Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926081

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G. A. Tolstikov[a]
[a] Institute of Chemistry, Bashkirian Branch of the USSR Academy of Sciences, Ufa, USSR

To cite this Article Tolstikov, G. A.(1983) 'The Reaction of Sulphur Dichloride with Olefins as a Pathway to the Synthesis of Thiacyclanes', Journal of Sulfur Chemistry, 3: 2, 39 — 65
To link to this Article: DOI: 10.1080/01961778308082443
URL: http://dx.doi.org/10.1080/01961778308082443

Sulfur Reports
Volume 3(2), May 1983, pp. 39–70
0196-1772/83/0302-0039/$12.00/0

Printed in the United States of America

THE REACTION OF SULPHUR DICHLORIDE WITH OLEFINS AS A PATHWAY TO THE SYNTHESIS OF THIACYCLANES

G. A. TOLSTIKOV

Institute of Chemistry, Bashkirian Branch of the USSR Academy of Sciences, SU-450054 Ufa, USSR

The synthesis of thiacyclanes which has been stimulated by studies of sulphur-containing components of petroleum[1] has attracted much interest based upon the discovery of a number of important properties of thiacyclanes[2] as well as the development of new approaches in organic synthesis using sulfur-containing intermediaries.[3,4]

The addition of sulphur dichloride to olefins is remarkable for its regio- and stereoselectivity which implies rich possibilities for the synthesis of thiacyclanes of various structures. The formation of α,α′-dichlorothiacyclanes is very important and contributes substantially to the value of this method. The high mobility of the chlorine atoms in nucleophilic substitution which is determined by the participation of thiiranium ions as intermediates allows SCl_2-olefin adducts to be used for the synthesis of a wide range of compounds. However, the literature has not yet reported the synthesis of thiacyclanes by this method, references[5–7] being the exception and dealing with only some points of those discussed below.

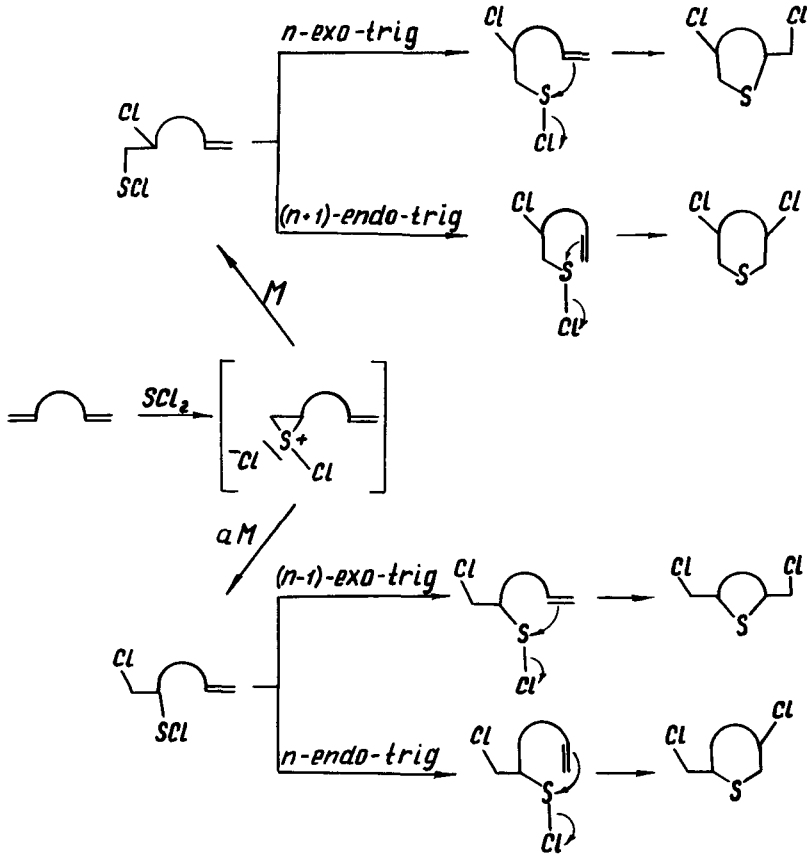
The present review covers some synthetic methods for obtaining thiamono-, thiabi-, and thiatricyclanes as well as sulphur-containing polyhedral compounds based on the reaction of sulphur dichloride with olefins. The formation of thiacyclanes by this method involves a two-step reaction of SCl_2 with compounds containing two active double bonds. Literature data show that aliphatic and cyclic di-, tri-, and tetraenes including those with functional groups have been used as substrates.

The reaction is usually run in non-polar solvents which implies the formation of either covalent intermediates of the σ-sulphurane type or ion pairs in both steps. According to recent statements,[8] the first step which proceeds through the intermediates under consideration may result in the formation of either the Markovnikov (M) or the anti-Markovnikov (aM) adduct. To describe the second step it seems useful to refer to the classification suggested in Reference.[9] Hence, the intramolecular cyclisation of M- and aM-sulphenyl chlorides can be represented as alternate exo-trig and endo-trig routes. The direction of cyclisation depends both on the thermodynamic stability of the cyclisation product α,α′-dichlorothiacyclane and on the kinetic conditions of the reaction.

In certain cases the kinetically favoured cyclisation products rearrange easily into thermodynamically more stable isomers resulting, as can be expected, in a ring size change. It should be emphasised that such reactions of α,α′-dichlorothiacyclanes lead to changes in the ring size as well. Since the use of polar solvents in nucleophilic substitution is an obligatory prerequisite, the assumption of ion pairs as intermediates must be valid.[8,10]

SYNTHESIS OF THIAMONOCYCLANES

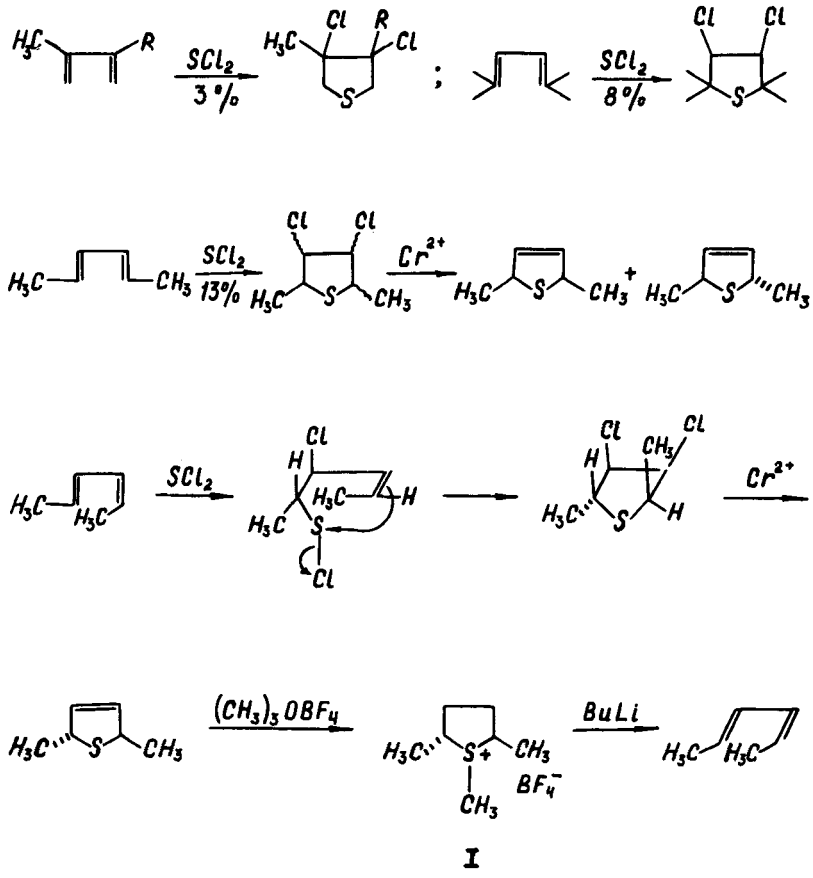
Syntheses of thiamonocyclanes containing five- to seven-membered rings by the addition of SCl_2 to aliphatic 1,3-, 1,4-, 1,5-, and 1,7-dienes as well as to dienes possessing functional groups have been described in the literature. The thiacyclane structures and the yields have been found to depend strongly on the structure of the diene and are controlled by steric and thermodynamic factors. Scheme 1 shows that the ring sizes can range from (n − 1) to (n + 1) where "n" is the number of carbon atoms in the diene chain. The formation of n-membered thiacyclanes proceeds by alternate n-exo-trig and n-endo-trig cyclisations of M- and aM-adducts. Only a single pathway seems to be possible for any thiacyclane with an (n − 1)- and (n + 1)-membered ring.



Scheme 1

The intermolecular interaction leading to oligomers and polymers is the reaction competing with cyclisation. Some pathways of formation of certain compounds of this type and their structures will be discussed below.

Concerning the dependence of the thiamonocyclane yield on the parent diene structure it should be noted that the yields have been found to be the lowest in the case of 1,3-dienes. In particular, the yield of 3-methyl-3,4-dichlorothiolane from isoprene and of 3,4-dimethyl-3,4-dichlorothiolane from 2,3-dimethyl-1,3-butadiene did not exceed 3%.[11]



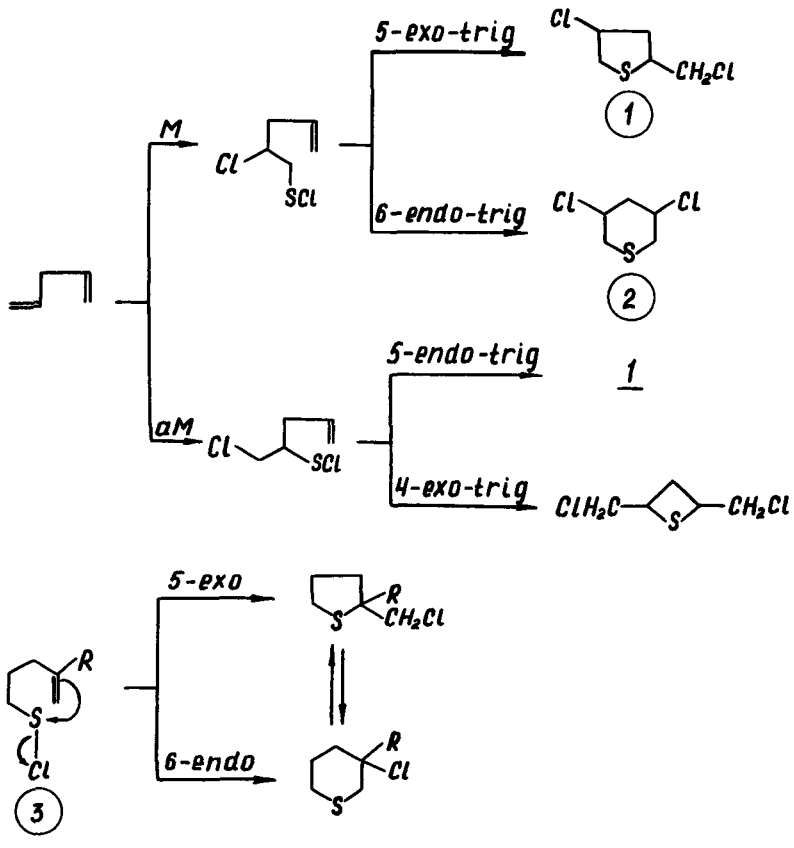
Scheme 2

Depending on the conditions, either 1,2,3,4-tetrachlorobutane[11] or bis-(2-chloro-3-butenyl) sulphide[12] was obtained instead of the expected thiolane.

However, the yields of 3,4-dichlorothiolanes showed a marked increase when dienes with non-terminal double bonds were subjected to the reaction with SCl_2.[13]

For example, 2,5-dimethyl-2,4-hexadiene was converted into 2,2,5,5-tetramethyl-3,4-dichlorothiolane and subsequently treated (without purification) with the chromium(II) acetate/ethylenediamine complex to give 2,2,5,5-tetramethyl-2,5-dihydrothiophene in a yield of 8% based on the diene. In a similar way, *cis*- and *trans*-2,5-dimethyl-2,5-dihydrothiophene were obtained in a yield of about 13%. The isomer ratio depends on the geometry of the double bonds in the initial dienes. Thus, a mixture of the *cis*- and *trans*-isomers in a 2:3 ratio was formed from (*E*,*E*)-2,4-hexadiene via 3,4-dichlorothiolanes. The reaction of (*E*,*Z*)-2,4-hexadiene with SCl_2 was more stereoselective since the content of *trans*-2,5-dimethyl-2,5-dihydrothiophene amounted to 90%.

The formation of thiolane derivatives from 1,3-dienes appears to proceed as an (n + 1)-endo-trig-cyclisation of an M-adduct, the stereoselectivity of which is controlled by steric factors operating in the intermediates. In fact, the high stereoselectivity of the reaction of (*E*,*Z*)-2,4-hexadiene can be explained by preference for a cyclisation which proceeds via sulphenyl chloride attack from the least hindered side. It should be noted



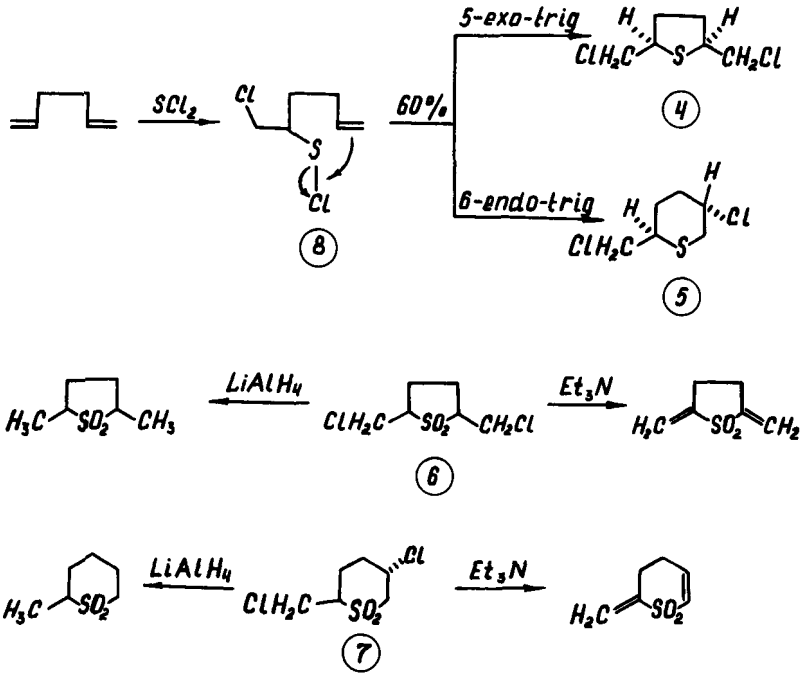
Scheme 3

that the fragmentation of the sulphonium salt **I** effected by butyllithium proceeds stereospecifically to give (*E,Z*)-2,4-hexadiene.

1,4-Pentadiene reacts with SCl_2 to form 2-(chloromethyl)-4-chlorothiolane and 3,5-dichlorothiane (**1**:**2** = 65:35).[14] This fact shows that the (n – 1)-exo-trig pathway leading to a thietane is not realised. The formation of thiolane and thiane can be represented respectively as 5-exo-trig and 6-endo-trig-cyclisations of the M-adduct. The cyclisation of the aM-sulphenyl chloride according to the 5-endo-trig pathway appears improbable.

From this viewpoint the cyclisation of unsaturated sulphenyl chlorides **3** (R = H, CH_3) is of special interest. According to Reference,[15] the initially formed products consist of mixtures with the thiolane as the major component (R = H: 79.6%; R = CH_3:95·6%). This was proven by oxidation to the corresponding sulphones. After keeping the mixtures at room temperature for a short period a change of the isomer ratio favouring the thianes (R = H: 82·0%; R = CH_3: 95·6%) occurred. Thus, the 5-exo-trig-cyclisation is kinetically favoured and gives thiolanes. However, the thiane derivatives are more stable thermodynamically.

According to Reference,[14] the reaction of 1,5-hexadiene with SCl_2 is stereo- and regiospecific to give *cis*-2,5-bis-(chloromethyl)-thiolane **4** in a yield of 60%.



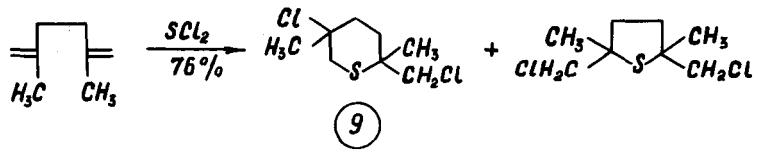
Scheme 4

Some recent data do not agree with these conclusions.[16] In particular, it has been established that the addition of SCl_2 to 1,5-hexadiene is not a regiospecific process, since even at -40 °C a mixture of **4** and *trans*-2-(chloromethyl)-5-chlorothiane **5** in a 3:2 ratio has been found to form. Storage at room temperature as well as vacuum distillation leads to irreversible isomerisation into a mixture with a reversed ratio of thiacyclanes (**4**:**5** = 35:65). The structures of the isomeric compounds have been determined by spectral studies of the crystalline sulphones **6** and **7**. E.g., the ^{13}C NMR spectrum of compound **6** shows only the expected three signals.

According to its ^1H NMR spectrum the sulphone **7** contains two equatorial substituents. These data unambiguously support the structures of the dichlorothiacyclanes **4** and **5** and allow to draw some conclusions concerning the stereo-orientation of the reaction of SCl_2 with 1,5-hexadiene. The reaction has been found to proceed through the kinetically favoured aM-sulphenyl chloride **8** in accord with the known statement[17] that the anti-Markovnikov addition of sulphenyl chlorides to alkenes is a kinetically controlled process taking place at low temperatures. The intramolecular cyclisation of **8** proceeds stereospecifically both via 5-exo-trig and 6-endo-trig schemes to give either a single isomer **4** or **5** in each case.

Further evidence for the thiacyclane structures is provided by reduction of the sulphones to *cis*-2,5-dimethylthiolane 1,1-dioxide under the action of $LiAlH_4$ as well as by their dehydrochlorination by triethylamine.

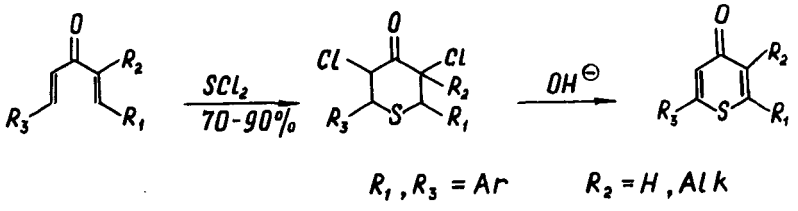
A mixture of thiacyclanes was obtained from 2,5-dimethyl-1,5-hexadiene in a 76% yield. Only 2-(chloromethyl)-2,5-dimethyl-5-chlorothiane **9** of unknown stereochemistry



Scheme 5

was isolated from the mixture.[14] No data concerning the structures of other reaction products were reported. In fact, the formation of stereoisomeric thiolanes and thianes can be expected.

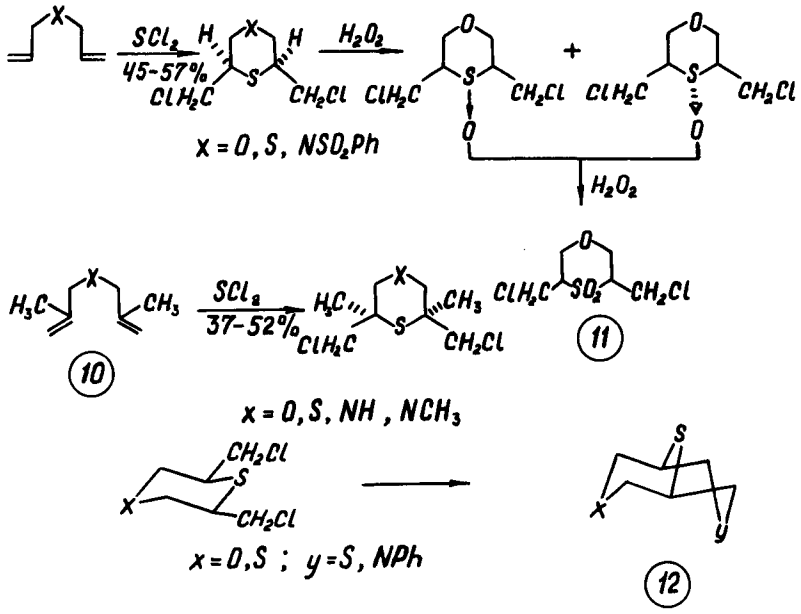
The reaction of 1,7-octadiene with SCl_2 proceeds as a stereospecific 7-exo-trig-cyclisation of the aM-adduct. However, the yield of *cis*-2,7-bis-(chloromethyl)-thiepane is rather low (13%).[14]



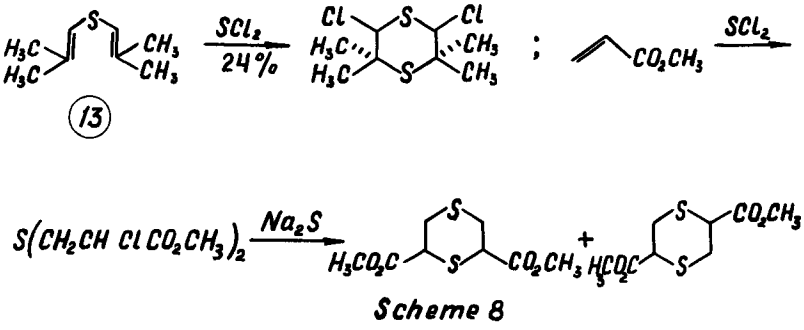
Scheme 6

The interaction of heteroatom-containing dienes with SCl_2 can serve as a convenient method for the preparation of a number of interesting sulphur-containing heterocycles. For example, the reaction with divinyl ketones has been utilised for the synthesis of thiopyrones. The formation of 3,5-dichlorotetrahydrothiopyrone-4 by 6-endo-trig-cyclisation of the M-adduct is the first step of this synthesis. Subsequent alkaline dehydrochlorination gives 4-thiopyrones in 70–90% yield based upon the divinyl ketones.[18]

The addition of SCl_2 to diallyl ether and to diallyl sulphide gives, respectively, 2,6-bis-(chloromethyl)-1,4-oxathiane and 2,6-bis-(chloromethyl)-1,4-dithiane in 42–44% yield.[14] The reaction of *N*,*N*-diallylbenzenesulphonamide proceeds in a higher yield to give the thiomorpholine.[19] Corresponding 2,2,6,7-tetrasubstituted heterocycles were obtained from dimethylallylic compounds of type **10**.[20] The addition of SCl_2 is both regio- and stereospecific since in all the reported cases the formation of *cis*-isomers has been observed, the structure of which has been proved by two independent methods. Thus, the oxidation of 2,6-bis-(chloromethyl)-1,4-oxathiane gave a mixture of two stereoisomeric sulphoxides which both could be converted to the same sulphone **11**.[14] The *cis*-arrangement of the chloromethyl groups follows also from the formation of bicyclanes of type **1** upon cyclisation with Na_2S or aniline.[21]



Scheme 7

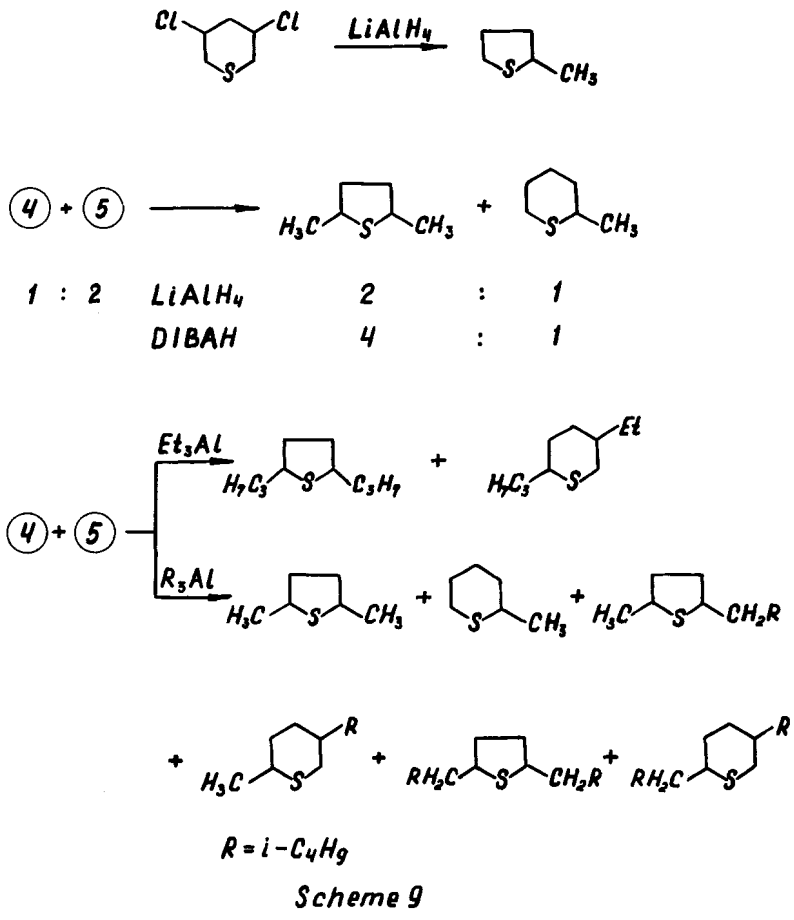


Scheme 8

Only one example of SCl_2 addition to divinyl sulphides has been reported. Thus, **13** gives rise to a mixture of stereoisomeric dithianes.[20] The synthesis of 1,4-dithianes can also be achieved by cyclisation of adducts of SCl_2 to mono-olefins with Na_2S, as has been shown by the corresponding transformation of methylacrylate.[22]

The further transformation of dichlorothiamonocyclanes by nucleophilic substitution and oxidation may become a convenient route for the preparation of many thiacyclanes which otherwise are difficult to obtain. Thus, the reduction by aluminium hydrides is accompanied by a change in the ring size. E.g., 3,5-dichlorothiane under the influence of $LiAlH_4$ undergoes quantitative transformation to 2-methylthiolane.[14] $LiAlH_4$ may be replaced by diisobutylaluminium hydride (DIBAH) which allows dechlorination under mild conditions (20 °C, 1 hr) in the presence of catalysts such as $TiCl_4$, $ZrCl_4$, and $Ni(acac)_2$.[23]

As evident from Scheme 9, hydrides cause an increase in the content of thiacyclanes with a smaller ring size.



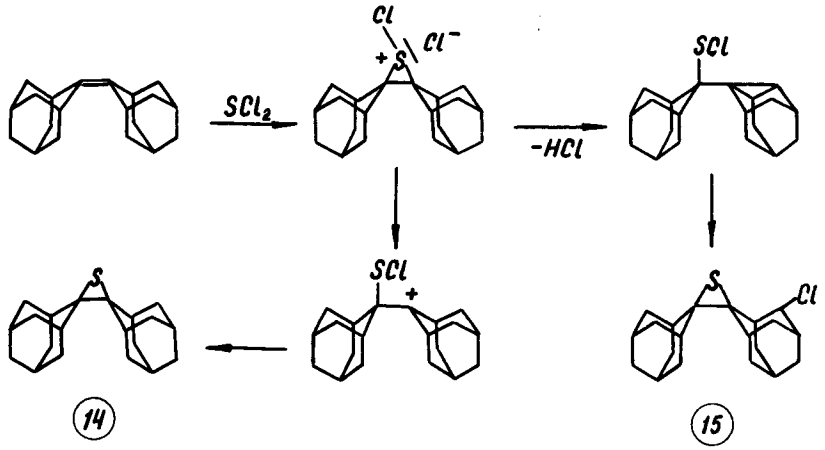
Scheme 9

The interaction of dichloro sulphides with trialkylalanes results in the formation of alkylation products. Thus, 2,5-dipropylthiolane and 2-propyl-5-ethylthiane were obtained from a mixture of the thiacyclanes **4** and **5** (2:1) under the action of triethylaluminium with the content of thiane increasing up to 75%. The reaction with triisobutylaluminium is more complicated since the formation of monoalkylation and dechlorination products has been established in addition to the formation of the dialkylation products.[23]

The reaction regarded below does not strictly relate to the transformation type discussed. However, we represent this reaction here since it is based on the interaction of SCl_2 with olefins on one hand and leads to thiamonocyclanes on the other.

The interaction of SCl_2 with adamantylideneadamantane, with an SCl_2-to-olefin ratio of 1:1.25, in chloroform at 20 °C was found[24] to give nearly instantaneously (5 min) thiirane **14** in 80% yield. (*e*)-4-Chloro-2,2′-epithio-2-(2′-adamantyl)-adamantane **15** was formed almost quantitatively in dichloromethane at 0° during 80 min. The structures of the thiiranes were confirmed by X-ray data.[24,25]

The mechanism of the thiirane formation involving a σ-sulphurane intermediate is represented in Scheme 10. The problem of synthesis of thiirane derivatives from monoolefins and sulphenyl halides has been discussed in the literature.[26,27-30]

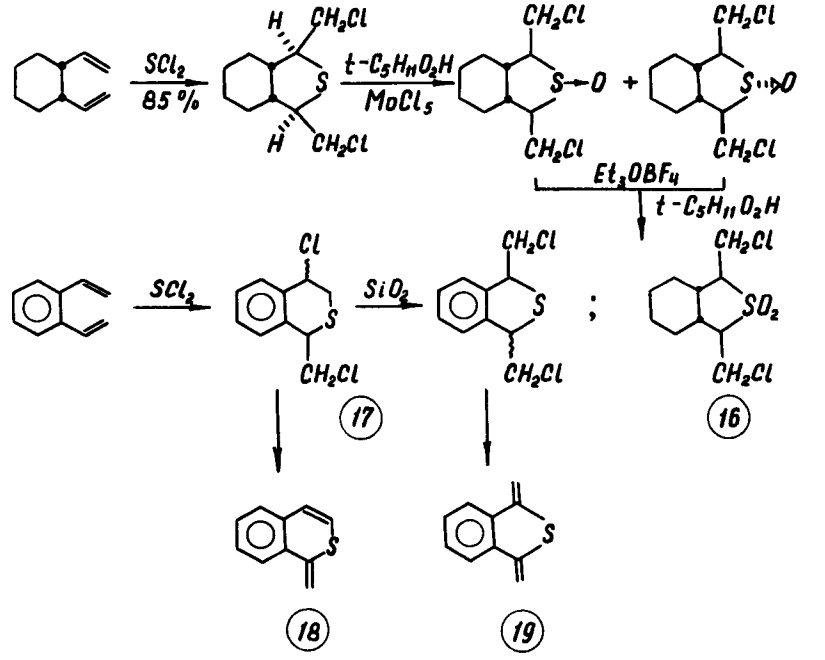


Scheme 10

SYNTHESIS OF THIABICYCLANES

The addition of SCl_2 to 1,2-divinylcyclanes, alkenylcyclanes, and cyclic dienes is commonly used to obtain thiabicyclanes.

The cyclisation of *cis*-1,2-divinylcyclohexane forming *cis*-1,3-bis-(chloromethyl)-perhydro-2-thiaindane proceeds smoothly and in high yield.[31] The orientation of the substitutents is supported by the fact that two epimeric sulphoxides are obtained with t-pentyl hydroperoxide in the presence of $MoCl_5$.[32,33] The oxidation product of both

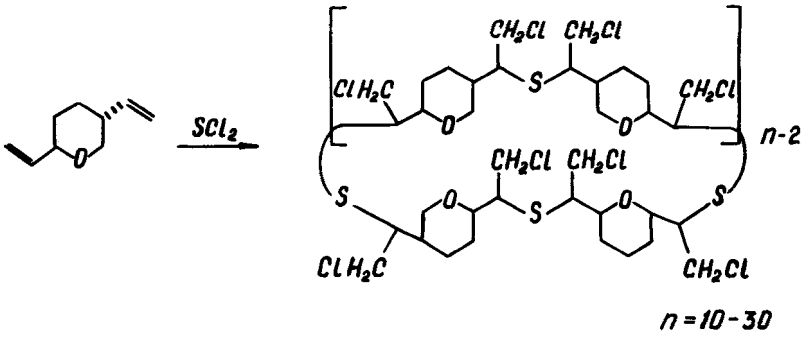


Scheme 11

sulphoxides is the sulphone **16**. Epimerization of the sulphoxide proceeds quantitatively under the influence of $[Et_3O]BF_4$.

In contrast to divinylcyclohexane, *o*-divinylbenzene reacts with SCl_2 to give the thiatetraline derivative **17** which chromotographed on silica gel gives a mixture of isomeric *cis*- and *trans*-1,3-bis-(chloromethyl)-1,3-dihydrobenzo[c]thiophenes.[34] Dehydrochlorination of the dichloro sulphides effected by azabicyclononane leads to compounds **18** and **19**.

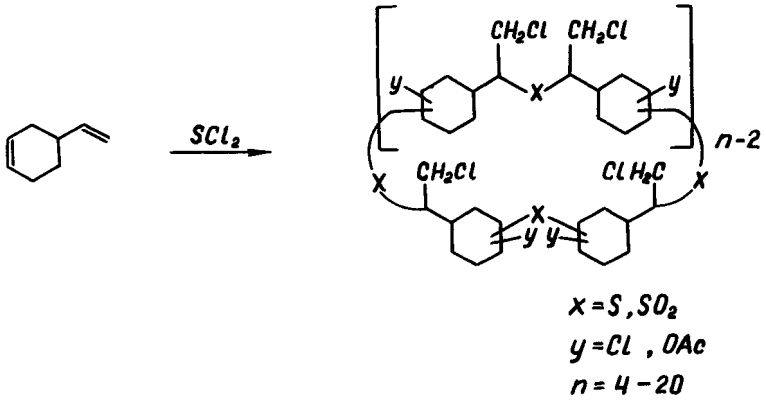
Therefore, the reactions lead to the formation of the thermodynamically favoured five- and six-membered heterocycles.



Scheme 12

When the vinyl groups occupy 1,4-positions intramolecular cyclisation does not occur. E.g., the reaction of SCl_2 with (*e*,*e*)-2,5-divinyltetrahydropyrane leads to macrocyclic oligomers with a molecular mass of about 8,000. According to ^1H NMR spectral data the oligomer units contain mainly anti-Markovnikov fragments.[35]

By itself, the formation of macrocyclic compounds is of considerable importance since it offers a convenient pathway for the synthesis of ionophore analogs and multidentate ligands. Macrocyclisation also occurs in reactions of 4-alkenylcyclohexenes with SCl_2, the yield of cyclooligomers depending on the double-bond reactivity towards electrophilic reagents. Thus, in the series: 4-vinylcyclohexene—1,4-dimethyl-4-vinylcyclohexene—



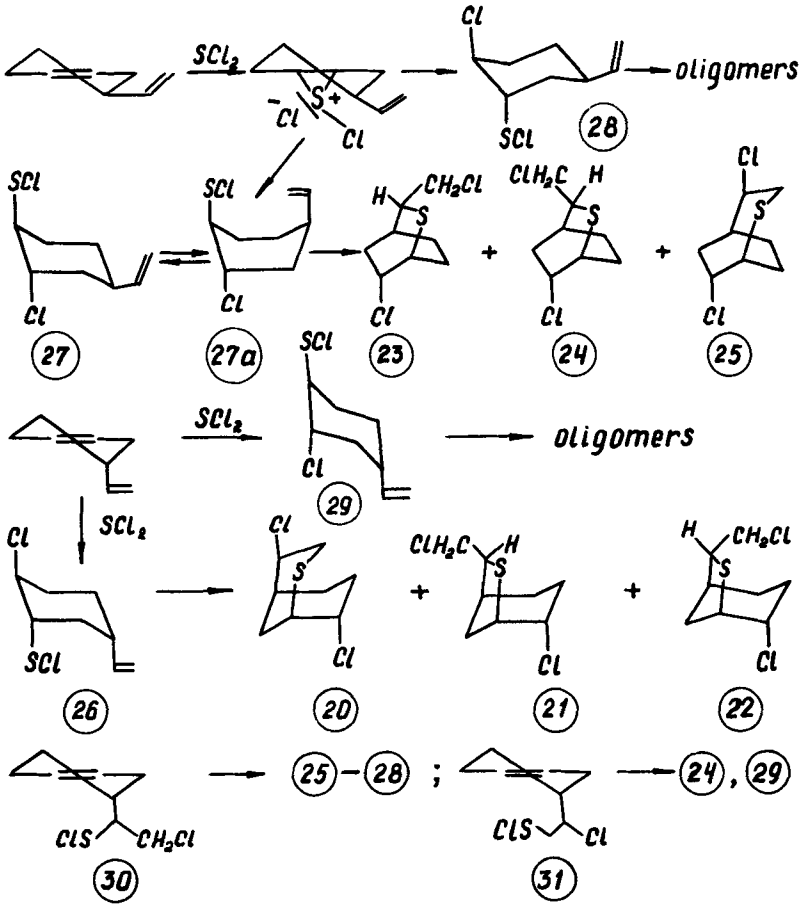
Scheme 13

1-methyl-4-isopropenylcyclohexene (dipentene) the yields of macrocyclic products from intermolecular cyclisation were 70%, 20%, and 15%, respectively.

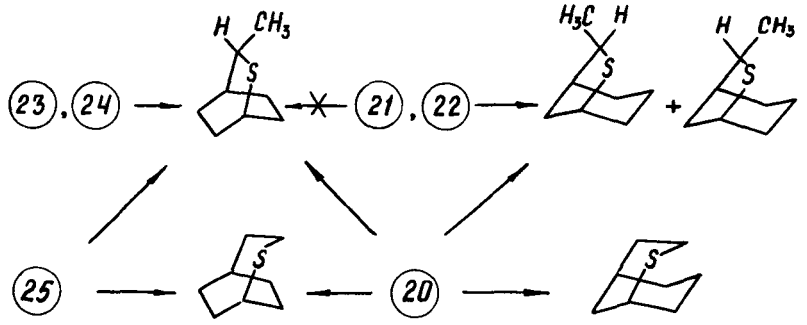
In the case of 4-vinylcyclohexene the formation of cyclooligomers was observed the molecular mass of which approached 5,000 depending on the reaction conditions and the solvent used. Scheme 13 represents their structures as assigned according to spectral data. The oligomers can be oxidized with hydrogen peroxide to sulphones and can be readily subjected to acetolysis as well.

Intramolecular cyclisation forms the thiabicyclanes **20–25**, their total yield not exceeding 30%.[35] It is to be noted, however, that the presence of four structural types of thiacyclanes was established in a mixture which had undergone distillation. Therefore, the possibility of thermal isomerization has to be taken into account.

The interaction of SCl_2 with 4-vinylcyclohexene can start with an attack at any of the double bonds. However, the addition across the cyclic bond seems to be preferred. This assumption agrees with the known data on selective reactions of 4-vinylcyclohexene with electrophilic reagents. E.g., epoxidation by peracids or hydroperoxides has been found to give exclusively 4-vinyl-1,2-epoxycyclohexane.[35]



Scheme 14

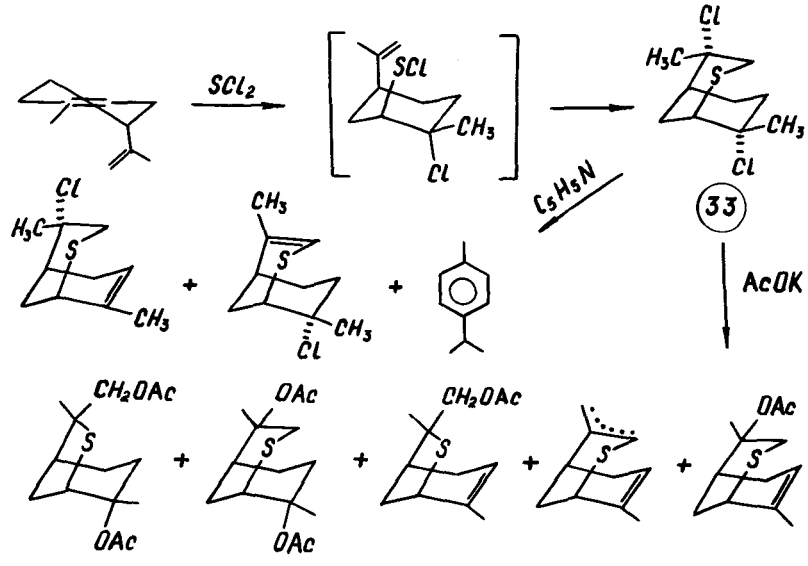


Scheme 15

Regarding the addition of SCl_2 to the cyclic double bond in conventional terms explains the observed formation of the four sulphenyl chlorides **26**–**29**. The isomer **26** with both reactive groups in the axial position can undergo a rapid intramolecular cyclisation to give the thiabicyclanes **20**–**22**. The cyclisation of sulphenyl chloride **27** appears to proceed at the moment of fixation of a boat conformation **28a** giving the thiabicyclanes **23**–**25**. The sulphenyl chlorides **28** and **29** can only interact intermolecularly to give cyclic oligomers.

Primary formation of the sulphenyl chlorides **30** and **31** is also possible. They can react both inter- and intramolecularly to give either thiabicyclanes described previously or oligomeric products.

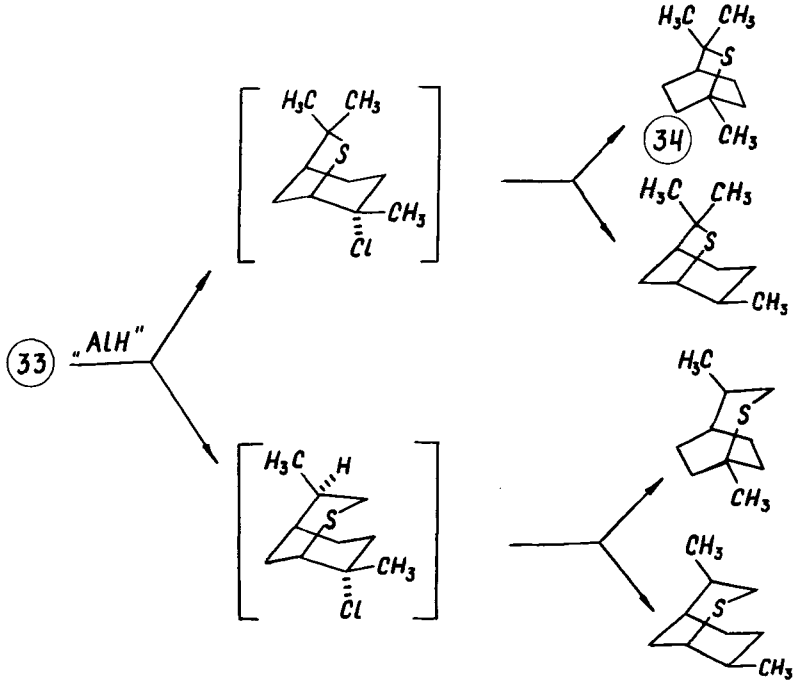
The evidence concerning the structures of the dichlorothiabicyclanes as well as their mutual transformations were obtained by reductive dechlorination. As was expected, the reduction resulted in five thiabicyclanes only, since the isomers **23** and **24** convert into the same sulphide of symmetrical structure.[32] The use of various reducing agents including DIBAH/Ni(acac)$_2$,[23] $LiAlH_4$, and $NaBH_4$ gave rise to mixtures of various thiabicyclanes. The conclusion has been drawn that reductive dechlorination is accompanied by



Scheme 16

skeletal rearrangement. Since two chlorine atoms are involved in reduction, double skeletal rearrangement is possible. Scheme 15 shows possible routes to thiabicyclanes on reduction.

The various possibilities for interconversions of chlorothiacyclanes in reductive dechlorination are evident in the example of the dipentene-SCl_2 adduct. As has been mentioned, in contrast to 4-vinylcyclohexene, dipentene gives mainly a product of intermolecular cyclisation. The reaction is regio- and stereospecific since a single product **33** is formed. Vacuum distillation or heating with pyridine gives two chlorothiacyclanes and *p*-cymene. Acetolysis with sodium acetate in acetic acid has been found to lead to two dienes as well as to mono- and diacetates both with unchanged and isomerized skeletons.

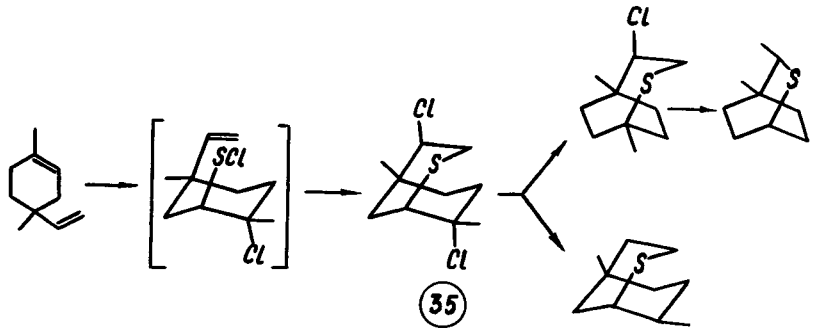


Scheme 17

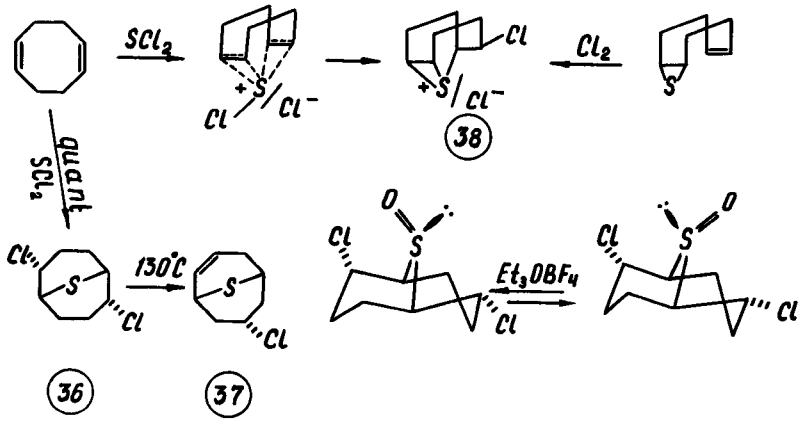
The reduction of adduct **33** leads to thiabicyclanes of four structural types.

The interaction of SCl_2 with 1,4-dimethyl-4-vinylcyclohexene is regio- and stereospecific and leads to the 2-thiabicyclo[3.3.1]nonane derivative **35**. The reduction effected by DIBAH/Ni(acac)$_2$ gives only two sulphides, one with unchanged skeleton, the other being the product of a double skeletal rearrangement.

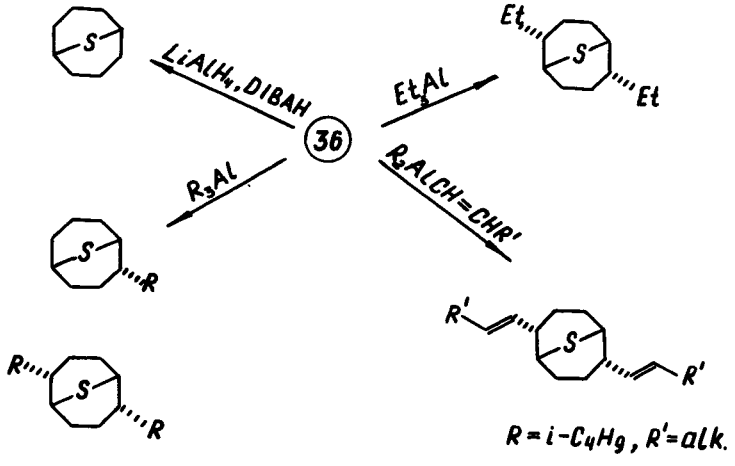
Interesting data have been obtained in investigations of transannular additions of SCl_2 to cyclodienes. Three independent research groups published nearly simultaneous reports[36–38] concerning a new approach to the synthesis of the otherwise difficultly available derivatives of 9-thiabicyclo[3.3.1]nonane. In particular, it has been established that 1,5-cyclooctadiene can readily be made to react with SCl_2 (no high-dilution technique is necessary) to form 2,6-dichloro-9-thiabicyclo[3.3.1]nonane **36** in almost quantitative yield. Its reduction with $LiAlH_4$ leads to 9-thiabicyclo[3.3.1]nonane. Taking into consideration the fact that its sulphoxide remains unchanged upon



Scheme 18



Scheme 19

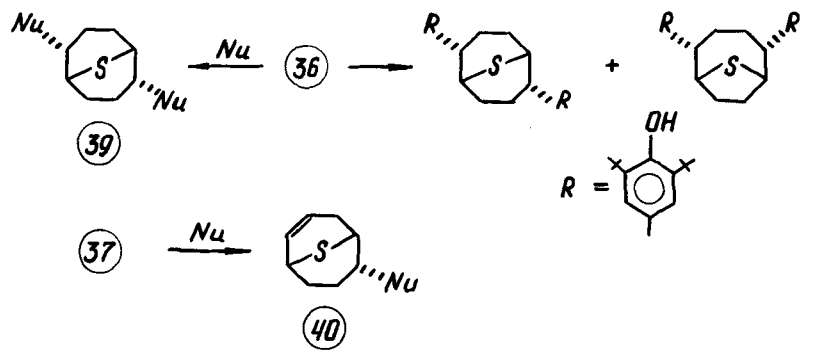


Scheme 20

attempted inversion with the well-known reagent Et_3OBF_4,[38] the structure of compound **36** has been unambigiously proven to be symmetrical. The spectral data are in accordance with an equatorial position of the chlorine atoms in compound **36**.[36] Upon heating of the dichloro sulphide over 130 °C elimination of HCl occurs to form the unsaturated compound **37**.

Regarding the mechanism of the reaction of cyclooctadiene with SCl_2, the participation of the thiiranium ion **38** has been suggested,[35] whose formation can proceed via an intermediate containing a pentacovalent sulphur atom. The conversion of cyclooctadiene monoepisulphide into **36** by chlorine is regarded as evidence for the existence of the thiiranium ion.[12]

Being readily available now adduct **38** has been used for the synthesis of a variety of sulphur-containing compounds. Thus, reduction and alkylation products result from the interaction with organoaluminium compounds in the presence of $Ni(acac)_2$.[23]



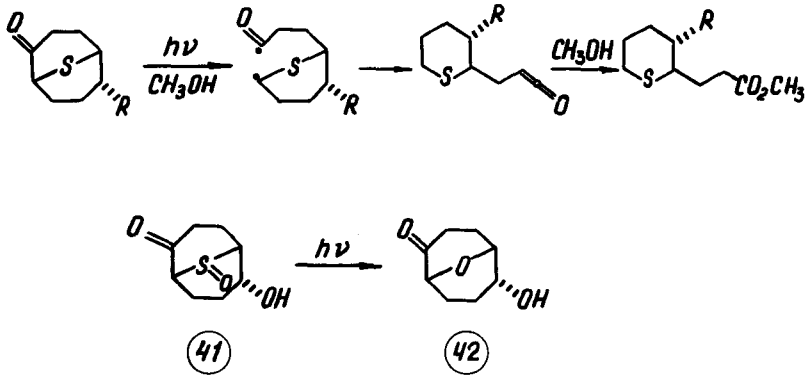
Scheme 21

The rearrangements involving a change in the ring size which take place during nucleophilic substitution have not been fully elucidated yet. According to Reference,[36] no rearrangement takes place in the reaction with nucleophiles such as F^-, I^-, OH^-, OAc^-, RO^-, ArO^-, ArS^-, $ArNH^-$, CN^-, SCN^-, $^-SP(S)(OR)_2$, and $^-SC(S)(NR_2)$. The formation of compounds of type **39** has been postulated. However, from the alkylation of 2,6-di-(*t*-butyl)-phenol with dichloro sulphide **36** in the presence of NaOH in dimethylformamide, two bisphenols have been isolated. They have been patented as antioxidants.[39]

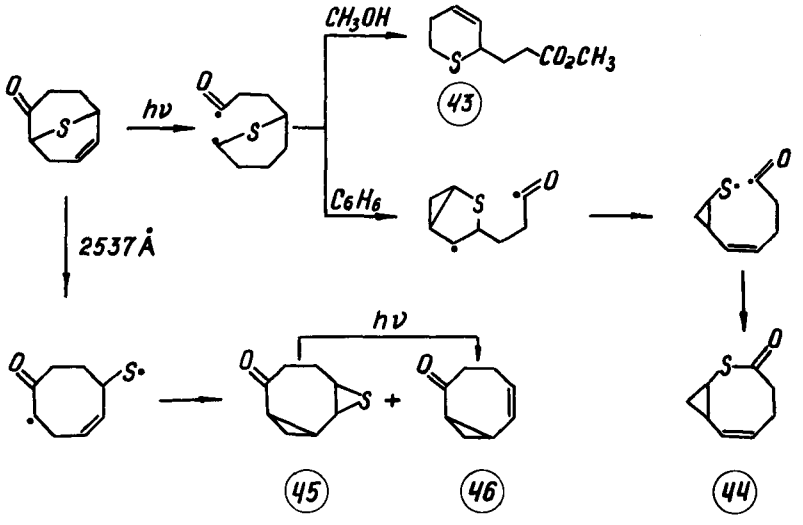
Nucleophilic substitution of the chlorine atom in the unsaturated sulphide **37** proceeds without any rearrangement. The reaction products **39** and **40** (Nu = ^-CN, ^-SCN, $^-SP(S)(OR)_2$, $^-SC(S)(NR_2)$) have been reported to possess high fungicidal, insecticidal, and amoebicidal activities.[40,41]

Interesting conversions of 9-thiabicyclo[3.3.1]nonane derivatives occur in photolysis. E.g., saturated α-keto sulphides were found to be converted to methyl esters of thiane derivatives upon UV irradiation in methanol.[42,43] The irradiation of the hydroxyketo sulphoxide **41** is accompanied by sulphur elimination to give the hydroxyketone **42**.[43]

The photoconversions of 9-thiabicyclo[3.3.1]-2-nonenone-6 take a different course. The unsaturated ester **43** was obtained in methanol solution, whereas the thiolactone **44** was formed in benzene solution. If the reaction was run using monochromatic light



Scheme 22

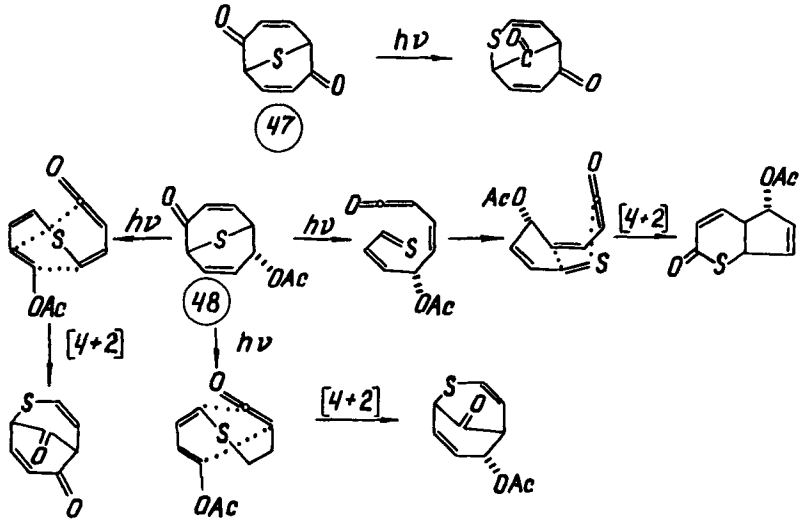


Scheme 23

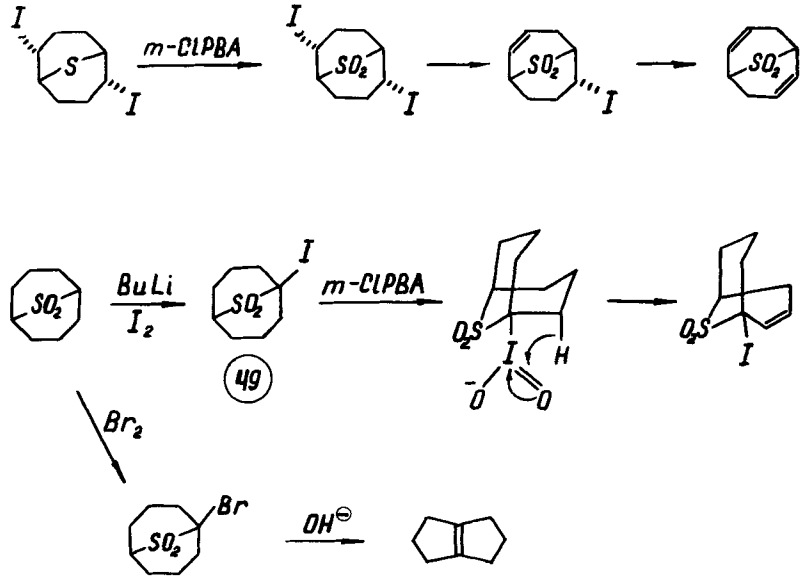
(λ = 2537 Å) formation of the ketones **45** and **46** was observed. The following explanations for the formation of these compounds have been suggested:[42,44,45]

Irradiation of diketone **47** and acetoxy ketone **48** causes complex rearrangements as shown in Scheme 24. While photolysis of the former gives a single diketone derived from 2-thiabicyclo[3.3.1]nonane, the latter **48** forms a variety of products. These transformations have been regarded[46] as a sequence of [4 + 2]-photocyclisations of ketene intermediates.

Some eliminations involving sulphones have been reported.[47] Thus, the oxidation of a diiodothiabicyclane with *m*-chloroperbenzoic acid leads to a sulphone which eliminates first one molecule of HI and then the second one while being treated with excess peracid. The assumption was made that the elimination proceeds via intermediates containing iodoxy groups. This is supported by experiments with the iodo sulphone **49** which is converted into an unsaturated compound in high yield upon oxidation with excess peracid.



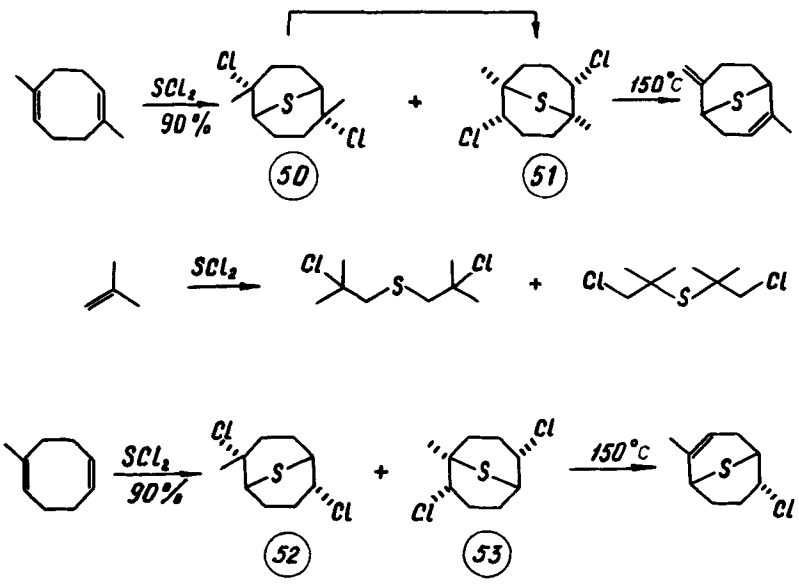
Scheme 24



Scheme 25

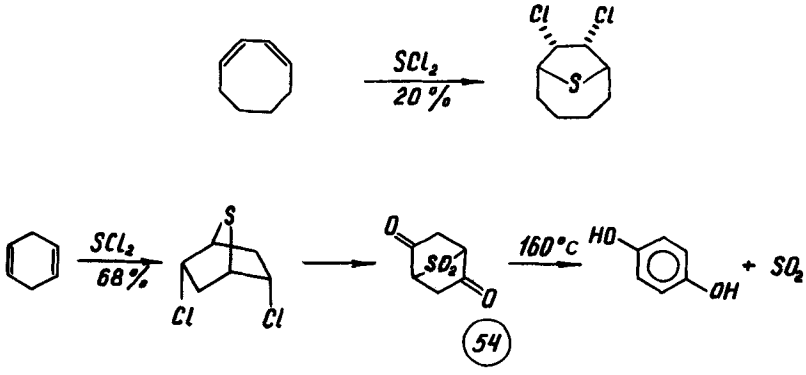
9-Thiabicyclo[3.3.1]nonane 9,9-dioxide has been used for synthesis of 1,5-bicyclo-[3.3.0]octene. A transannular Ramberg-Bäcklund rearrangement is the key step.[48]

Rapid isomerisation of thiacyclanes has been established in the reaction of SCl_2 with 1-methyl- and 1,5-dimethyl-1,5-cyclooctadiene.[23] Thus, a mixture of adducts was obtained from 1,5-dimethylcyclooctadiene at $-50\,^{\circ}C$, where a "Markovnikov" isomer prevailed (**50**:**51** = 75:25). While keeping this mixture at temperatures from $+5$ to $+20\,^{\circ}C$ for 5 days spontaneous rearrangement occurred to form essentially the aM-adduct **51**. This process is considerably promoted at elevated temperatures: e.g., heating the mixture up to 100 °C for several minutes results in mixtures whose main component is **51** (95%).



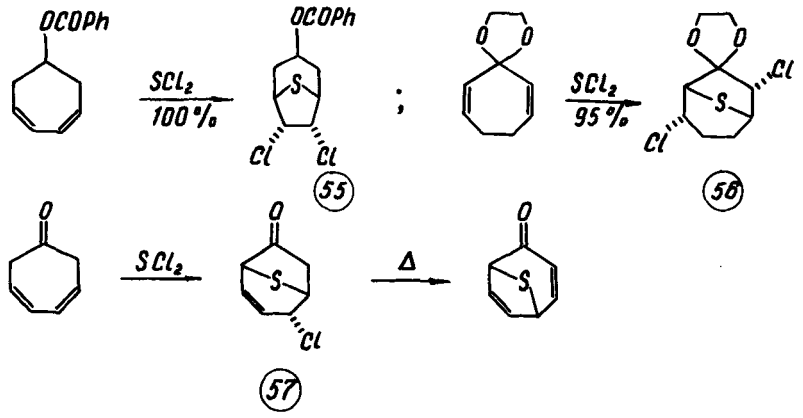
Scheme 26

It should be noted that upon heating the isobutylene-SCl_2 adduct (2:1), the isomer ratio in the originally obtained mixture M:aM = 46:54 is reversed to give M:aM = 65:35. This fact can be explained by a higher thermodynamic stability of the M-adduct.[5] The isomerisation of the bicyclane **50** to **51** may be related to a higher thermodynamic stability of the isomer containing two angular methyl groups. This is supported by the somewhat different behaviour of the 1-methylclooctadiene-SCl_2 adduct. Freshly prepared it consists of a mixture of isomers **52**:**53** = 62:38, while after standing or after a short period of heating the ratio is reversed to become 30:70. Thus, the presence of a single methyl group imparts no sufficient improvement in the stability of isomer **53** to obtain it as a single product. The difference in behaviour of the adducts during thermolysis is of special interest. While **51** eliminates two HCl molecules to form the corresponding diene, the mixture of **52** and **53** gives a chloro sulphide.[23]



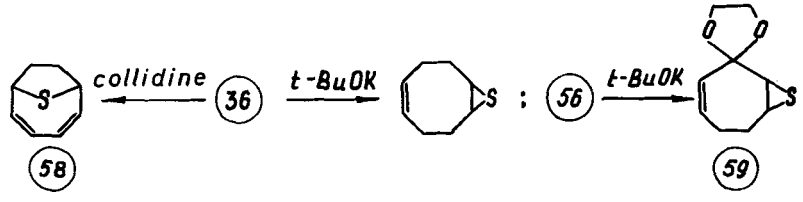
Scheme 27

The addition of SCl_2 to 1,3-cyclooctadiene results in a low yield of the single isomer 7,8-dichloro-9-thiabicyclo[4.2.1]nonane.[36] Strong dilution (1:500) is required to obtain a satisfactory yield (68%) of the corresponding adduct of 1,4-cyclohexadiene.[37] It should be emphasized that both chlorine atoms in the adduct are *endo*-oriented. The diketo sulphone **54**, readily available from the corresponding adducts, eliminates SO_2 to give hyroquinone[49] when heated to 160 °C.



Scheme 28

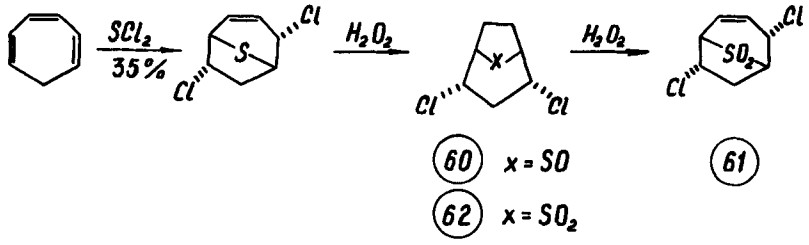
Thia-analogs of tropane alkaloids containing the 8-thiabicyclo[3.2.1]octane skeleton can be obtained from cycloheptadiene derivatives.[50] E.g., 1,3-cycloheptadien-6-yl benzoate upon addition of SCl_2 is quantitatively converted to the thiacyclane **55**. The dichloro sulphide **56** is obtained from 1,5-cycloheptadiene-7-one ethylene ketal. The addition of SCl_2 to 1,3-cycloheptadiene-6-one is accompanied by elimination of HCl and rearrangement to the unsaturated compound **57** which upon heating gives the photolabile 8-thiabicyclo[3.2.1]-3,6-octadiene-2-one.



Scheme 29

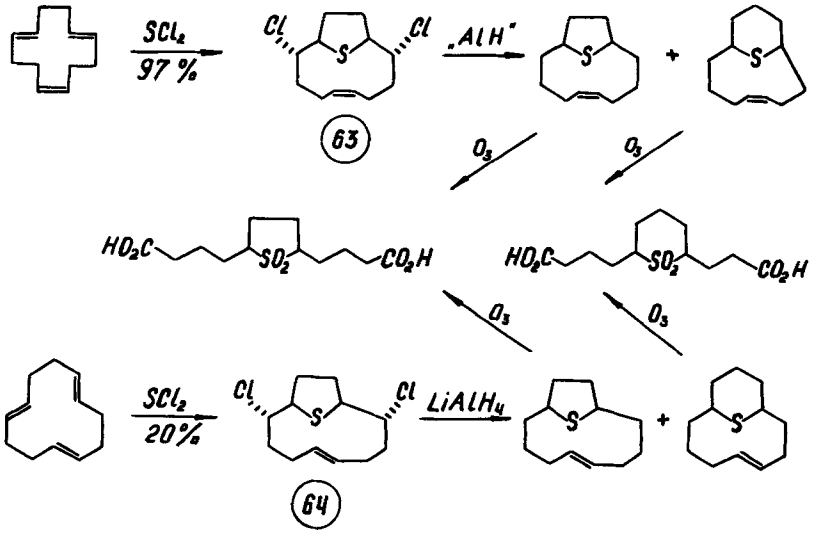
As a rule, the elimination of two HCl molecules from dichlorothiabicyclanes effected by bases is accompanied by some rearrangement. Thus, compound **36**, refluxed in collidine, forms **58**.[51] Treatment with potassium *t*-butoxide in dimethyl sulphoxide leads to thiiranes. E.g., cyclooctadiene monoepisulfide is obtained from **36**, whereas **56** is smoothly converted to **59**.[52]

Several cyclic trienes and tetraenes have been used for the synthesis of thiabicyclanes. Thus, SCl_2 can be added to 1,3,5-cycloheptatriene to give 2,6-dichloro-8-thiabicyclo [3.2.1]octene. Oxidation of this compound results in rather interesting conversions. Treatment with H_2O_2 in acetic acid leads to the sulphoxide **60** with a rearranged skeleton.



Scheme 30

Further oxidation under the same conditions surprisingly gives the sulphone **61** with an unchanged skeleton. The rearranged skeleton was retained in sulphone **62** which results when the oxidation is carried out with H_2O_2 in acetone.[39]

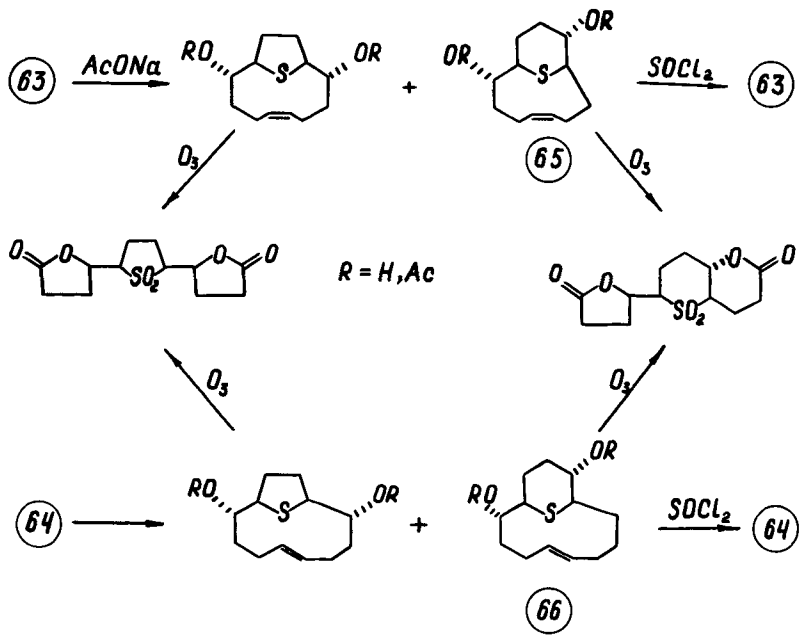


Scheme 31

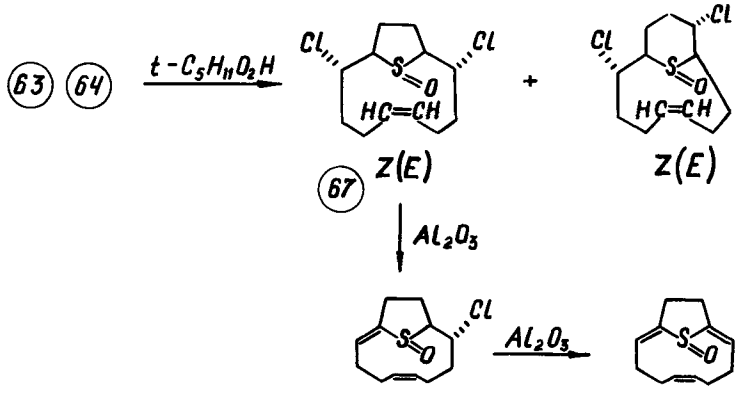
The reaction of (*E*,*E*,*Z*)- and (*E*,*E*,*E*)-1,5,9-cyclododecatriene with SCl_2 has been investigated in detail.[53–59] The formation of adduct **63** from the (*E*,*E*,*Z*)-triene was established to proceed quantitatively whereas the yield of thiabicyclane **64** from the (*E*,*E*,*E*)-isomer under optimal conditions does not exceed 20%. A water soluble salt of unknown structure[55–57] appears to be the main reaction product. Upon reduction of both thiabicyclanes with $LiAlH_4$, rearrangement takes place to form thiane derivatives in a yield of 80%. Thiabicyclanes with an unchanged skeleton amount only to 20%. The ratio of thiane to thiolane was reversed (15: 85) when the reagent DIBAH/$Ni(acac)_2$[23] was used as reductant.

Ozonolysis of thiabicyclenes appears to be a convenient way for obtaining the otherwise difficultly accessible 2,5-disubstituted sulpholanes and 2,6-disubstituted thianes.[57]

The acetolysis of the dichloro sulphides is accompanied by partial isomerisation.[58–59] However, the content of the thiane derivatives **65** and **66**, their structure being proved by X-ray structural analysis,[60] does not exceed 20%. It should be noted that the possibility



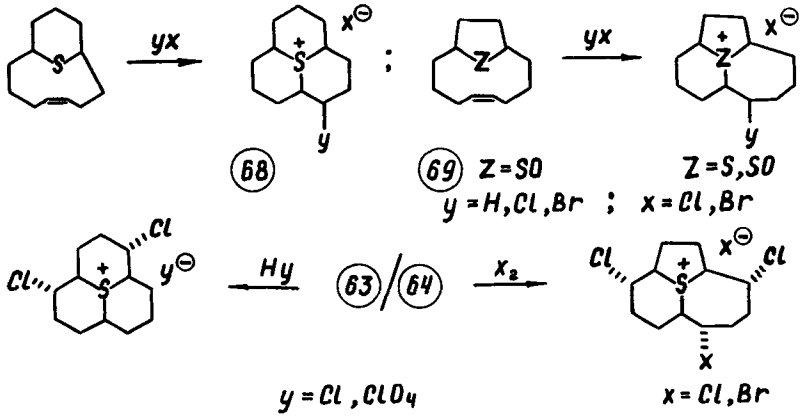
Scheme 32



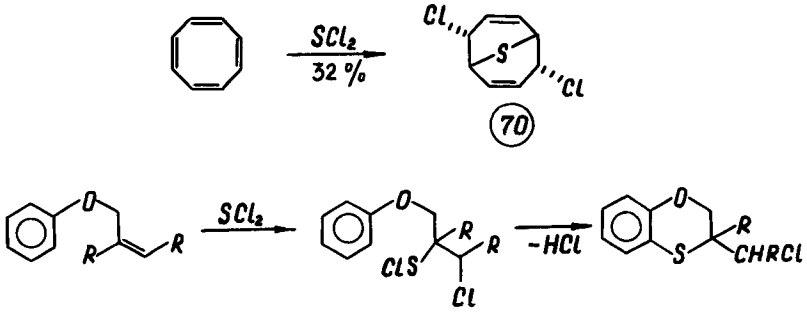
Scheme 33

of a reverse rearrangement of the thiane derivatives to the original structures has been demonstrated by conversion of the diols (R = H) to the adducts **63** and **64**, respectively, by means of $SOCl_2$.[59] The ozonolysis of the diols was used for obtaining polyfunctional sulpholane and thiane derivatives.[57–59] Certain ozonolysis products possess high antiinflammatory activity.[61]

Rearrangement with ring expansion is observed in the interaction of **63** with KSCN, $NaNO_2$, NaCN, and $NaOCH_3$[56,62] as well as in the oxidation of the dichloro sulphides. Thus, together with the sulphoxides **67** thiane oxides[33,56,63–66] were obtained under the influence of t-$C_5H_{11}O_2H$ in the presence of $MoCl_5$. The former are subject to smooth dehydrochlorination upon contact with Al_2O_3.[56]



Scheme 34



Scheme 35

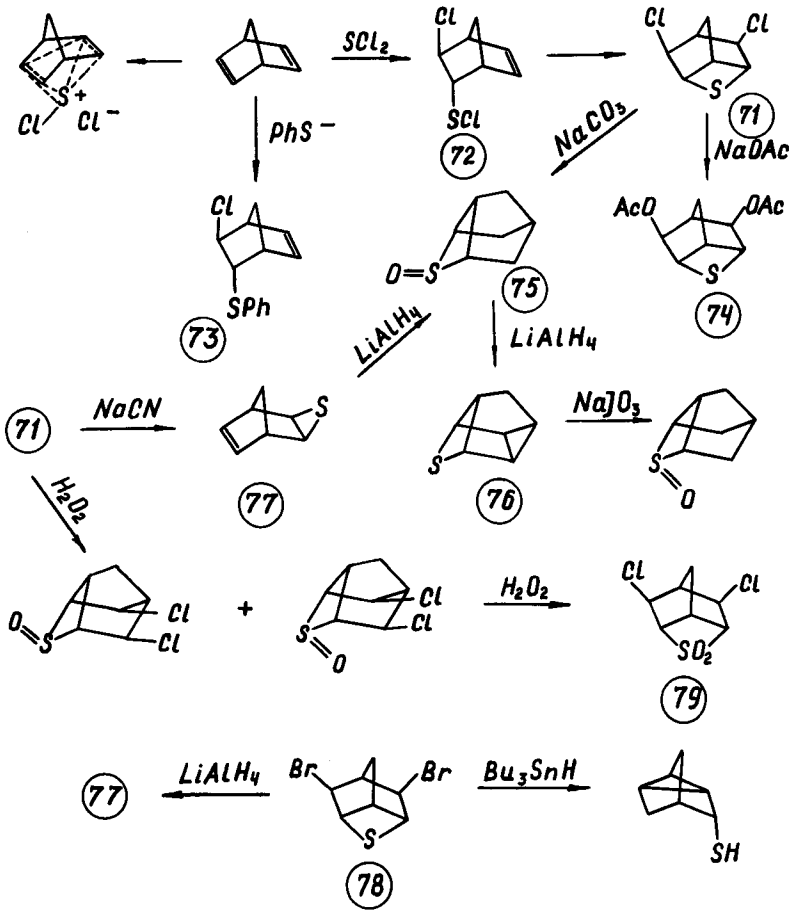
Transannular reactions involving the sulphur atom and a double bond take place when thiabicyclenes are treated with HCl, $HClO_4$, Cl_2, or Br_2. The corresponding sulphonium salts are obtained. It should be emphasised that no isomerisation is caused by Cl_2 and Br_2 while HCl and $HClO_4$ give the sulphonium salts **68**.[56] The sulphoxide **69** reacts with HCl and Br_2 to form sulphoxonium salts.[56,66–68]

The conversion of 1,3,5,7-cyclooctatetraene to 2,6-dichloro-9-thiabicyclo[3.3.1]-3,7-nonadiene **70** appears to be the only example of reactions of tetraenes with SCl_2.[53,69]

A different case is the synthesis of 2,3-dihydro-1,4-benzoxathiines from phenylallyl ethers involving the spontaneous cyclisation of the intermediate sulphenyl chlorides with elimination of HCl.[70]

THE SYNTHESIS OF THIATRICYCLANES AND POLYHEDRAL COMPOUNDS

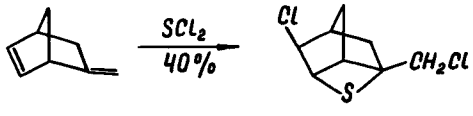
Sulphur dichloride quite easily adds to norbornadiene yielding about 80% of *exo,exo*-3,5-dichloro-8-thiatricyclo[2.2.1.$1^{2,6}$]octane.[71] The asymmetrical structure is supported by the oxidation to two stereoisomeric sulphoxides, which interconvert under the action of Et_3OBF_4 and form the same sulphone upon further oxidation.[71] The addition of SCl_2 to norbornadiene is considered to occur via an intermediate containing pentacovalent



Scheme 36

sulphur. We believe the reaction to start with an SCl_2 attack across one of the double bonds with the formation of the *exo*-chloro *endo*-sulphenyl chloride **72**. The possibility of obtaining *exo*-chloro *endo*-sulphides **73** from norbornadiene and arenesulphenyl chlorides constitutes reliable proof.[72,73]

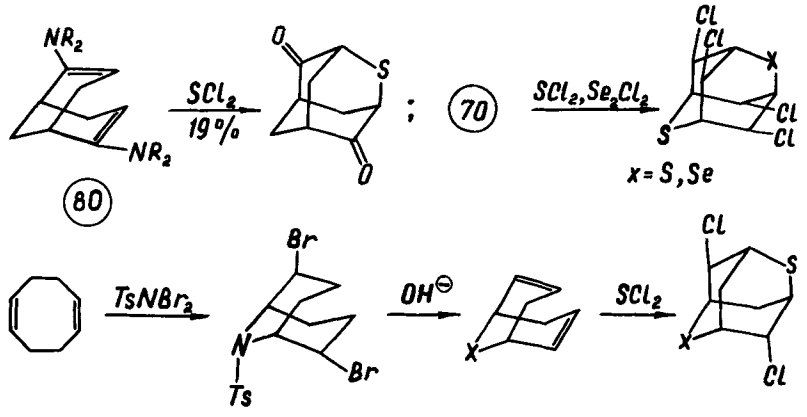
The stereoorientation of the second stage is determined by the conformation of the adduct **72**. Some interesting transformations of **71** take place during nucleophilic substitution. Thus, acetolysis proceeds without rearrangement to give the diacetate **74**,[74] whereas hydrolysis with aqueous Na_2CO_3 leads to a sulphoxide[75] with a tricyclane structure.[75] A stereoisomeric sulphoxide can be obtained from **75** in two steps: reduction of **75** with $LiAlH_4$ to form **76** which subsequently is oxidised with $NaIO_3$.[76]



Scheme 37

It should be noted that the sulphoxide **75** can be obtained by reduction of thiirane **77** with $LiAlH_4$ as well. Compound **77**, in turn, is formed either by treatment of the dichloro sulphide **71** with sodium cyanide or by reduction of the dibromo sulphide **78** with $LiAlH_4$. The action of tributylstannane on **78** gives a rearranged thiol. Sulphone **79** has been patented as a monomer.[77]

The addition of SCl_2 to 2-methylenenorbornene proceeds stereospecifically to yield *exo*-2-(chloromethyl)-*exo*-5-chloro-8-thiatricyclo[2.2.1.$1^{2,6}$]octane.[14]



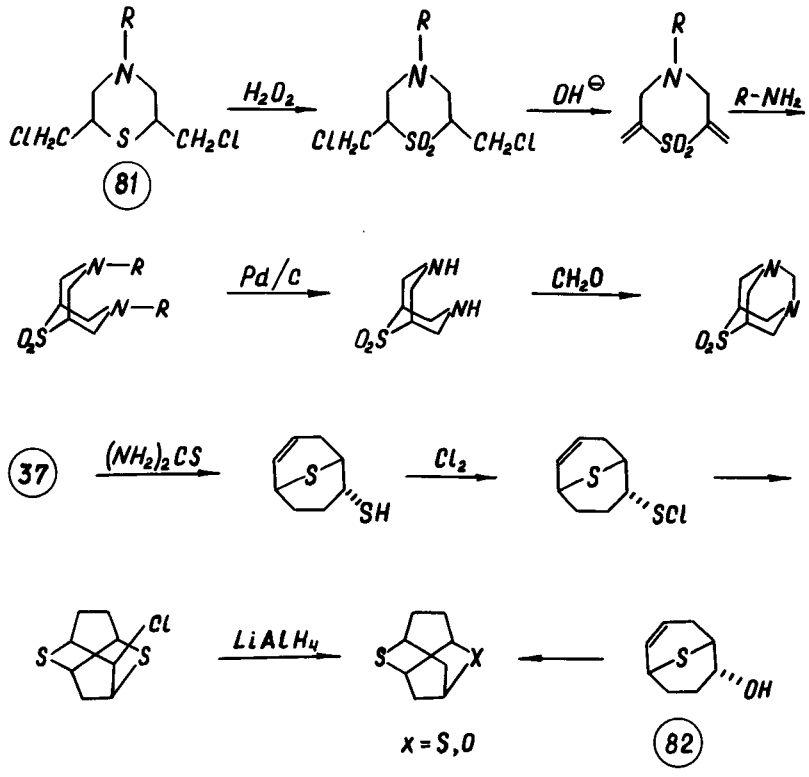
Scheme 38

Several synthetic pathways leading to sulphur-containing polyhedral compounds are known. Thus, enamine **80** has been converted to a diketothiaadamantane in 19% yield.[78] 4,8,9,10-Tetrachloro-2,6-dithiaadamantane can be obtained by subsequent addition of two SCl_2 molecules.[53,69] Treatment of monoadduct **70** with Se_2Cl_2 gives 4,8,9,10-tetrachloro-2-thia-6-selenoadamantane.[79] The addition of SCl_2 to 9-oxa- and 9-arylsulphonylazabicyclo[3.3.1]octadienes was used as a convenient pathway for obtaining 2-oxa(aza)-6-thiaadamantane derivatives.[80–82] Also, transannular addition of *N*,*N*-dibromo-*p*-toluenesulphonamide to 1,5-cyclooctadiene has been used to obtain azabicyclooctadiene.[80]

The five-step conversion of adduct **81** including sulphur atom oxidation, dehydrochlorination, nucleophilic addition of benzylamine, hydrogenolysis, and condensation with formaldehyde has been carried out in the synthesis of 6-thia-1,3-diazaadamantane. An original synthesis of 2,7-dithiatwistane has been performed based on sulphide **37**.[83] Conversion of the hydroxy sulphide **82** to thiaoxatwistane has been described.[84]

In conclusion, the addition of sulphur dichloride to olefins can be recommended as a most convenient method for the synthesis of thiacyclanes the structure of which can be easily modified by choosing starting compounds with two active double bonds.

However, for the sake of justice it should be noted that this method is most convenient for obtaining five- and six-membered thiacyclanes. No systematic studies on the pathways of synthesis of sulphur-containing heterocycles of larger size have been conducted. Only little is known concerning the synthesis of thiabicyclanes containing functional groups. Nucleophilic substitution of chlorine atoms and its triggering of skeletal izomerisations has not been sufficiently highlighted yet. Future more detailed studies of these aspects will, hopefully, allow us to devise more general methods for the synthesis of specific thiacyclanes.



Scheme 39

APPENDIX

Since commercially available sulphur dichloride is of consistently poor quality the author recommends its preparation by chlorination of disulphur dichloride. The following procedure has been found useful: Disulphur dichloride (600 ml) is placed in a 1 l two-necked round-bottomed flask, 2 g of iron power is added, and gaseous chlorine, dried by passing through H_2SO_4 and a tube filled with $CaCl_2$, is led in to the point of saturation. Subsequently 1 to 2 g of PCl_3 are added and the mixture left to stand for 1 hr. The fraction boiling between 55 and 63 °C is collected by distillation and then redistilled with a long Vigreux column to yield pure sulphur dichloride, b.p. 58–60 °C. When kept in dark glass vessels this product remains useful for 5 days. Older samples should be discarded.

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