 (58mg, 31%) as a colourless oil; b.p. 60-62°, 0·1mmHg; $\nu_{max}^{CCl_4}$ 2980, 2888, 1735, 1650, 1458, 1430, 1397, 1265, 1210, 1177, 1138, 1076, 1044, 1000, 979, 949, 690, 665 and 637 cm^{-1}; $\delta(CDCl_3)$ 2·30 (m, 4H, cycloheptene $C\underline{H}_2$), 2·71-3·13 (m, 1H, C(6)$\underline{H}$), 3·27 (d, J=7Hz, 1H, C(7) $\underline{H}$), 4·02 (m, 4H, dioxolane $C\underline{H}_2$) and 5·71 (m, 2H, olefinic $\underline{H}$); m/e 184 (M^+), 152, 151, 118, 112, 79 and 68. The lower band gave a yellow oil which consisted largely of 38 (59mg, 25%), as shown from spectral comparisons.[37]

(b) Addition of 35 to $KOBu^t$

To a stirred solution of $KOBu^t$ (705mg, 6·3mmol) in t-butanol

(50ml) was added 35 (765mg, 3·0mmol) at 30°. The reaction mixture, which turned pale yellow after 5 min, was heated at 80° for 2 hr, then worked up as in the reaction of 9 with $KOBu^t$. Solvent removal afforded a dark-red oil (480mg), which on purification by preparative t.l.c. (ether-petroleum spirit, 3:7) gave 44 (210mg, 37%) and 38 (36mg) (slightly impure).

Reaction of 40 with $KOBu^t$

40 (127·5mg, 0·5mmol) and $KOBu^t$ (117·5mg, 1·05mmol) were reacted according to the procedure used for 35, in (a). The same work-up, followed by removal of ether, afforded a yellow oil (99mg), whose p.m.r. spectrum clearly showed the presence of a mixture of starting material (40) and unsaturated episulphide (44). Partial purification was achieved by crystallisation of 40 (10·1mg) from ether as yellow prisms. The mother liquor, on removal of ether, was distilled to give 44 (25mg, 41%) as a colourless oil, b.p. 72-75°, 0·15mmHg. The residue from the distillation consisted of a mixture and was not further purified.

Treatment of a mixture of 36 and 41 with $KOBu^t$

To a stirred solution of a 1:2 mixture of 36 and 41 (31·6mg, 0·092mmol) in t-butanol (15ml) was added a solution of $KOBu^t$ (21·6mg, 0·193mmol) in t-butanol (5ml) over 2 min at 40°, during which a dark-yellow colour developed and a precipitate formed. The reaction mixture was heated at 50° for 24 hr, then poured into ice-cold water

(10ml) and extracted with ether (2 x 30ml). The combined ether extracts were washed with brine (2 x 20ml), water (2 x 20ml) and dried. Removal of ether gave a yellow oil (16mg) which, on passage through a plug of alumina (0·5g) using ether as eluent, yielded, on removal of solvent, 44 (10mg, 59%) as a colourless oil.

Hydrolysis and isomerisation of 35 by silica or alumina

Analytical t.l.c. (ether-petroleum spirit, 3:7) of a pure sample of 35 showed three spots with Rf values 0·1, 0·5 and 0·7. Preparative t.l.c. (silica gel) of 35 (100mg) gave three bands. Extraction of the uppermost band yielded colourless prisms of 40 (10·6mg) m.p. 110-112°. Anal. calc. for $C_9H_{12}Cl_2O_2S$; C 42·36, H 4·74%. Found: C 42·20, H 4·67%; ν_{max}^{KBr} 2984, 2946, 2908, 1332, 1250, 1205, 1184, 1150, 1074, 1060, 1042, 1001, 969, 957, 849, 811, 748, 732, 660 and 585 cm^{-1}; $\delta(CDCl_3)$ 1·72-2·44 (br env, 2H, C(6,7) $\underline{H}_2$), 2·60-3·03 (m, 2H, C(6,7) $\underline{H}_2'$), 3·71 (m, 2H, C(1,5) $\underline{H}_2$), 4·01-4·47 (m, 4H, dioxolane $C\underline{H}_2$) and 4·54 (d, J=2Hz, 2H, C(2,4) $\underline{H}_2$); m/e (258, 256 and 254) (M^+), 221, 219, 183, 120 and 99. The middle band furnished 35 (27mg), spectroscopically identical with the sample applied to the plate. Extraction of the lowest band yielded colourless prisms of 38 (22·6mg) m.p. 84-86°. Anal. calc. for $C_9H_{13}ClO_3S$: C 45·66, H 5·54%. Found: C 45·34, H 5·76%; ν_{max}^{KBr} 3540, 2958, 2895, 1396, 1300, 1201, 1148, 1115, 1041, 1032, 985, 951, 870, 747 and 654 cm^{-1}; $\delta(CDCl_3)$ 1·83-2·60 (br env, 4H, C(3,4) $\underline{H}_2$), 2·86 (d, J=12Hz, 1H, O$\underline{H}$), 3·19 (m, 1H, C(1)$\underline{H}$), 3·33 (m, J=6 and 4Hz, 1H, C(5) $\underline{H}$), 3·94 (m, J=12 and 4Hz, 1H, C(2) $\underline{H}$),

4·11 (m, 4H, dioxolane $\underline{CH}_2$) and 4·59 (d, J=6Hz, 1H, C(6) $\underline{H}$); m/e (238 and 236) (M^+), 220, 218, 201, 183, 138, 125 and 118. Passage of 35 (400mg) through a column (23cm x 1cm i.d. column, 16g of alumina) with ether-petroleum spirit, 3:2, as eluent gave 40 (30mg). Further elution with chloroform yielded 38 (320mg).

2,5-Bis-endo-dichloro-7-thiabicyclo (2.2.1) heptane (50)[28]

Cyclohexa -1,4-diene (3·0ml, 31·5mmol) and SCl_2 (2·1ml, 32·2mmol) each in dry methylene chloride (18ml) were simultaneously added dropwise over 12 hr to gently refluxing methylene chloride (500ml). The yellow solution was then concentrated to about 20ml, shaken with dilute hydrochloric acid and brine, dried, and added dropwise to n-pentane (100ml) to precipitate a white, odourless, highly insoluble polymer. The filtrate, on removal of pentane, yielded a yellow semi-solid, which on sublimation ("cold finger") at aspirator vacuum and 90° gave 50 (1·51g, 26%) as a colourless, waxy solid, m.p. 91-94° (lit.[28] m.p. 93-94°, sealed tube); $\nu_{max}^{CCl_4}$ 2960, 1446, 1319, 1264, 1182, 946, 906, 870, 698, 663, 645 and 596 cm^{-1}; $\delta(CDCl_3)$ 2·25-2·60 (m, 4H, $\underline{CH}_2$), 3·56-3·79 (m, 2H, $\underline{H}$-C-S) and 4·18-4·70 (m, 2H, $\underline{H}$-C-Cl); m/e (186, 184 and 182) (M^+), (149 and 147) (M^+-Cl), 115, 113, 111 and 86.

Treatment of 50 with $KOBu^t$

$KOBu^t$ (369mg, 3·29mmol) and 50 (153mg, 0·836mmol) were mixed as in the reaction of 9 with $KOBu^t$. The reaction mixture was heated

at 80° for 120 hr, the solution remaining colourless. On work-up and removal of solvent, starting material (50) (125mg, 82%) alone was recovered.

Treatment of 51 with $KOBu^t$

$KOBu^t$ (25·9mg, 0·231mmol) and 51 (30mg, 0·11mmol), following the procedure in the reaction of 9 with $KOBu^t$, also failed to react. Thus, after the reaction mixture was heated at 50° for 24 hr, worked up and ether removed, starting material (51) (24mg, 80%) remained.

3,5-Bis-exo-dichloro-8-thiatricyclo (2.2.1.$1^{2,6}$) octane (1)[39]

A solution of norbornadiene (32·2g, 350mmol) in hexane (250ml) and a solution of SCl_2 (36·0g, 350mmol) in hexane (250ml) were added dropwise at equal rates to rapidly stirred hexane (100ml) over a period of 6 hr with cooling, maintaining the internal temperature at 0-5°. Solvent was removed to give a light-yellow oil, which on distillation (92-96°, 0·5mmHg) gave 1 (45·2g, 66%) as a colourless liquid which solified on standing, m.p. 38-44° (lit.[39] m.p. 39-42°); ν_{max}^{KBr} 3000, 2984, 2961, 1452, 1310, 1283, 911, 860, 770, 744 and 690 cm^{-1}; $\delta(CDCl_3)$ 2·07 (bs, 2H, C(7) H), 3·19-3·26 (m, 3H, C(2,6) H and C(4) H), 4·00 (m, 1H, C(1) H) and 4·63 (bs, 2H, C(3,5) H); m/e (198, 196 and 194) (M^+), (161 and 159) (M^+-Cl), 125, 124, 123, 100, 91 and 66.

Reaction of 1 with $KOBu^t$

To a stirred solution of $KOBu^t$ (2·96g, 26·4mmol) in t-butanol (60ml) was added 1 (1·03g, 5·28mmol) at 40°. The dark brown suspension was refluxed for 24 hr, poured into ice-cold water (60ml) and extracted with ether (2 x 120ml). Combined extracts were washed with brine (6 x 50ml), water (4 x 50ml) and dried. Removal of ether afforded a brown oil (520mg). Analytical t.l.c. (petroleum spirit) showed one principal component (Rf=0·4) and one minor component (Rf=0·2). A trace amount of t-butanol was present as shown by p.m.r. Distillation gave 3 (208mg, 32%) as a colourless liquid b.p. 32-45°, 0·5mmHg (lit.[18] b.p. 35-50°, 0·5mmHg); $\nu_{max}^{CCl_4}$ 3078, 3034, 2988, 2970, 2938, 2870, 1642, 1460, 1332, 1295, 1243, 1040, 913, 846 and 655 cm^{-1}; $\delta(CDCl_3)$ 2·10 (bs, 2H, $C\underline{H}_2$), 3·07 (m, 2H, allylic $\underline{H}$), 3·20 (m, 2H, $\underline{H}$-C-S) and 5·73 (m, 2H, olefinic $\underline{H}$); m/e 124 (M^+), 123, 92, 91 and 66. The residue from the distillation, on preparative t.l.c. (alumina, petroleum ether) gave one band, which on extraction yielded 62 (30mg, 2·3%) as yellow crystals, m.p. 152-153°; $\nu_{max}^{CCl_4}$ 3076, 2986, 2944, 2874, 1570, 1450, 1296, 1264, 1229, 1205, 1120, 1081 and 713 cm^{-1}; $\delta(CDCl_3)$ 1·97 (m, 2H, $C\underline{H}_2$), 2·04 (m, 2H, $C\underline{H}'_2$), 3·20 (m, 4H, bridgehead $\underline{H}$) and 6·63-6·95 (m, 4H, olefinic $\underline{H}$); m/e 244 (M^+), 218, 217, 211, 185 and 121.

Part 2

Electrophilic Additions to Diene Monoepisulphides.

Introduction

In 1920 Delepine prepared[47] the first pure aliphatic thiirane, ethylene sulphide, and noted it reacted with bromine to form a viscous, coloured substance. He recognised the importance of thiiranes as reactive substances suitable for a variety of reactions and observed that ethylene sulphide, on storing at room temperature, gradually polymerised to form a white mass.[47,48]

Surprisingly, almost thirty years elapsed before Culvenor published[49] the first detailed account of the preparation and reactions of aliphatic episulphides. The revival of interest in the chemistry of episulphides most likely arose from the results of technological studies, which indicated that they might have industrial applications as synthetic polymers[49,50] and in the modification of wool fibres.[51]

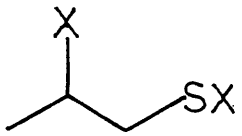
It was noted that many of the reactions and properties of the episulphides could not have been deduced, by analogy, from a knowledge of the chemistry of epoxides. In particular, an outstanding property of the episulphides was their tendency to undergo polymerisation under a variety of conditions - low molecular weight members forming polymers at ordinary temperatures with water containing small traces of acid or alkali.[47,49] Interestingly, cyclohexene sulphide reacted with chlorine to yield 1,2-dichlorocyclohexane in addition to a large proportion of polymer.[49]

Stewart and Cordts reported,[52] in 1952, that the reaction of chlorine and bromine with propylene sulphide, in non-aqueous solution,

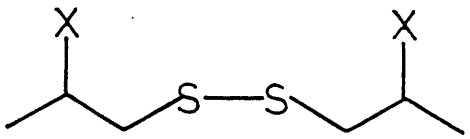
resulted in ring opening with the formation of a halosulphenyl halide (69)or the corresponding disulphide (70), depending on the amount of halogen used (Scheme 23). 70 was considered to arise by reaction of initially formed sulphenyl halide (69) with unreacted substrate.[52] Reaction of 69 with propylene sulphide did, in fact, yield the same disulphide (70) obtained by using a deficiency of halogen.[52] Later, however, other authors reported[53] that the initially formed sulphenyl halide had structure 71 and the disulphide had structure 72, at variance with Stewart and Cordts results. This difference of opinion has not yet been resolved[54] with certainty.

Halogenolysis of 70 with chlorine or bromine[54] yields the corresponding sulphenyl halide (69). Indeed, halogenolysis of disulphides in general, at low temperature in carbon tetrachloride or methylene chloride, represents a standard preparation[54,55] of alkanesulphenyl halides. Organic sulphenyl iodides, on the other hand, are generally obtained by an alternative route which involves oxidation[54,56] of thiols by the appropriate halogen since iodine, unlike chlorine and bromine, is incapable[56] of cleaving a disulphide under anhydrous conditions. A familiar reaction is the oxidation of thiols to disulphides by iodine, which proceeds via a sulphenyl iodide intermediate (Scheme 24),[56] this being one of the best methods of preparing disulphides.[57]

Helmkamp and Pettitt[58] studied the interaction between iodine and but-2-ene sulphide, their interest in this being initiated by their previous observation that desulphurisation of the latter with methyl iodide led,[59] under certain conditions, to the formation of molecular

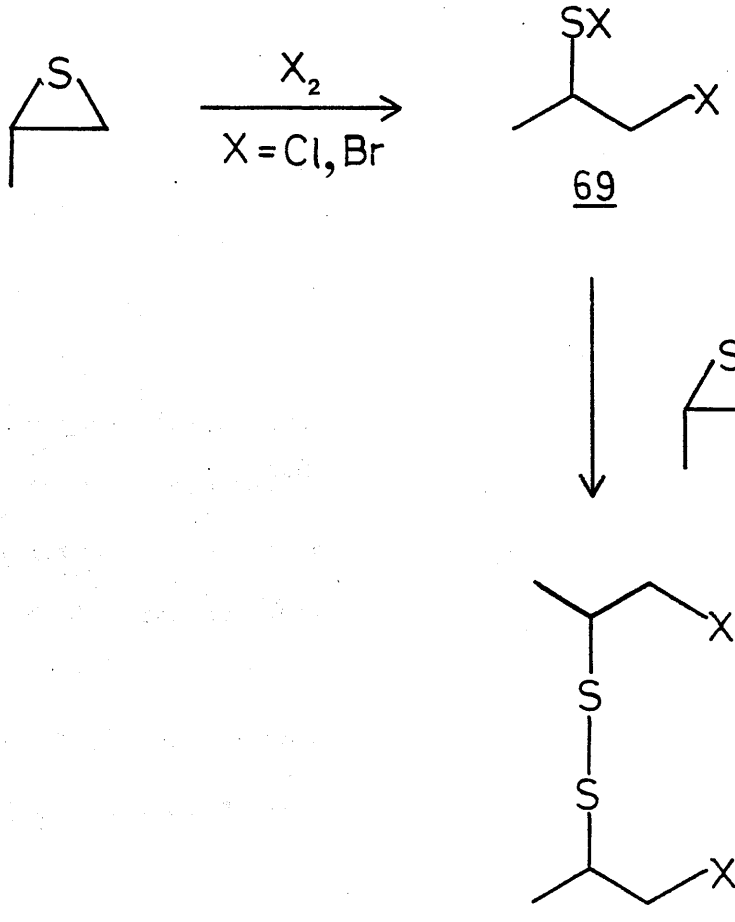


71



72

Scheme 23



Scheme 24

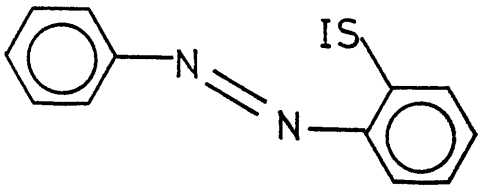
$$R{-}SH + I_2 \longrightarrow 2\,R{-}SI + HI \xrightarrow{R'SH} RS{-}SR' + HI$$

iodine. They showed that iodine reacted with meso- and dl-but-2-ene sulphide in benzene with stereospecific loss of sulphur to give but-2-ene in moderate yield. Scheme 25 depicts the proposed route to cis-but-2-ene. The meso-sulphide (73) was considered to react with iodine to form sulphenyl iodide (74) then disulphide (75), either of which could undergo a trans elimination. However, the nature of this process was not determined and it was not known if 75 reverted back to 74 prior to desulphurisation.

Unlike sulphenyl iodides, much work has been done with sulphenyl chlorides and bromides,[54,56] mainly because of their greater stability and ease of purification. An outstanding feature of organic sulphenyl chlorides is their highly electrophilic character derived from the partial ionic nature of the S-Cl bond. These compounds can attack unshared electron pairs on the oxygen, phosphorous, sulphur and nitrogen atoms of molecules.[60] Much of the chemistry of sulphenyl bromides is identical to that of the corresponding chlorides, but generally the bromides are less stable.

Sulphenyl iodides are highly reactive but intrinsically rather stable.[56] Only in few instances have they been isolated in quite stable forms.[56] These include sterically hindered protein sulphenyl iodides[61-63] and azobenzene-2-sulphenyl iodide (76).[64] The two characteristic reactions of sulphenyl iodides are displacement of iodide ion from sulphur by nucleophilic attack on the latter and disproportionation to disulphide and iodine.

One of the most interesting reactions of sulphenyl halides is



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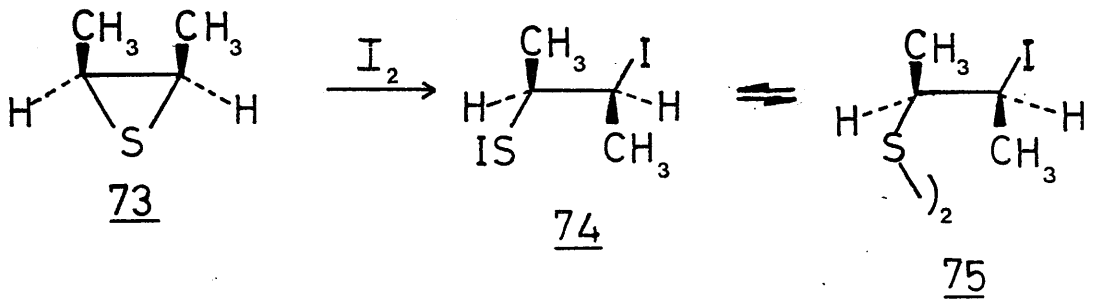
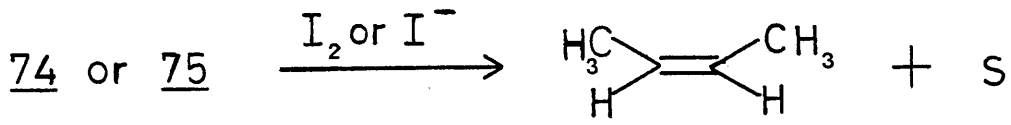
Scheme 25

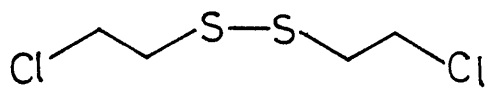


73 74 75



their additon to alkenes. Early studies by Fuson and co-workers[55] on the reaction of sulphenyl chlorides with olefins showed that 2-chloroethylsulphenyl chloride (78), made by chlorinolysis of disulph (77), condensed with ethylene to produce bis(2-chloroethyl) sulphide (79) (Scheme 26). This important result substantiated the hypothesis of Conant,Hartshorn and Richardson[65] that 78 is an intermediate in the preparation of 79 from condensation[65] of SCl_2 with ethylene. Interest in 79, commonly known as "Mustard Gas", stemmed from its extreme toxicity and unique biological properties. The toxicity, which led to its extensive use in chemical warfare during World War I, has been attributed[66] to its ease of penetration through the body tissue combined with intracellular evolution of hydrogen chloride by sulphur-assisted hydrolysis (Scheme 27). An early important use of 79 was in the treatment of cancer. The basis of this use rests on the fact that rapidly dividing tumour cells are particularly sensitive to destruction by chemical agents or by ionising radiation. 79 acts *in vivo* as an electrophilic reagent alkylating essential cellular macromolecules, presumably cross-linking them, therefore disrupting cellular processes and causing tumour inhibition.[67] Early encouraging results led to the synthesis and testing of related systems[68] in attempts to obtain agents which maintained their anti-tumour potency but had less severe side-effects. Compound 80 is currently used in the treatment of head and neck cancer through injection directly into blood vessels supplying the tumour.[67]

Fuson[55] also showed that cyclohexene reacted with 78 to give an unsymmetrical dichlorosulphide (81) (Scheme 28). Similarly, a mixed halosulphide (83) was obtained on addition of 2-chloroethylsulphenyl



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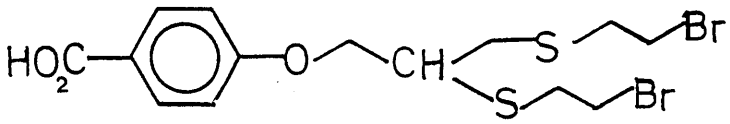
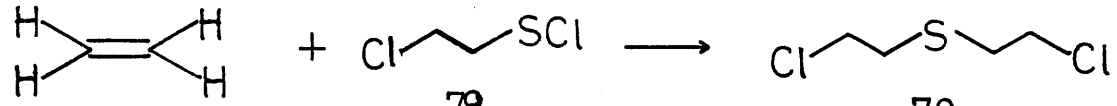


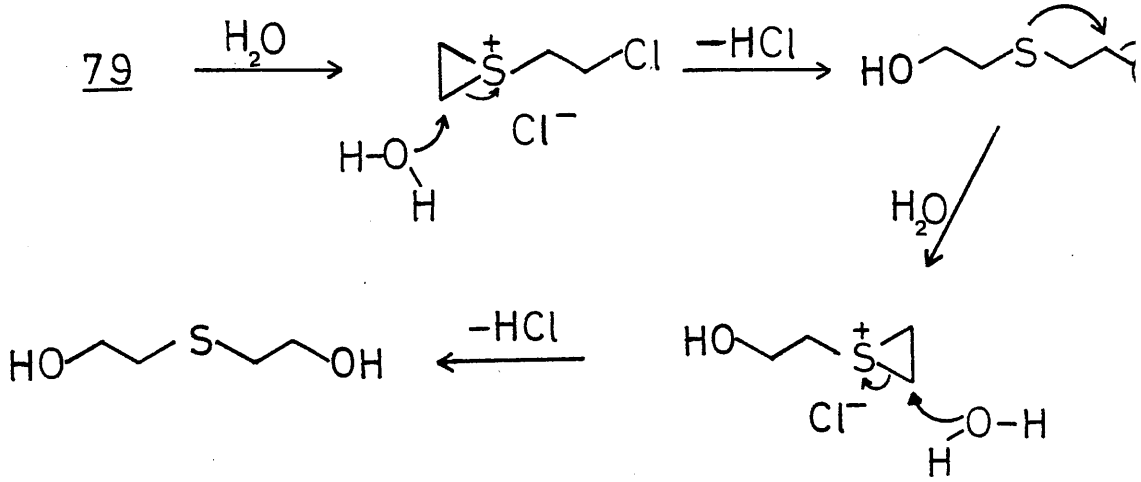
80

Scheme 26



78 79

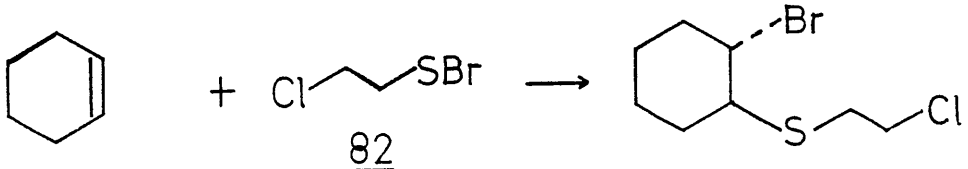
Scheme 27



Scheme 28

78 81

Scheme 29



82 83

bromide (82) (prepared by brominolysis of 77) to cyclohexene (Scheme 2

Many examples of the condensation of sulphenyl chlorides[69] and bromides with alkenes are now known. Addition of alkane- and arenesulphenyl chlorides is believed[39,70,114] to proceed by formation of a π-complex and an episulphonium ion (84) (Scheme 30). Ring opening of the latter usually gives the Markovnikov product (85)[53] but in certain cases the anti-Markovnikov adduct (86)[70,71] predominates. The intermediacy of 84 accounts for the trans-stereospecific addition for such reactions. Sulphenyl bromides add to alkenes in a similar manner.

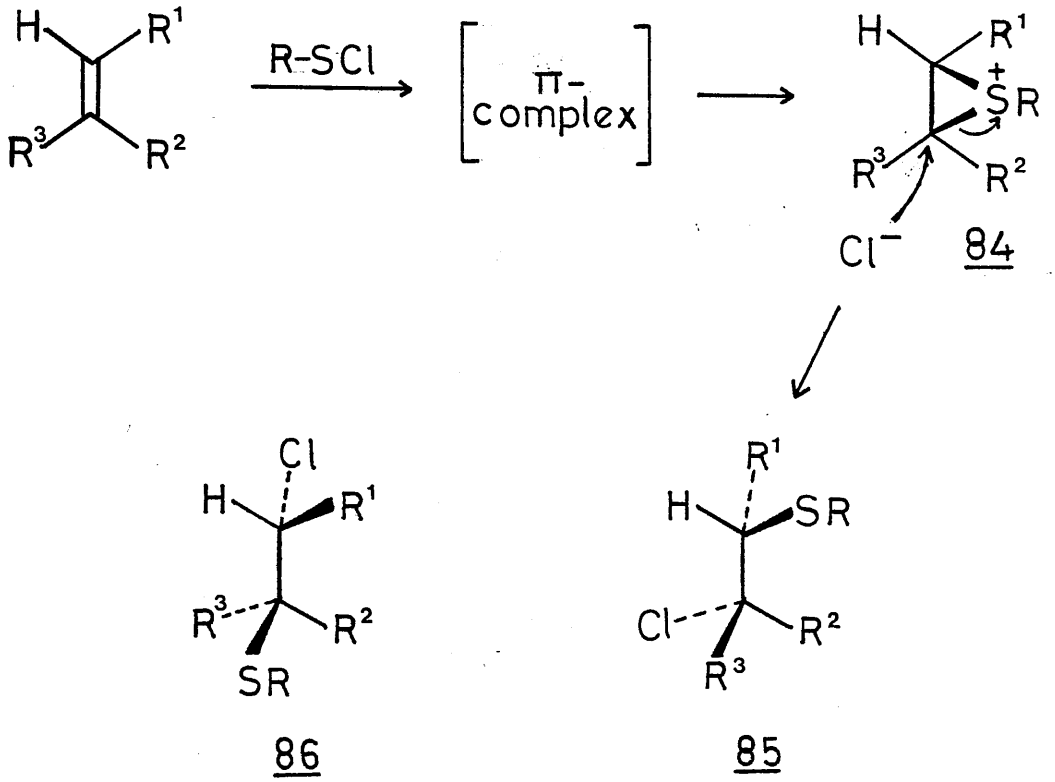
Mueller and Butler[70] suggested that the relative importance of electronic and steric factors controls the formation of products. Rece studies by Morita and Oae[72] on the intramolecular cyclisation of unsaturated sulphenyl halides (87), generated by halogenolysis of the corresponding disulphide (88) and not isolated, support this view. Thus, disulphide (89) on halogenative cyclisation gave a mixture of 90 and 91 in which the smaller ring compound (90), the anti-Markovnikov addition product and the less stable isomer,[73] was the major component (Scheme 31). This result indicates that there is little or no partial charge developed on the carbon atoms involved in the intermediate (92). Therefore, steric factors control the formation of 90.

The reactions of SCl_2 with alkenes are particularly interesting because β-chloroalkylsulphenyl chlorides are initially formed which can react further with unreacted alkene to produce the important β,β'-dichloroalkyl sulphides, such as 79 (*vide supra*). Surprisingly, only in recent years has the synthetic utility of SCl_2 been fully

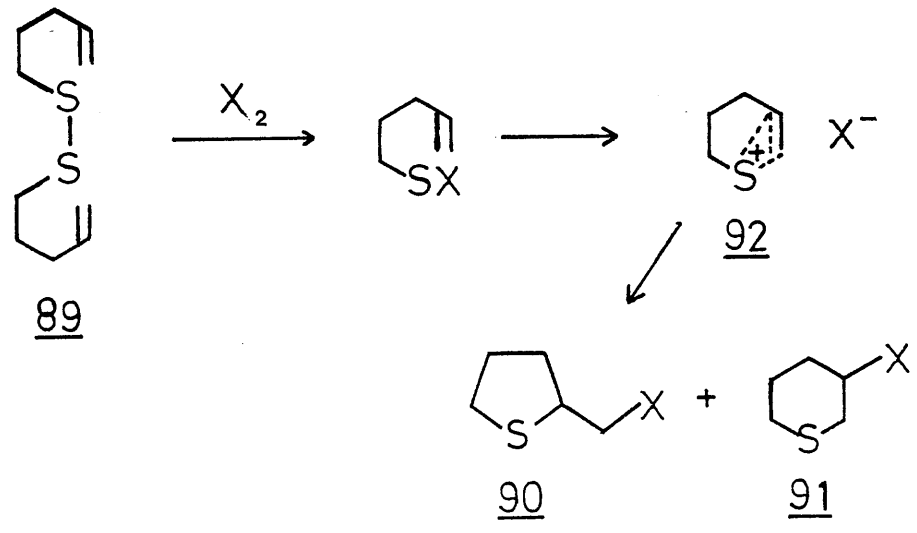
$CH_2{=}CH(CH_2)_nSX$ — 87

$(CH_2{=}CH(CH_2)_nS\rightarrow)_2$ — 88

Scheme 30



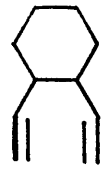
Scheme 31



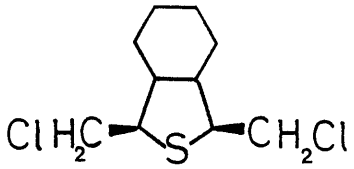
realised. Reactions of SCl_2 with a wide variety of unsaturated system (recently reviewed[74]) including dienes,[19,28,30,39] acetylenes,[75] enol ethers and enamines,[76] oximes[77] and nitriles[78] have in recent year yielded novel sulphur-containing products. In particular, the additio of SCl_2 to cyclic polyolefins[81] has been widely used for the preparati of thiabicyclic systems.

In 1966 the transannular addition of SCl_2 to cis,cis-cycloocta-1,5-diene (93) was described independently by three research groups.[19,28,39] This reaction gave dichloride (8) in high yield and provided the first convenient synthetic entry into 9-thiabicyclo (3.3.1) nonane (Scheme 32). The anti configuration of the carbon-chlorine bonds of 8 relative to the sulphur bridge is accounted for by the postulation of an episulphonium intermediate (94), however, there is no evidence for the formation of 2,5-dichloro-9-thiabicyclo (4.2.1) nonane in this reaction. Thus it is expected here that thermodynamic control is operative, the resulting molecular framework comprising two six-member rings in the chair-chair conformation which allows the most favourable staggering of the carbon-hydrogen bonds. It was also shown that cycloocta-1,3-diene, on SCl_2 addition, gave 31,[19] a structural isomer of 8, and that cyclohexa-1,4-diene yielded 50.[28] Other additions of SCl_2 to dienes have since been reported, including the recent addition to 95 which furnishes 96.[79]

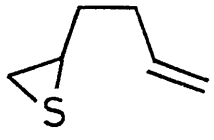
Functional group modification of these dichloroalkyl sulphides is generally made easier by the participation of the sulphur lone-pair in the displacement of the chloride ions, which manifests itself in the high rates of solvolyses and the retention of the bis-endo



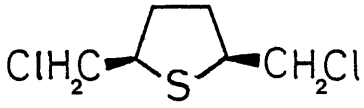
95



96

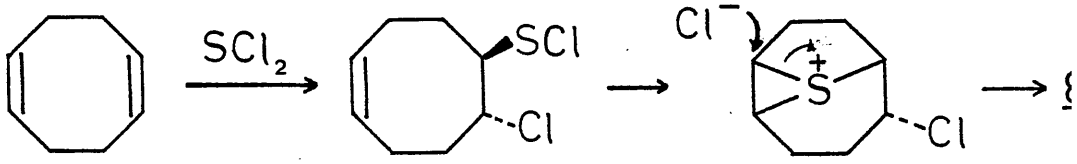


97



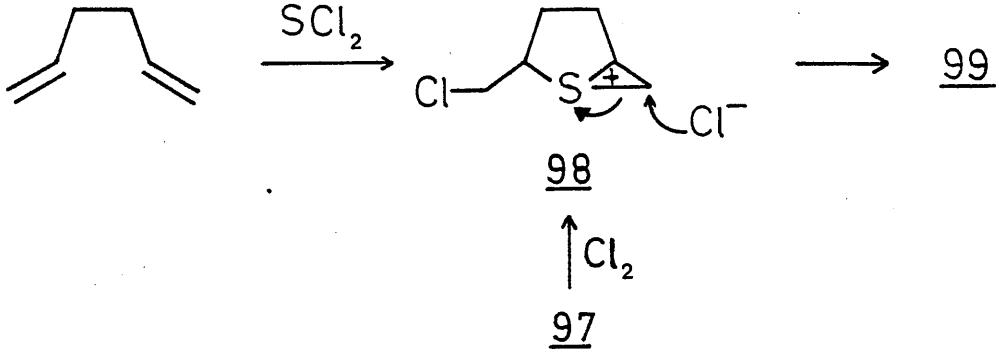
99

Scheme 32



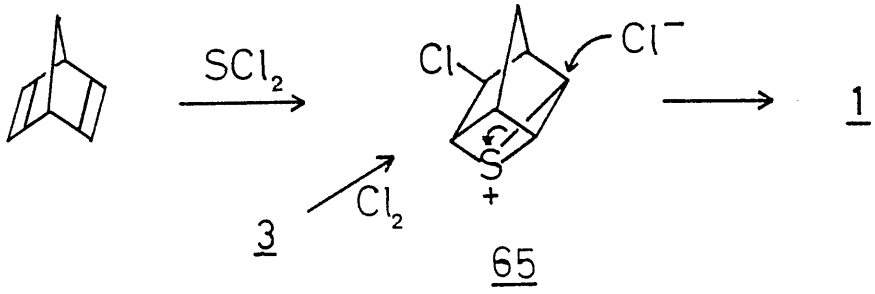
93 94

Scheme 33



98 97 99

Scheme 34



3 65 1

configuration of the β-substituents. Clearly, then, sulphur dichloride condensations with dienes provide a valuable route to sulphur-bridged carbocyclic systems.

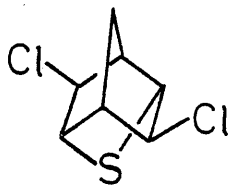
Of particular relevance to the present study is the closely related formation of β,β'-dichloroalkyl sulphides by chlorine addition to unsaturated thiiranes. Lautenschlaeger[30] showed that 8 could readily be obtained from unsaturated episulphide (11) in high yield by reaction with chlorine. Furthermore, norbornadiene monoepisulphide (3) and 97 gave 1 and 99 respectively, on reaction with chlorine, these products being identical with those obtained from SCl_2 additions to the corresponding dienes. These intriguing results suggested that the intermediates in both types of reaction were identical. This implies that, generally, in the case of an episulphide of a diolefin in which intramolecular attack of SCl_2 occurs, the addition of chlorine should lead to the formation of a cyclic dichloroalkyl sulphide, identical with the SCl_2 addition product to the diolefin.

Mueller[80] suggests that both types of reaction proceed through a common episulphonium ion intermediate which readily accounts for the stereospecific formation of product. Thus chlorine addition to 11, for example, gives 94 which, on chloride attack, yields 8. Also SCl_2 addition to hexa-1,5-diene or reaction of chlorine with its monoepisulphide (97) generates 98 which rearranges to 99 (Scheme 33). Mueller[80] favours an episulphonium intermediate (65) in the formation of 1 from 3 and norbornadiene (Scheme 34). However, Lautenschlaeger[39] argues that the assumption of 65 as an intermediate is unsatisfactory. He proposes that 100 is thermodynamically more stable than 1, because of better staggering of its bonds and the involvement of the sulphur in

the five-membered ring in preference to the four-membered ring, and should therefore be formed preferentially from 65. Postulation of a resonance stabilised intermediate such as 4, he argued, best explained the results.

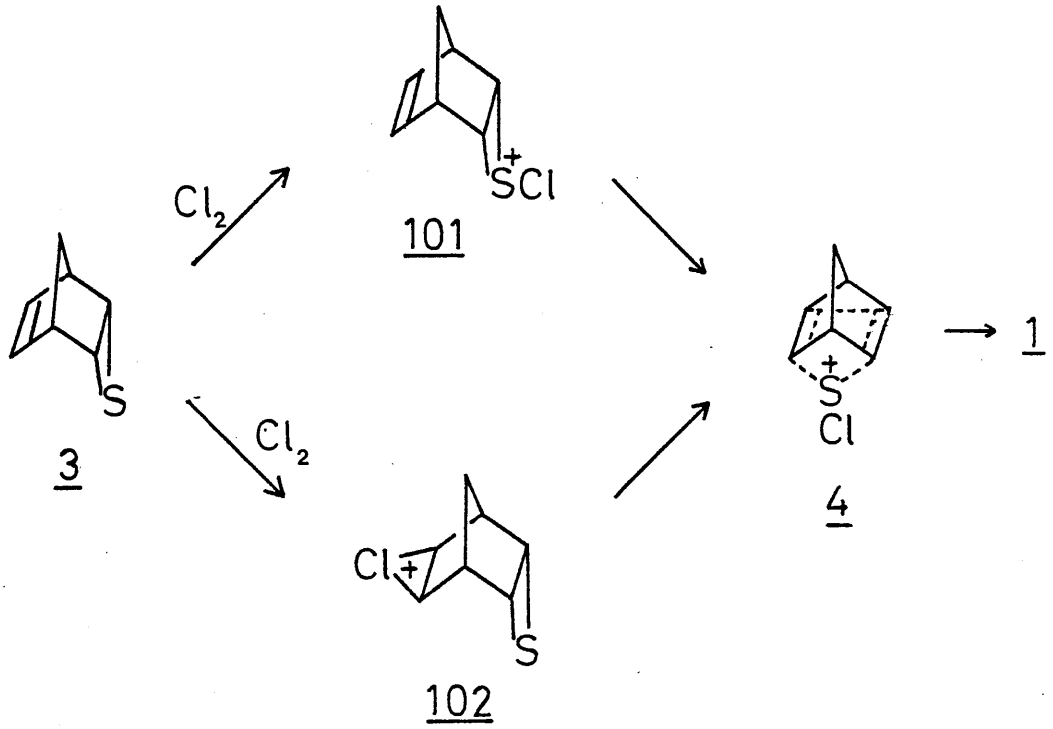
Another important mechanistic point concerns the mode of addition of chlorine to unsaturated episulphides i.e. whether initial addition of chlorine occurs to the sulphur atom or to the double bond, since transannular rearrangement could lead to a common intermediate. Thus 3, for example, on chlorine addition may initially give rise to 101 or 102 either of which could rearrange to 4 (Scheme 35).

In this section, the preparation of sulphur-bridged compounds by chlorine addition to unsaturated episulphides is extended to include bromine and iodine additions. Furthermore, the site of initial electrophilic attack is clearly established and a novel route to a 1,2-dithiolane described.



100

Scheme 35

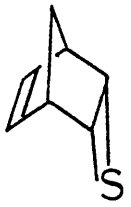


Discussion

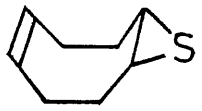
The addition of chlorine to diene monoepisulphides was studied to provide on alternative route (vide supra) to cyclic sulphides and to clarify mechanistic aspects of the addition. Moreover, it was projected that bromine and iodine reactions with unsaturated thiiranes should furnish dibromo- and diiodoalkyl sulphides, which cannot be obtained directly from dienes since stable SBr_2 and SI_2 are unknown. In some cases these bromides or iodides may be prepared by appropriate halide treatment of the corresponding dichloroalkyl sulphide but this method fails if there is insufficient sulphur-participation and/or steric hindrance to substitution.

The diene monoepisulphides chosen for study were those of corresponding dienes which readily react with SCl_2 to give dichlorosulphides. Furthermore, to simplify the reactions and to study the effect of ring size the research was restricted to cyclic substrates 3, 11, 44 and 57. The choice of these reduces complications due to electronic effects which control the formation of Markovnikov products.

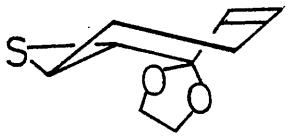
The method of Hinshaw[5] was used to prepare 11 (Scheme 36) in 18% yield (lit. 26%). This involves trans addition of iodine thiocyanate selectively across one double bond of 93 to form a β-iodothiocyanate, which on base hydrolysis yields episulphide (11). Iodine thiocyanate was generated from an equimolar mixture of iodine and thiocyanogen. Limited spectroscopic evidence[82] suggests an equilibrium is set up with an appreciable quantity of iodine thiocyanate



3

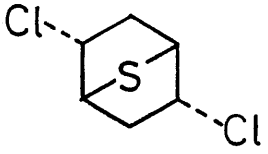


11

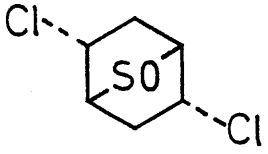


44

57

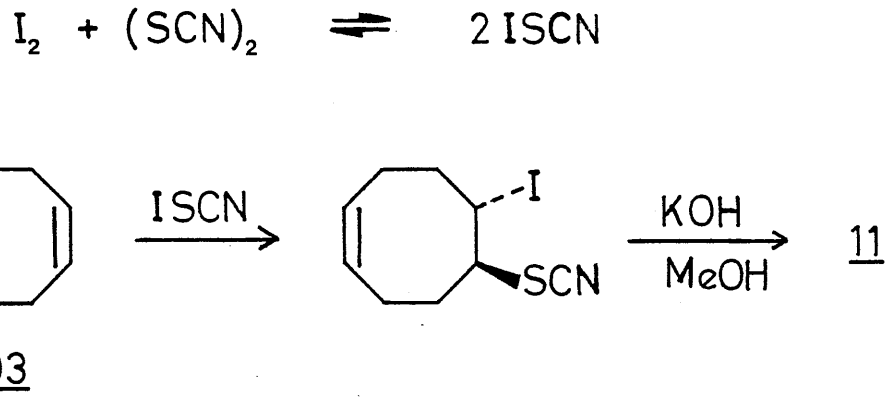


50



103

Scheme 36



Scheme 37

$$Pb(NO_3)_2 + 2\,NaSCN \longrightarrow Pb(SCN)_2\downarrow + 2\,NaNO_3$$

$$Pb(SCN)_2 + Br_2 \longrightarrow (SCN)_2 + PbBr_2$$

formed. Thiocyanogen,[31] prepared as in Scheme 37, is sensitive to heat, light and moisture, being readily hydrolysed to thiocyanic acid (HSCN) and hypothiocyanous acid (HOSCN).

Cyclohexa-1,4-diene monoepisulphide (57) was prepared from cyclohexa-1,4 -diene in an overall yield of 25% using the same procedure as for 11. After purification by column chromatography, 57 was obtained as a colourless oil with a powerful, sulphury odour. Mass spectral peaks appeared at m/e 112 (M^+) and 79 (M^+-HS) while the infra-red spectrum possessed an olefinic stretching band at 1663 cm^{-1} along with strong absorptions at 1086 and 671 cm^{-1}, attributed to the episulphide moiety. The p.m.r. spectrum exhibits three narrow multiplets centred at δ2·70 (4H), 3·24 (2H) and 5·47 (2H) corresponding to methylenic, H-C-S and olefinic absorptions respectively. 3 and 44 were obtained from $KOBu^t$ treatments of 1 and 35 respectively (See Part 1). 11 was also prepared by this method.

Electrophilic additions to 7-thiabicyclo (4.1.0) hept-3-ene (57)

Following Lautenschlaeger's procedure[30] for reaction of chlorine with 11, dry chlorine gas was bubbled through a solution of 57 in methylene chloride. The crude product was shown, by p.m.r. and mass spectroscopy, to consist of dichlorosulphide (50) and its sulphoxide (103), in the approximate ratio 2:5 (p.m.r. integration). Purification by preparative t.l.c. gave 103 as colourless prisms (21%) but failed to yield 50. Apparently 50 had decomposed on the silica plate. The

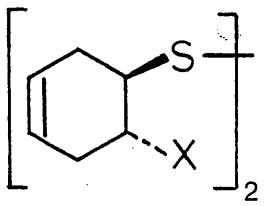
low recovery of 103 from the purification suggested that this is also sensitive to silica gel. Assignment of structure 103 was based on the p.m.r. and mass spectra. The p.m.r. spectrum exhibited two well-spaced two-proton methylene envelopes centred at δ2·40 and 2·74. These are assigned to the endo and exo methylenic hydrogens on C-3 and C-6, the exo protons occurring at lower field because of their proximity to the sulphoxide group. A significant feature was the large separation of the H-C-Cl one-proton multiplets at δ4·04-4·50 and 4·73-5·24 which contrasts with a two-proton multiplet at δ4·18-4·70 for the H-C-Cl absorption for sulphide (50) (*vide infra*). This large downfield shift of one of the H-C-Cl atoms in the spectrum of 103 compared with that of 50 is most satisfactorily explained on the basis that this proton is in the deshielding zone of the sulphoxide group. Also consistent with compound 103 was a broad two-proton multiplet at δ3·59 (bridgehead H).

It is noteworthy that, when the above chlorinolysis prodedure was carried out with 11 as substrate, sulphide (8) was formed, unaccompanied by sulphoxide. Thus, it appears that 50 is more susceptible to air oxidation in the presence of chlorine than 8.

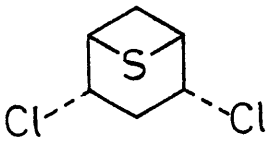
Sulphuryl chloride, SO_2Cl_2, proved to be more convenient for chlorinolysis of 57 than chlorine gas, since, with SO_2Cl_2, no undesirable over-oxidised products were formed. Treatment of episulphide (57) with an equimolar amount of SO_2Cl_2 in methylene chloride at 0°, gave exclusively dichlorosulphide (50) (94%). The product was obtained as a colourless, crystalline solid, m.p. 89-92°

(lit.[28] m.p. 93-94°, sealed tube). The p.m.r. spectrum supports the bis-endo orientation of the chlorine substituents on C-2 and C-5, since the observed coupling constant between the H-C-Cl and bridgehead protons is ca. 3·5Hz and not zero as would be expected if the chlorine atoms were exo. For comparison, the observed coupling constant between the exo-methylene and bridgehead protons in the norbornyl system[83] is 3-6Hz, whereas that for the corresponding endo methylene protons is zero. The methylenic resonances, for 50, appear as a four-proton doublet of quartets at δ2·25-2·60. Bridgehead absorptions are present at δ3·56-3·79 (m, 2H) while H-C-Cl resonances consist of a two-proton sextet at δ4·18-4·70. A molecular formula of $C_6H_8Cl_2S$ was evident from the presence of mass spectral ions at m/e 182, 184 and 186 (intensity 9:6:1). These spectral features were in agreement with those of an authentic sample of 50.

The observation by Stewart and Cordts[52] that the product formed on reaction of halogen with episulphide depended on the relative amounts of substrate and reagent, prompted the treatment of 57 with ½mol of SO_2Cl_2. The product obtained, on solvent removal, was a colourless oil, b.p. 95-100° at 0·03mmHg. This was identified as di-(2-chlorocyclohex-4-enyl) disulphide (104) (97%) on the following evidence. Microanalysis indicated a molecular formula of $C_{12}H_{16}Cl_2S_2$ and was in agreement with the mass spectrum which displays parent ions at m/e 294, 296 and 298 (intensity 9:6:1). The p.m.r. spectrum shows broad, overlapping multiplets in the region δ2·0-3·5 (10H), these being consistent with the methylene and H-C-S protons of 104. A two-proton multiplet at δ4·17-4·60 is assigned to H-C-Cl absorption

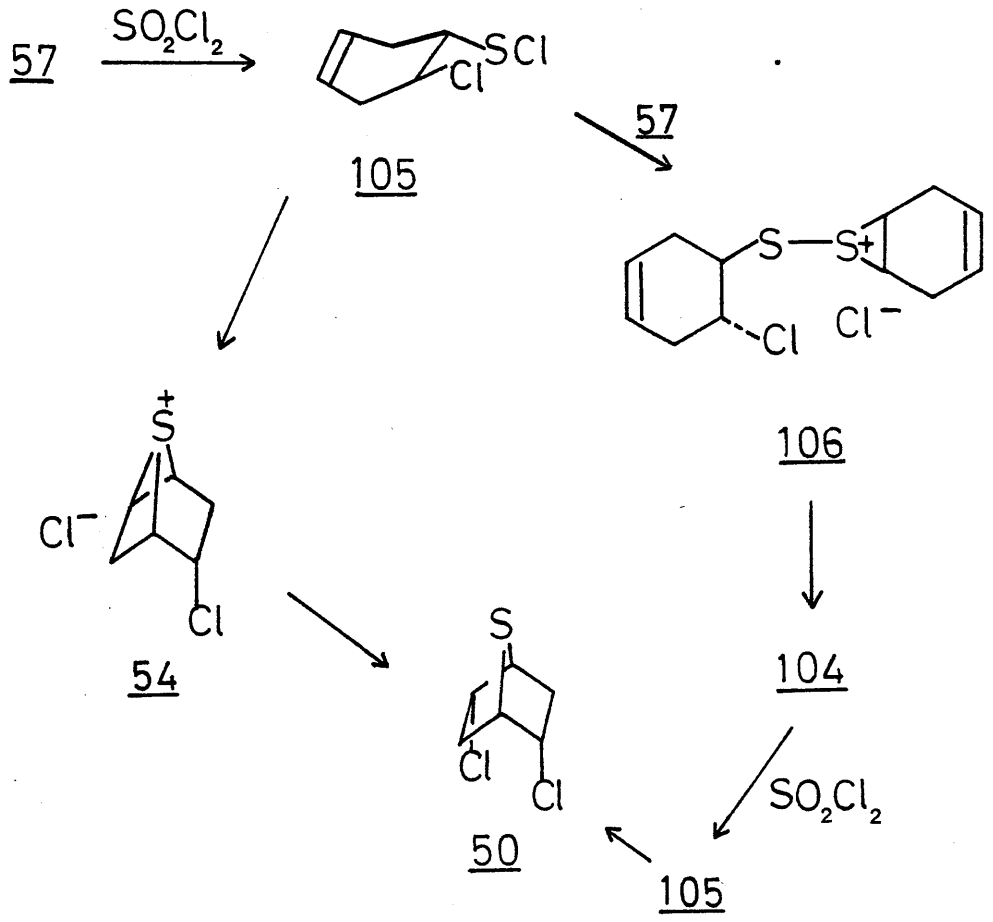


104 X = Cl
108 X = Br



107

Scheme 38



while an olefinic resonance is centred at δ5·66 (4H). In the infra-red spectrum, a double bond stretching absorption appears at 1663 cm^{-1}.

It is considered that reaction of SO_2Cl_2 with 57 initially gives rise to a chloroalkylsulphenyl chloride (105) which can condense intermolecularly with unreacted substrate (57) to form disulphide (104) or cyclise intramolecularly to yield 50 (Scheme 38), depending upon the amount of SO_2Cl_2 present. With a 2:1 ratio of 57 to SO_2Cl_2, 105 reacts with the remaining substrate (57) to give 104, presumably via 106. That 105, in the presence of 57, undergoes intermolecular conversion to 104, rather than intramolecular reaction to 50, indicates that the likely sulphonium intermediate (54) in the latter process is highly strained.

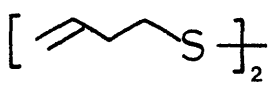
With equimolar quantities of 57 and SO_2Cl_2, formation of 105 is followed by partial conversion to 104 (the latter's presence during the reaction being indicated by analytical t.l.c.) by condensation with episulphide (57), the latter process being relatively fast. However, it is expected that 104 is readily cleaved by the remaining SO_2Cl_2 to regenerate 105 which, in the absence of 57, undergoes intramolecular cyclisation to 50. The absence of the (3.1.1) isomer (107) is readily explained on the basis of a thermodynamically controlled process, in which the more stable (2.2.1) ring compound (50) is formed.

Bromine treatment of 57 gave results which paralleled those of the SO_2Cl_2 reactions. Thus, reaction of 57 with ½mol of bromine gave disulphide (108) in high yield (94%). Its p.m.r. spectrum was similar in appearance to that of 104 and satisfactory microanalytical data and

spectra were obtained. Reaction of 57 with an equimolar amount of bromine gave 2,5-bis-endo-dibromo-7-thiabicyclo (2.2.1) heptane (51) (86%) as a colourless, semi-crystalline solid. Microanalysis and a mass spectrum confirmed a molecular formula of $C_6H_8Br_2S$ and the p.m.r. spectrum closely resembled that of 50. In particular, the value of the coupling constant between the H-C-Br and bridgehead protons indicated the bis-endo orientation of the bromine substituents.

That bromine cleavage of the disulphide (108) occurs was proved by its treatment with bromine which gave 51, quantitatively, supporting the pathway depicted in Scheme 39, for conversion of 57 to 51. For comparison, brominolysis of disulphide (109) has been reported[72] to furnish 3-bromothiacyclopentane (110) rather than the more strained four-membered compound (111).

Additional evidence for the proposed pathway was gained from a low temperature 90MHz p.m.r. study. P.m.r. spectra were recorded continuously after the addition of an 0·5 molar equivalent of bromine to a solution of 57 in deuteriochloroform, at a sample temperature of -40°. New signals appeared at δ5·63, 4·56 and in the H-C-S and methylenic regions. These were attributed to the disulphide (108), by spectral comparisons. After 15 min at -40°, the sample consisted entirely of 108. The sample temperature was gradually raised to 35° over a period of 2 hr 40 min but spectra recorded at 20 min intervals were essentially the same, indicating no further reaction. When the temperature was lowered to -50° and 0·5 molar equivalent of bromine added, complete transformation to 51 took place.



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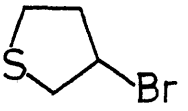

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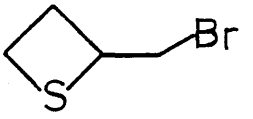
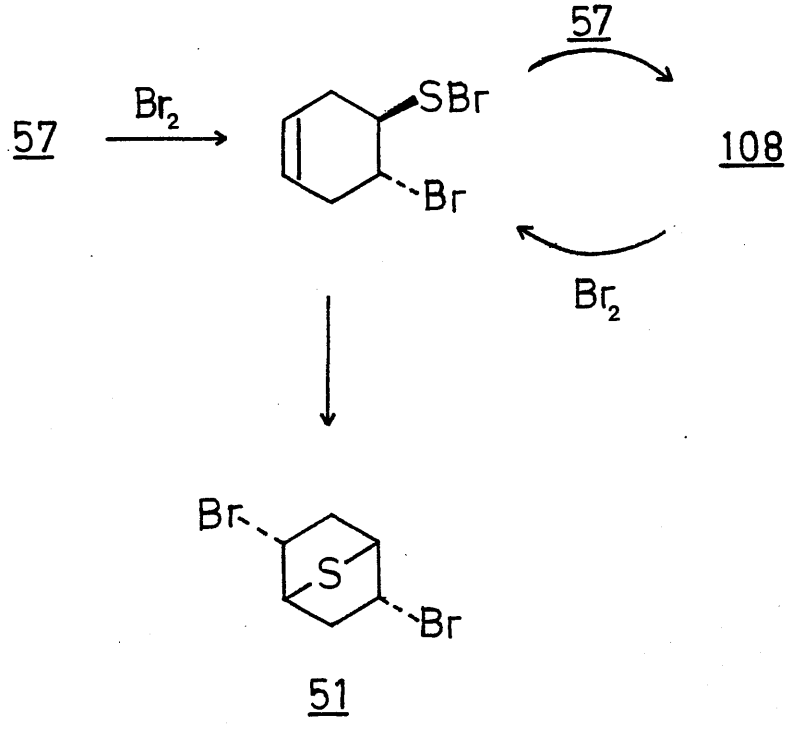


111

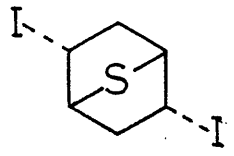
Scheme 39



51

Reaction of 57 with an equimolar quantity of iodine at -35° in the absence of light gave, on solvent removal after workup, a colourless oil, b.p. 90-100° at 0·04mmHg (decomposes). This compound underwent slow decomposition on standing. That this product was the disulphide (112), formed in 80% yield, was evident from its p.m.r. spectrum, which closely resembled those of 104 and 108. Furthermore, a molecular ion was present at m/e 478 in addition to a large daughter ion peak at m/e 351 (M^+-I). A mass measurement of the molecular ion confirmed the molecular formula of $C_{12}H_{16}I_2S_2$. The infra-red spectrum showed double bond absorption at 1658 cm^{-1}.

It was noted that, on addition of an 0·5 molar equivalent of iodine to 57, the purple iodine colour remained, although t.l.c. indicated complete reaction of 57. This observation was taken as evidence that some disproportionation of initially formed sulphenyl iodide (113) occurs, giving 112 and iodine (Scheme 40), in addition to intermolecular reaction of 113 with 57. Prolonged reactions of 57 with equimolar amounts of iodine over a range of temperatures (-35° to +35°) gave, in each case, the same product, viz 112. Thus, reaction of iodine with 57 differs from the previous SO_2Cl_2 and bromine additions in that a bicyclic thioether is not formed. The absence of 52 from the iodine reaction may be due, in part, to the inability[56] of iodine to cleave the disulphide linkage of 112, therefore preventing 113 from being regenerated. Furthermore, it is considered that intramolecular addition of the sulphenyl iodide moiety of 113 to the double bond to form 52 does not occur because of the high strain engendered in forming 56. Instead, facile transformation to 112



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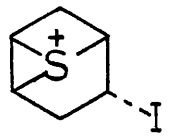

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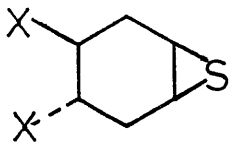
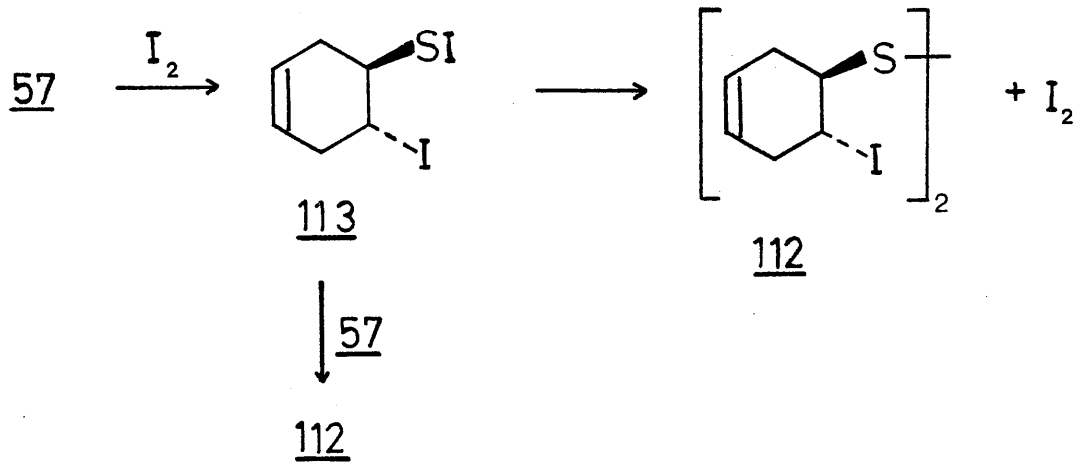
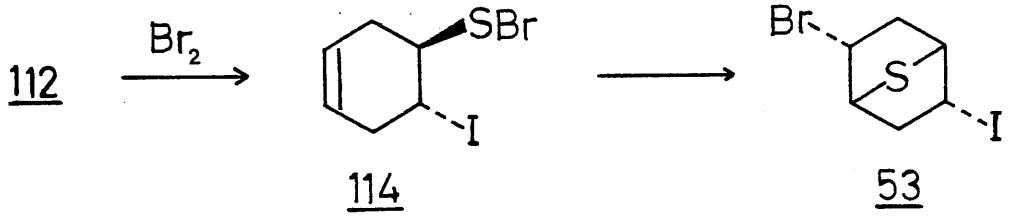


117

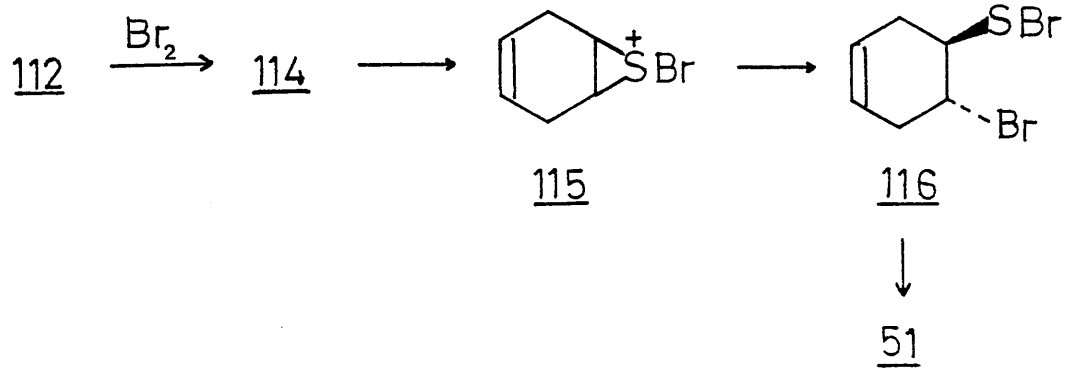
Scheme 40



Scheme 41



Scheme 42



takes place.

A low temperature 90MHz p.m.r. study of the reaction of 57 with iodine supported the above results. Spectra were recorded before and after the addition of ½mol of iodine to a solution of 57 in trichlorofluoromethane at -100°. At this temperature, no reaction took place. The sample temperature was gradually raised to 0° over 50 min, spectra being recorded at intervals. Slow conversion of 57 to disulphide (112) took place. A further ½mol of iodine was added to complete the reaction. The p.m.r. spectrum, recorded at a sample temperature of 10°, was identical to that of 112 and showed no starting material.

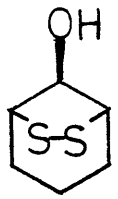
It was expected that treatment of 112 with bromine would readily yield 2-bromo-5-iodo-7-thiabicyclo (2.2.1) heptane (53), via 114 (Scheme 41). To test this hypothesis, a freshly prepared sample of 112 was treated with an equimolar amount of bromine at 0°. Since both t.l.c. and p.m.r. indicated the formation of a complex mixture, a further equivalent of bromine was added. Preparative t.l.c. of the crude reaction mixture gave one major band which contained dibromosulphide (51). 51 may have formed by the sequence shown in Scheme 42. Initially generated sulphenyl bromide (114) may undergo facile conversion to 116 via an easily accessible sulphonium ion (115). In the absence of 57, 116 should spontaneously cyclise to 51.

It is noteworthy in the above discussion that the intermediates of the halogenolyses are disulphides and not dihaloepisulphides of the type 117 (X=Cl, Br, I). These results clearly indicate that halogenolyses of unsaturated episulphides proceed via initial electrophilic ring opening of the thiirane moiety and not by halogenation of the double bond.

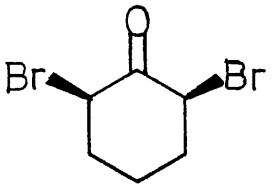
The formation of disulphides in halogenolyses of 57 raised the possibility of creating an intramolecular S-S link by an analogous ring opening process with sulphur dichloride (Scheme 43). Initially formed thiosulphenyl chloride (118), in the absence of unreacted substrate, could undergo intramolecular addition of the S-Cl moiety across the double bond to form either 120 or 121, via 119.

The technique of simultaneous dropwise addition of 57 and an equimolar quantity of SCl_2 (both in equal volumes of methylene chloride) into a large volume of methylene chloride, a procedure employed by Corey,[28] was followed. This had the two-fold advantage of slowing down the overall reaction, by aiding in the dissipation of evolved heat, and reducing the amount of polymeric by-products.

The major product from the reaction crystallised from ethyl acetate-hexane as yellow, microcrystalline prisms, m.p. 133-137°. Microanalysis of this compound corresponded to a molecular formula of $C_6H_8Cl_2S_2$ and the presence of two chlorine atoms was supported by molecular ions at m/e 214, 216 and 218 of intensity 9:6:1. Major fragments ions at m/e 113 and 115 (intensity 3:1), resulting from loss of a chlorine atom and H_2S_2, further supported this formula. The 60MHz p.m.r. spectrum (Figure 6) was in accord with structure 120 (42%). This spectrum discloses four methylene proton resonances. In 121, only two separate methylenic proton absorptions would be expected and the spectrum should resemble that of 50, which shows a simple absorption pattern.



122



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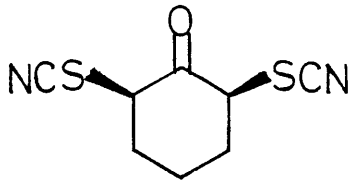
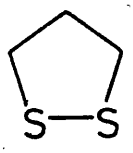


124



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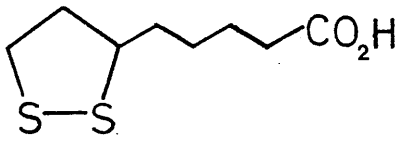
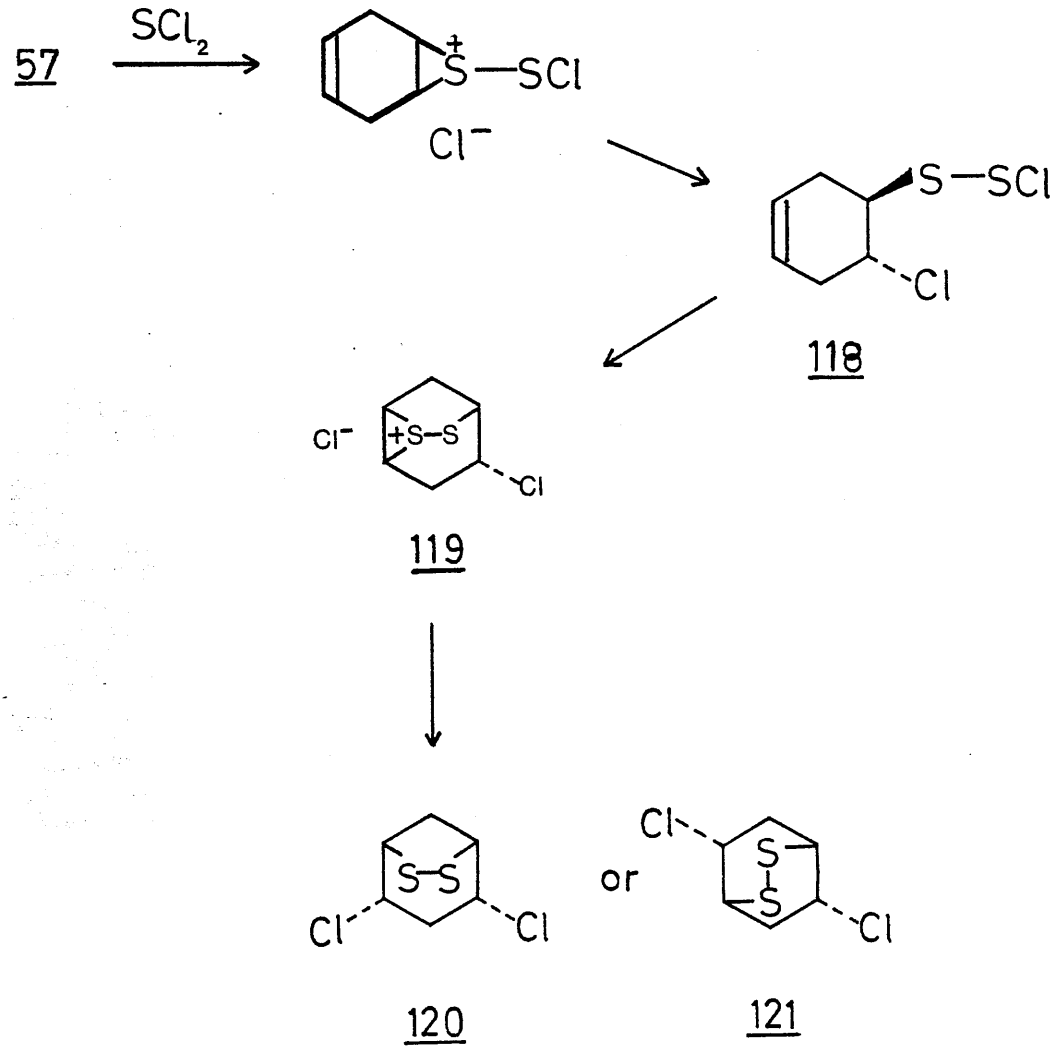


126

Scheme 43



The structure was firmly established as 120 from the noise-decoupled ^{13}C n.m.r. spectrum which showed four distinct carbon resonances, whereas 121 should exhibit only three absorptions. Significantly, the ultraviolet spectrum of the product showed absorptio similar to those reported[84] for 122 (276 (ε23) and 369nm (65)).

The mother liquor of crystallisation of 120 was stripped of solve to leave a yellow oil, shown by p.m.r. to be a mixture of 120 and an alkene. Preparative t.l.c. of this oil furnished a liquid product as the major component, the identity of which could not be established due to the presence of minor impurities. It is possible that this alkene arose by intermolecular reaction of initially formed thiosulphenyl chloride (118). The remainder of the t.l.c. plate contained insignificant amounts of extractable material. Apparently, 120 had decomposed on the silica gel.

The above reaction offers a facile synthesis of simple bicyclic disulphides which are difficult to prepare by other routes. An important feature of the ring system of 120 is that the dihedral angle between the two C-S bonds is, of necessity, very close to 0^{o}. Wilson[84] pointed out that the nature of a disulphide linkage is significantly altered by changes in the dihedral angle. Reduction of this angle increases the interaction between the two lone pairs of 3p non-bonding electrons on the sulphur atoms. Thus, disulphides with small dihedral angles absorb light at longer wavelengths and have lower ionisation potentials than do disulphides with larger dihedral angles. The same author described the synthesis of 122 in only 35% yield from 123 via

124. Clearly, if 57 could be obtained in high yield then the SCl_2 reaction with 57 would represent an improved method for preparing such disulphides.

In contrast to the parent, 1,2-dithiolane (125), 120 is quite stable and does not seem to polymerise, even on storage for several months. This stability is remarkable because the planar 1,2dithiolanes embody C-S dihedral angles considerably distorted from the preferred 90^{o} (vide supra).

The 2,3-dithiabicyclo (3.2.1) octane system has been prepared in certain steroid molecules[85] and the ease of cleavage of the S-S bond in the 1,2-dithiolane structure, resulting from the high ring strain, is extremely important because of the role of lipoic acid (126) as a growth promoting agent.[86]

Bromine addition to endo-2,3-epithio-norborn-5-ene (3)

It is surprising that reaction of 3 with chlorine, studied by Lautenschlaeger,[18] gives 1 and not, what appears to be, the thermodynamically more stable isomer (100). To determine if a change in the nature of the halogen would affect the course of reaction, 3 was treated with an equimolar quantity of bromine. Sublimation of the crude product produced colourless crystals, m.p. $79-82^{o}$, identified from spectroscopic evidence as 3,5-bis-exo-dibromo-8-thiatricyclo ($2.2.1.1^{2,6}$) octane (2) (lit.[20] m.p. $81-83^{o}$). Mass spectral ions at

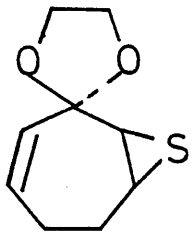
m/e 282, 284 and 286 (M^+) (intensity 1:2:1) indicated the presence of two bromine atoms and its p.m.r. and infra-red spectra were similar to those of dichloride (1) (See Part 1).

Thus, reaction of 3 with bromine parallels its reaction with chlorine, in that the apparently less stable isomer (2) is again formed. The criterion of thermodynamic stability of product, in the determinatio of the course of the reaction, cannot apply here. Rather, the stability of the intermediate is considered to be of critical importance in this reaction. It is proposed that sulphenyl bromide (127) is initially formed which rearranges to 2 via sulphonium ion (128) rather than a less stable ion (129) (Scheme 44). 130, unlike 2, cannot readily be formed from 128.

Electrophilic additions to 44

Reaction of 44 with an equimolar quantity of sulphuryl chloride gave, on recrystallisation of the crude product, colourless needles, m.p. 113-115°. This material was clearly identified as dichloride (35) (83% yield), by direct spectral comparison with authentic 35 (See Part 1 In an attempt to isolate a possible disulphide species, 44 was treated with ½mol of SO_2Cl_2. P.m.r. and mass spectroscopic analysis of the reaction mixture indicated the presence only of starting material and 35. No disulphide was detected.

To account for the absence of disulphides it is prooosed that



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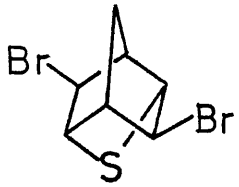

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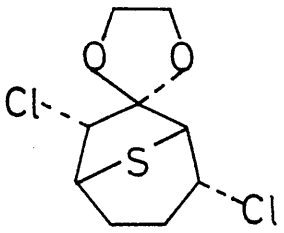

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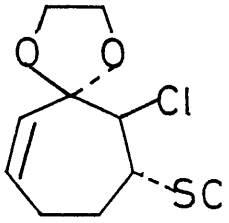
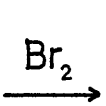
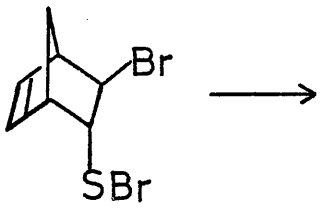


47

Scheme 44

3





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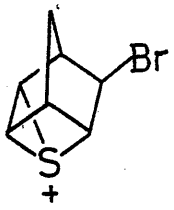

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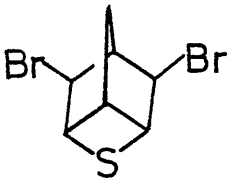
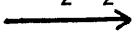
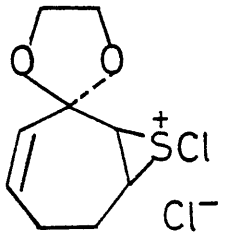


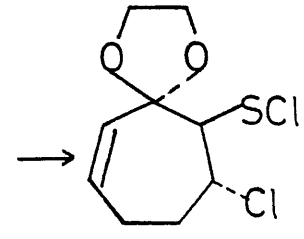
2

Scheme 45

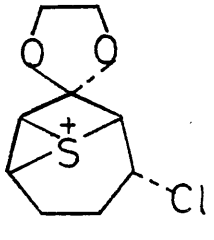
44







48



131

35

initially formed sulphenyl chloride (48) undergoes facile intramolecular cyclisation, via 131, to 35 (Scheme 45), since intermolecular attack of 48 by unreacted substrate (44) is severely hindered. Formation of 48, rather than the alternative sulphenyl chloride (47) is assumed, since 47 would yield a mixture of 35 and 40 (See Part 1). 48, on the other hand, cyclises to 35 rather than the thermodynamically less stable isomer (49).

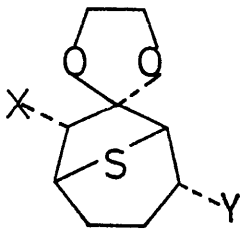
Reaction of 44 with an equimolar quantity of bromine furnished an oil, whose p.m.r. spectrum indicated the presence of a mixture of 36 and 41, in the approximate ratio 1:2 (from p.m.r. integration). This was supported by a mass spectrum, which showed a molecular ion triplet at m/e 342, 344 and 346 of intensity 1:2:1. Partial purification was achieved by crystallisation of the mixture from ethyl acetate. 41 precipitated as colourless prisms, m.p. 106-108° (35% yield), and was identified from the following evidence. Microanalysis was consistent with a molecular formula of $C_9H_{12}O_2Br_2S$, as was the mass spectrum. The infra-red spectrum had the same general appearance as that of 40, which was markedly different from the infra-red spectrum of 35. The p.m.r. spectrum also resembled that of 40; in particular, it showed two well-separated two-proton methylenic resonances at δ1·66-2·42 and 2·53-3·14 corresponding to the C-6 and C-7 hydrogens which are syn and anti respectively to the C-S bonds. Furthermore, a two-proton doublet (J=2Hz) at δ4·75 is consistent with structure 41 and not 36.

Distillation of the remaining mixture failed to separate the

isomers and further purification was not attempted in view of their expected susceptibility to isomerisation and hydrolysis (See Part 1). Formation of both 36 and 41 in the reaction indicates the intermediacy of 132 (Scheme 46). It is likely that 132 and 133 are initially generated, the former being predominant and giving rise to 36 and 41. 133 would undergo cyclisation to 36 only.

Recent work by Haufe[87] on the transannular reaction of cyclohepta-1,4-diene with N-bromosuccinimide in the presence of water, which gives low yields of 134 and 135, lends indirect support for the mechanism shown in Scheme 46.

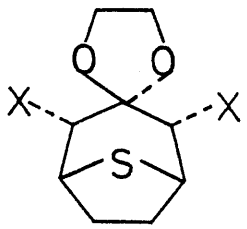
The absence of disulphides as intermediates in the halogenolyses of 44 was supported by the reaction of 44 with iodine (1·1 molar equivalent) which gave non-olefinic material, indicating intramolecular cyclisation of initially formed sulphenyl iodide (136). The p.m.r. spectrum of the crude reaction mixture resembled the spectrum of a mixture of 36 and 41. Thus, it was deduced that 37 and 42 had formed. However, passage through a column of alumina gave only one identifiable compound, obtained as colourless prisms. This compound, which had a wide melting point range, gradually became yellow on standing. Its mass spectrum had a parent ion at m/e 328 and major fragment ions at 311 (M^+-OH) and 201 (M^+-I). A strong hydroxyl stretching band was present in the infra-red spectrum at 3572 cm^{-1} and the presence of this group was confirmed by a deuterium oxide exchangeable O<u>H</u> doublet (1H, J=10Hz) at δ2·89 in the p.m.r. spectrum. <u>H</u>-C-O and <u>H</u>-C-I resonances were present at δ3·84 (m, 1H) and 5·03 (d, J=5Hz, 1H) and



37 X=Y=I

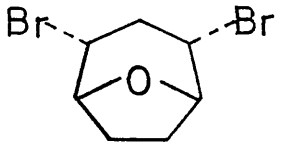
38 X=Cl, Y=OH

39 X=I , Y=OH

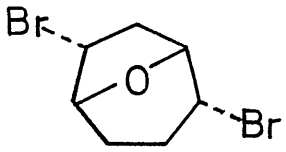


40 X=Cl

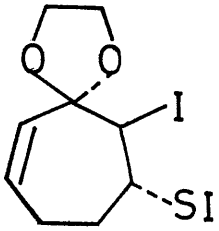
42 X=I



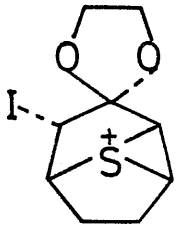
134



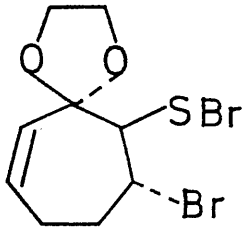
135



136

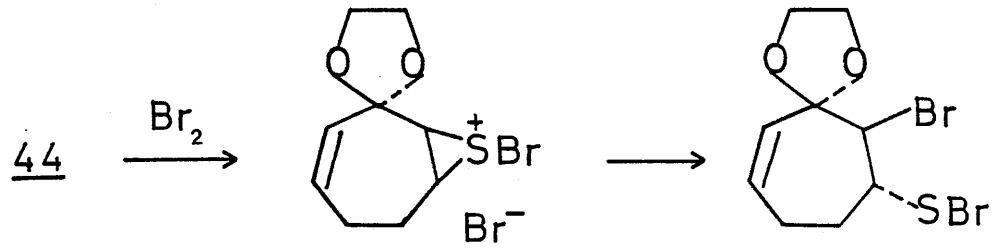


137

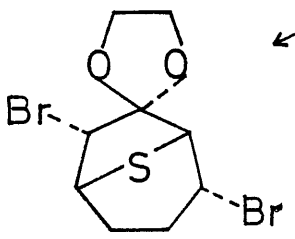


133

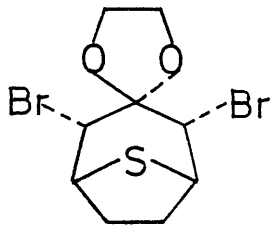
Scheme 46



132



36

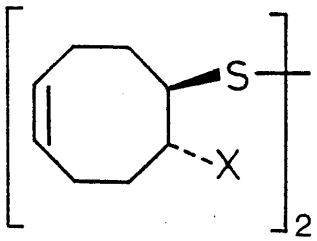


41

the appearance of the spectrum was similar to that of 38. This compound was assigned as 39, the iodine analogue of 38. That 39 had arisen from hydrolysis and isomerisation of the reaction product (s), on passage through the column, was evident by the absence of absorption signals of 39 from the p.m.r. spectrum of unpurified reaction mixture. Transformation of 37 and 42 to 39 likely occurs *via* a readily accessible sulphonium ion (137). Further material was collected from the column but gave rise to broad infra-red and p.m.r. absorptions and was not identified.

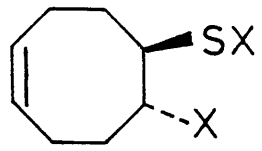
Electrophilic additions to 11

Chlorine addition to 11 gave dichloride (8), in accord with Lautenschlaeger's[30] result. To test for the possible intermediacy of disulphides, a low temperature p.m.r. study of this reaction was undertaken. 90MHz p.m.r. spectra were recorded after the addition of an excess of chlorine in carbon tetrachloride solution to a sample tube containing 11 in the same solvent at -30°. New absorptions at δ4·71 (H-C-Cl), 2·82 (H-C-S) and in the methylenic region were attributed to formation of 8. The sample was warmed to -20° and, when the spectrum was re-run, complete reaction to 8 had taken place. Thus, the reaction is similar to the halogenolyses of 44, in that disulphide species do not form. The absence of disulphide (138) is taken to imply that the initially produced sulphenyl chloride (139) undergoes rapid transformation to 8, *via* 94 (See Scheme 32), formation of the latter being facilitated by the conformational flexibility of the eight-membered ring.



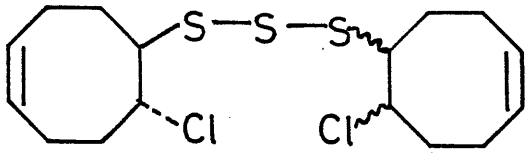
138 X = Cl

140 X = I



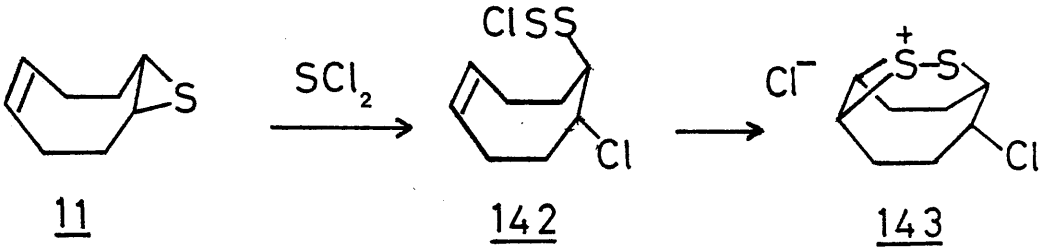
139 X = Cl

141 X = I

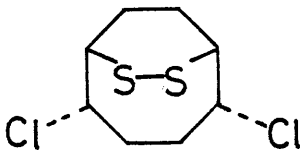


146

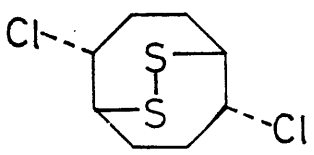
Scheme 47



11 142 143



144



145

Treatment of 11 with an equimolar quantity of bromine in methylene chloride at -20° gave, on recrystallisation from heptane-benzene, colourless prisms of 2,6-dibromo-9-thiabicyclo (3.3.1) nonane (9), m.p. 133-135° (lit.[19] m.p. 134·5-135·5°), in a yield of 85%. The spectra of the product were identical with those of an authentic sample of 9, prepared from 8 (See Part 1). A low temperature (-50°) 90MHz p.m.r. study of the reaction failed to show the presence of intermediates, the only observable resonances being associated with either 9 or 11. Thus, brominolysis of 11, like chlorinolysis, does not involve disulphide species.

Reaction of 11 with an equimolar amount of iodine furnished colourless prisms. This product was identified as diiodoalkyl sulphide (10), m.p. 144-146° (lit.[19] m.p. 145-146°), by spectral comparisons. As with the previous halogenolyses of 11, a low temperature (-60°) 90MHz study of this reaction failed to show any intermediate species. Formation of 10 is good evidence for the non-intermediacy of disulphides in the halogenolyses of the eight-membered compounds since 140 cannot be cleaved by iodine to form sulphenyl iodide (141) (cf. six-membered case).

Prompted by the isolation of 120 from the reaction of 57 with sulphur dichloride, a similar reaction was carried out using 11. It was expected that electrophilic ring opening would take place to generate 142, which would undergo facile intramolecular cyclisation to 144 or 145 via 143 (Scheme 47).

However, the p.m.r. spectrum of the crude product, a viscous oil, resembled that of 8. Distillation of this oil gave a colourless semi-solid which had a wide melting point range, m.p. 85-97°. Infra-red and mass spectroscopy confirmed the identity of the product as 8. It was noteworthy that no mass spectral peaks appeared above the parent ion triplet for 8, suggesting the absence of disulphides (144 and 145). However, from the low yield of 8 obtained, partly due to losses encountered in the distillation, bridged disulphides could possibly have been generated.

The formation of 8 in the above reaction may be rationalised if initially formed 142 condenses with unreacted substrate to give a tri-sulphide (146). Reaction of 146 with SCl_2 may generate 139, which can form 8 (vide supra) as the thermodynamically favoured product. It is likely that polymerisation occurs to a certain extent and this would account for the low recovery from the distillation.

E X P E R I M E N T A L

Preparation of ISCN[5,31]

To an ice-cold solution of lead nitrate (45g, 0·136mol) in water (100ml) was added a cold solution of sodium thiocyanate (25g, 0·309mol) in water (100ml). Lead thiocyanate, which precipitated as a white powder, was collected by filtration, washed free of nitrates with water, and then dried in vacuum over phosphorous pentoxide in the dark. The dry solid (40g, 0·124mol) was stirred in dry CCl_4 (200ml) to form a suspension and cooled to 5-10°. A solution of Br_2 (18g, 0·113mol) in the same solvent (180ml) was slowly added with vigorous stirring. The suspended solids were allowed to settle and the thiocyanogen solution decanted into an ice-cooled vigorously stirred suspension of I_2(34g, 0·134mol) in dry CCl_4 (200ml). The cooled mixture was stirred in the absence of light for 15 min before use.

Reactions of ISCN with dienes

(a) Preparation of 57

Cyclohexa-1,4-diene (18·1g, 0·226mol) in CCl_4 (100ml) was added dropwise to the stirred ISCN solution (prepared above) at 5-10°. After stirring for 2 hr at 5-10°, a solution of KOH (25·2g, 0·45mol) in methanol (200ml) was added and the mixture vigorously stirred at 25° for 3 hr. The mixture was poured on to ice, washed with aqueous sodium thiosulphate, water and dried. Removal of solvent afforded a yellow oil (16·1g) which was chromatographed over alumina (240g).

Elution with ether-petroleum spirit (1:19) yielded 57 as a colourless oil (6·3g, 56mmol, 25%), b.p. 71-73°, 12mmHg (lit.[13] b.p. 69°, 10mmHg); $\nu_{max}^{CCl_4}$ 3042, 3015, 2978, 2924, 2835, 1663, 1431, 1384, 1211, 1086, 902, 671 and 591 cm^{-1}; δ ($CDCl_3$) 2·50-2·93 (m, 4H, $\underline{CH}_2$), 3·13-3·37 (m, 2H, H-C-S) and 5·34-5·60 (m, 2H, olefinic H); m/e 112(M^+), 80, 79, 78, 77, 51 and 39.

(b) Preparation of 11

The above procedure was repeated using cyclocta-1,5-diene (24·4g, 0·226mol) as substrate. Removal of solvent afforded a yellow oil (18g). Purification as above yielded 11 as a colourless oil (5·2g, 18%) (lit.[5] 26%), identical with the previously prepared 11 (See Part 1). Unreacted alkene (3g, 21mmol) was also obtained from the column.

Chlorinolyses of 57

(i) Reaction of 57 with Cl_2

Chlorine gas, dried by passage through calcium chloride, was bubbled through a solution of 57 (85mg, 0·759mmol) in CH_2Cl_2 (15ml) at -40° for 1 hr. The solution was allowed to warm to room temperature, washed with aq.$Na_2S_2O_3$, water and dried. Solvent removal gave a colourless liquid (111mg) whose p.m.r. and mass spectra indicated a mixture of 2,5-dichloro-7-thiabicyclo (2.2.1) heptane (50) and sulphoxide

(103) in the approximate ratio 2:5 (p.m.r. integration). m/e (202, 200 and 198) (M^+, 103) and (186, 184 and 182).

Preparative t.l.c. (ether-petroleum spirit, 1:1) gave one major band which furnished slightly yellow prisms of 103 (32mg, 21%), m.p. 95-115°; $\delta(CDCl_3)$ 2·40 (m, 2H, CH_2), 3·59 (m, 2H, H-C-SO), 4·04-4·50 (m, 1H, H-C-Cl) and 4·73-5·24 (m, 1H, H-C-Cl). Minor bands, on extraction gave insignificant amounts of material. 50 was not recovered from the plate.

(ii) Reaction of 57 with SO_2Cl_2

2,5-dichloro-7-thiabicyclo (2.2.1) heptane (50)

A solution of SO_2Cl_2 (162mg, 1·20mmol) in CH_2Cl_2 (5ml) was added dropwise to a stirred solution of 57 (135mg, 1·20mmol) in CH_2Cl_2 (15ml) at 0°. Analytical t.l.c. (ether-petroleum spirit, 1:49) indicated complete reaction ater 30 min. The solution was allowed to warm to room temperature and solvent removed to give 50 as a viscous, colourless oil which solidified on standing (209mg, 1·14mmol, 94%), m.p. 89-92° (lit.[28] m.p. 93-94°, sealed tube). Infra-red, p.m.r and mass spectra were identical with those of an authentic sample of 50 (See Part 1).

di-(2-chlorocyclohex-4-enyl) disulphide (104)

SO_2Cl_2 (81mg, 0·60mmol) in CH_2Cl_2 (5ml) was added to 57 (135mg, 1·20mmol) in CH_2Cl_2 (15ml) as above. After 1 hr, solvent was removed to give disulphide (104) as a colourless liquid (173mg, 97%); b.p. 95-100°, 0·03mmHg. Anal. calc. for $C_{12}H_{16}Cl_2S_2$: C 48·82, H 5·46%. Found: C 48·83, H 5·28%; $\nu_{max}^{CCl_4}$ 3040, 2938, 2900, 1663, 1431, 1220, 952, 910, 685 and 664 cm^{-1}; $\delta(CDCl_3)$ 2·00-3·50 (br env, 10H, CH_2 and H-C-S), 4·17-4·60 (m, 2H, H-C-Cl) and 5·66 (m, 4H, olefinic H); m/e (298, 296 and 294) (M^+), (184, 182 and 180), 161, 159, 149, 147, 115 and 112.

Brominolyses of 57

2,5-dibromo-7-thiabicyclo (2.2.1) heptane (51)

A solution of Br_2 (110mg, 0·69mmol) in CH_2Cl_2 (5ml) was added dropwise to a stirred solution of 57 (77mg, 0·69mmol) in CH_2Cl_2 (10ml) at 0°. Removal of solvent, after 1 hr, gave waxy dibromide (51) (188mg, 100%) which sublimed (105°, 46mmHg) as a colourless, semi-crystalline solid (162mg, 86%), m.p. 60-62°. Anal. calc. for $C_6H_8Br_2S$: C 26·49, H 2·96%. Found: C 26·38, H 2·94%; $\nu_{max}^{CCl_4}$ 2992, 2950, 1443, 1313, 1240, 1158, 938, 909, 656, 604 and 585 cm^{-1}; $\delta(CDCl_3)$ 2·33-2·80 (m, 4H, CH_2), 3·63-3·83 (m, 2H, H-C-S) and 4·30-4·72 (m, 2H, H-C-Br); m/e (274, 272 and 270) (M^+), (193 and 191) (M^+-Br), (159 and 157) (M^+-H_2SBr), 147,

145 and 111 (M^+-HBr_2).

di (2-bromocyclohex-4-enyl) disulphide (108)

The procedure above was repeated using 57 (150mg, 1·34mmol) in CH_2Cl_2 (15ml) and Br_2 (107mg, 0·67mmol) in CH_2Cl_2(3ml) to give disulphide (108) as a colourless liquid (241mg, 94%); b.p. 125-130°, 0·15mmHg. Anal. calc. for $C_{12}H_{16}Br_2S_2$: C 37·54, H 4·20%. Found: C 37·40, H 4·17%; $\nu_{max}^{CCl_4}$ 3042, 2936, 2895, 1661, 1428, 1420, 1323, 1213, 1167, 1044, 910, 882, 686 and 660 cm^{-1}; δ($CDCl_3$) 2·00-3·60 (br env, 10H, $C\underline{H}_2$ and $\underline{H}$-C-S), 4·37-4·77 (m, 2H, $\underline{H}$-C-Br) and 5·63 (m, 4H, olefinic $\underline{H}$); m/e (386, 384, 382) (M^+), (306, 304 and 302), (225 and 223), 193, 191, 161, 159 and 112.

Iodinolyses of 57

di (2-iodocyclohex-4-enyl) disulphide (112)

A solution of I_2 (353mg, 1·39mmol) in CH_2Cl_2 (10ml) was added dropwise to a stirred solution of 57 (156mg, 1·39mmol) in CH_2Cl_2 (25ml) at -35°, in the absence of light. After 15 min, the purple solution was decolourised with aq. $Na_2S_2O_3$, washed with water and dried. Solvent removal gave disulphide (112) as a colourless liquid (312mg, 90%); b.p. 90-100°, 0·04mmHg (decomposes). Mass calc. for $C_{12}H_{16}I_2S_2$: 477·87865. Found: 477·87815; $\nu_{max}^{CCl_4}$ 3035, 2922, 2888, 2836, 1658,

1430, 1215 and 1208 cm^{-1}; $\delta(CDCl_3)$ 2·03-3·60 (br env, 10H, $\underline{CH}_2$ and $\underline{H}$-C-S), 4·50-4·95 (m, 2H, $\underline{H}$-C-I) and 5·64 (m, 4H, olefinic $\underline{H}$); m/e 478 (M^+), 398 ($M^+-C_6H_8$), 351 (M^+-I), 271, 254, 239, 207, 127 and 79. Prolonged reactions of equimolar amounts of 57 and I_2, over a range of temperatures (-35° to 25°), gave disulphide (112) as the only product in each case.

Brominolysis of 112

I_2 (196mg, 0·77mmol) in CH_2Cl_2 (20ml) was added dropwise to a stirred solution of 57 (172mg, 1·53mmol) in CH_2Cl_2 (20ml) at 0°, in the absence of light. After 15 min, a solution of Br_2 (123mg, 0·77mmol) in CH_2Cl_2 (5ml) was added at 0°. Solvent was removed after 15 min to give a dark-red oil, whose p.m.r. spectrum ($CDCl_3$) indicated the presence of a complex mixture. On removal of $CDCl_3$, the oil was dissolved in CH_2Cl_2 (20ml), the solution stirred at 0° and Br_2 (123mg, 0·77mol) in CH_2Cl_2 (5ml) added. After 15 min, the solution was washed with aq. $Na_2S_2O_3$, water and dried. Removal of solvent afforded a viscous, yellow oil (460mg)whose p.m.r. spectrum was similar to that of 51. Preparative t.l.c. (ether-petroleum spirit, 1:49) of 100mg of this oil gave one major band, which furnished 51 (51mg), identified from its p.m.r. and mass spectra. Extraction of minor bands gave insignificant amounts of material.

Low temperature p.m.r. study of iodinolysis of 57

I_2 (44mg, 0·17mmol) was added to a p.m.r. tube containing a solution of 57 (39mg, 0·35mmol) in $CFCl_3$ (0·5ml) at -100° (liquid N_2). The tube was immediately inserted into the instrument probe at -100° and 90MHz spectra continuously recorded. At this temperature no reaction occurred. The sample was warmed to 0° over 50 min, at which temperature a new olefinic signal appeared at δ 5·64(m), accompanied by new absorptions in H-C-I, H-C-S and methylenic regions. These signals continued to increase in intensity at the expense of substrate. After a total of 2 hr 30 min, a further amount of I_2 (44mg), was added at 10°. The resulting spectrum was identical to that of disulphide (112), no starting material being present.

Low temperature p.m.r. study of brominolysis of 57

Br_2 (39mg, 0·25mmol) was added to a p.m.r. tube containing 57 (54·7mg, 0·49mmol) in $CDCl_3$ (0·5ml) at -40° (acetone/dry ice). 90MHz p.m.r. spectra, at this temperature, indicated reaction occurring by the appearance of new signals at δ 5·63 (olefinic H), 4·56 (H-C-Br) and in the H-C-S and methylenic regions. After 15 min at -40°, the peaks due to starting material had completely disappeared, having been replaced by the spectrum of 108 (*vide supra*). The sample was warmed to 35° over 2 hr 40 min, during which spectra run at 20 min intervals remained essentially unchanged. The sample temperature was lowered to -50° and further Br_2 (39mg, 0·25mmol) added. A spectrum recorded immediately

was that of dibromosulphide (51), remaining unchanged on warming to 20°.

Reaction of 57 with SCl_2

57 (56mg, 0·5mmol) and SCl_2 (51·5mg, 0·5mmol), each dissolved in CH_2Cl_2 (25ml), were simultaneously added dropwise, over 30 min, to CH_2Cl_2 (200ml) which was stirred at -50°. The solution was maintained at this temperature for 15min after the additions, allowed to warm to room temperature, washed with aq.$NaHCO_3$, brine, water and dried. Removal of solvent gave a yellow semi-solid (105mg), whose p.m.r. spectrum was complex. Analytical t.l.c. (ether-petroleum spirit, 1:24) showed two spots (Rf values 0·1 and 0·6). Recrystallisation from ethyl acetate-hexane furnished yellow, microcrystalline prisms of 120 (45mg, 42%), m.p. 133-137°. Anal. calc. for $C_6H_8Cl_2S_2$: C 33·50, H 3·75%. Found: C 33·74, H 3·50%; ν_{max}^{KBr} 2966, 2956, 1443, 1417, 1347, 1320, 1246, 1021, 949, 903, 854, 817 and 609 cm^{-1}; $\delta(CDCl_3)$ 1·83-2·57 (overlapping d of m, 2H, H-C-(6) and H-C(8)), 2·87-3·40 (d of t, J=16 and 4Hz, 1H, H-C-(8)), 3·71 -4·06 (d of m, J=13Hz, 1H, H-C-(6)) and 4·10-4·43 (m, 4H, H-C-S and H-C-Cl); m/e (218, 216 and 214) (M^+), (181 and 179), (115 and 113), 80, 79 and 77; λ_{max}^{MeOH} 361 (ε66) and 270 nm (33).

The mother liquor was stripped of solvent to leave a viscous, yellow oil which was a mixture of 120 and an alkene (from p.m.r.). Preparative t.l.c. (ether-petroleum spirit, 3:2) gave one major band, which yielded a colourless oil (14mg); $\nu_{max}^{CCl_4}$ 3620, 3570, 2934, 1421,

1374, 1215, 1172, 947 and 683 cm^{-1}; $\delta(CDCl_3)$ 1·20-3·30 (br env), 4·30-4·62 (m) and 5·68 (s, olefinic H); m/e (268 and 266), 210, 208, 147 and 112. This oil could not be identified from these spectra due to the presence of minor impurities. Further purification was not attempted. Extraction of minor bands failed to give any significant amount of material.

Brominolysis of 3

Br_2 (160mg, 1mmol) in CH_2Cl_2 (10ml) was added dropwise to a stirred solution of 3 (124mg, 1mmol) in CH_2Cl_2 (15ml) at 0°. After 2 hr, the solution was washed with aq. $Na_2S_2O_3$, water and dried. Removal of solvent afforded 2 (270mg) as a crystalline solid which sublimed at 30°, 0·05mmHg ("cold finger") to furnish colourless crystals (221mg, 75%), m.p. 78-82° (lit.[20] m.p. 81-83°); $\nu_{max}^{CCl_4}$ 2997, 1453, 1288, 1277, 1159, 1094, 909, 859, 715, 635 and 620 cm^{-1}; $\delta(CDCl_3)$ 2·26 (s, 2H, CH_2), 3·36 (s, 2H, H-C-S), 3·46 (d, J=1Hz, 1H, H-C(4)), 4·00 (m, 1H, H-C(1)) and 4·72 (s, 2H, H-C-Br); m/e (286, 284 and 282) (M^+), (205 and 203) (M^+-Br), 124, 123, 91 and 83.

Chlorinolyses of 44

SO_2Cl_2 (25·6mg, 0·19mmol) in CH_2Cl_2 (5ml) was added dropwise to a stirred solution of 44 (32·5mg, 0·17mmol) in CH_2Cl_2 (10ml) at 0°. Solvent was removed after 2 hr to leave a crystalline solid (41·4mg) which recrystallised from ethyl acetate as colourless needles of 35

(37·3mg, 83%), m.p. 113-115°. Its spectra were identical to those of an authentic sample of 35 (See Part 1). The above procedure was repeated using half the amount of SO_2Cl_2. Removal of solvent gave a semi-solid (39mg), shown to consist of a mixture of starting material and 35 from p.m.r. and mass spectroscopy. The absence of mass spectral ions above m/e 258 indicated no disulphide present and purification was thus not attempted.

Brominolysis of 44

Br_2 (35·2mg, 0·22mmol) in CH_2Cl_2 (5ml) was added to 44 (36·8mg, 0·2mmol) in CH_2Cl_2 (10ml) at 0°. After 2 hr, the solution was washed with aq. $Na_2S_2O_3$, water and dried. Removal of CH_2Cl_2 afforded a viscous, yellow oil (70mg), shown to consist of a mixture of 36 and 41 (1:2) from its p.m.r. spectrum. Crystallisation from ethyl acetate furnished 41 as colourless prisms (26mg, 35%), m.p. 106-108°. Anal. calc. for $C_9H_{12}O_2Br_2S$: C 31·42, H 3·52%. Found: C 31·63, H 3·26%; ν_{max}^{KBr} 2962, 2908, 1460, 1331, 1199, 1140, 1075, 1056, 1042, 1000, 970, 953, 809, 710, 619 and 556 cm^{-1}; δ($CDCl_3$) 1·66-2·42 (br env, 2H, C(6,7) $\underline{H}_2$), 2·53-3·14 (m, 2H, C(6,7) $\underline{H}_2'$), 3·88 (m, 2H, C(1,5) $\underline{H}_2$), 4·03-4·54 (m, 4H, dioxolane $C\underline{H}_2$) and 4·75 (d, J=2Hz, 2H, C(2,4) $\underline{H}_2$); m/e (346, 344 and 342) (M^+), (313, 311 and 309), (265 and 263), 183, 151 and 99. Removal of ethyl acetate from the mother liquor and distillation of the remaining oil (44mg) at 120-130°, 0·3mmHg gave a colourless liquid (28mg) which was still a mixture. A mass spectrum of the distillate was identical to that of 41. No further purification

was attempted.

Iodinolysis of 44

I_2 (81·3mg, 0·32mmol) in CH_2Cl_2 (15ml) was added to 44 (53·2mg, 0·29mmol) in CH_2Cl_2 (15ml) at -50°, under nitrogen, in the absence of light. After 6 hr, the solution was washed with aq. sodium metabisulphite, water and dried. Removal of CH_2Cl_2 afforded a viscous yellow oil (90mg) which p.m.r. indicated to consist of a mixture of 37 and 42, by spectral comparisons. Passage through a column of alumina (6g) with petroleum spirit as eluent gave a yellow oil (12mg) which exhibited broad absorptions in its p.m.r. and infra-red spectra and was not further analysed. Elution with ether-petroleum spirit (1:1) gave 39 as colourless prisms (20mg), m.p. 75-88°; $\nu_{max}^{CCl_4}$ 3372, 2960, 2900, 1438, 1400, 1299, 1215, 1165, 1110, 1040, 984 and 625 cm^{-1}; $\delta(CDCl_3)$ 1·80-2·51 (br env, 4H, C(3,4) $\underline{H}_2$), 2·89 (d, J=10Hz, 1H, O$\underline{H}$), 3·13 (m, 1H, C(1) $\underline{H}$), 3·33 (m, 1H, C(5) $\underline{H}$), 3·84 (m, J=10 and 3Hz, 1H, C(2) $\underline{H}$), 4·07 (m, 4H, dioxolane, C$\underline{H}_2$) and 5·03 (d, J=5Hz, 1H, C(6) $\underline{H}$); m/e 328 (M^+), 311 (M^+-OH), 201 (M^+-I), 183, 157 and 125.

Chlorinolysis of 11[30]

Dry chlorine gas was bubbled through a stirred solution of 11 (104mg, 0·743mmol) in CH_2Cl_2 (40ml) at 0-5° for 1 hr. The solution was allowed to warm to room temperature, allowing excess chlorine to escape and washed with aq. $Na_2S_2O_3$, water and dried. Removal of

CH_2Cl_2 gave yellow crystals (150mg) which recrystallised from benzene to furnish 8 (130mg, 83%), m.p. 99-101° (lit.[30] m.p. 100-101°); ν_{max}^{KBr} 2933, 1485, 1159, 949 and 689 cm^{-1}; $\delta(CDCl_3)$ 2·09-2·65 (br env, 8H, CH_2), 2·82 (m, 2H, H-C-S) and 4·71 (m, 2H, H-C-Cl).

Brominolysis of 11

Br_2 (114mg, 0·714mmol) in CH_2Cl_2 (5ml) was added dropwise to a stirred solution of 11 (100mg, 0·71mmol) in CH_2Cl_2 (5ml) at -20°. After 30 min, the solution was washed with aq. $Na_2S_2O_3$, water and dried. Removal of solvent afforded a crystalline solid (204mg) which recrystallised from heptane-benzene as colourless prisms of 9 (182mg, 85%), m.p. 133-135° (lit.[19] m.p. 134·5-135·5°). Its infra-red, p.m.r. and mass spectra were identical with those of an authentic sample of 9 (See Part 1).

Iodinolysis of 11

The procedure above was repeated using I_2 (54·3mg, 0·214mmol) in CH_2Cl_2 and 11 (30mg, 0·214mmol) in CH_2Cl_2 (5ml) to furnish a yellow semi-crystalline solid (176mg). Recrystallisation from heptane-benzene gave colourless prisms of 10 (61mg, 72%), m.p. 144-146° (lit.[19] m.p. 145-146°), with identical spectra to those of an authentic sample of 10 (See Part 1).

Low temperature p.m.r. study of halogenolyses of 11

(a) Chlorinolysis

To a p.m.r. tube containing 11 (40mg, 0·286mmol) in CCl_4 (0·5ml) at -30°, was added a solution of chlorine (excess) in the same solvent. 90MHz p.m.r. spectra, run at -30°, showed emergent signals at δ4·71 (m, H-C-Cl), 2·82 (m, H-C-S) and in the methylenic region. These absorptions increased in intensity at the expense of substrate. It was necessary to raise the temperature to -20° to effect complete reaction, the resulting spectrum being identical to that of 8.

(b) Brominolysis

Br_2 (45·8mg, 0·286mmol) was added dropwise to a p.m.r. tube containing a solution of 11 (40mg, 0·286mmol) in $CDCl_3$ (0·5ml) at -50°. 90MHz spectra, recorded at -50° after each addition, showed new absorptions at δ4·70-5·19 (H-C-Br), 2·79-3·15 (H-C-S) and 2·10-2·79 (CH_2), attributed to 9. The sample was warmed to 10° and further Br_2 (20mg) was added which effected complete conversion of 11 to 9.

(c) Iodinolysis

I_2 (36·3mg, 0·143mmol) was added to a p.m.r. tube containing 11 (40mg, 0·286mmol) in CD_2Cl_2 (0·5ml) at -60°. 90MHz spectra, recorded

at this temperature, gave new signals which corresponded with those of 10. To effect complete reaction, two further amounts of I_2(36·3mg) were added at 20°, the resulting spectrum being identical to that of 10.

Reaction of 11 with SCl_2

11 (44·2mg, 0·316mmol) and SCl_2 (35·8mg, 0·348mmol), each dissolved in CH_2Cl_2 (10ml), were simultaneously added dropwise over 10 min to CH_2Cl_2 (30ml) which was stirred at 0°. The solution was maintained at this temperature for 2 hr after the additions, allowed to warm to room temperature, washed with aq. $NaHCO_3$, brine, water and dried. Removal of solvent gave a viscous yellow oil (75mg) whose p.m.r. spectrum was similar to that of 8. Distillation at 50-75°, 0·1mmHg furnished 8 (slightly impure) as a colourless semi-solid (20mg, 30%), m.p. 85-97°. Spectra were similar to those of an authentic sample of 8 (vide supra).

Part 3

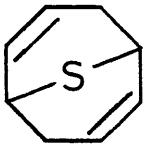
Novel Eliminations of Halo-9-thiabicyclo (3.3.1) nonanes.

Introduction

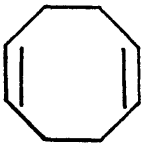
Base treatments of 8, discussed in Part 1, have yielded substitution or elimination-rearrangement products. Thus, synthesis of 9-thiabicyclo (3.3.1) nona-2,6-diene (13) from a bicyclic precursor has never been achieved but 13 can be formed in 22% yield from addition of sodium sulphide to cis-3,7-dibromocycloocta-1,5-diene (147),[88] this condensation occurring because of the cis orientation of the bromine atoms. 147 was obtained from cycloocta-1,5-diene (93) in ca. 7% and therefore the preparation of 13 from 93 (overall yield ca. 1·5%) is clearly unsatisfactory.

In 1971, the reaction of 10 with excess meta-chloroperbenzoic acid (m-CPBA) was found to give a small amount of alkene, in addition to the desired sulphone (148)[89]. Structures 149 and 150 were considered for the alkene, 149 being favoured by spectral comparisons. Until recently, this reaction was not closely investigated because it was of little significance to the research being conducted at that time. Nevertheless, this elimination process was previously unknown and thus warranted further investigation.

At the outset of the present study it was known[90] that reaction of peracetic acid with cyclohexyl iodide yielded products derivable from the interaction of cyclohexene, iodonium ion and solvent. The major product on treatment of cyclohexyl iodide (151) with peracetic acid in acetic acid was 1-iodo-2-acetoxycyclohexane (152) (70-80%) (Scheme 48) when the ratio of acid to substrate was low (0·42-0·76:1)



13



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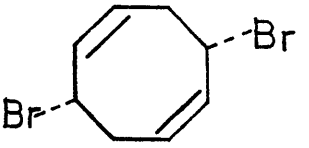

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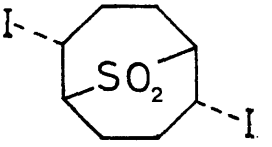
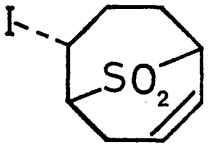
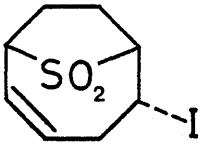


148

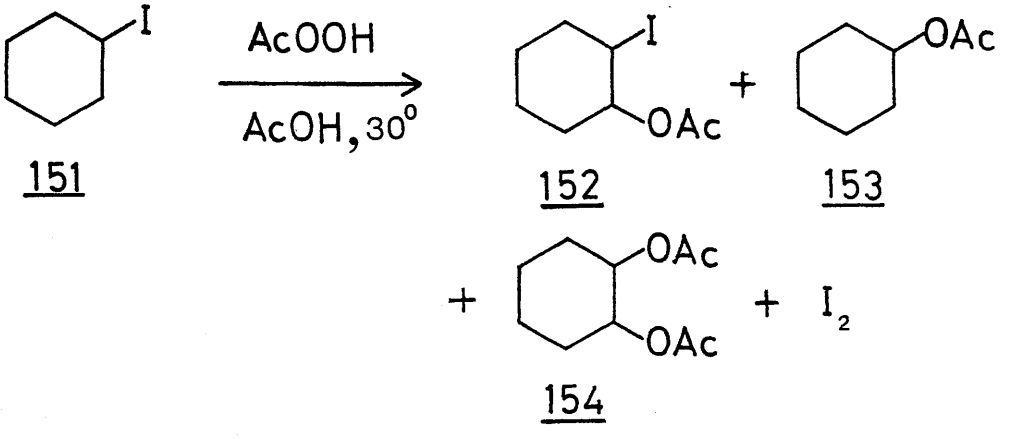


149



150

Scheme 48



151

152

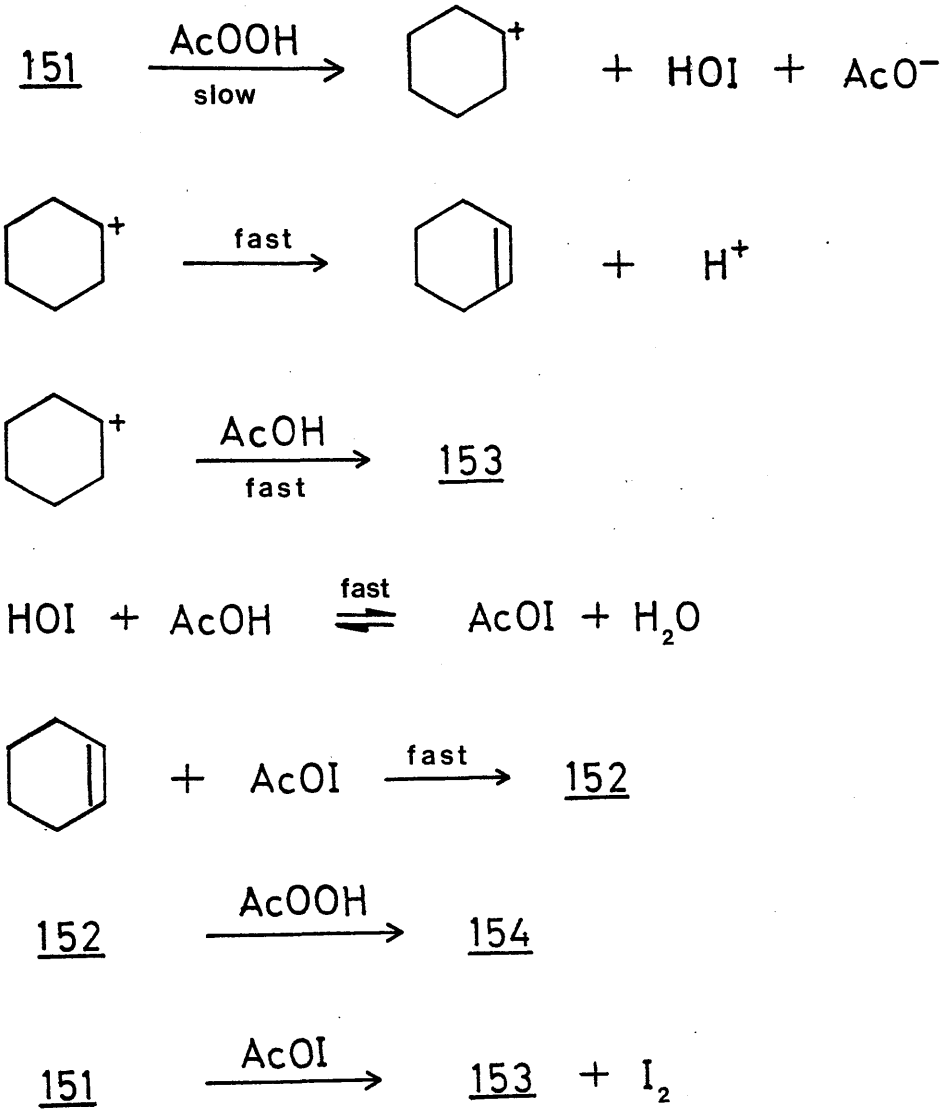
153

154

Other products, formed in small amounts, were cyclohexyl acetate (153), 1,2-diacetoxycyclohexane (154), and iodine. When the ratio was raised to 1·71:1, 152 disappeared and 154 was obtained as the principal product together with 153 and iodine. Ogata suggested that cyclohexene is an intermediate in the reaction (Scheme 49)[90] but kinetic studies[90] did not provide unequivocal proof of the mechanism depicted. The important step is the abstraction of iodide ion by peracetic acid, forming cyclohexyl cation, which is deprotonated to cyclohexene. Solvolysis of the cation would yield 153 or the latter might be formed from 151 by direct displacement. The hypoiodous acid generated may be oxidised by peracid to acetyl hypoiodite, which then adds to cyclohexene to give 152. Attack of acetyl hypoiodite on 151 would produce iodine while excess peracid may convert 152 to 154. Peracetic acid reacts with other alkyl iodides in the presence of cyclohexene to yield 152 in varying amounts.[90]

The behaviour of 151 towards peracetic acid resembles both the Prévost reaction,[91] in which acetyl hypoiodite adds to cyclohexene to give an iodoacetate, and the silver nitrate treatment of 151 which yields cyclohexene.[92] The latter reaction probably proceeds by initial abstraction of iodide by silver ion giving rise to a carbonium ion which eliminates a proton. In non-polar media, where carbonium ion formation is disfavoured, substitution of halogen by nitrate ion may occur in a concerted push-pull process.[93] Indeed, substitutions of alkyl halides with silver salts are widely used synthetic methods.[93]

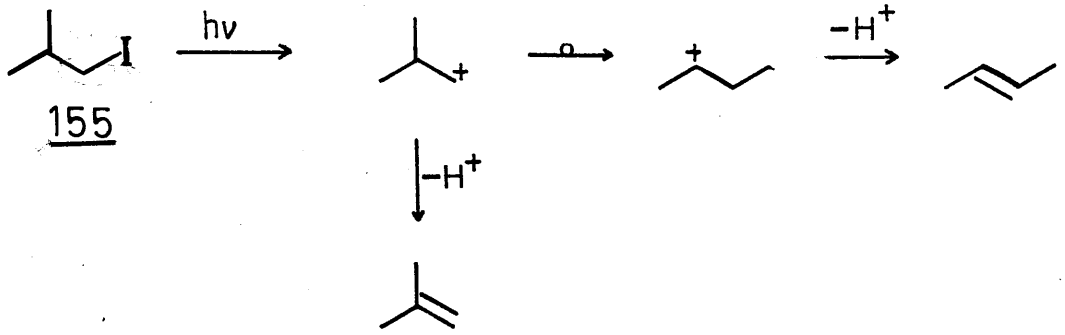
Scheme 49


151
AcOOH
slow
+ HOI + AcO⁻
fast
+ H⁺
AcOH
fast
153
HOI + AcOH
fast
AcOI + H₂O
+ AcOI
fast
152
152
AcOOH
154
151
AcOI
153 + I₂

Recent photochemical studies[94-97] have shown that irradiation of alkyl bromides and, particularly, iodides in solution is also a convenient method for the generation of carbocations. Kropp suggested[94-97] that involvement of cationic intermediates in the photochemistry of alkyl iodides provides obvious answers to some of the apparent anomalies in early literature, which were inexplicable because only radical intermediates had been considered. Thus, for example, isobutyl iodide (155) was found to afford a mixture of isobutene and but-2-ene.[98] Formation of the latter most likely occurs *via* rearrangement of the iso-butyl cation (Scheme 50).[97] Similarly, irradiation of diiodide (156) yielded substantial amounts of 2-methyl-but-2-ene (157),[99] the formation of which is explained on the basis of rearrangement of neopentyl cation (Scheme 51).[97] These results clearly show that, in solution, the initially generated radical pair (158) can undergo subsequent electron transfer to afford an ion pair (159) and, ultimately, carbocationic products (Scheme 52). Furthermore, there is a marked contrast in behaviour between alkyl iodides and the corresponding bromides, the latter giving rise to radical derived products. For example, irradiation of 2-exo-iodonorbornane (160) in ether solution afforded a mixture of 161 and 162 in yields of 81% and 19% respectively (Scheme 53).[94] In contrast, the corresponding bromide afforded only the reduction product, norbornane (92%), on irradiation in ether.

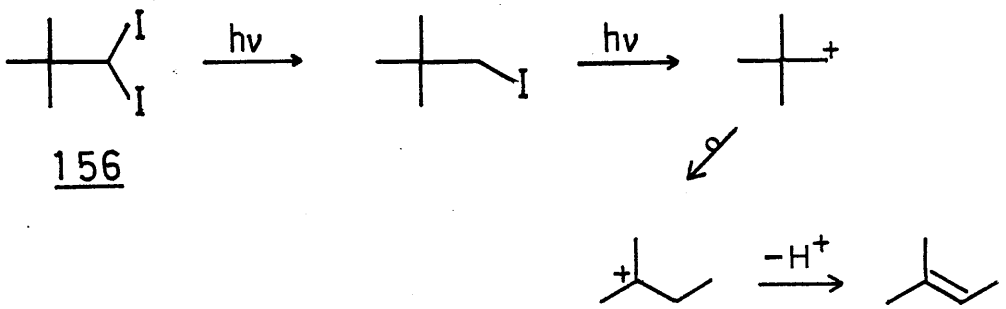
It was considered that the study of the photolyses of 2,6-dihalo-9-thiabicyclo (3.3.1) nonanes in conjunction with their reactions with m-CPBA would assist in the understanding of both processes. Additional information was thought to be attainable from attempts to effect

Scheme 50



155

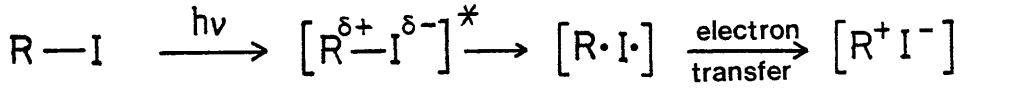
Scheme 51



156

157

Scheme 52



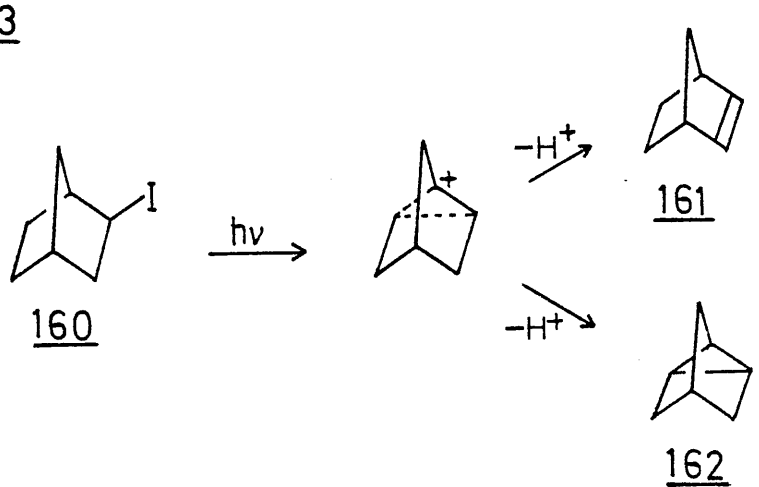
158

159

radical products

carbocationic products

Scheme 53



160

161

162

dehydroiodination under a variety of conditions eg. base and silver ion treatments, ozonolysis and pyrolysis. For comparison, reactions of m-CPBA with an acyclic iodide were also investigated.

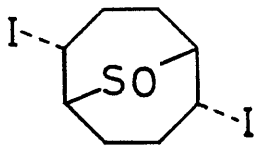
m-CPBA treatments of bicyclic dihalosulphides 8, 9 and 10

Reactions of 10 with varying amounts of m-CPBA in chloroform, conveniently followed by analytical t.l.c., were carried out and the results summarised in the Table. A 1:1·1 ratio yielded sulphoxide (163), m.p. 154-158°. An infra-red spectrum indicated the sulphoxide grouping by the presence of strong bands at 1059 and 1045 cm^{-1}. This was supported from a p.m.r. spectrum which, in contrast to that of 10, exhibited two separate H-C-I resonances (m, 1H). A mass spectral ion at m/e 410 (M^+) together with daughter ion at 287 (M^+-I) was also consistent with 163.

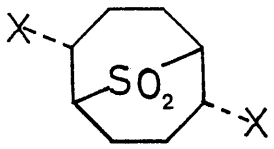
On increasing the peracid/substrate ratio to 2:1, a mixture of 163 and sulphone (148) resulted. A 3:1 ratio succeeded in reacting all of 163, t.l.c. giving rise to a new spot with different Rf value from those of 148 and 163. The p.m.r. spectrum of the reaction mixture, before purification, exhibited low intensity olefinic signals. Recrystallisation, however, failed to yield olefinic product, the colourless prisms obtained being identified as diiodosulphone (148). Strong sulphone bands appeared in the infra-red spectrum at 1305 and 1128 cm^{-1}. The H-C-I resonance in the p.m.r. spectrum consisted of a two-proton multiplet centred at δ5·21 while a bridgehead multiplet, δ3·39 (2H), a methylenic envelope, δ2·20-2·98 (8H), and a parent mass spectral ion at m/e 426 confirmed this structure.

Table Products formed on reaction of 10 with m-CPBA

Molar ratio, 10: m-CPBA	Products (Yield)
1:1·1	163 (85%)
1:3	148 (82%), 149 (trace)
1:6	149 (62%), 148 (15%)
1:10	164 (70%), 149 (7%)

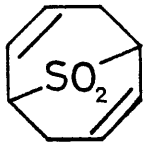


163



20 X = Cl

166 X = Br

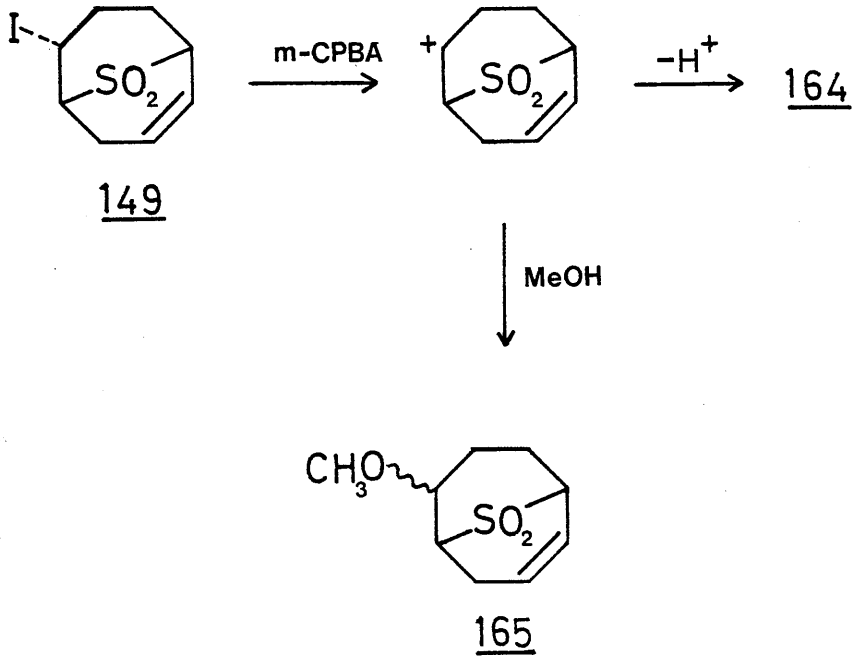


164

182 X = OCH_3

183 X = I

Scheme 54



With six mol of peracid, the initially formed 163 was gradually replaced by 148 and an alkene, the latter being the major component (by p.m.r.). Separation, by preparative t.l.c., gave 148 (15%) and monoalkene (149) (62%), m.p. 130-131°, whose structure was firmly established on the basis of the following evidence. Microanalysis was in agreement with a molecular of $C_8H_{11}O_2IS$ and the mass spectrum supported this, by indicating a molecular weight of 298. The infra-red spectrum showed strong sulphone bands at 1301 and 1118 cm^{-1}. A 90MHz p.m.r. spectrum exhibited two separate one-proton olefinic resonances, δ5·43-5·85 (m, H-C-2), 5·90-6·34 (m, H-C-3) and a one-proton H-C-I multiplet, δ4·92 (H-C-6). Two distinct bridgehead resonances were centred at δ3·30 (m, 1H, H-C-5, non-allylic H) and 3·65 (m, 1H, H-C-1, allylic H). An allylic two-proton multiplet was present at δ2·92-3·33 (H-C-4) and non-allylic methylenic resonances at δ1·65-2·80 (complex m, 4H, H-C-7 and H-C-8). While this spectrum confirms the compound as a monoelimination product, it does not unequivocably distinguish between two possible monoenes, viz 149 and 150. Proton decoupling confirmed the product as 149. Decoupling of the H-C-I proton sharpened the bridgehead resonance at δ3·30 and collapsed splitting in the non-allylic methylene signals, the splitting pattern of the H-C-4 methylene resonance remaining essentially unaltered. Irradiation of the non-allylic bridgehead proton collapsed the H-C-I multiplet to a triplet (J=7Hz), while decoupling of non-allylic methylenic H reduced the H-C-I multiplet to a doublet (J=4Hz).

Increasing the peracid to substrate ratio to 10:1 gave rise to a fourth product. This sublimed as colourless prisms and was identified

as 9-thiabicyclo (3.3.1) nona-2,6-diene 9,9-dioxide (164) on the following evidence. Microanalysis was in agreement with a molecular formula of $C_8H_{10}O_2S$, as was the presence of mass spectral ions at m/e 140 (M^+) and 105 (M^+-HSO_2). The infra-red spectrum showed strong sulphone absorptions in addition to a weak olefinic band at 1645 cm^{-1}. A p.m.r. spectrum exhibited a four-proton olefinic resonance at δ5·82 (m) along with a bridgehead mulitiplet, δ3·35-3·65 (2H), and a methylenic envelope, δ2·35-3·25 (4H). In addition to 164, isolated in 70% yield, a small amount of 149 (7%) was obtained. That sulphur lone-pairs were not required to effect the eliminations was shown by reacting sulphone (149) with excess m-CPBA, which furnished diene (164) (88% yield). A radical pathway for this elimination was thought to be unlikely and this was supported from an e.s.r. study at 298K and 77K which failed to reveal the presence of radicals.

If carbonium ions are intermediates, as suggested by Ogata for the case of cyclohexyl iodide, reaction in the presence of nucleophilic species could lead to products derived from nucleophilic attack on these ions. On treatment of 149 with excess m-CPBA using methanol as solvent, a mixture of 164 and methyl ether (165) resulted. Preparative t.l.c. failed to give a pure sample of 165, a mixture being obtained in which 164 was present in small amount. A mass spectrum showed a molecular ion at m/e 202 (M^+, 165) accompanied by a daughter ion at 186 (M^+-O). The p.m.r. spectrum exhibited a three-proton singlet at δ3·33, associated with the methoxy protons of 165, and a broad olefinic multiplet at δ5·35-6·20. An absorption at δ3·25-3·70 was attributed to the bridgehead and H-C-6 resonances of 165, its complexity preventing

determination of the coupling constant between the H-C-5 and H-C-6 protons. A control experiment in which 149 was stirred in methanol, in the absence of m-CPBA, showed no reaction. Thus, formation of 165 is strong evidence for the intermediacy of a carbonium ion in the reaction of 149 with m-CPBA (Scheme 54).

Conversion of 149 to 165 suggests a new route to ethers which could be of particular utility for hindered iodide substrates and where elimination is disfavoured eg. formation of 182 from 183. Moreover, the peracid treatment of iodides could generate strained carbocations.

Reactions of dichloride (8) and dibromide (9) with large excesses of m-CPBA for prolonged periods gave only the corresponding sulphones, 20 and 166.

Other attempts to dehydroiodinate bicyclic iodides 10, 148, and 149

Pyrolysis of 8 effects dehydrochlorination to 25,[19] although diene (24) also forms on prolonged[89] heating. In contrast, pyrolysis of 10 failed to yield olefinic product. A viscous brown oil was obtained, whose p.m.r. spectrum indicated that substantial decomposition had occurred. Since the pyrolysis conditions employed for 10 were milder than those used for 8, it was considered that 10 would not cleanly undergo elimination of HI on heating and therefore further pyrolyses were not carried out.

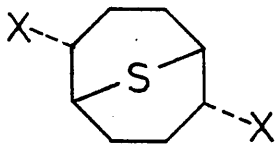
In an alternative approach 10 was treated with silver nitrate in a mixture of methylene chloride and water. A colourless precipitate (silver chloride) deposited. The organic layer yielded a colourless solid which decomposed at its melting point, 76-78°. Indeed, this crystalline material on standing overnight in the dark decomposed to a yellow, frothy mass with a smell reminiscent of nitric oxide. However, the pure reaction product was stable in chloroform solution and satisfactory spectra were obtained. The p.m.r. spectrum displayed a complex multiplet in the methylenic region, which integrated for eight hydrogens, and a H-C-S resonance at δ2·87-3·20 (2H). A two-proton triplet of doublets, with J=10 and 5Hz respectively, at δ5·33-5·84, was consistent with the hydrogens at C-2 and C-6 of dinitrate (167). Strong absorptions in the infra-red spectrum at 1635 and 1278 cm^{-1} were attributed to asymmetrical and symmetrical stretching of the N-O bonds. The mass spectrum, obtained on a freshly prepared sample, showed a parent ion at m/e 264 with daughter ions at m/e 202 (M^+-NO_3), 201 (M^+-HNO_3) and 138 (M^+-2HNO_3), consistent with 167. It was noted that mass spectra taken after the sample had stood at room temperature for a prolonged period did not show any of these peaks, but the identity of the decomposition product was not determined. Although nitrate ion is a poor nucleophile, formation of substitution product (167) is enhanced by the sulphur lone-pairs, which assist in the expulsion of iodide ions. It has since been shown[100] that the corresponding chloride (8) undergoes an analogous displacement reaction with silver nitrate.

An attempt to dehydroiodinate 149 with silver nitrate in dimethyl

sulphoxide was unsuccessful. Thus, after a prolonged period (2 days) only starting material was recovered. This result perhaps indicates that m-CPBA is a more powerful iodide abstracter than silver ion, though this cannot be deduced with certainty since complexation of silver ion with solvent would reduce its electrophilic character. It also shows the importance of sulphur participation in the previous reaction.

2,4,6-Collidine, a hindered base, also failed to react with 149. Reaction of 148 with potassium hydroxide in methanol afforded starting material and a mixture containing dimethyl ether (168) (major) and 169. Although this mixture could not be separated, the presence of 168 was indicated by a mass spectral ion at m/e 426 (M^+). Also, the p.m.r. spectrum exhibited a singlet at δ3·40 (methoxy protons) and a triplet of doublets, with J=10 and 5Hz respectively, at δ4·03 (H-C-OMe), in addition to methylenic and bridgehead resonances. Scheme 55 depicts a possible mechanism for the conversion of 148 to 168, which is analogous to that proposed[22,23] for the formation of 19 from $KOBu^t$ treatment of 17 (Scheme 10).

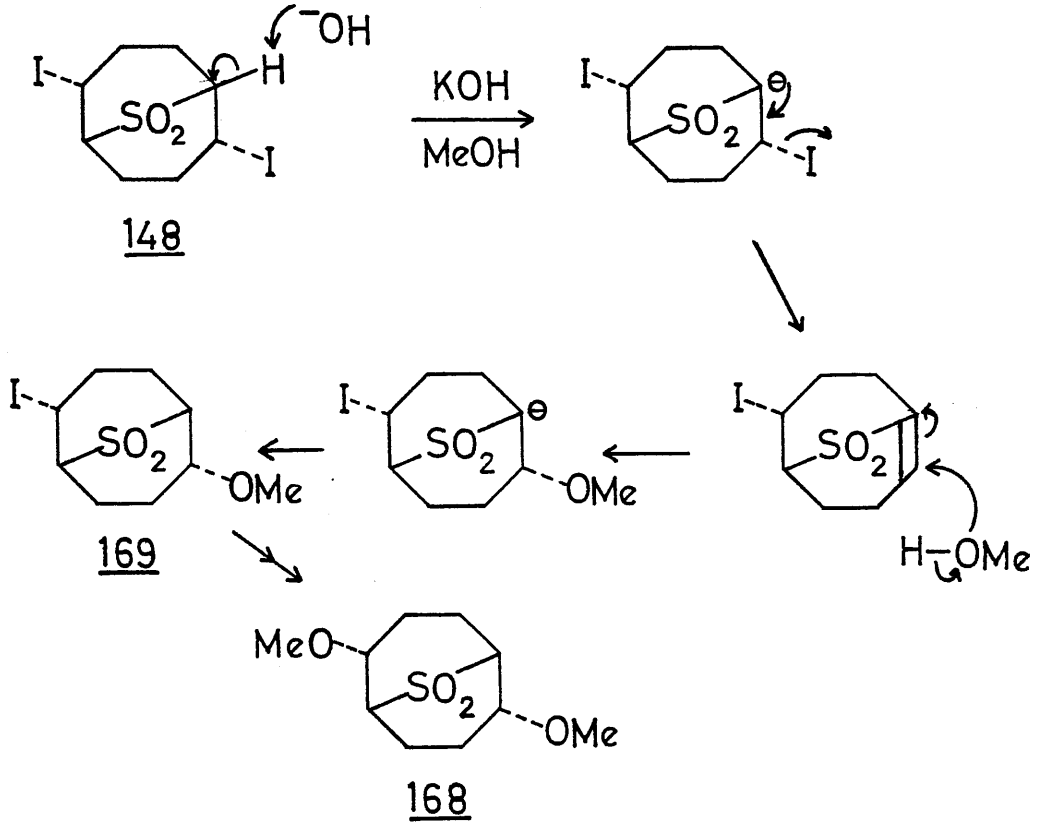
It was conceivable that the observed dehydroiodinations with m-CPBA took place via the intermediacy of alkyl iodoso or iodoxy compounds. Thus 148, for example, on m-CPBA treatment may give rise to an iodoso compound (170) which could eliminate HOI (Scheme 56) in a stepwise process involving a carbonium ion intermediate. It is noteworthy that aromatic iodoso[101] and iodoxy[102] compounds have been isolated but stable aliphatic analogues are unknown. Since



10 X = I

167 X = ONO_2

Scheme 55

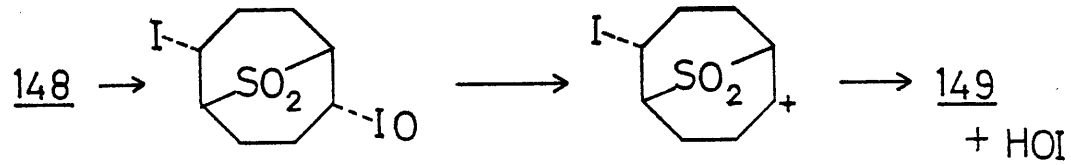


148

169

168

Scheme 56



148

170

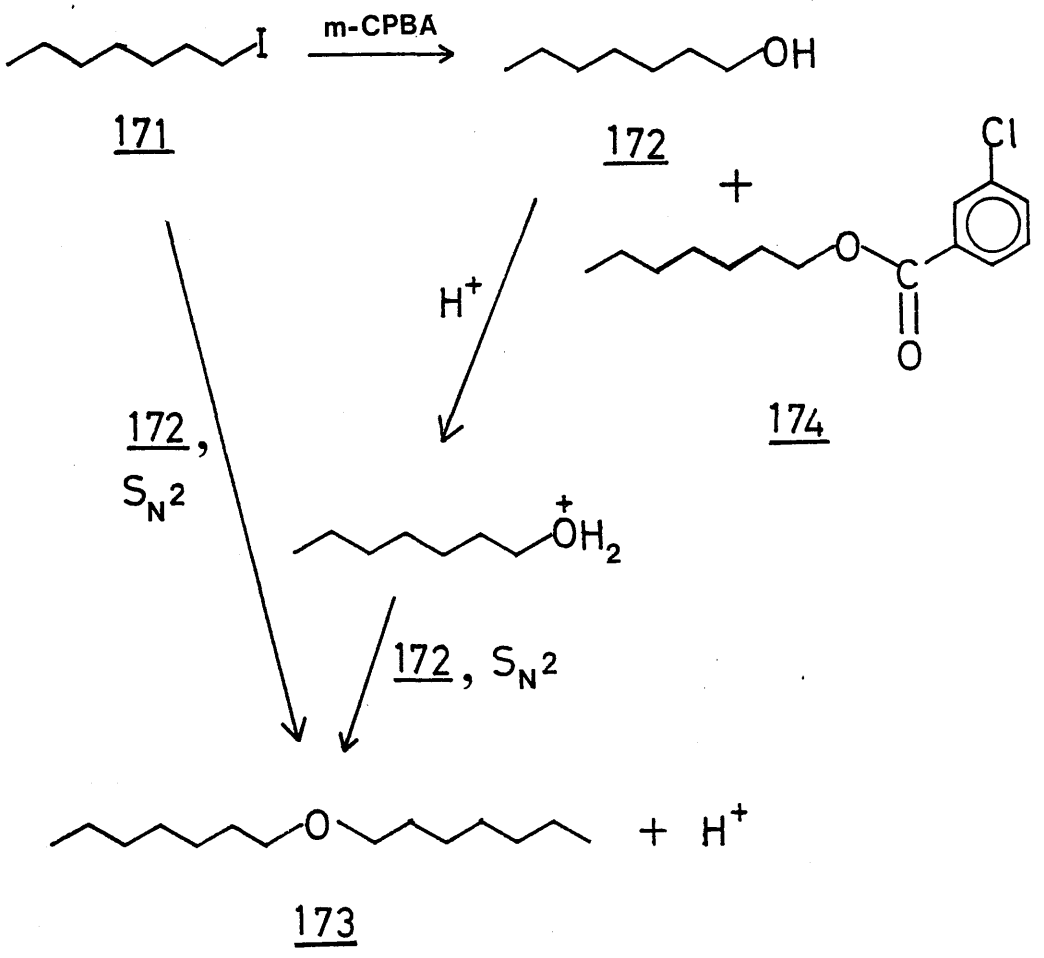
149 + HOI

aromatic iodides are converted to hypervalent iodine compounds by ozone[103] it was considered that 148, for example, might undergo elimination in the presence of ozone. To test this, an oxygen-ozone mixture was passed through solutions of 148 and 171 in ethyl acetate. No reaction took place in each case. However, the inertness of these iodides to ozone does not disprove the intermediacy of iodoso or iodoxy species in m-CPBA dehydroiodination reactions.

Reactions of simple alkyl iodides with m-CPBA

Reaction of 171 with an equimolar amount of m-CPBA produced an almost immediate iodine colour and heat evolution. However, t.l.c. after 2 hr indicated the presence of a substantial amount of starting material and therefore a further mol of peracid was added. The suspension was stirred for 15 days, t.l.c. showing gradual conversion of 171 to a mixture of products. Preparative t.l.c. of the oily residue gave three bands, the most mobile of which contained starting material (4%). The middle band afforded a colourless, sweet-smelling, oil, b.p. 70-80°, 0·04mmHg, whose p.m.r. spectrum exhibited a complex multiplet at δ0·87-2·10 and a triplet (J=6Hz) at δ3·36, the relative intensities being 13:2. The most striking feature of the infra-red spectrum was the presence of a strong C-O stretching band in the region 1070-1150 cm^{-1}, the remainder of the spectrum resembling that of 171. This compound was assigned as di-n-heptyl ether (173), (23% yield), which was in agreement with a molecular ion at m/e 214 in the mass spectrum. Although mass spectral peaks were also present at m/e 254 and 256 of intensity 3:1, these were attributed to a trace

Scheme 57



amount of n-heptyl meta-chlorobenzoate (174), whose presence was revealed from a high amplitude p.m.r. spectrum and a weak infra-red absorption at 1729 cm^{-1} (C=O). The least mobile band yielded 172 (27%), identified from a p.m.r. spectrum which showed, in addition to CH resonances, a deuterium oxide exchangeable OH absorption.

An S_N2 type reaction of 172 with protonated alcohol or unreacted iodide (171) (Scheme 57) readily explains the formation of 173, though the mechanism of formation of 172 itself is not immediately obvious. Acid catalysed hydrolysis of initially formed ester (174) is a possible source of 172, but generation from 171 via an iodoso intermediate cannot be dismissed. 174 is likely formed by direct nucleophilic displacement of iodide from 171 by meta-chlorobenzoate ion. At higher acidity (10:1 ratio of peracid to 171), 173 was the principal product. In contrast, the industrial preparation of low molecular weight ethers involves the reaction of excess alcohol with concentrated sulphuric acid at 140°.

It is unlikely that elimination takes place in the reaction of 171 with excess m-CPBA since no evidence for olefins or olefin adducts, such as vicinal iodoesters or di-esters, was found.

Reactions of ethyl, cyclohexyl and neopentyl[104] iodides with a large excess of m-CPBA in $CHCl_3$, gave, in each case, complicated mixtures of alcohols, esters and ethers. No attempt was made to separate these but it is noteworthy that their p.m.r. spectra did not exhibit olefinic resonances. Thus, it was not ascertained whether

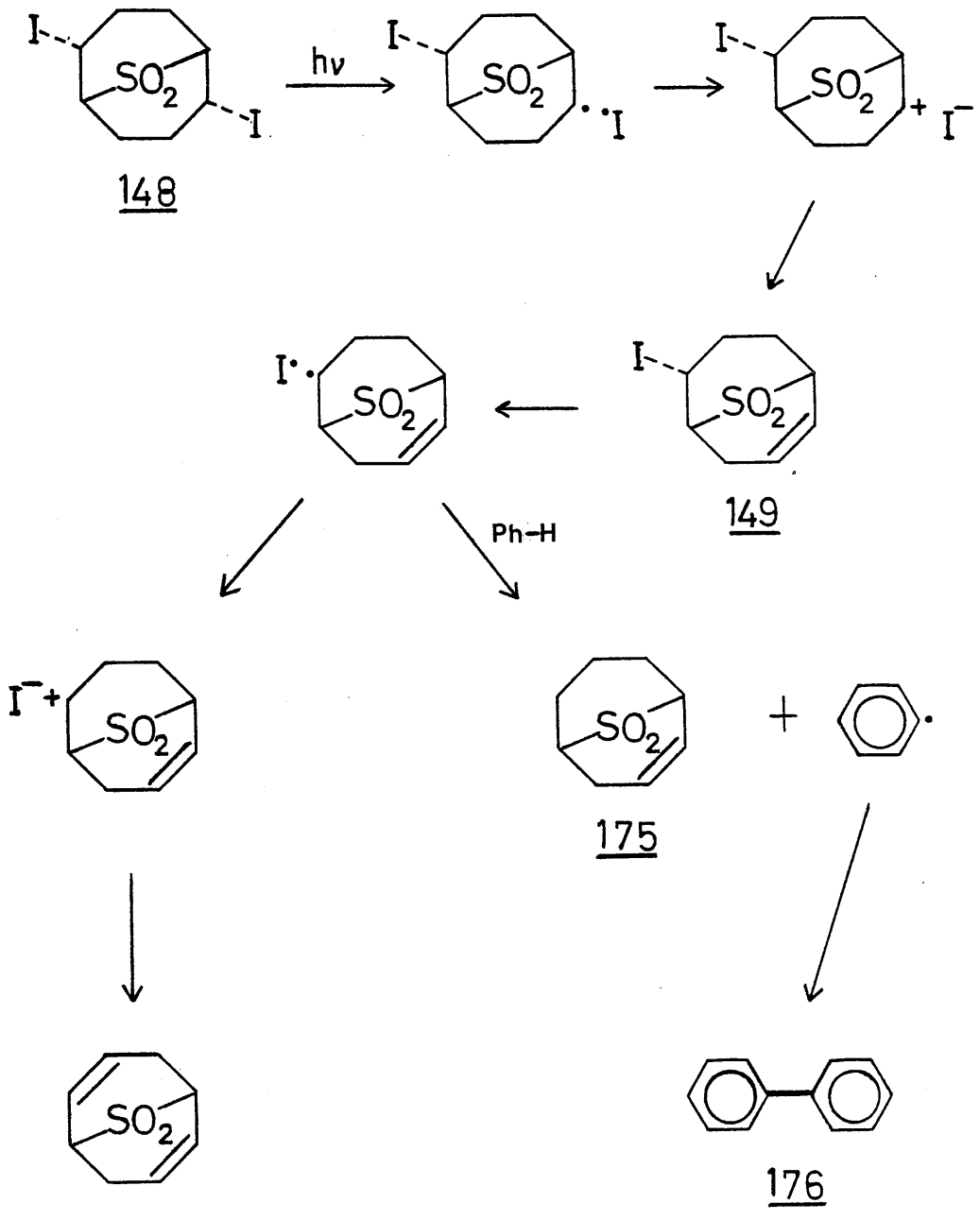
olefin derived products were actually formed.

Photolyses of 2,6-dihalo-9-thiabicyclo (3.3.1) nonanes

The ultraviolet spectrum of 148 exhibits a single absorption maximum (halogen, $n \rightarrow \sigma^*$) at 265nm ($\log \varepsilon$ 3·07). Excitation of these electrons by photolysis of 148 in benzene through quartz resulted in double dehyroiodination to afford 164 (73% yield on purification). The p.m.r. spectrum of crude material displayed additional olefinic signals, attributable to 175. No resonances due to 149 were present, and, since the solution in which the photolysis was carried out was dilute (ca. 6×10^{-4} M), it was considered that dimerisation by radical coupling was unlikely. That some photoreduction had occurred was evident from the presence of a small amount of biphenyl (176) (δ7·20-7·80) in the photolysis mixture. Because of the low yields of 175 and 176, neither was isolated.

Scheme 58 depicts a possible pathway to the observed products. Initial $n \rightarrow \sigma^*$ excitation in the iodine atom generates a radical pair. Electron transfer affords an ion pair and deprotonation yields 149. Similarly, homolysis of the C-I bond of the latter, followed by electron transfer and proton loss produces 164. 175 is formed by hydrogen atom abstraction from solvent, which generates phenyl radicals, these coupling to give 176. The postulation of carbonium ion intermediates satisfactorily explains the high yield of 164, which is of the same order of magnitude as that in the m-CPBA conversion

Scheme 58


I
SO2
I
hν
I
SO2
I
I
SO2
+ I⁻
148
I
SO2
149
I
SO2
Ph-H
I⁻+
SO2
SO2
175
+
SO2
164
176

of 10 to 164, and the low yield of photoreduction product.

Irradiation of 163 for 3 hr produced a complex mixture of decomposition products and no attempt was made to separate and identify the components. It is likely that C-S bond cleavage takes place after $n \rightarrow \sigma^*$ excitation of the sulphur lone-pair electrons. This, together with $n \rightarrow \sigma^*$ transitions in the iodine atoms and subsequent C-I cleavage, elimination or photoreduction would lead to a variety of products.

The ultraviolet spectrum of 10 possesses two absorption maxima attributable to $n \rightarrow \sigma^*$ transitions in halogen[105] and in sulphur.[106] These occur at 265 ($\log \varepsilon$ 3·71) and 245nm ($\log \varepsilon$ 3·51) respectively and are close to a major emission (254nm) of the mercury irradiation lamp. Thus, photochemical excitation of 10 may lead to formation of diene (13) and other products. However, irradiation of 10 for 2 hr afforded a mixture in which 176 was the major constituent. Formation of the latter, isolated as colourless crystals, m.p. 68-70°, is a possible indication of considerable photoreduction.

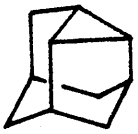
The ultraviolet spectrum of dibromosulphone (166) exhibits a single absorption maximum (halogen, $n \rightarrow \sigma^*$)[105] at ca. 220nm (inflection) ($\log \varepsilon$ 2·77). Irradiation of 166 gave a number of compounds which separated on preparative t.l.c. into three bands, the uppermost containing biphenyl. The middle band afforded a mixture of 177 and 178 (in ca. 24% combined yield) in the approximate ratio 1:1. Structural assignments are based on p.m.r. and mass spectra of the

mixture as further t.l.c. failed to separate these compounds.

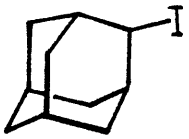
The lowest band yielded colourless crystals whose p.m.r. and mass spectra indicated a mixture of 175 and 179 (ca. 1:1). Sublimation afforded 175 (ca. 24% yield) as prisms. Although spectra showed the presence of a trace amount of 179, satisfactory microanalytical data were obtained, confirming a molecular formula of $C_8H_{12}O_2S$. The mass spectrum showed a parent ion at m/e 172 and strong sulphone bands were present in the infra-red spectrum. In particular, the p.m.r. spectrum exhibited two separate one-proton olefinic resonances at δ5·51-5·90 (m) and 5·95-6·25 (m), these having a similar profile to the olefinic absorptions of 149. The distillation residue consisted of decomposed material and therefore 179 was not recovered.

Products 178 and 179 are formed *via* initial homolytic cleavage of the C-Br bonds followed by hydrogen atom abstraction from benzene. This is supported by the presence of 176. Elimination products 175 and 177 may arise from electron transfer within radical pair cages and deprotonation of the resultant cations (Scheme 59). Photoreduction thus appears to be a more important process for 166 than for 148; consequently electron transfer after initial homolysis is more facile for 148.

Irradiation of 9 for 20 hr produced a complicated mixture containing biphenyl, while irradiation for 5 hr yielded predominantly starting material. The photochemical reactivity of 9 is consistent with the ultraviolet absorption maxima of 249nm (log ε 2·83) ($n \rightarrow \sigma^*$

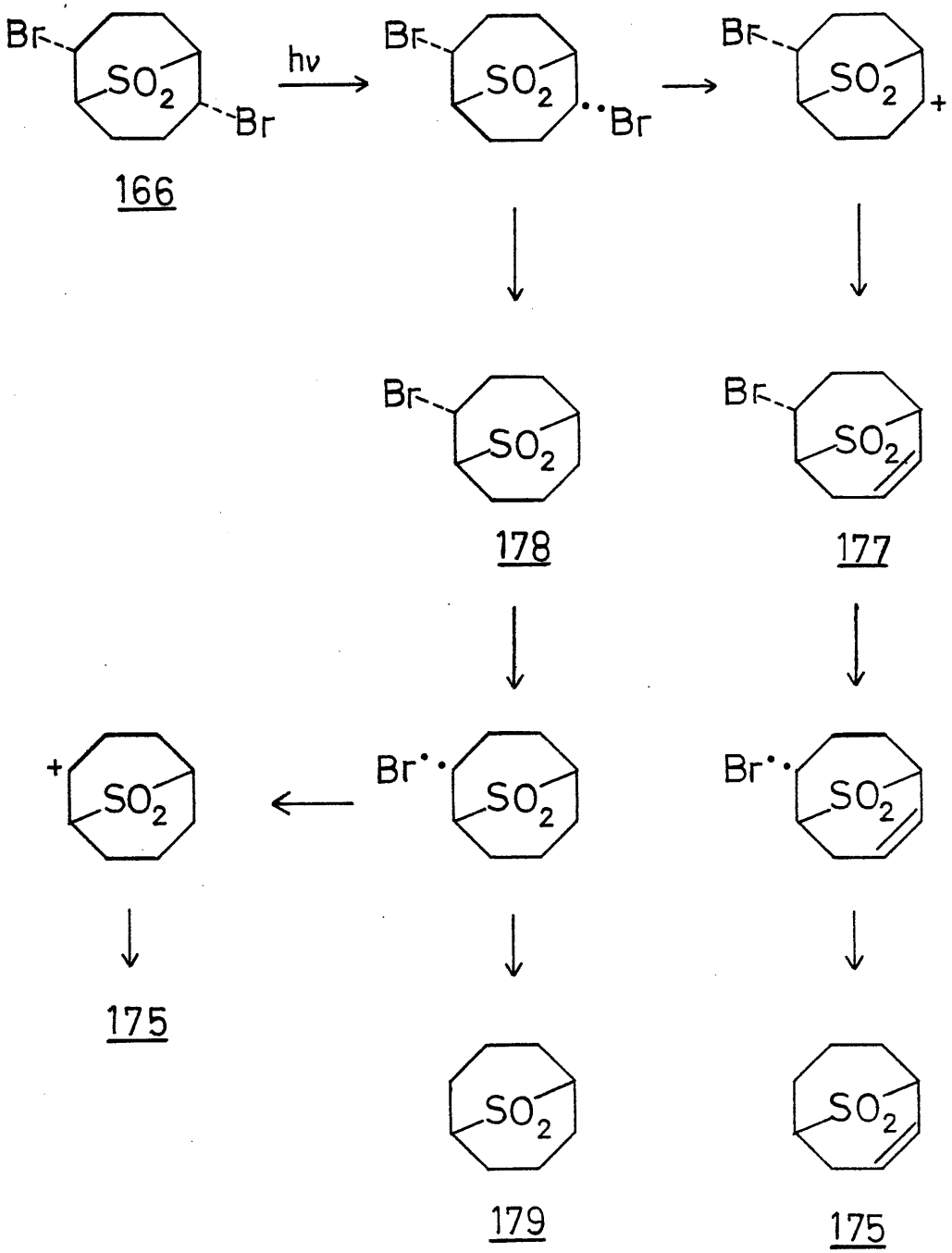


180



181

Scheme 59



for S) and 222nm (log ε 3·69) ($n \rightarrow \sigma^*$ for Br) which, being within the broad spectral emission of the mercury lamp, would lead to C-S and C-Br cleavage resulting in a variety of products.

Dichlorosulphone (20) proved inert to irradiation, reflecting its transparence above 205nm in the ultraviolet spectrum.

These photolysis results support Kropp's conclusion that alkyl bromides show greater radical behaviour on irradiation than the corresponding iodides. Since photolysis and m-CPBA treatment of iodides both provide carbonium ions, the isolation of a strained elimination product, *viz* 180 from 181,[107] suggests a further (*vide supra*) application of the alkyl iodide-peracid reaction.

Recently, examples of dehydroiodination by peracetic[108] and m-CPBA[109] have been reported. The oxidative eliminations were suggested to involve a hypervalent iodine compound which undergoes pericyclic syn elimination as for sulphoxides[110] and selenoxides.[111] This intermediate may also rearrange to an alkyl hypoiodite (*via* an ion pair) which is converted to an alcohol.

EXPERIMENTAL

Reaction of 10 with m-CPBA

(i) 2,6-diiodo-9-thiabicyclo (3.3.1) nonane 9-oxide (163)

A solution of m-CPBA (189mg, 1·1mmol) in $CHCl_3$ (15ml) was added dropwise over 15 min to a stirred solution of 10 (394mg, 1mmol) in the same solvent (15ml) at 0°. After 3 hr at 0° the yellow mixture was washed with aq. $Na_2S_2O_3$, aq. $NaHCO_3$, water and dried. Removal of the solvent and recrystallisation from methanol-chloroform afforded 163 as colourless prisms (360mg, 85%), m.p. 154-158°; ν_{max}^{KBr} 2982, 2960, 2938, 2911, 1480, 1202, 1059, 1045, 1036 and 789 cm^{-1}; $\delta(CDCl_3)$ 1·80-3·05 (br env, 8H, CH_2), 3·23-3·60 (m, 2H, bridgehead H), 4·42-4·95 (m, 1H, H-C-I) and 5·10-5·60 (m, 1H, H-C-I); m/e 410 (M^+), 283 (M^+-I), 267 and 233.

(ii) 2,6-diiodo-9-thiabicyclo (3.3.1) nonane 9,9-dioxide (148)

A repeat of the above procedure using m-CPBA (516mg, 3mmol) in $CHCl_3$ (15ml) and 10 (394mg, 1mmol) in $CHCl_3$ (15ml) gave 148 as a colourless semi-solid. Recrystallisation from methanol-chloroform removed traces of 149 and yielded 148 as prisms (349mg, 82%), m.p. 198-202°; ν_{max}^{KBr} 2969, 2930, 1481, 1435, 1305, 1266, 1217, 1128,

1050, 862, 814 and 537 cm^{-1}; $\delta(CDCl_3)$ 2·20-2·98 (br env, 8H, $C\underline{H}_2$), 3·39 (m, 2H, bridgehead $\underline{H}$) and 5·21 (m, 2H, $\underline{H}$-C-I); m/e 426 (M^+), 299 (M^+-I), 233, 207 and 107; λ_{max}^{EtOH} 265nm (log ε 3·07).

(iii) 6-iodo-9-thiabicyclo (3.3.1) non-2-ene 9,9-dioxide (149)

Following the previous procedures, m-CPBA (1·03g, 6mmol) in $CHCl_3$ (20ml) and 10 (394mg, 1mmol) in $CHCl_3$ (20ml) were reacted. A pink colour developed and substantial precipitation occurred. Solvent removal after workup afforded a mixture of 148 and 149. Purification was achieved by preparative t.l.c. (ether-petroleum spirit, 2:3). The upper band, on ether extraction, yielded 148 (64mg, 15%) while the lowest band afforded 149 (206mg, 62%) as colourless prisms, m.p. 130-131°. Anal. calc. for $C_8H_{11}O_2IS$: C 32·34, H 3·73%. Found: C 32·18, H 3·75%; ν_{max}^{KBr} 2942, 1443, 1301, 1242, 1190, 1118, 1063, 991, 872, 820 and 710 cm^{-1}; $\delta(CDCl_3)$ 1·65-2·80 (complex m, 4H, $\underline{H}$-C-7 and $\underline{H}$-C-8), 2·92-3·33 (m, 2H, $\underline{H}$-C-4), 3·33-3·50 (m, 1H, $\underline{H}$-C-5), 3·50-3·81 (m, 1H, $\underline{H}$-C-1), 4·72-5·22 (m, 1H, $\underline{H}$-C-6), 5·43-5·85 (m, 1H, $\underline{H}$-C-2) and 5·90-6·34 (m, 1H, $\underline{H}$-C-3); m/e 298 (M^+), 206, 171, 141, 105 and 91.

(iv) 9-thiabicyclo (3.3.1) nona-2,6-diene 9,9-dioxide (164)

The procedure in (i) was repeated using m-CPBA (1·72g, 10mmol)

in $CHCl_3$ (50ml) and 10 (394mg, 1mmol) in $CHCl_3$ (20ml) at 25°. During the addition, heat was evolved and a deep purple colour appeared. After 3 hr, the colourless solution was washed as in (i) and dried. Removal of $CHCl_3$ and washing the remaining semi-solid (190mg) with ether yielded 164 as colourless prisms (102mg, 60%) which sublimed at 115°, 0·1mmHg; m.p. 164-167° (lit.[88] m.p. 165-167°). Anal. calc. for $C_8H_{10}O_2S$: C 56·45, H 5·9%. Found: 56·22, H 5·7%; ν_{max}^{KBr} 2911, 1645, 1333, 1302, 1245, 1200 and 1121 cm^{-1}; $\delta(CDCl_3)$ 2·35-3·25 (br env, 4H, CH_2), 3·35-3·65 (m, 2H, bridgehead H) and 5·51-5·99 (m, 4H, olefinic H); m/e 170 (M^+), 105 (M^+-HSO_2), 91, 78 and 65. Preparative t.l.c. (ether) of the ether washings gave two bands. Ether extraction of the upper band afforded 149 (20mg, 7%) while the lower band yielded 164 (17mg, 10%).

Reaction of 149 with m-CPBA

(a) $CHCl_3$ as solvent

The procedure in (i) was repeated using m-CPBA (756mg, 4·4mmol) in $CHCl_3$ (35ml) and 149 (298mg, 1mmol) in $CHCl_3$ (15ml) at 25° to give colourless crystals of 164 (150mg, 88%), identified from its p.m.r. and mass spectra.

(b) MeOH as solvent

m-CPBA (756mg, 4·4mmol in MeOH (15ml) was added dropwise to a

stirred solution of 149 (298mg, 1mmol) in MeOH (25ml) at 25° over 15 min. After 3 hr, the clear solution was stripped of solvent and $CHCl_3$ (30ml) added. The pink solution was washed with aqueous sodium metabisulphite, aq. $NaHCO_3$, water and dried. Removal of $CHCl_3$ gave a colourless oil (218mg). Preparative t.l.c. (ethyl acetate-petroleum spirit, 1:1) showed one major band. Ether extraction furnished a colourless semi-solid (93mg) which consisted of a mixture of 164 and 165 (major component); $\delta(CDCl_3)$ 2·00-3·20 (br env, $C\underline{H}_2$), 3·25-3·70 (m, $\underline{H}$-C-OCH_3 and bridgehead $\underline{H}$), 3·33 (s, $C\underline{H}_3$-O) and 5·35-6·20 (m, olefinic $\underline{H}$); m/e 202 (M^+, 165), 186 (M^+-O), 170 (M^+, 164), 156, 139, 105 and 91. Further purification was not attempted. Minor bands gave insignificant amounts of material.

Attempted reaction of 149 with MeOH in the absence of m-CPBA

A solution of 149 (298mg, 1mmol) in MeOH (40ml) was stirred at 25° for 3 hr, during which the solution remained clear. Removal of MeOH yielded starting material (298mg), identified from its p.m.r. spectrum.

Reaction of 149 with m-CPBA (e.s.r.)

A 1:4 molar ratio of 149 (50mg, 0·17mmol) to m-CPBA (117mg, 0·68mmol) was stirred in chloroform-toluene (3:2, 3·3ml) at 25° for 15 min, whereupon a purple colour developed. An aliquot (ca. 0·1ml) was removed and high resolution e.s.r. spectra were recorded on it

at 298K and 77K. No radicals were detected.

Reaction of 8 with excess m-CPBA

m-CPBA (3·36g, 20mmol) in $CHCl_3$ (50ml) was added over 15 min to a stirred solution of 8 (422mg, 2mmol) in $CHCl_3$ (30ml) at 25°. After 3 days, during which a colourless precipitate formed, the mixture was washed with aq. $Na_2S_2O_5$, aq. $NaHCO_3$, water and dried. Solvent removal yielded 20 (480mg) as crystals. Recrystallisation from ethanol-chloroform furnished colourless prisms (413mg, 85%), m.p. 176-177° (lit.[19] m.p. 175-176°); ν_{max}^{KBr} 1310, 1130, 833, 545 and 437 cm^{-1}; $\delta(CDCl_3)$ 2·01-3·02 (br env, 8H, CH_2), 3·01-3·35 (m, 2H, bridgehead H) and 4·60-5·18 (m, 2H, H-C-Cl); λ_{max}^{EtOH} - no absorption above 200nm.

Reaction of 9 with excess m-CPBA

The procedure above was repeated using m-CPBA (3·36g, 20mmol) and 9 (600mg, 2mmol). On workup after 3 days, 166 (652mg) was obtained as colourless crystals. Recrystallisation from methanol-chloroform furnished prisms (578mg, 87%), m.p. 195-197°. Anal. calc. for $C_8H_{12}O_2Br_2S$: C 28·9, H 3·61%. Found: C 29·0, H 3·78%; ν_{max}^{KBr} 2978, 2937, 1480, 1309, 1296, 1267, 1186, 1132, 820 and 541 cm^{-1}; $\delta(CDCl_3)$ 2·08-2·90 (br env, 8H, CH_2), 3·05-3·35 (m, 2H, bridgehead H) and 4·65-5·16 (m, 2H, H-C-Br); m/e (334, 332 and 330) (M^+), (269, 267 and 265), (253 and 251) and (189 and 187); λ_{max}^{EtOH} ~220nm (log ε 2·77).

Pyrolysis of 10

10 (394mg, 1mmol) was pyrolysed in a 6"long, flame dried, vacuum sealed Pyrex tube (i.d. 1cm) at 150° for 4 hr. Purple vapour appeared as 10 assumed a grey colour before melting. The brown oil which resulted was extracted with ether and $CHCl_3$, leaving an insoluble residue. Filtration followed by removal of solvent gave a brown oil whose p.m.r. spectrum exhibited broad multiplet signals and indicated that substantial decomposition had taken place by the absence of H-C-S and H-C-I absorptions. No olefinic resonances were present.

Reaction of 10 with $AgNO_3$

$AgNO_3$ (429mg, 2·52mmol) in water (2ml) was added to a stirred solution of 10 (500mg, 1.26mmol) in CH_2Cl_2 (5ml). A colourless precipitate deposited and after 30 min the organic layer was collected, washed with water, dried and solvent removed to yield a colourless solid, m.p. 65-68°. Recrystallisation from $CHCl_3$ furnished colourless crystals of 167 (155mg, 47%), m.p. 76-78° (decomposes); $\nu_{max}^{CHCl_3}$ 2900, 1635, 1350, 1278, 870 and 850 cm^{-1}; $\delta(CDCl_3)$ 1·69-2·70 (complex m, 8H, CH_2), 2·87-3·20 (m, 2H, H-C-S) and 5·33-5·84 (t d, J=10 and 5Hz, 2H, H-C-ONO_2); m/e 264 (M^+), 202 (M^+-NO_3), 201, 172 (M^+-2NO_2), 139 and 138. 167 decomposes on standing but is relatively stable in solution ($CHCl_3$).

Collidine treatment of 149

A solution of 149 (356mg, 1·2mmol) in 2,4,6-collidine (5ml) was stirred at 80° for 5 hr. The solution was allowed to cool, added to ethyl acetate (15ml) and washed with dilute hydrochloric acid (4 x 10ml), brine and dried. Removal of solvent gave starting material (265mg, 74%), identified from a p.m.r. spectrum.

$AgNO_3$ treatment of 149

$AgNO_3$ (85mg, 0·5mmol) was added to a stirred solution of 149 (149mg, 0·5mmol) in dimethyl sulphoxide (15ml). After 48 hr, chloroform (30ml) was added and the extract washed with water (10 x 15ml) then dried. Removal of solvent gave starting material (142mg).

Ozone treatment of 148 and 171

An oxygen-ozone mixture was bubbled through a solution of 148 (104mg, 0·24mmol) in ethyl acetate (70ml) at -40° for 30 min. The deep blue solution decolourised on standing. Zinc (30mg, 0·45mmol) and acetic acid (one drop) were added and the suspension stirred at room temperature for 15 min. Filtration and removal of solvent afforded 148 (96mg), as shown from p.m.r. and mass spectra.

Similar ozone treatment of 1-iodoheptane (171) (0·24mmol) at room temperature for 2 hr, and without reductive workup, gave starting material (0·24mmol).

Reaction of 148 with KOH

To a stirred solution of 148 (213mg, 0·5mmol) in methanol (40ml) at reflux was added potassium hydroxide pellets (62mg, 1·1mmol). The clear solution was refluxed for 2 hr and solvent removed to leave a colourless solid whose p.m.r. indicated the presence of 148 (major), 168 and 169. The solid was re-dissolved in hot methanol, the stirred solution refluxed and further KOH (124mg, 2·2mmol) added. After 12 hr, MeOH was removed and the residual solid taken up in $CHCl_3$, washed with brine and dried. Evaporation of solvent yielded colourless crystals (150mg). Preparative t.l.c. (ether-petroleum spirit, 1:1) showed three bands. The uppermost and middle bands contained 148 (8mg) while the lowest band gave slightly yellow crystals (122mg), consisting of 168 and small amounts of 148 and 169; δ ($CDCl_3$) 1·60-2·80 (br env, CH_2), 3·20 (m, bridgehead H), 3·40 (s, CH_3O), 4·03 (t d, J=10 and 5Hz, H-C-O) and 5·11 (m, H-C-I); m/e 426 (M^+, 148), 330 (M^+, 169), 234 (M^+, 168), 219, 204 and 203. Further preparative t.l.c. (ether-petroleum spirit, 4:1) and a recrystallisation from ether-hexane failed to separate this mixture.

Reaction of 1-iodoheptane (171) with m-CPBA

m-CPBA (0·86g, 5mmol) in $CHCl_3$ (20ml) was added dropwise over 15 min to a stirred solution of 171 (1·13g, 5mmol) in $CHCl_3$ (20ml) at room temperature. A purple colour developed during the addition and heat was evolved. Ananlytical t.l.c. after 2 hr indicated incomplete reaction and therefore further m-CPBA (0·86g) was added. The mixture was stirred for 15 days, washed with aq. $Na_2S_2O_3$, dilute sodium hydroxide, brine and dried. Solvent removal afforded a viscous yellow oil (617mg). Preparative t.l.c. (carbon tetrachloride) gave three bands, the uppermost consisting of 171 (49mg, 4%). The middle band gave di-n-heptyl ether (173) as a colourless oil (123mg, 23%), b.p. 70-80°, 0·04mmHg (lit[112] b.p. 259°, 760mmHg); $\nu_{max}^{CCl_4}$ 2956, 2926, 2856, 1467, 1376 and 1110 cm^{-1}; $\delta(CDCl_3)$ 0·87-2·10 (complex m, 26H, $C\underline{H}_2$ and $C\underline{H}_3$) and 3·36 (t, J=6Hz, 4H, $\underline{H}$-C-O); m/e 214 (M^+), 199, 185, 171, 157 and 143. Both bands contained a trace amount of 174 which gave rise to a two-proton triplet (J=6Hz) at δ4·30 and aromatic resonances at δ7·30-8·00 (m, 4H) in the p.m.r. spectra. Infra-red absorptionsat 1729 and 2790 cm^{-1} and mass spectral peaks at m/e 254 and 256 (M^+) were attributed to 174.

Ether extraction of the lowest band afforded heptan-1-ol (172) (154mg, 27%); $\delta(CDCl_3)$ 0·87-2·20 (complex m, 13H, $C\underline{H}_2$ and $C\underline{H}_3$), 2·37 (s, 1H, O$\underline{H}$) and 3·63 (t, J=6Hz, 2H, $\underline{H}$-C-OH).

A repeat of the above reaction using m-CPBA (50mmol) in $CHCl_3$ (50ml) and 171 (5mmol) in $CHCl_3$ (25ml) gave, on similar workup after

12 hr, a mixture which consisted largely of 173, together with small amounts of 172 and 174, identified from the p.m.r. spectrum. Purification was not attempted.

Reaction of simple alkyl iodides with excess m-CPBA

Separate reactions of ethyl, cyclohexyl and neopentyl iodides (1mmol) in $CHCl_3$ (25ml) with m-CPBA (10mmol) in $CHCl_3$ (25ml) were carried out at room temperature. In each case a purple colour appeared and heat was evolved. On workup after 12 hr, a p.m.r. spectrum revealed the presence of a mixture of the corresponding alcohol, ether and ester, in each case. No olefinic products were formed and purifications were not attempted.

Photolysis of 148

A solution of 148 (48mg, 0·11mmol) in benzene (190ml) was irradiated for 15 hr. The solution became yellow, darkening to violet-brown as irradiation continued. Removal of solvent yielded a viscous brown oil (29mg). Preparative t.l.c. (ether) gave one band which afforded 164 (14mg, 73%) as colourless crystals, m.p. 165-167°, identified from spectral comparisons,

Photolyses of 10 and 163

Irradiation of a solution of 10 (79mg, 0·20mmol) in benzene (190ml) for 2 hr afforded a dark brown oil on removal of solvent. A p.m.r. spectrum indicated the presence of a complex mixture. Preparative t.l.c. (ether-petroleum spirit, 1:9) gave one major band which yielded colourless crystals of biphenyl (176) (10mg). Sublimation at 70-80° (aspirator vacuum) gave star-shaped crystals, m.p. 68-70° (lit.[113] m.p. 69-72°). Anal. calc. for $C_{12}H_{10}$: C 93·46, H 6·54. Found: C 93·1, H 6·27; $\delta(CDCl_3)$ 7·20-7·80 (complex m); m/e 154 (M^+), 128, 115, 92, 79 and 77. Ether extraction of minor bands gave insignificant amounts of material while the base line afforded a brown oil (32mg) whose p.m.r. was complex and indicated a mixture. Further purification was not attempted. Photolysis of 10 (158mg) for 9 hr gave a similar result.

Irradiation of 163 (96mg, 0·23mmol) in benzene (190ml) for 3 hr yielded, on removal of solvent, a dark brown oil which consisted of a complex mixture containing bipbenyl (from p.m.r. and t.l.c.). Purification was not attempted.

Photolysis of 166

166 (90mg, 0·27mmol) in benzene (190ml) was irradiated for 2 hr. Removal of benzene afforded starting material. Irradiation

for a further 14 hr yielded a brown oil on evaporation of solvent. Preparative t.l.c. (ether) gave three bands, the uppermost, on $CHCl_3$ extraction, giving biphenyl (22mg). The middle band afforded a colourless semi-solid (23mg) whose spectra were consistent with a mixture of 177 and 178 (ca. 24% combined yield) (~1:1); $\delta(CDCl_3)$ 1·40-3·52 (br env, $C\underline{H}_2$ and $\underline{H}$-C-SO_2), 4·95 (m, $\underline{H}$-C-Br) and 5·51-6·30 (m, olefinic $\underline{H}$); m/e (254, 252 and 250) (M^+, 177 and 178), (187 and 185) and 173. Further preparative t.l.c. (ether-petroleum spirit, 9:1) failed to separate this mixture.

The lowest band furnished colourless crystals (16mg) which consisted of a mixture of 175 and 179 (~1:1 from p.m.r. integration); m/e 174 (M^+, 179), 172 (M^+, 175), 109, 107, 93, 91 and 79. Sublimation afforded 175 (slightly impure) as colourless prisms (8mg, 24%), m.p. 235-245° (lit.[19] m.p. 253-255°). Anal. calc. for $C_8H_{12}O_2S$: C 55·78, H 7·02%. Found: C 55·98, H 6·88%; ν_{max}^{KBr} 2927, 1625, 1433, 1282, 1113, 810 and 700 cm^{-1}; $\delta(CDCl_3)$ 1·49-3·25 (br env, 9H, $C\underline{H}_2$ and $\underline{H}$-C-5), 3·30-3·65 (m, 1H, $\underline{H}$-C-1), 5·51-5·90 (m, 1H, $\underline{H}$-C-2) and 5·95-6·25 (m, 1H, $\underline{H}$-C-3); m/e 172 (M^+), 107 (M^+-HSO_2) 93, 91 and 79.

Photolysis of 9

9 (124mg, 0·41mmol) in benzene (190ml) was irradiated for 20 hr. Evaporation to dryness left a brown oil. Preparative t.l.c. (CCl_4)

gave a broad band which afforded a brown oil (42mg). This consisted of a complex mixture containing biphenyl, as shown by p.m.r., and further purification was not attempted. Photolysis of 9 for 5 hr yielded predominantly starting material.

Photolysis of 20

A solution of 20 (121mg, 0·5mmol) in benzene (190ml) was irradiated for 24 hr. The p.m.r. spectrum of the colourless solid (115mg) on removal of benzene was identical to that of starting material but contained additional signals due to biphenyl.

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