THE SYNTHESIS OF STERICALLY HINDERED OLEFINS

a thesis presented by

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in partial fulfilment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

Chemistry Department,
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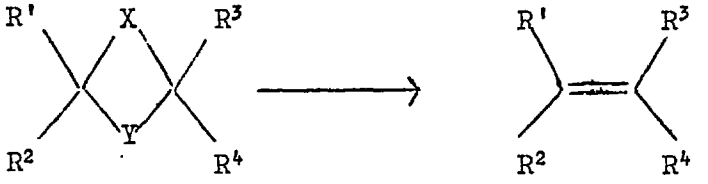
June, 1971.

Et tout le reste est littérature.

PAUL VERLAINE.

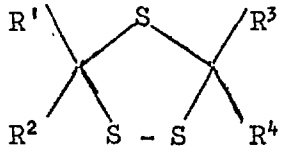
ABSTRACT

There are many olefin-forming reactions, but there is still need for a general preparation of sterically hindered olefins from readily available reagents and in good yields. Conventional olefin-forming reactions are seriously affected by steric hindrance. A new approach to olefin synthesis is outlined which should be particularly applicable to highly hindered olefins. In principle, the twofold extrusion process [(A) → (B)], where R' etc are alkyl, aralkyl, aryl etc and X and Y are easily extrudable fragments, would enable highly hindered olefins to be synthesized. This is because both olefin bonds would be formed intramolecularly, and the nature of X and Y can be chosen to avoid problems of steric compression.



(A) (B)

This present work investigates the potential of several of these systems:



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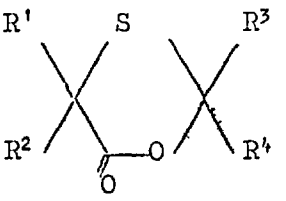

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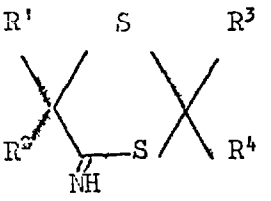

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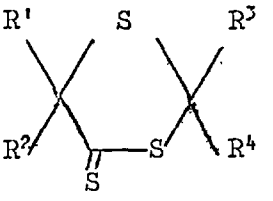

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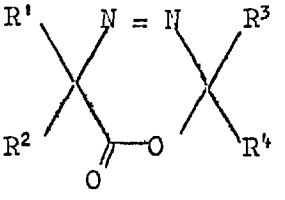

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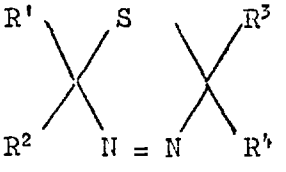

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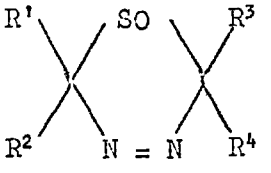

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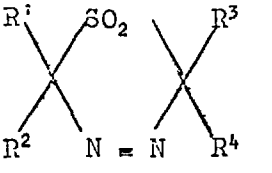


(XII)

The trithia compound [(V); R^1, $R^2 = R^3$, $R^4 = (CH_2)_5$] does not undergo desulphurisation to the corresponding olefin. Heating 1,3-oxathiolan-5-ones (VI) with tervalent phosphine reagents yields highly hindered olefins with ease, but only when conjugating residues are present to facilitate the extrusion of carbon dioxide. Systems (VII) and (VIII) are new. The compound [(VIII); $R^1, R^2 = R^3, R^4 = (CH_2)_5$]

is not desulphurised by tris(diethylamino) phosphine at 190°. The azo-lactone system (IX) is also new. The compound [(IX); $R'=R^2$ = Et and R^3,R^4 = cholestanyl] readily pyrolyses to diethylketen and cholestanone, whereas photolysis yields the mixed azine and carbon dioxide. The most promising system investigated is the new azo-sulphide system (X). Pyrolysis of the compound [(X); $R',R^2 = R^3,R^4 = (CH_2)_5$] yields the corresponding thiiran, whereas pyrolysis in the presence of tervalent phosphine yields bis-cyclohexylidene. Photolysis of this compound yields cyclohexanoneazine and sulphur. The azo-sulphoxide [(XI); $R',R^2 = R^3,R^4 = (CH_2)_5$] and the azo-sulphone [(XII); $R',R^2 = R^3,R^4 = (CH_2)_5$] afford only poor yields of bis-cyclohexylidene on pyrolysis, and low yields of cyclohexanoneazine on photolysis.

ACKNOWLEDGEMENTS

I thank Professor D.H.R. Barton, F.R.S. for allowing me the privilege to work under his guidance.

I also thank Mr. K.I. Jones for his analytical service, Mrs. Boston and Mrs. Lee for n.m.r. and m.s. services, and the technical staff of the new Hofmann laboratory for their assistance.

Brian Willis,
Hofmann Laboratory,
June, 1971.

CONTENTS

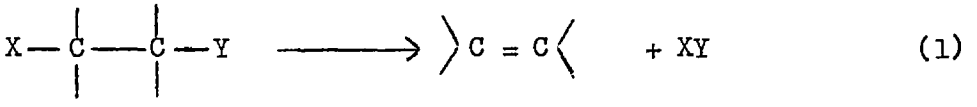
REVIEW

METHODS FOR INTRODUCING OLEFINIC BONDS

1. Elimination reactions

a) E1 and E2 reactions in solution

Nearly all olefin forming elimination reactions of synthetic importance are β-eliminations, in which two groups are lost from adjacent carbon atoms (equation 1).



$$X-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-Y \longrightarrow \rangle C=C\langle + XY \qquad (1)$$

One of these groups is usually hydrogen.

The E2 (bimolecular elimination) reactions of alkylhalides and tetraalkylammonium salts, the acid-catalysed E1 (unimolecular elimination) dehydration of alcohols, and the reaction of p-toluenesulphonates with halide ion are but three of many known synthetically useful β-elimination reactions which occur in solution.

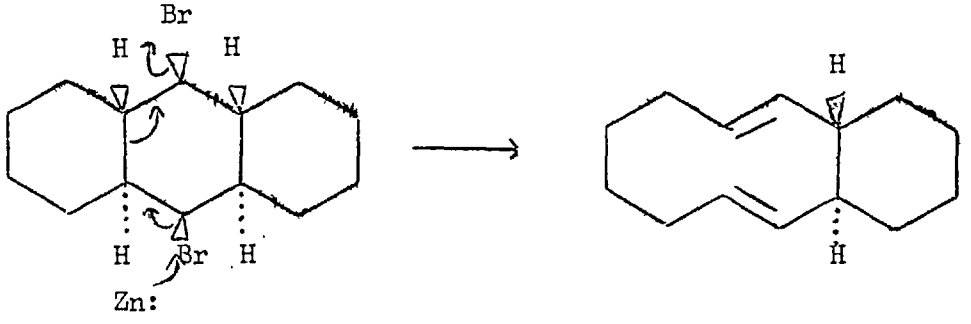
b) Thermal eliminations in the gas or liquid phase:

Olefin forming reactions in the gas or liquid phase can also be represented by equation 1, and once again there are several possibilities, since X can be halide, ester, xanthate, alcohol, amine, chloroformate etc. Of these the pyrolyses of esters and xanthates have been widely used for preparative purposes.

Olefin forming eliminations in solution and in the gas phase have been reviewed in fine detail.[1]

c) Eliminations from disubstituted systems.

Such eliminations have provided a general route for the introduction of the olefinic bond into medium-ring cyclic derivatives.[2] Even dibromides can eliminate (scheme 2). The anion has been generated in a number of ways.[3]



Scheme 2

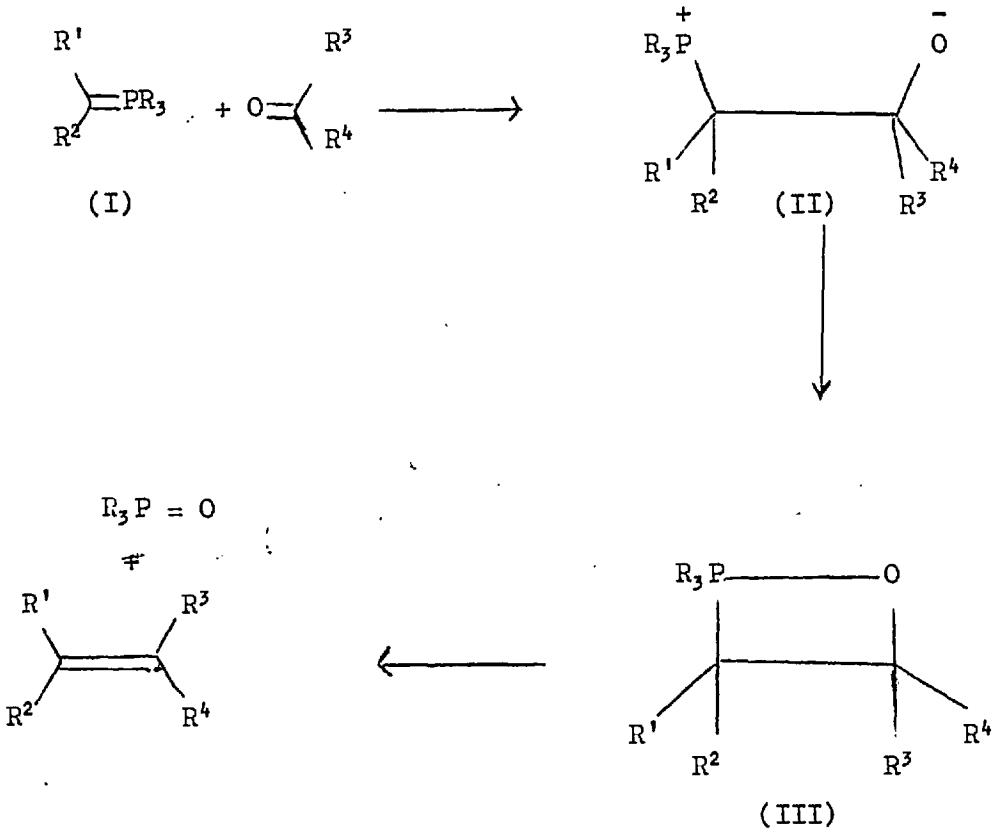
2. From carbonyl compounds

a) The Wittig reaction and its modifications.

The Wittig reaction is undoubtedly the most important olefin forming reaction to date. It has been considered to proceed in three steps (scheme 3). The standard method for preparing the Wittig reagent (I) is by the reaction of the phosphonium salt $R'R^2CHPR_3^+X^-$ with base. Addition of this phosphorane to a carbonyl compound produces a presumed, but as yet undetected, zwitterion (II). Phosphorus-oxygen bond formation, followed by collapse of the cyclic oxaphosphetan intermediate (III) yields the cis- or trans-olefin.

Resonance stabilised phosphoranes eg.

$R_3\overset{+}{P}\overline{C}HCO_2Et \leftrightarrow R_3\overset{+}{P}CH = \underset{\underset{O^-}{|}}{C}OEt$ give predominantly trans-olefins.[4]

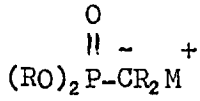


Scheme 3.

Addition of protic solvents or Lewis acids favours the formation of cis-olefins,[5] as a result of oxygen atom coordination in the intermediate betaine.

The majority of Wittig reagents are non-stabilised and behave differently. Under salt-free conditions the cis-olefin is formed with high selectivity,[6] whereas quenching the intermediate betaine with a lithium salt, followed by treatment of the salt so formed with butyl lithium and then with t-butanol gives almost pure trans-olefin.[7] There have been several reviews of the Wittig reaction.[8]

Phosphonate carbanions (IV) and phosphonothioate esters (V) condense with carbonyl compounds to give olefins.[9]



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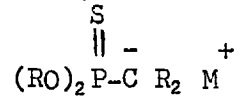
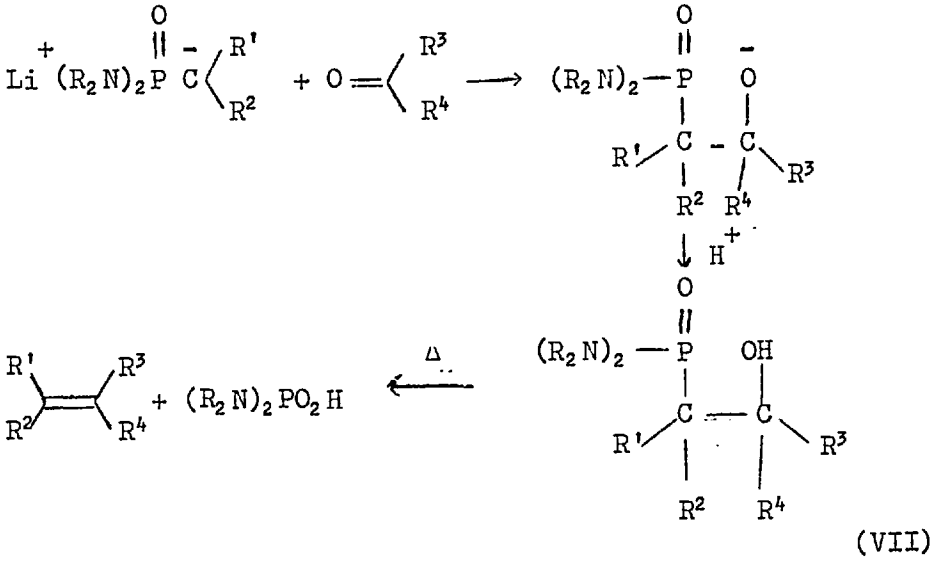


(V)

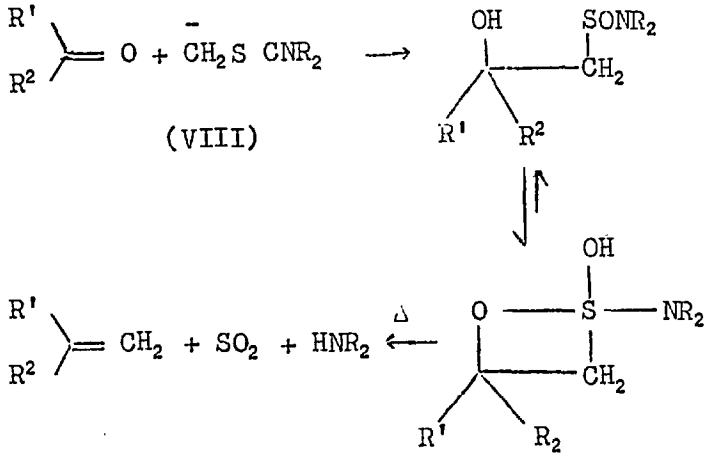
Recently, the phosphonamide reagents (VI) have been developed (scheme 4).[10]



(VII)

Scheme 4

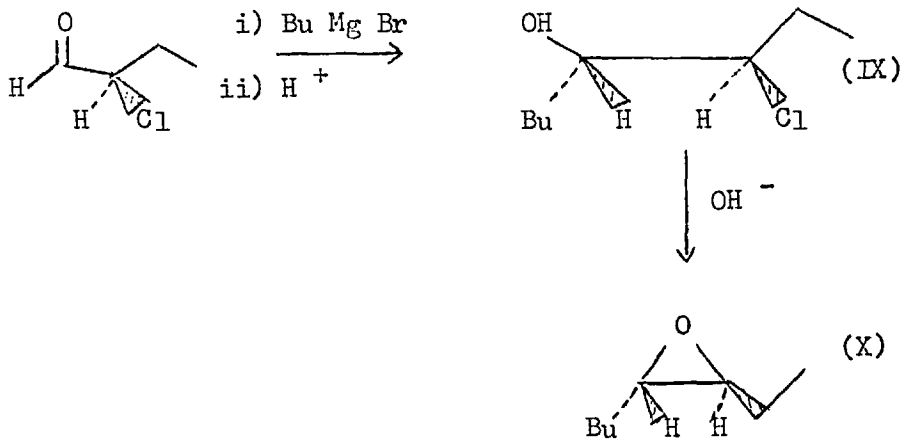
The adducts (VII) can be isolated, permitting some control over stereochemistry. The threo-alcohols yield the pure trans-olefins and the erythro isomers the pure cis-olefins. Sulphinamides (VIII) also react with carbonyl compounds to give olefins, but with limited synthetic scope (scheme 5).[11]



Scheme 5

b) α-Chlorocarbonyl compounds.

At low temperature the most favourable conformation of α-chlorocarbonyl compounds during Grignard addition is with the carbonyl and chlorine groups antiperiplanar. Addition occurs from the least hindered side to give only one chlorohydrin. The chlorohydrin (IX) produced from 2-chlorobutanol and butylmagnesium bromide gives the trans-epoxide (X) according to scheme 6.[12]



Scheme 6

Expoxides are readily deoxygenated stereospecifically to olefins (see later).

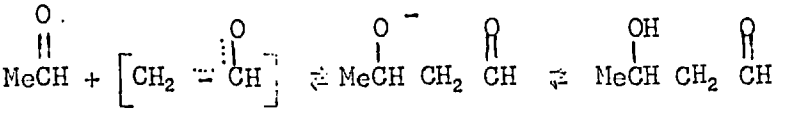
c) Condensation reactions

Condensation reactions important in olefin synthesis result from carbanion attack upon the electrophilic carbon of carbonyl compounds, with subsequent dehydration.

i) Aldol Condensations.

These condensations are catalysed by bases and by acids, as illustrated (scheme 7).

BASE CATALYSIS



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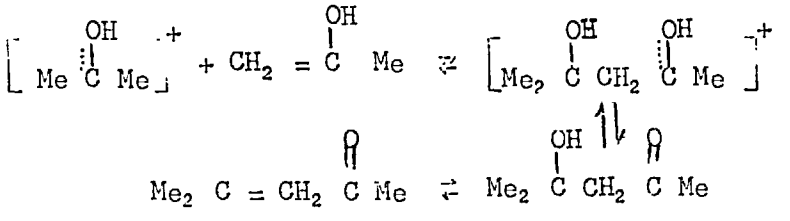
ACID CATALYSIS



(XII)

Scheme 7

Dehydration of aldols such as (XI) and (XII) proceed more readily in acid solution, although with aromatic carbonyl compounds the unsaturated ketone is obtained directly, even under alkaline conditions.

The Perkin reaction is the base catalysed condensation of an anhydride with an aromatid aldehyde.

ii) The Knoevenagel condensations.

Compounds containing an active methylene group will often condense with carbonyl compounds in the presence of base as illustrated (equation 8).

$$PhCHO + MeNO_2 \xrightarrow{NaOH} PhCH(OH)CH_2NO_2 \xrightarrow{HCl} PhCH = CHNO_2 \qquad (8)$$

The Stobbe condensation is similar (equation 9).

$$Ph_2C = O + \begin{matrix} CH_2CO_2Et \\ | \\ CH_2CO_2Et \end{matrix} \xrightarrow{NaH} Ph_2C = \begin{matrix} C\ CO_2H \\ | \\ CH_2CO_2Et \end{matrix} \qquad (9)$$

In the Reformatsky reaction the carbanion is produced by the attack of zinc on α-haloesters.

Alkene forming condensation reactions have been reviewed at length.[1]

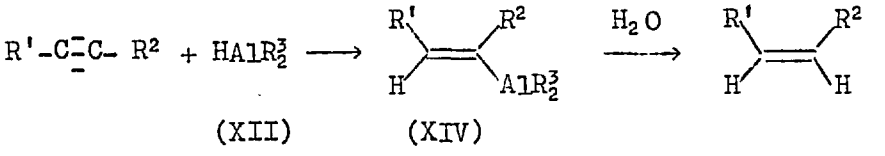
3. From acetylenes

a) Reduction

Acetylenes are reduced to cis-olefins by catalytic reduction over poisoned catalysts,[13] whereas reduction with sodium in liquid ammonia yields trans- olefins.[14] Lithium aluminium hydride has been used for the reduction of disubstituted acetylenes.[15]

Di- or tri-alkylalanes add to acetylenes to yield di-, tri-, or tetrasubstituted olefins in a controlled manner, illustrated by the addition of dialkylalanes (XIII) to acetylenes. Acid hydrolysis of the alanes (XIV) liberates the olefins in high yields (scheme 9).[16]

Similarly, hydroboration can be used to reduce acetylenes.

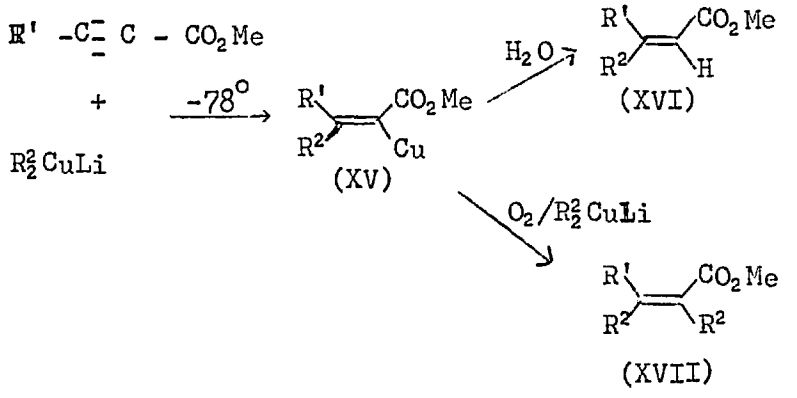


(XII) (XIV)

Scheme 9.

b) Additions

Acids add across acetylenes, often in a stereospecific trans manner.[17] Alkylcopper-lithium complexes have been used to add alkyl groups across acetylenic esters. Quenching the intermediate (XV) with water yields the unsaturated ester (XVI), or oxidation with air in the presence of excess reagent yields the dialkylated product (XVII). All the reactions proceed stereospecifically at low temperature (scheme 10).[18]



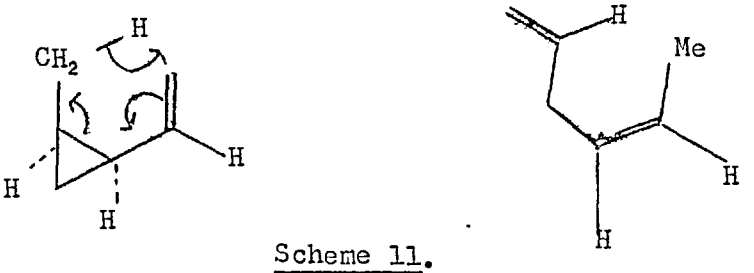
(XV) (XVI) (XVII)

Scheme 10.

4. Rearrangements

a) Thermal

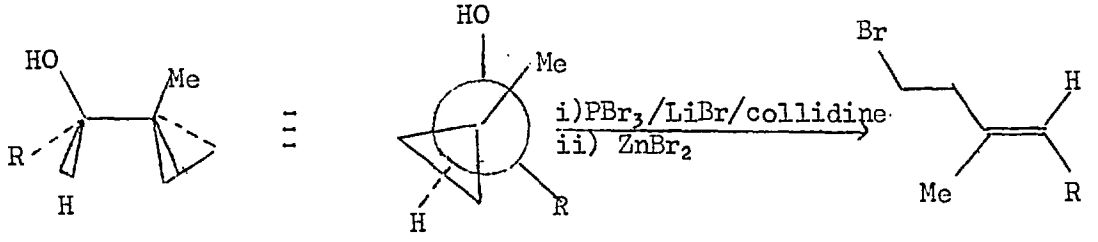
Olefins are often formed from thermal electrocyclic processes.[19] The Claisen and the Carroll rearrangements are two well-known examples. A more recent example is illustrated (scheme 11).[20]



Scheme 11.

b) α-Cyclopropylcarbinols

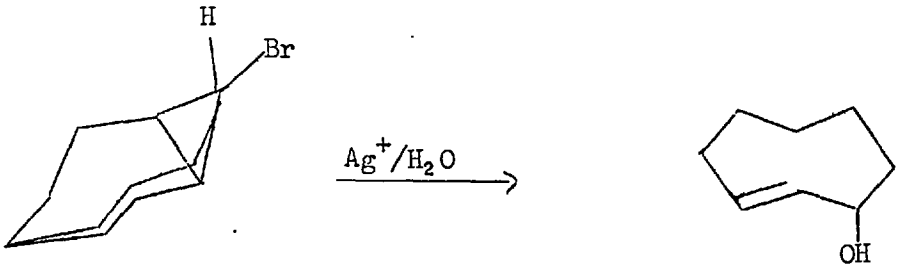
α-cyclopropylcarbinols are cleaved by acid to olefins, as illustrated by the stereospecific synthesis of tri-substituted olefins (scheme 12).[21]



Scheme 12.

c) Halogenocyclopropanes

Pyrolysis or solvolysis of halogenocyclopropanes has been used to prepare medium ring cycloalkenes, as illustrated (scheme 13).[6]

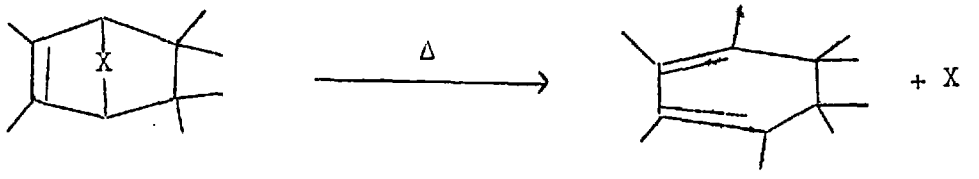


Scheme 13.

5. Extrusion Reactions

a) Retro - Diels Alder reactions.[22]

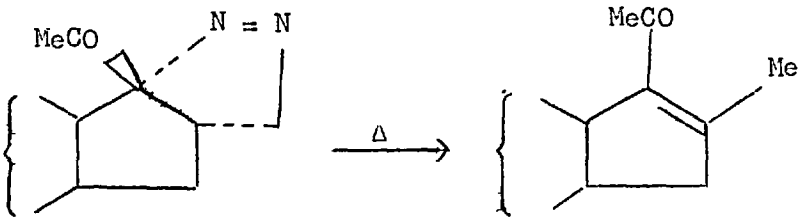
Those reactions of use in olefin synthesis can be expressed in a general form, where X is a readily extrudable fragment such as carbon monoxide, carbon dioxide, or sulphur dioxide (scheme 14). The extrusion does not proceed if the double bond is absent and is easier when the 5,6-double bond is also present.



Scheme 14.

b) Pyrazolines

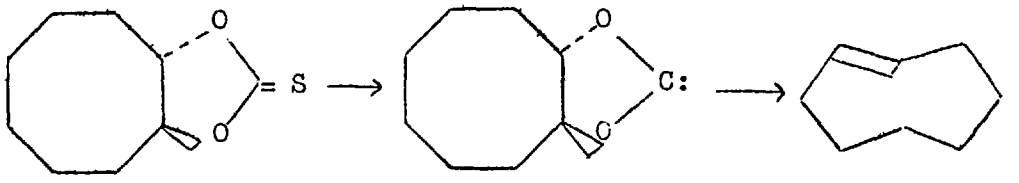
The common side-reaction which occurs during the pyrolysis of pyrazolines is the formation of olefins. This is especially useful with certain steroid derivatives, which give little or none of the corresponding cyclopropane derivatives. The 1-pyrazoline of 3β-acetoxypregna-5,16-diene-20-one yields the 16-methyl-5,16-diene-20-one derivative (scheme 15).[23]



Scheme 15.

c) Cyclic thiocarbonates

The elimination reactions of cyclic thionecarbonates have recently been developed for controlled olefin formation. Treatment of the thionecarbonate of 1,2-trans-cyclooctanediol (XVIII) with tervalent phosphine reagents produces a carbene, which extrudes carbon dioxide to give the trans-olefin (equation 16).[24] Trithiocarbonates behave similarly.[25] Two related olefin-forming reactions have appeared recently, utilizing 2-substituted-1,3-dioxazolidines.[26]



(16)

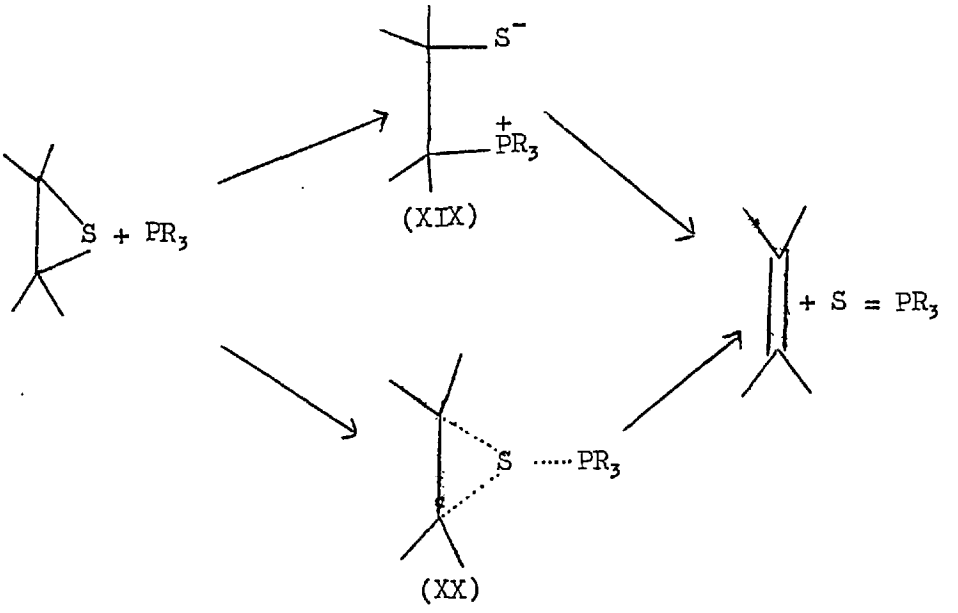
(XVIII)

d) From 3-membered rings

(i) Thiirans.[27]

Thermal desulphurisation of thiirans is often accompanied by dehydrogenation, whereas chemical methods proceed at lower temperatures and usually without side-reactions.

Thiirans react readily with tervalent phosphorus reagents to give olefins (scheme 17). The intermediacy of the betaine (XIX) is uncertain. Mechanistic studies support direct abstraction of sulphur (XX).[28]



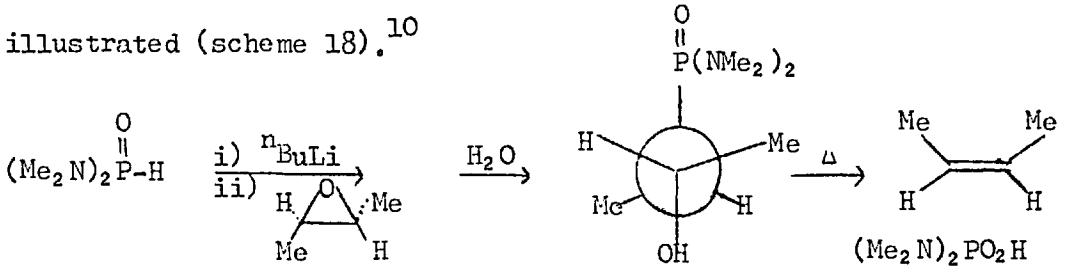
Scheme 17.

Recently organolithium reagents have found increasing use in the desulphurisation of thiirans.[29] Other reagents that have been used include Grignard reagents, lithium aluminium hydride, potassium butoxide, methyl iodide and iodine. Treatment of thiiranium salts with nucleophiles also yields olefins.[30]

ii) Oxirans.

Oxirans are readily converted into thiirans by a variety of methods.[27] Alternatively they may be deoxygenated by tervalent

phosphorus reagents,[31] or by pyrolysis of their β-hydroxyphosphonamides formed by treatment of the oxiran with diamidophosphite anion as illustrated (scheme 18).[10]



Scheme 18.

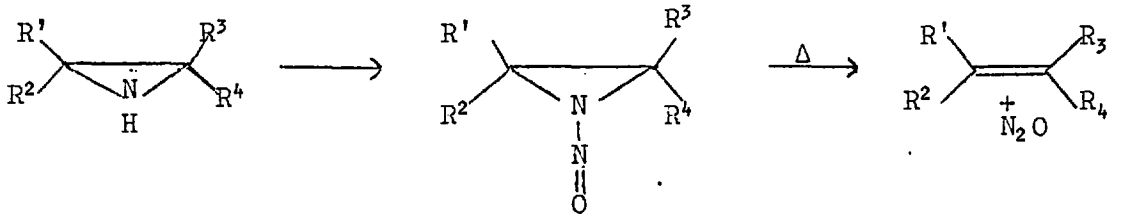
iii) Thiiran oxides

Most thiiran-1,1-dioxides decompose near room temperature to give sulphur dioxide and alkenes in a stereospecific manner.[32] In solution the rate of decomposition to olefins has been found to correlate with the ionizing power of the medium.[33]

The indications are that thiiran-1-monoxides also decompose thermally to give olefins, but at a higher temperature.[34]

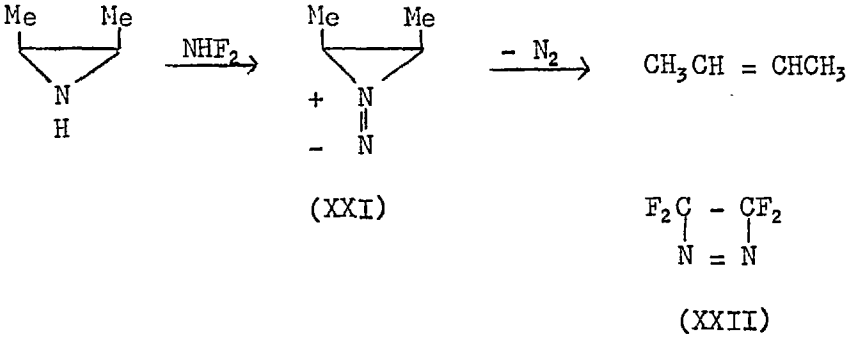
iv) Aziridines

Thermal decomposition of nitrosoaziridines yields olefins in a stereospecific manner (scheme 19).[35]



Scheme 19.

It has been proposed that the stereospecific deamination of aziridines by difluoramine to give nitrogen and olefins proceeds via the ethyleneazamines (XXI) (scheme 20.)[36]



(XXI)

(XXII)

Scheme 20.

(v) Cyclopropanones.

Hot-tube pyrolysis of 2,2-dimethylcyclopropanone at 250° yields isobutene and carbon monoxide, whereas vapour phase chromatography results in rearrangement to methylisopropenyl ketone.[37]

e) From 4-membered rings.

(i) Δ'-1,2-diazetines.

Pyrolysis of tetrafluoro-Δ'-1,2-diazetene (XXII) at 240° yields nitrogen and tetrafluoroethylene.[38]

(ii) β-lactones.

β-lactones readily extrude carbon dioxide on pyrolysis to form olefins.[39] Recently the elimination has been shown to be stereospecific.[40] Only one example of the pyrolysis of β-thiolactones to carbonyl sulphide and olefin has been reported.[41]

THE PREPARATION OF STERICALLY HINDERED OLEFINS.

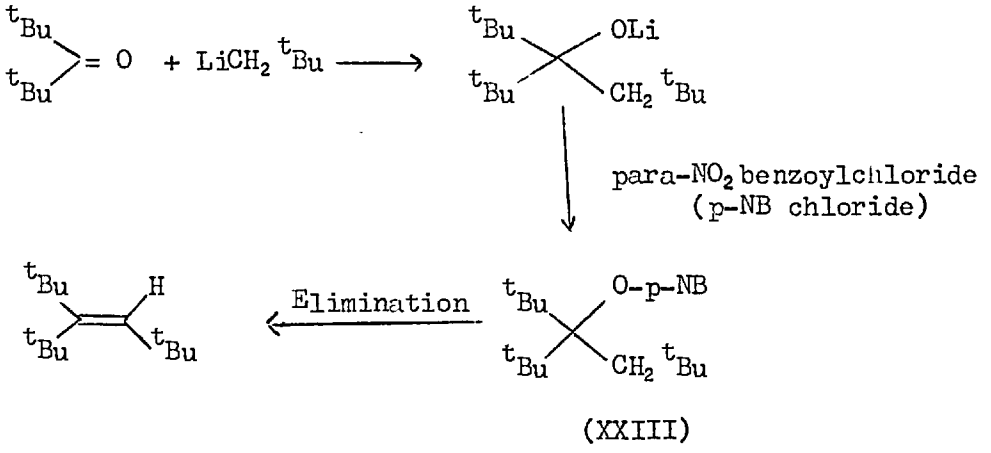
The Wittig reaction has shown itself to be an excellent preparative method for the synthesis of disubstituted olefins. The review articles available[8] illustrate that yields are generally lower in the case of trisubstituted olefins. That few tetrasubstituted olefins have been reported, and yields have not been quoted or are low, is indicative that the Wittig reaction cannot be used to prepare sterically hindered olefins. Recent ramifications[10,11] have been used to prepare simple unhindered olefins, but there is no reason why these procedures should have any advantage over the normal Wittig reaction in the preparation of sterically hindered olefins.

Hydroalumination and hydroboration of acetylenes[16,42] are experimentally inconvenient reactions because of their sensitivity to oxygen and protic solvents. Moreover, their usefulness in preparing even simple tetrasubstituted olefins is severely limited.

The extrusion reactions already discussed (page 18-19 , types c and d) have been used for the interconversion of cis- and trans- olefins, but since olefins are generally the starting materials for such sequences they do not constitute a general preparation of olefins.

Elimination reactions have provided an important synthetic route to olefins, but the intermediates become progressively less accessible with increasing substitution. Nevertheless, they have provided a useful route to otherwise inaccessible olefins, albeit in low yields, as illustrated by the preparation of tri-t-butyl ethylene (scheme 21).

The nitrobenzoate (XXIII) was prepared in a yield



(XXIII)

Scheme 21.

of 51%.[43] Solvolysis in 60% dioxan/water gave tri-t-butylethylene in a yield of 3%, whereas pyrolysis at 160° gave a yield of 32%.[44]

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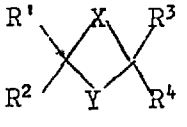
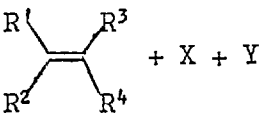
DISCUSSION

There are many olefin-forming reactions, of which the Wittig reaction is of special significance. However, there is still need for a general olefin synthesis which will afford sterically hindered olefins in good yields and from readily available reagents. The Wittig reaction starts from readily available carbonyl compounds, but it has been mainly applied to the preparation of disubstituted olefins. Trisubstituted olefins are formed in lower yields and tetrasubstituted olefins generally in poor yields. These results reflect that formation of the intermediate oxaphosphetans is seriously affected by steric hindrance. Chemists requiring a particular hindered olefin have frequently been forced to use less facile procedures, where yields are low and where purification is often baulked by the propensity of the various precursors for rearrangement.

All conventional olefin-forming reactions are seriously affected by steric hindrance. In principle a twofold extrusion process of the type [(A) → (B)] where R', etc are alkyl, aralkyl, aryl, etc., and where X and Y are easily extrudable fragments would enable highly hindered olefins to be synthesised, since now both olefin bonds would be formed intramolecularly, and the nature of X and Y can be chosen to avoid problems of steric compression.

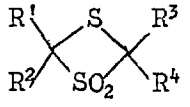


(A)

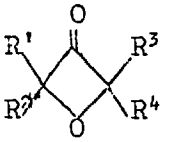


(B)

There are many possibilities for X and Y that can be considered. Those discussed in this present work include:



(I)



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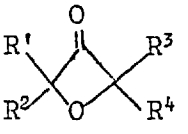

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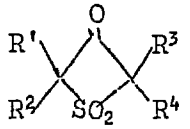

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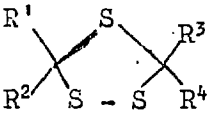

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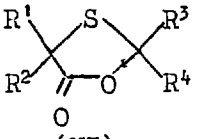

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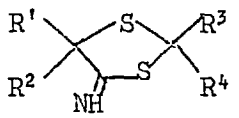

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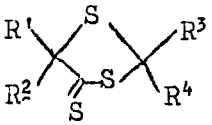

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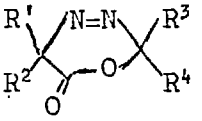

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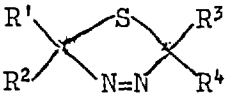

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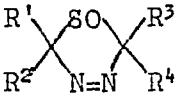

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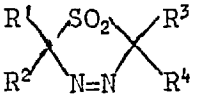

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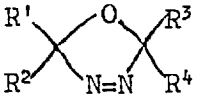

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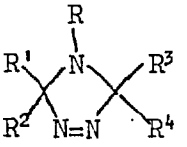


(XIV)

The choice of X and Y will obviously govern the conditions under which a system undergoes the required twofold extrusion process. One might expect extrusions to proceed readily when the extruded species have low enthalpies and when the intermediates are

externally stabilized. It is possible that a further driving force for such extrusions may be derived from the entropy gain resulting from the extrusion of a symmetrical species, although in the synthesis of hindered olefins by extrusion processes this may be outweighed by the enthalpy lost in producing a strained product.

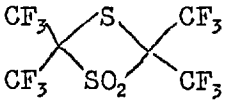
An approximate ranking of the ease of extrusion of inorganic molecules by comparable mechanisms has been proposed:[1]

$N_2 > CO_2 \gtrsim CO \gtrsim$ 'SO' $> SO_2 > O_2 \gtrsim S > O$.

External stabilization, by substituents at the terminal carbon atoms which are capable of delocalising the radicals or charges within the intermediate, may be indistinguishable from the promotion of electron assymmetry and the subsequent operation of an ionic mechanism. Extrusions proceeding via ionic mechanisms may also be effected chemically, as in the removal of sulphur from episulphides by tervalent phosphorus reagents. Such extrusions provide useful and sometimes more facile alternatives to pyrolytic extrusions, and generally do not require terminal stabilization. Extrusions proceeding via intermediates which are not terminally stabilized can often be effected by photolysis. However, so far as this present study is concerned, it is emphasized that a general route to sterically hindered olefins which does not involve photolytic extrusion and which utilises readily available reagents is required.

The 1,3-dithietan-1,1-dioxide (XV) is reported to lose sulphur dioxide at 600° to give a thiiran.[2] Cyclobutan-1,3-diones (II)

obtained by keten dimerization, undergo photochemical decarbonylation to give olefins. The intermediacy of ketens, which are also primary fission products has not been discounted.[3] Tetramethyloxetan-3-one (XVI), prepared in four steps from 2,5-dimethyl-2,5-dihydroxy-3-hexyne, afforded small amounts of tetramethylethyleneoxide on photolysis.[4] Recently it has been reported that flash thermolysis of thietan-3-one-1,1-dioxides (IV) at 930-950° yields olefins.[5] Clearly none of these systems would provide a general synthesis of



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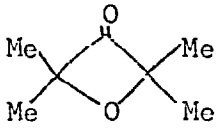
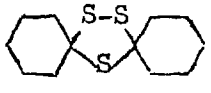


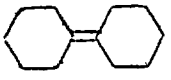
(XVI)

sterically hindered olefins.

1,2,4-Trithiolanes (V) are well known, and those derived from ketones are reported to be remarkably stable, since they do not react with aqueous acids, bases, heavy-metal salts, mercury, triethylphosphite or triphenylphosphine.[6] The readily available[7] (XVII) was prepared and found to resist attack by many tervalent phosphorus reagents [triethylphosphite, triphenylphosphine, tris(diethylamino)phosphine], and when treated with tributylphosphine at 200° it was slowly desulphurised, but no bis-cyclohexylidene (XVIII) was formed.

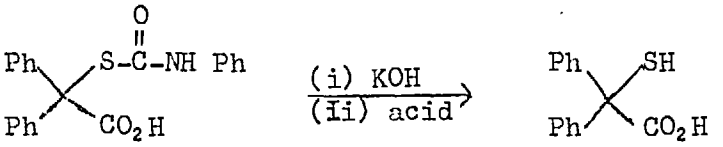


(XVII)



(XVIII)

1,3-Oxathiolan-5-ones (VI) are also well known,[8] prepared by the acid catalysed condensation of 2-mercaptoacids with carbonyl compounds. Attempts at preparing thiobenzilic acid (XX) from the thiocarbamate (XIX) according to the method of Becker and Bistrzycki[9] gave the potassium salt of thiobenzilic acid as colourless needles m.p. 150-150.5° (from toluene). The preparation was modified and free thiobenzilic acid obtained as colourless plates m.p. 152-153° (from acetone/hexane) (lit.[9] 147.5-149° from toluene or acetic acid).



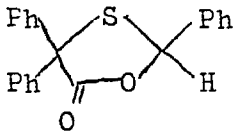
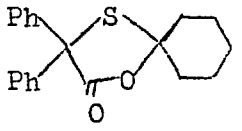
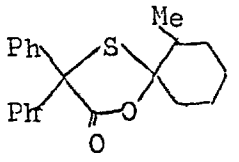
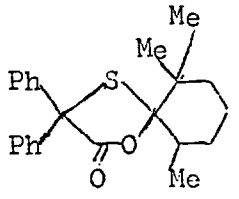
(XIX) (XX)

The acid catalysed condensation of thiobenzilic acid with benzaldehyde and with various ketones gave the oxathiolan-5-ones (XXI), (XXII), (XXIII) and (XXIV) (see Table 1). The best results were obtained using toluene-p-sulphonic acid (azeotropic removal of water) or boron trifluoride gas.

The lower yield of the oxathiolan-5-one (XXIV) was a consequence of the instability of 2,2,6-trimethylcyclohexanone and the final oxathiolan-5-one to the condensation conditions. An investigation into alternative catalysts for use with labile carbonyl compounds might be useful. The n.m.r. spectra of compounds (XXIII) and (XXIV) showed that each was a mixture of two isomers. An attempt to prepare the oxathiolan-5-one (XXI) direct from the thiocarbamate (XIX) and

benzaldehyde, using hydrogen chloride gas and glacial acetic acid was unsuccessful.

TABLE 1

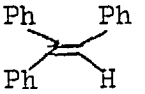
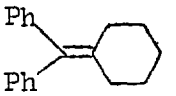
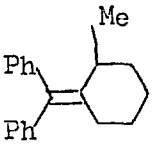
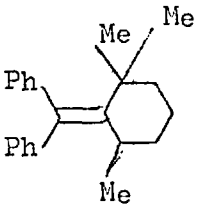
Oxathiolan-5-one		YIELD (%) Hydrogen chloride	Toluene-p-sulphonic acid	Boron trifluoride Catalyst
	(XXI)	77	94	not tried
	(XXII)	78	83	84
	(XXIII)	74	low	not tried
	(XXIV)	< 5	0	34

Compounds (XXIII) and (XXIV) were mixtures of two isomers, which were not separated.

Heating the various oxathiolan-5-ones in the presence of tris(diethylamino) phosphine gave good yields of the corresponding olefins (XXV), (XXVI), (XXVII) and (XXVIII) respectively (see Table 2).

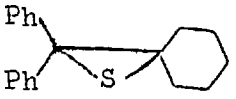
The formation of the highly hindered olefin (XXVIII) is noteworthy. The u.v. spectra of compounds (XXVI), (XXVII) and (XXVIII) are interesting since increasing the methyl substitution of the cyclohexane ring results in a small hypsochromic shift and a large hypochromic effect, a direct consequence of the increased steric interaction (see Experimental).

TABLE 2

Oxathiolan-5-one		Olefin formed		
(XXI)	150-160°, 2 hr.		(XXV)	(95%)
(XXII)	160-200°, 5 hr.		(XXVI)	(82%)
(XXIII)	200-240°, 6 hr.		(XXVII)	(81%)
(XXIV)	180-230°, 4 hr.		(XXVIII)	(80%)

Pyrolysis of the oxathiolan-5-one (XXII) at 210° in the absence of phosphine gave a mixture containing diphenylcyclohexylidene (XXVI), its thiiran (XXIX) and triphenylmethane. Pyrolysis of the olefin (XXVI) at 210° in the presence of sulphur gave triphenylmethane and

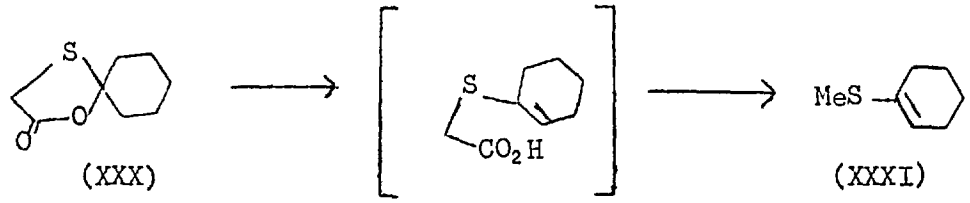
other non-polymeric products. The isolation of the thiiran (XXIX) confirms that the extrusion of carbon dioxide is the first step of the twofold process. This is followed by the removal of sulphur when the pyrolysis is conducted in the presence of a tervalent phosphorus reagent.



(XXIX)

Pedersen,[10] whilst attempting to prepare isobenzothiophenes, reported that pyrolysis of oxathiolan-5-ones derived from aliphatic carbonyl compounds and thiobenzilic acid gave complex mixtures, containing up to ten components, which were not characterized. Benzaldehyde derivatives gave thiirans, which afforded olefins (and sulphur) in relatively low yields.

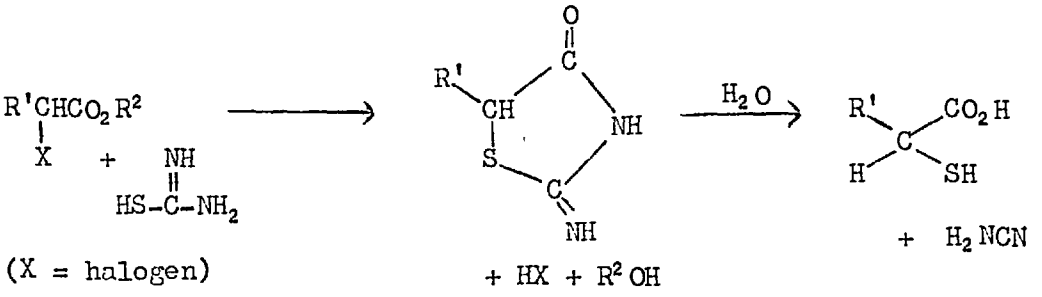
That the oxathiolan-5-one (XXI) expels carbon dioxide some 50-70° lower than the oxathiolan-5-ones (XXII), (XXIII) and (XXIV) is a result of the extra stabilization provided by the third terminal phenyl group. Although this synthesis affords highly hindered olefins with ease, it is not applicable unless phenyl or other conjugating residues are present to facilitate the loss of carbon dioxide. Thus pyrolysis of the oxathiolan-5-one (XXX) at 220° in the presence of triphenylphosphine gave only 1-methylthiocyclohex-1-ene (XXXI).



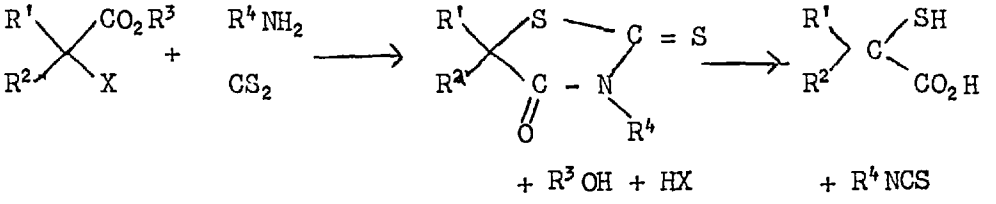
(XXX) (XXXI)

A more attractive way of collapsing oxathiolan-5-ones would result if the sulphur bridge could be extruded first to give β-lactones, which are known to afford olefins and carbon dioxide at relatively low temperatures.[11] Thermally it should be easier to extrude sulphur dioxide than elemental sulphur from five-membered rings, but oxidation to the 1,3-oxathiolan-5-one-1,1-dioxides offers no advantage since the extrusion of carbon dioxide should still be the first step of the twofold extrusion process.[1] The removal of sulphur from five-membered rings by chemical methods, with concomitant formation of a bond between the carbon atoms previously joined to sulphur has never been reported. The affinity of perchloropolysilanes for oxygen[12] prompted an investigation into their use for removing sulphur from oxathiolan-5-ones as the first step of the extrusion process. However, hexachlorodisilane did not react with the oxathiolan-5-one (XXII) under a variety of conditions.

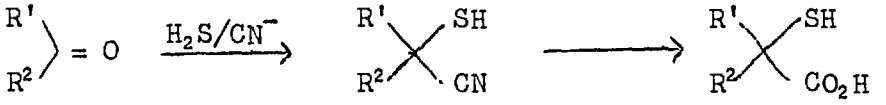
2-Mercaptoacids are generally prepared from their corresponding 2-haloacids (or esters) by treatment with potassium hydrogen sulphide, or by hydrolysis of their pseudothiohydantoins (scheme 1) or rhodanins (scheme 2). Treatment of 2-bromocyclohexanecarboxylic acid (or its ethyl ester) with thiourea failed to give the required pseudothiohydantoin. Consequently a one-step preparation of 2-mercaptonitriles from carbonyl compounds was considered (scheme 3). It is reported[13] that when hydrogen sulphide is passed into an aqueous solution of an alkali cyanide 5-amino-2-thiocarbamylthiazole (chrysean) is formed.



Scheme 1.



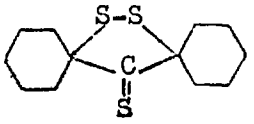
Scheme 2.



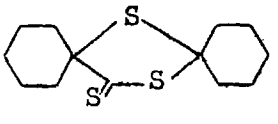
Scheme 3.

Therefore a preliminary study of the reaction between gem-dithiols and cyanide ion was carried out. The readily available[14] cyclohexane-1,1-dithiol (XXXII) was treated with one equivalent of potassium cyanide in dioxan/water at 23°. Monitoring of the reaction by t.l.c. indicated the rapid formation of two products, which were separated by column chromatography. The first component crystallised from light petroleum as orange plates m.p. 53.5-54°,

and analysed correctly for $C_{13}H_{20}S_3$. Two possible structures for this compound were considered, the thioketone (XXXIII) or the dithioester (XXXIV). The reported[15] i.r. absorption frequencies for the



(XXXIII)

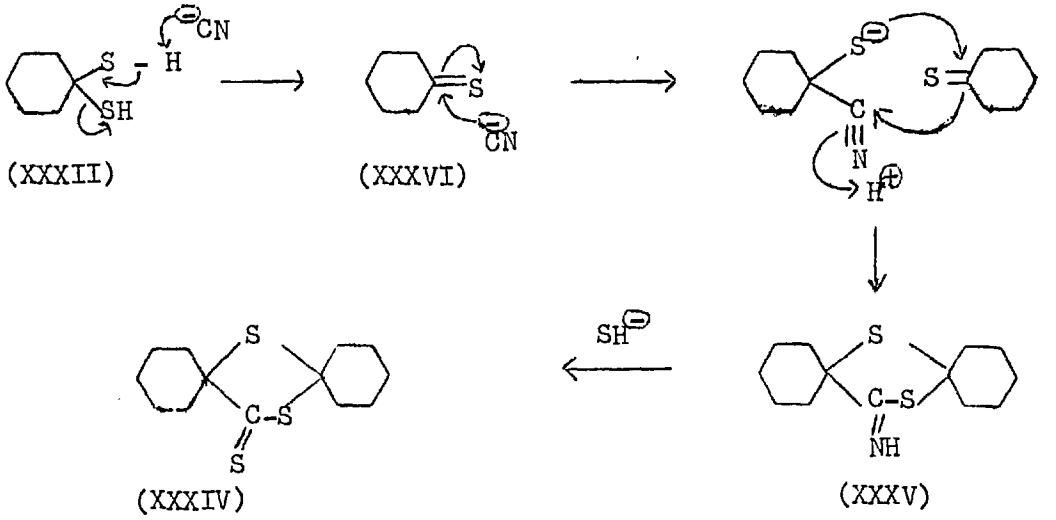


(XXXIV)

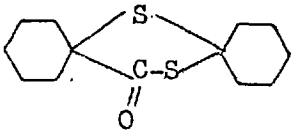
thiocarbonyl groups of thiofenchone, aromatic thioketones, and dithioesters are 1180, 1207-1224, and 1190-1225 cm^{-1} respectively. Consequently the i.r. spectrum of the unknown cannot be used to distinguish between the two structures. The u.v. spectrum of the unknown has an absorption band at 321 nm. (ε 10,700), which confirms that the compound has structure (XXXIV). The thioketone should exhibit absorption bands at 240-245 and 210-220 nm., whereas the dithioester should absorb at 300-320 nm. (ε ca. 10,000).[16] The instability of aliphatic thioketones is attributed to thioenolisation and subsequent polymerisation, since sulphur does not readily form a $p\pi p\pi$ bond. This is because carbon and sulphur belong to different groups, and overlap of the $2p\pi$ orbital of carbon with the $3p\pi$ orbital of sulphur is not favoured.[17] Since compound (XXXIII) is unable to enolise one might expect its stability to be comparable with that of thiofenchone. Component two crystallised from light petroleum as colourless needles m.p. 85.0-85.5°, and analysed correctly for $C_{13}H_{21}NS_2$. The n.m.r. and i.r. spectra of this compound

confirmed the presence of an imine group, and by analogy the compound was assigned the structure (XXXV). There is strong mechanistic support for the structures (XXXIV) and (XXXV), which also explains the pink colour observed during the reaction (attributed to the thiocarbonyl compound (XXXVI) (mechanism 1).

Mechanism 1.

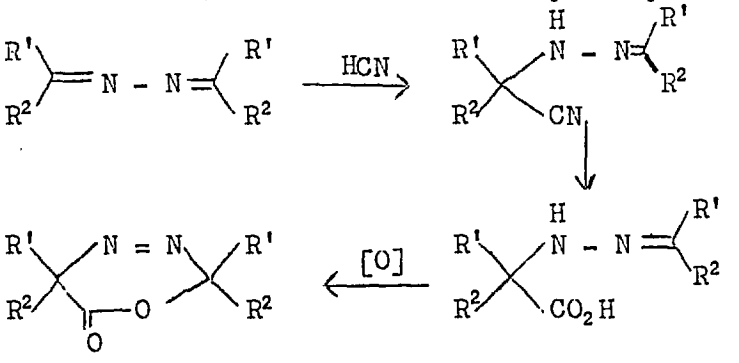


This mechanism was confirmed in part by treating the iminoester (XXXV) with hydrogen sulphide gas, whereupon the dithioester (XXXIV) was formed. Attempts to prepare the dithioester directly from cyclohexanone, potassium cyanide and hydrogen sulphide gas were unsuccessful. Systems (VII) and (VIII) are new. Experiments are at present underway in this laboratory to determine whether or not compounds (XXXIV), (XXXV) and (XXXVI) undergo the twofold extrusion process.

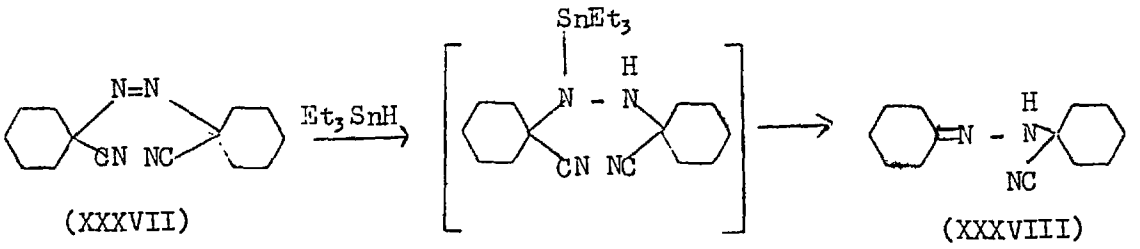


(XXXVI)

An apparently attractive olefin synthesis would result if X were nitrogen and Y were carbon dioxide in (A), as in system (IX). Now, the more facile extrusion of nitrogen may be the expected first step of the twofold extrusion process to give β-lactones, which might extrude carbon dioxide under the reaction conditions.[11] Two approaches to this hitherto unknown system were considered. The first was essentially the addition of one equivalent of hydrogen cyanide to an azine, followed by hydrolysis to the acid and oxidative cyclization to the azo-lactone (scheme 4). This was not investigated because of the difficulty envisaged in adding only one equivalent of hydrogen cyanide to an azine, although the azodinitrile (XXXVII) is reported[18] to have been converted into the nitrile (XXXVIII) in relatively low yield (scheme 5).



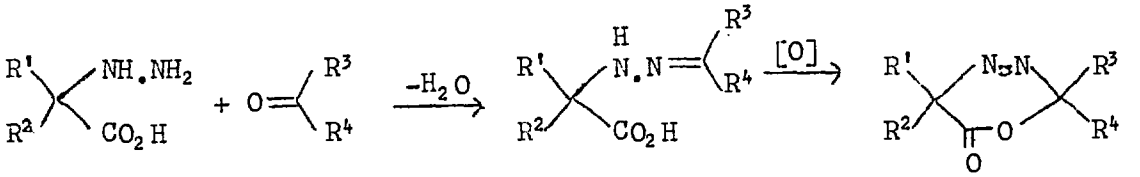
Scheme 4.



(XXXVII) (XXXVIII)

Scheme 5.

The second, and more attractive method, involved the condensation of carbonyl compounds with readily available[19] 2-hydrazinoacids, and oxidative-cyclization of the hydrazones to the azo-lactone ring system (scheme 6).

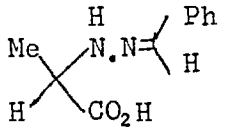


(XXXIX)

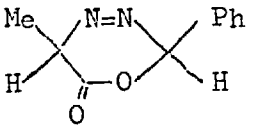
Scheme 6.

The hydrazones (XXXIX) were prepared in high yields under very mild conditions. All of these condensation products exhibit characteristic carboxylic acid absorption bands in the i.r., confirming that they exist in the open-chain form. It is interesting that in solution the carboxyl carbonyl absorption bands are between 1710 and 1720 cm^{-1}, whereas in mulls the absorption bands are between 1600-1610 cm^{-1}, indicating the tendency of these compounds to exist in the ionised form in the solid state.

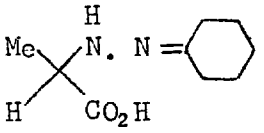
Attempted oxidation of the hydrazone derived from 2-hydrazino-propionic acid and benzaldehyde (XL) with lead tetra-acetate at 0° gave an unstable oil, having an i.r. absorption band at 1770 cm^{-1}. The azo-lactone (XLI) might be expected to absorb in this region, bearing in mind that the double bond introduces some ring strain. The product could not be crystallised, even at low-temperature, and was unstable to chromatography.



(XL)



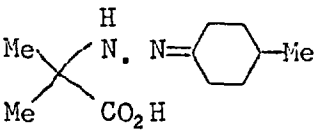
(XLI)



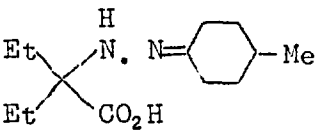
(XLII)

Oxidation of the hydrazone (XLII) with activated manganese dioxide gave a reaction product which did not show any i.r. absorption bands above 1710 cm^{-1}.

It was reasoned that suitably chosen tetra-alkyl-substituted azo-lactones would be more easily crystallised, and more stable than those having terminal phenyl groups. Oxidation of the hydrazones (XLIII) and (XLIV) with lead tetra-acetate at - 15° gave oils having i.r. absorption bands at 1740 and 1750 cm^{-1} respectively, but which once again could not be purified by low-temperature crystallisation or by chromatography. Pyrolysis experiments were conducted on these oils, but no olefinic products were observed.

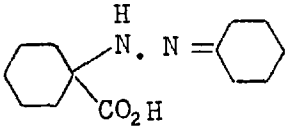


(XLIII)

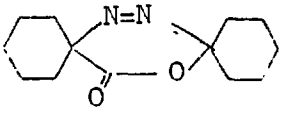


(XLIV)

The hydrazone (XLV) was prepared from 2-hydrazinocyclohexane-carboxylic acid and cyclohexanone. Oxidation of the hydrazone with lead tetra-acetate at - 15° gave an unstable solid. Crystallisation from diethyl ether/light petroleum at low temperature gave colourless plates, which appeared to decompose slowly at room temperature, noticeably at 60°, and vigorously with solution at 90°. The i.r. spectrum of these crystals showed a strong absorption at 1750 cm^{-1} (lactone CO) and a weak absorption at 1595 cm^{-1} (-N=N-), both attributed to the azo-lactone (XLVI). A weak, yet sharp absorption at 2120 cm^{-1} indicated a keten impurity. Pyrolysis of this product at 100° or in refluxing toluene gave no trace of bis-cyclohexylidene (XVIII).



(XLV)

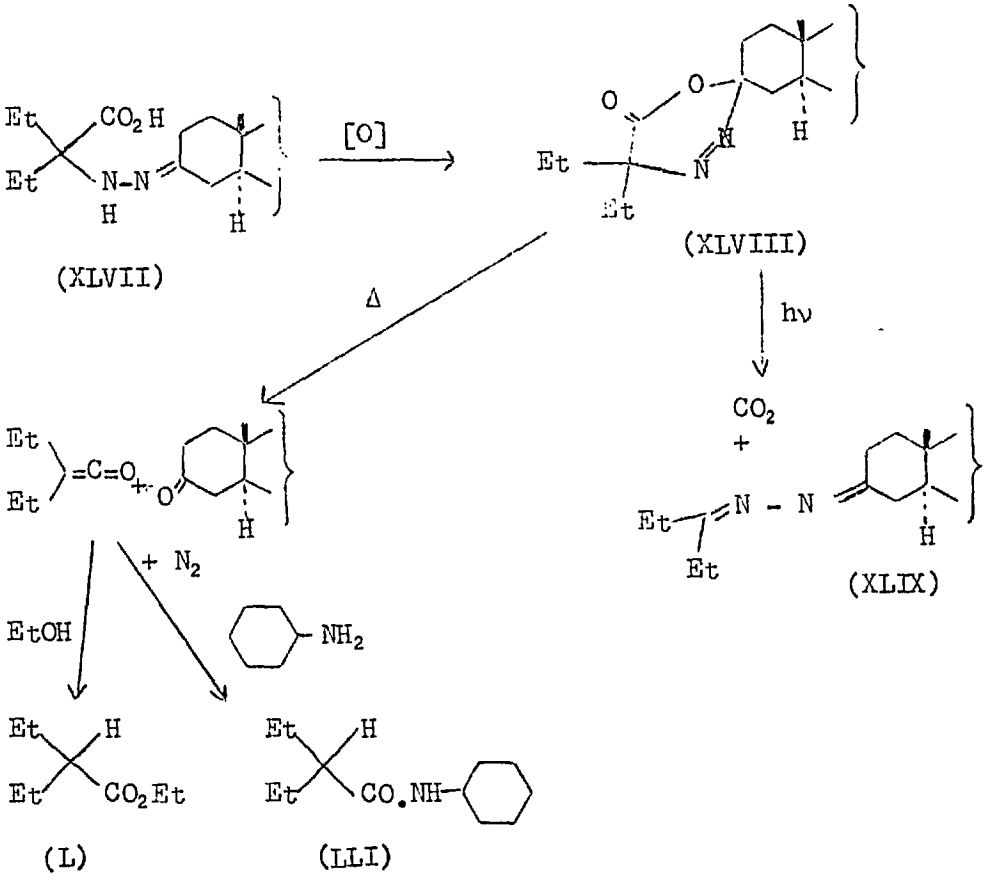


(XLVI)

Condensation of cholestanone with 2-ethyl-2-hydrazinobutyric acid in ethanol gave the hydrazone (XLVII). Oxidation of the latter with lead tetra-acetate at - 18° gave a thermally unstable solid. The i.r. spectrum of this solid showed a strong absorption at 1740 cm^{-1} attributed to the azo-lactone (XLVIII), and a much weaker absorption at 1635 cm^{-1} attributed to azine impurity.

The cyclised product could not be purified by recrystallisation alone and was unstable to chromatography. Purification was achieved using gel filtration through Sephadex LH20, in the dark but at room temperature. The separation was monitored by observing the $\pi \rightarrow \pi^{*}$ transition of the azo chromophore at 368 nm. The azo-lactone (XLVIII) had the expected spectral properties and gave a correct analysis.

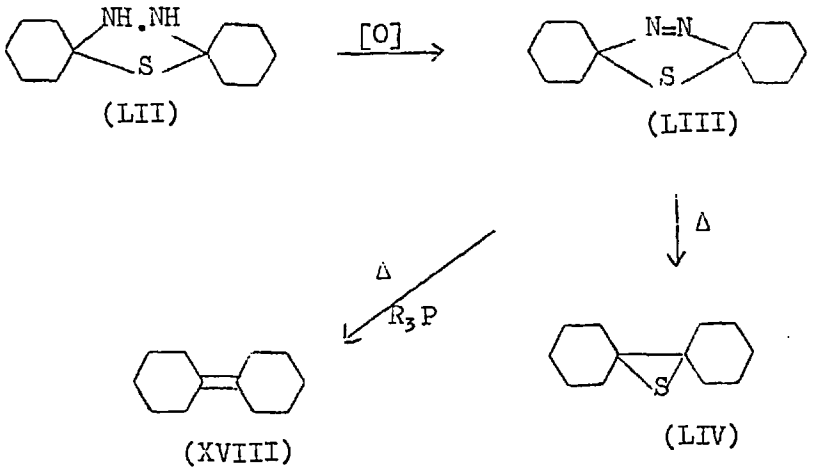
Pyrolysis of (XLVIII) at 115° gave smoothly diethylketen and cholestanone. The keten was flushed from the pyrolysis vessel with a stream of nitrogen, and identified by its characteristic i.r. spectrum and by trapping with ethanol and cyclohexylamine.



The products were identical with authentic samples of the ester (L) and the amide (LI). The pyrolysis residue was identified as cholestanone. There was no trace of the expected olefin.

Photolysis of the azo-lactone (XLVIII) in cyclohexane, using a medium-pressure mercury arc lamp and pyrex apparatus at 19°, gave smoothly carbon dioxide and the mixed azine (XLIX). The extrusion of carbon dioxide was illustrated by passing the gas from the photolysis apparatus through lime water, which gave a precipitate of calcium carbonate. The mixed azine was identified by its characteristic i.r. absorption band at 1635 cm^{-1} and by an exact mass measurement. This compound was not analysed because it was considered that the mixed azine might have been dissociating into two symmetrical azines, although the mass spectrum showed no evidence of this.

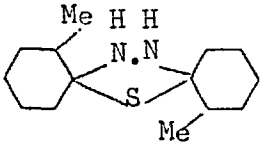
In principle one would expect the azo-sulphide system (X) to undergo the twofold extrusion process to give olefins. The most obvious route to this system is oxidation of the readily available[20] 1,3,4-thiadiazolidines. Compound (LII) was prepared from cyclohexanone, hydrazine hydrate and hydrogen sulphide, and oxidised with lead tetra-acetate at 0° to the azo-sulphide(LIII) (99%). The oxidation was also accomplished by D.D.Q. at 0° (91%). Pyrolysis of the azo-sulphide at 100° gave the thiiran (LIV), whereas pyrolysis in the presence of triphenylphosphine or tris(diethylamino)phosphine gave bis-cyclohexylidene (XVIII) (75% and 77% respectively).



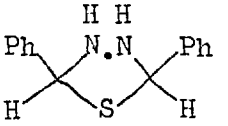
(LII) (LIII) (XVIII) (LIV)

It was found that the thiadiazolidine (LII) could be prepared by treating solutions of cyclohexanoneazine with hydrogen sulphide. When the addition of hydrogen sulphide to cyclohexanoneazine was carried out in the presence of 4-methylcyclohexanone no incorporation of the latter was detected. When solutions of cyclohexanoneazine were treated with hydrogen sulphide in a converted atmospheric hydrogenation apparatus quantitative yields of the thiadiazolidine were obtained, and no further purification was necessary. Bis-cyclohexylidene was obtained in an overall yield of 73% from cyclohexanoneazine when the reaction sequence was conducted without purification of the intermediates. Photolysis of the azo-sulphide (LIII) in cyclohexane, using a medium-pressure mercury arc lamp and pyrex apparatus gave cyclohexanoneazine (52%), but no bis-cyclohexylidene. Attempts to prepare the thiadiazolidines (LV) and

(LVI) by addition of hydrogen sulphide to the corresponding azines were unsuccessful.



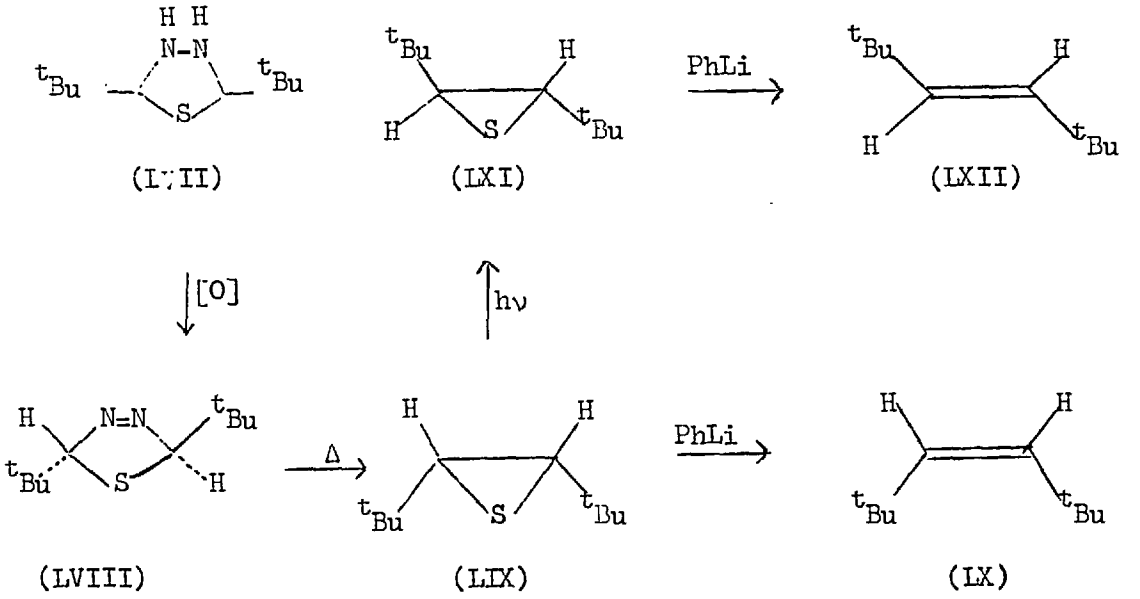
(LV)



(LVI)

While our publications were in preparation Kellogg and Wassenaar also reported[21] the formation of the azo-sulphide(LIII) by oxidation of the thiadiazolidine (LII) with diethylazodicarboxylate. Pyrolysis gave the thiiran (LIV), which gave bis-cyclohexylidene on treatment with butyl lithium. Very recently these same authors[22] have quite elegantly illustrated the stereospecificity of twofold extrusions from azo-sulphides. The highly unstable thiadiazolidine (LVII) was prepared by reacting pivalaldehydeazine with hydrogen sulphide under pressure, and this was oxidised to the trans-thiadiazoline (LVIII) with diethylazodicarboxylate at - 10°. Pyrolysis (85-100°) gave the cis-thiiran (LIX), which gave the cis-olefin (LX) on treatment with phenyl lithium. Photolysis of the cis-thiiran gave the trans-thiiran (LXI), which gave the trans-olefin (LXII) on treatment with phenyl lithium.

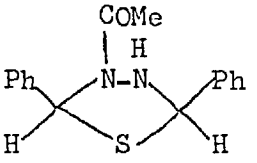
The addition of hydrogen sulphide to azines is reversible, and the formation of the highly unstable thiadiazolidine (LVII) may well represent the limit of this reaction in its present form, because hydrogen sulphide gas is easily liquified.



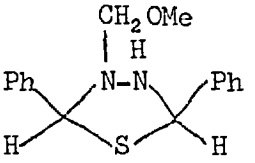
In situ oxidation may provide the necessary driving force for the preparation of more-hindered azo-sulphides, but finding a reagent that will effect thiadiazolidine oxidation yet not oxidise hydrogen sulphide to sulphur will be no easy task. It is encouraging that the thiadiazoline (LIII) is stable to hydrogen sulphide. The oxidation of the thiadiazolidine (LII) with a reagent that does not oxidise hydrogen sulphide has not yet been achieved.

Alternatively, the formation of N-substituted thiadiazolidines in situ should provide the necessary driving force for the addition as well as useful intermediates to the azo-sulphides. The 3-acetylthiadiazolidine (LXIII) was not formed when a solution of benzalazine in acetic anhydride and acetone was treated with hydrogen sulphide. Similarly, no useful product was obtained when

a solution of benzalazine, methylal, and boron trifluoride etherate was treated with hydrogen sulphide in an attempt to prepare the thiadiazolidine (LXIV).

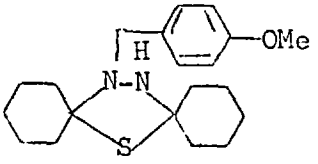


(LXIII)

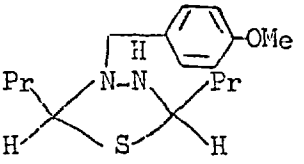


(LXIV)

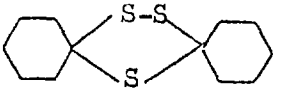
Attempts at forming the 3-substituted thiadiazolidine (LXVa) from p-methoxybenzylhydrazine, cyclohexanone and hydrogen sulphide or potassium hydrogen sulphide, in the presence of triethylamine, gave no trace of the required compound. The only sulphur containing product observed was the trithiolane (XVII). Similarly, none of the thiadiazolidine (LXVb) was formed when p-methoxybenzylhydrazine, n-butyraldehyde and anhydrous sodium sulphide were heated together in absolute ethanol.



(LXVa)



(LXVb)

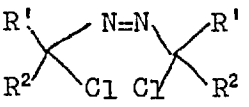


(XVII)

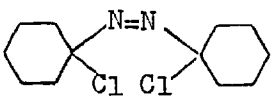
The direct addition of elemental sulphur to azines might in principle give azo-sulphides directly. However, treatment of cyclohexanoneazine with flowers of sulphur and pyridine under a variety of conditions gave no trace of the required products (LIII), (LIV) or (XVIII). Atomic sulphur is a possible alternative, but

here the problem is how to generate it in the presence of azines. Attempts to produce atomic sulphur from hydrogen sulphide and sulphur dioxide in the presence of cyclohexanoneazine gave acidic azine-sulphur dioxide reaction products. The photolysis of carbonyl sulphide has been used to generate triplet or singlet state sulphur atoms,[23] which have been reacted with olefins in the gas, liquid or solid phase. This method of producing atomic sulphur is experimentally inconvenient. Moreover, azines may interfere with the photochemical excitation of carbonyl sulphide, since the photolysis is usually carried out at 229 nm., and azines in general absorb in the region 205 - 267 nm.

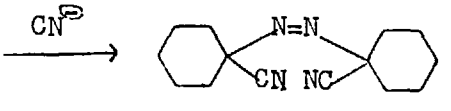
Azines are readily converted into the corresponding α,α'-dichloroazoalkanes (LXVI)[24] by low temperature chlorination. Both chlorine atoms undergo nucleophilic displacement by cyanide, azide, thiols, and carboxylates. Therefore, one might expect to obtain the required azo-sulphide ring system by treating α,α'-dichloroazoalkanes with sodium sulphide. Treatment of (LXVII) with sodium cyanide in water-acetone-methanol (1:2:2 by volume) at 21° gave the azodinitrile (LXVIII) (67%). Treatment of (LXVII) with sodium sulphide under identical conditions gave a mixture of cyclohexanone and cyclohexanone-azine. There was no trace of the required azo-sulphide (LIII) or of compounds (LIV) and (XVIII).



(LXVI)

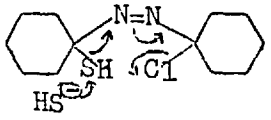


(LXVII)

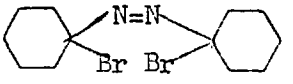


(LXVIII)

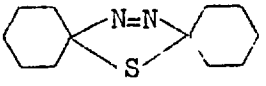
The formation of cyclohexanone can be explained in terms of hydrolysis to α-hydroxy intermediates, which can undergo stepwise or concerted cleavage. The formation of cyclohexanoneazine must be explained in terms of oxidation of sulphide ion, perhaps involving the intermediate (LXIX).



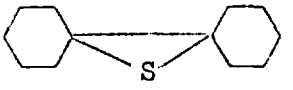
(LXIX)



(LXX)



(LXIII)



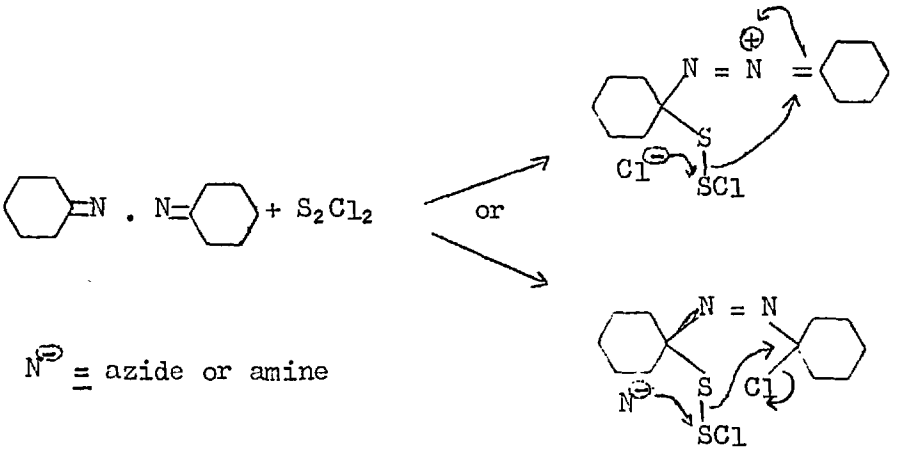
(LIV)

The conditions under which the dichloroazoalkane (LXVII) was treated with sodium sulphide were varied and the results have been summarised (Experimental, Table 1). Cyclohexanone and cyclohexanone-azine were generally the products, although in one experiment where (LXVII) was treated with sodium sulphide hydrate in collidine at 95°, a 10% yield of the required episulphide (LIV) was isolated. The thiadiazoline (LIII) was isolated unchanged after treatment with

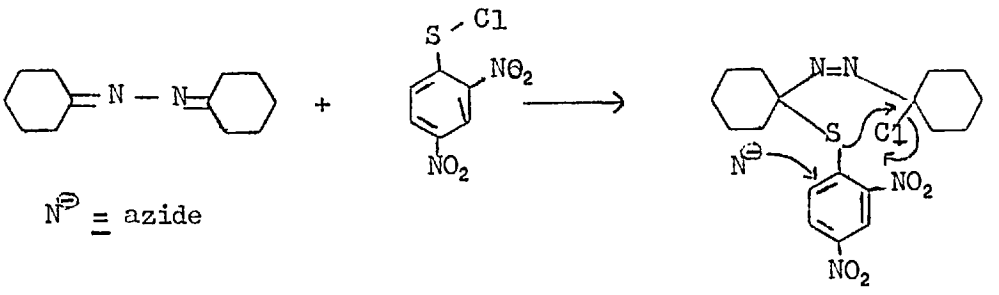
sodium sulphide hydrate in dimethylformamide at 20°, illustrating its stability to such conditions.

Treating the dichloroazoalkane (LXVII) with hydrogen sulphide-triethylamine, or potassium hydrogen sulphide-collidine, did not give the required azo-sulphide, episulphide or olefin.

Attempts to prepare the α,α'-dibromoazoalkane (LXX) by treating cyclohexanoneazine with bromine or with dioxan dibromide at low temperature gave unstable oils. Treating these oils with anhydrous sodium sulphide did not give any of the required products. It was considered possible that disulphur dichloride might add to cyclohexanone-azine according to scheme 7, but dropwise addition of disulphur-dichloride to a solution of cyclohexanoneazine at low temperature gave intractable gums. Moreover, the milder 2,4-dinitrobenzenesulph-enyl chloride did not add to cyclohexanoneazine in the desired manner (scheme 8).

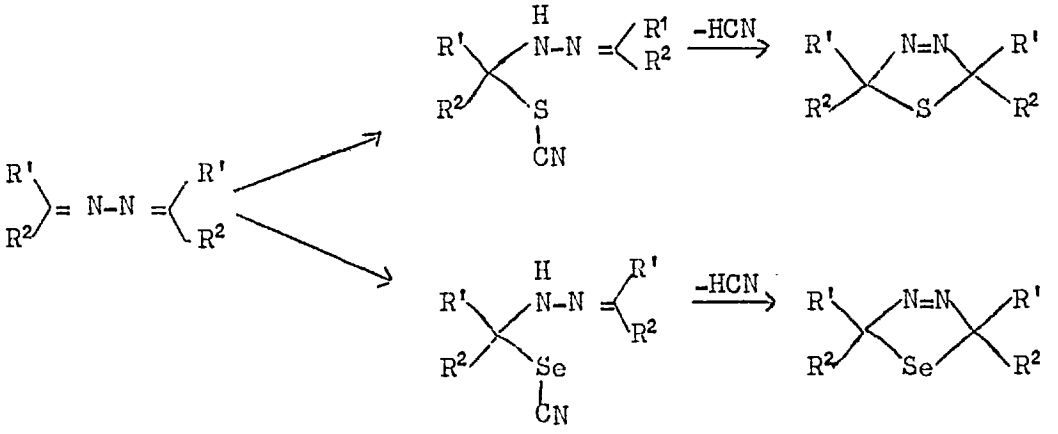


Scheme 7.



Scheme 8.

The addition of one equivalent of hydrogen thiocyanate or hydrogen selenocyanate to an azine should provide useful intermediates to the azo-sulphide or azo-selenide systems (scheme 9). However, attempts to add potassium thiocyanate or potassium selenocyanate to acetophenoneazine or cyclohexanoneazine in the presence of trimethylamine hydrochloride were unsuccessful.



Scheme 9.

It has been reported[25] that treatment of benzophenoneazine with sodium or potassium in tetrahydrofuran yields a dianion. Quenching

the dianion with methyl iodide, 1,3-dibromopropane, or 1,4-dibromobutane resulted in alkylation on the benzylic carbon and adjacent nitrogen, consistent with a 1,2-dianionic structure (LXXI). Attempts were made to induce bis-carbon alkylation, since the 1,4-dianion (LXXII) is a resonance hybrid, but quenching with methylene iodide or 1,2-dibromoethane gave benzophenoneazine (and presumably ethylene).

$$Ph_2C{=}N{-}N{=}C\ Ph_2 \xrightarrow{M \text{ in THF}} [Ph_2\overset{\ominus}{C}{-}N{-}N{=}C\ Ph_2\overset{\ominus}{}]\ 2M^{\oplus}$$

(LXXI) $\updownarrow$

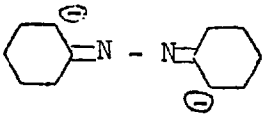
$$[Ph_2C{-}N{=}N{-}\overset{\ominus}{C}\ Ph_2]\ 2M^{\oplus}$$

(LXXII)

Conceivably, aliphatic azines might behave differently to benzophenoneazine since anionic delocalisation is reduced, in which event a 1,4-dianion appears favourable. Treatment of 1,4-dianions of azines with monosulphurdichloride, ditosylsulphide, or an alkylthioamine could in principle give azo-sulphides.

Cyclohexanoneazine did not react with sodium in tetrahydrofuran, even when heated at reflux. When lithium-ethylamine complex was added to a solution of cyclohexanoneazine in ethylamine at -76° it was quickly decolourised, until two equivalents had been added, whereupon decolouration became very slow. Quenching the dianion with water gave cyclohexanoneazine, quenching with methyliodide gave 2-methylcyclohexanoneazine, and quenching with alkylthioamine (followed by work up with water) gave cyclohexanoneazine.

No azo-sulphide was observed in any of these experiments. These results are consistent with the formation of the dianion (LXXIII), the formation of which may be explained in terms of hydrogen transfer.

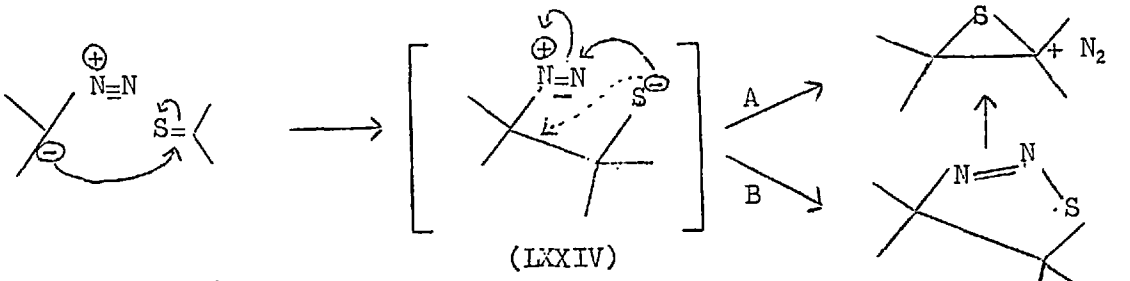


(LXXIII)

An alternative explanation is that the decolouration observed was a result of azine-catalysed decomposition of the lithium-ethylamine complex to lithium ethylamide. A solution of lithium-naphthalene reagent was added to a solution of cyclohexanoneazine in tetrahydrofuran at -19°, until a permanent green colour was observed. Quenching with methyl iodide and work up with water gave several products.

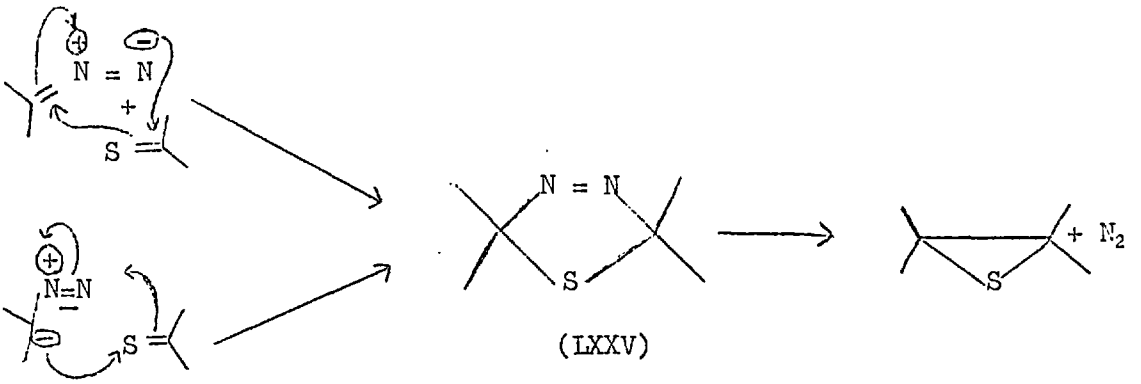
Several aromatic thiirans have been prepared by the reaction of diazoalkanes with thioketones,[26] and thioketones are reported to have been generated <u>in situ</u> from aromatic diazo-compounds and sulphur.[27] The observation that nitrogen is evolved spontaneously from these reactions might be interpreted mechanistically in terms of an intermediate (LXXIV), resulting from the attack of the negative carbon atom of the diazoalkane at the thiocarbonyl carbon atom. This intermediate may then collapse to thiiran and nitrogen by one of two pathways (A or B, scheme 10). Alternatively, we considered the possible intermediacy of Δ^3-1,3,4-thiadiazolines (LXXV),

arising from attack of the negative nitrogen atom of the diazoalkane at the thiocarbonyl carbon atom, or even the direct attack of the negative carbon atom of the diazoalkane at the sulphur atom of the thiocarbonyl compound. (scheme 11).



(LXXIV)

Scheme 10.

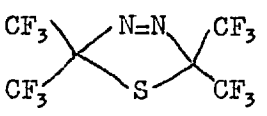


(LXXV)

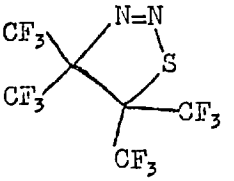
Scheme 11.

With aromatic diazoalkanes and thioketones the external stabilisation resulting from the terminal phenyl groups would make the extrusion of nitrogen extremely facile, and consequently the intermediate thiadiazolines would not be observed. Recently, the formation of the azo-sulphide (LXXVI) was observed in the reaction between the

corresponding thioketone and diazoalkane. That the compound isolated was (LXXVI) and not the Δ^2-1,2,3-thiadiazoline (LXXVII) was demonstrated unequivocally by fluorine atom n.m.r. spectroscopy. A study of the possible intermediacy of azo-sulphides in the reactions between aliphatic thioketones and aliphatic diazoalkanes not having strongly electronegative substituents was undertaken. Aliphatic thioketones with α-hydrogen atoms readily enolise and are unstable except at low temperatures. Consequently the idea of preparing them from diazoalkanes in situ was most attractive.

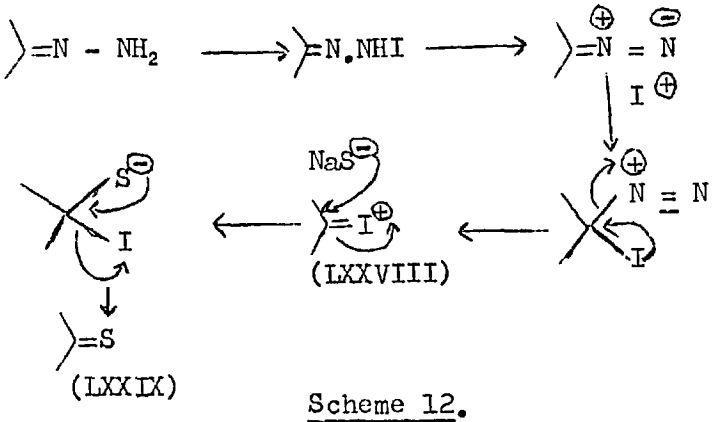


(LXXVI)



(LXXVII)

The mechanism proposed by Barton[29] for the oxidation of hydrazones by iodine invokes an intermediate (LXXVIII), which if treated with sodium sulphide might yield the thioketone (LXXIX) (scheme 12).



(LXXVIII)

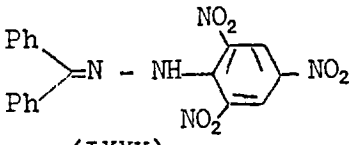
(LXXIX)

Scheme 12.

However, iodine was found to react very quickly with sodium sulphide. Even so this sequence was attempted using 3-pentanonehydrazone, but azine was recovered quantitatively. Alternatively, it was considered that the whole sequence might be accomplished with elemental sulphur alone, but as expected sulphur was not a strong enough oxidising agent.

In order to investigate the reaction of aliphatic diazoalkanes with aliphatic thioketones it was necessary to develop a mild, low-temperature method for the preparation of aliphatic diazoalkanes from hydrazones. The method most widely used for the preparation of diazoalkanes from hydrazones involves heterogeneous oxidation by heavy metal oxides,[30] but yields are low in the case of aliphatic hydrazones. Other preparative methods are either too involved or require drastic reaction conditions. The diazo-transfer method described by Anselme[31] is one of the mildest homogeneous procedures available, but the diazoalkanes are generated in the presence of excess butyl lithium.[32] Benzophenonehydrazone was chosen for the initial oxidation experiments, since the formation of diphenyldiazomethane is self-indicating. Treatment of this hydrazone with Cookson's reagent gave benzophenoneazine and 4-phenylurazole. Benzoyl peroxide did not react with benzophenonehydrazone. The hydrazone (LXXX) was obtained when benzophenonehydrazone was treated with picrylazide. In no case was the characteristic crimson colour of diphenyldiazomethane observed. However, a quantitative yield of diphenyldiazomethane was obtained when

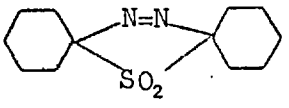
benzophenonehydrazone was treated with lead tetra-acetate in the presence of triethylamine.



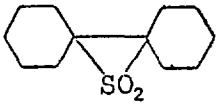
(LXXX)

Experiments are at present underway to extend this oxidation procedure to aliphatic hydrazones, and to investigate the reaction of aliphatic diazoalkanes with non-enolisable thioketones and with thioketones generated in situ at low temperature.

In principle one might expect the azo-sulphone system (XII) and the azo-sulphoxide system (XI) to be susceptible to the twofold extrusion process. It has already been shown[33] that sulphur dioxide will not add to cyclohexanoneazine or benzalazine at atmospheric pressure, and the logical extension of this investigation was to try to add sulphur dioxide to azines under pressure. A series of autoclave experiments was conducted using cyclohexanoneazine, but in no case was the azo-sulphone (LXXXI), the episulphone (LXXXII), or bis-cyclohexylidene (XVIII) observed.



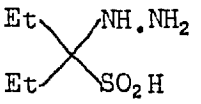
(LXXXI)



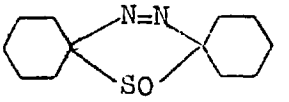
(LXXXII)

Attempts at adding sulphoxylic acid or sodium sulphoxylate to 3-pentanonehydrazone to give the 2-hydrazinosulphinic acid (LXXXIII)

(or its sodium salt) were unsuccessful.



(LXXXIII)



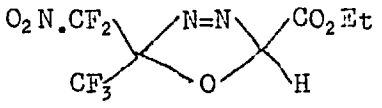
(LXXXIV)

There is some evidence in the literature that the azo-sulphone system would not undergo the twofold extrusion process in the desired manner.[34] It was therefore decided to prepare the azo-sulphoxide (LXXXIV) and the azo-sulphone (LXXXI) by oxidation of the azo-sulphide (LIII), and submit them to the extrusion process. Oxidation of the azo-sulphide with hydrogen peroxide in acetic acid gave the azo-sulphoxide which was oxidised further with peracetic acid in dichloromethane to the azo-sulphone. Pyrolysis of the sulphoxide or sulphone gave only poor yields of bis-cyclohexylidene (XVIII) (11 and 12% respectively). Photolysis afforded cyclohexanoneazine (54 and 18% respectively), but no olefin.

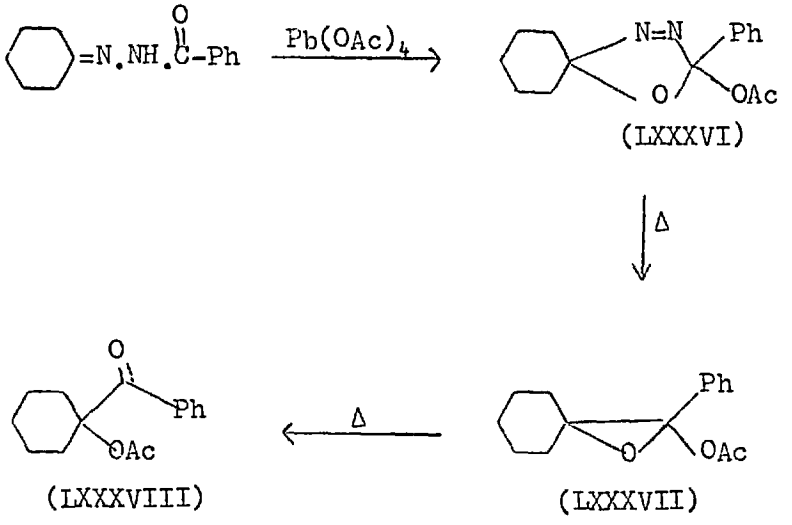
It therefore seems likely that the azo-sulphoxide and azo-sulphone systems are of no use in the synthesis of olefins by twofold extrusion processes, unless they are first reduced to the azo-sulphide system.

Δ^3-1,3,4-Oxadiazolines (XIII) might be expected to undergo the twofold extrusion process to give olefins. The oxadiazoline (LXXXV) is reported[35] to have been prepared from nitro-perfluoroacetone and ethyldiazoacetate at -40°. The reaction mixture slowly lost nitrogen on heating to 165-170° to give the corresponding oxiran in

low yield. The oxadiazoline (LXXXVI) has also been prepared, and is reported[36] to yield the keto-acetate (LXXXVIII) on pyrolysis, by way of the oxirane (LXXXVII) (scheme 13).

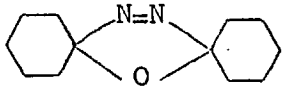


(LXXXV)



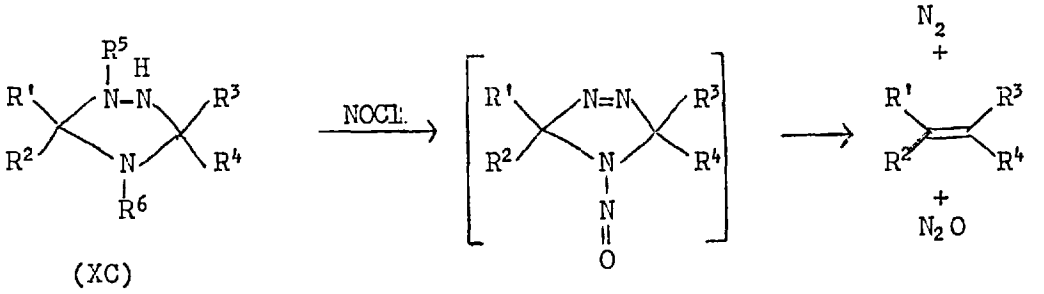
Scheme 13.

Attempts to prepare the oxadiazoline (LXXXIX) from cyclohexanone-azine and potassium hydroxide in the presence of various oxidising agents were unsuccessful.



(LXXXIX)

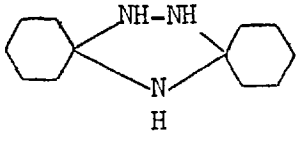
Triazolines (XIV) are of interest since they might be expected to extrude nitrogen to give aziridines, which are readily converted into olefins. In principle the whole sequence might be achieved by treating a suitably substituted triazolidine (XC) with nitrosyl chloride, and warming (scheme 14).



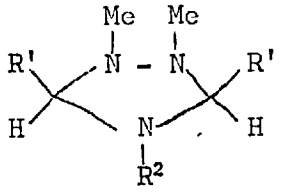
(XC)

Scheme 14.

Attempts at forming the triazolidine (XCI) by treating cyclohexanoneazine with sodamide or ammonia were unsuccessful. Similarly, benzylamine did not add to cyclohexanoneazine under a variety of conditions.



(XCI)

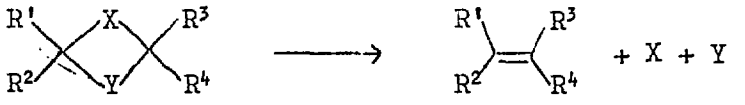


(XCII)

Substituted 1,2,4-triazolidines (XCII) are readily prepared from sym-dimethylhydrazine, aldehydes and primary amines.[37] However, the reaction could not be extended to p-methoxybenzylhydrazine.

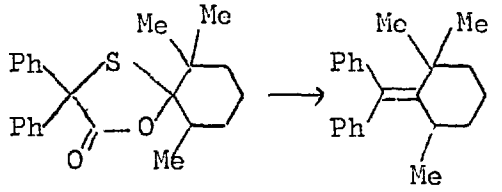
Conclusions

The twofold extrusion process [(A) → (B)] offers an attractive route to sterically hindered olefins and, as expected, the choice of X and Y governs the conditions under which the extrusion occurs.



(A) (B)

Of several systems that have been examined two have proven useful in olefin synthesis by twofold extrusion processes. Heating oxathiolan-5-ones with tervalent phosphine affords hindered olefins with ease, but only when conjugating residues are present to facilitate the loss of carbon dioxide. Pyrolysis of compound (XXIV) at 180 - 230° in the presence of tris(diethylamino)phosphine gave the highly hindered olefin (XXVIII) in 80% yield.



(XXIV) (XXVIII)

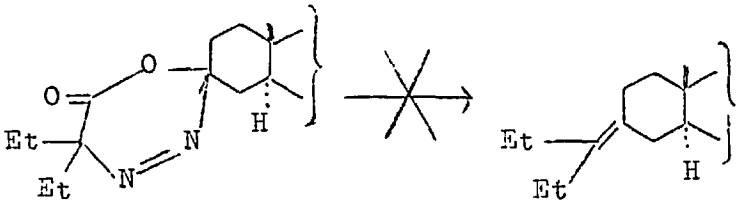
The 1,3,4-thiadiazoline system is very promising, since in this case the extrusion process occurs at relatively low temperature, and does not require conjugating residues to be present. Pyrolysis of compound (LIII) in the presence of tervalent phosphine gave bis-cyclohexylidene (XVIII) in high yield. Several different

routes to azo-sulphides

(LIII) (XVIII)

have been investigated in an attempt to extend the usefulness of this system.

That systems involving six-membered rings are probably less useful than those with five-membered rings was demonstrated by the pyrolysis and photolysis reactions of compound (XLVIII), neither of which gave any trace of the expected olefin.



(XLVIII)

Several other systems have been investigated but did not provide useful olefin syntheses.

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EXPERIMENTAL

Unless otherwise stated, the following data applies to this section:

Melting points were determined on a Kofler block and are uncorrected. Infrared (i.r.) spectra were recorded on a Unicam SP200 or a Perkin Elmer 257 spectrometer as solutions in chloroform or carbon tetrachloride, or as mulls with nujol or hexachlorobutadiene. Nuclear magnetic resonance (n.m.r.) spectra were taken in deuterochloroform or carbon tetrachloride with a Varian A60 or T60 spectrometer. Ultraviolet (u.v.) spectra were recorded on a Unicam SP800B spectrometer. Mass spectra (m.s.) were recorded with a Perkin Elmer 270 low-resolution or an A.E.I. MS9 high-resolution spectrometer.

The following symbols are used for i.r. data:

w ..... weak

m ..... medium

s ..... strong.

The following symbols are used for n.m.r. data:

s ..... singlet

d ..... doublet

t ..... triplet

q ..... quartet

bs..... broad singlet

m ..... multiplet.

Benzene, diethyl ether, light petroleum and hexane were dried over sodium wire. Tetrahydrofuran was distilled from lithium aluminium hydride before use. Dichloromethane was distilled from phosphorus pentoxide. Triethylamine was distilled from sodium wire. Lead tetra-acetate was washed free from acetic acid with dry light petroleum and dried in vacuo. Liquid reagents were generally redistilled before use and solids recrystallised if far different from their literature m.p. Nitrogen was dry and essentially oxygen free.

"Worked up in the usual way" implies successive washings with saturated sodium bicarbonate or 2% sodium carbonate solution, followed by washing with water to neutrality.

Solutions of organic compounds were dried with anhydrous sodium sulphate. Evaporation of solvents was effected in vacuo using minimum temperatures. Solids were dried in vacuo at room temperature. Alumina grade III and silica gel MFC were used for column chromatography. "Light petroleum" refers to that fraction boiling between 40 - 60°.

1,2,4-Trithiolan-3,5-bis(spiro-1'-cyclohexane) (XVII).

This compound was prepared according to the method of Asinger.[1] Recrystallisation from ethanol gave colourless plates m.p. 49.0 - 49.5° (lit. 50°). Spectral data was in accordance with this structure.

Desulphurisation of (XVII) with tervalent phosphorus reagents.

a) Tris(diethylamino)Phosphine.

Trithiolane (0.25 g.) and tris(diethylamino)phosphine[2] (0.8 g.) were heated together under nitrogen at 150 - 160°. After 1 hour the reaction temperature began to fall as diethylamine started refluxing. After 2.1/2 hours the reaction temperature had fallen to ca. 110°. Thin layer chromatography (t.l.c.) indicated the formation of several minor components and the presence of unreacted trithiolane. Column chromatography (alumina, light petroleum then benzene) gave no bis-cyclohexylidene (XVIII).

b) Tri-n-butylphosphine.

Trithiolane (0.25 g.) and tri-n-butylphosphine (0.6 g.) were heated together under nitrogen at 160° for 1.1/2 hours, and then at 200° for 3 hours. No bis-cyclohexylidene was observed.

c) Triethylphosphite.

Trithiolane (0.25 g.) and triethylphosphite (0.5 g.) were heated together at reflux under nitrogen for 4 hours. No bis-cyclohexylidene was observed.

d) Triphenylphosphine.

Trithiolane (0.25 g.), triphenylphosphine (0.8 g.), toluene (1.0 ml.) and benzoylperoxide (0.05g.) were heated together at reflux under nitrogen for 3 hours. No bis-cyclohexylidene was observed.

N-phenyl-S-benzhydrylthiocarbamate-2-carboxylic acid (XIX).

This compound was prepared according to the method of Becker and Bistrzycki.[3] Recrystallisation from methanol/water gave colourless prisms m.p. 138 - 138.5° (lit. 140.5°).

Potassium 2-mercaptodiphenylacetate.

Attempts to prepare 2-mercaptodiphenylacetic acid according to the method of Becker and Bistrzycki[3] gave the potassium salt as colourless needles m.p. 150 - 150.5° (decomp.) from toluene; ν_{max}(mull) 2600 m, 1590 s and 1330 s (ionised carboxyl group) cm^{-1}.

2-Mercaptodiphenylacetic acid (XX).

Potassium hydroxide (10.5 g.) was dissolved in water (750 ml.) and the solution heated at reflux under nitrogen to remove dissolved air. After cooling, N-phenyl-S-benzhydrylthiocarbamate-2-carboxylic acid (30.0 g.) was added and the mixture heated at reflux for 1 hour with stirring. The solution was cooled and any solid present removed by filtration. The pH of the solution was adjusted to 3 by the dropwise addition of dilute hydrochloric acid, with stirring at 4°. The precipitate was collected, thoroughly washed with water, dissolved in diethyl ether, and stirred with

dilute hydrochloric acid (100 ml.) for 30 minutes. The ethereal layer was separated, washed once with water (50 ml.) and dried. Evaporation of the solvent gave the free acid as a white solid which crystallised from acetone/hexane as colourless plates, m.p. 152 - 153°, 83% theor. (lit.[3] 147.5 - 149° from toluene or acetic acid); ν_{max} ($CHCl_3$) 2600 (SH), 2900 (OH), 1700 s and 1265 s (free carboxylic acid) cm^{-1}; τ 6.85 (1H, s), 2.65 (10 H, m), -1.80 (1H, bs); (M^+) $^m/_e$ = 244.

2,4,4-Triphenyl-1,3-oxathiolan-5-one (XXI).

a) Hydrogen chloride catalyst.

Dry hydrogen chloride was passed into a mixture of potassium-2-mercaptodiphenylacetate (1.89 g.), glacial acetic acid (5.0 ml.) and benzaldehyde (0.9 g.) at 30°. After 80 minutes the reaction product was decomposed by the careful addition of ice-water. The precipitate was collected, worked up in the usual way, and dried, m.p. 97 - 97.5°, 77% theor. (lit.[4] 94 - 95°); ν_{max}(mull) 3050, 1755 s (lactone CO) cm^{-1}.

b) Toluene-p-sulphonic acid catalyst.

2-Mercaptodiphenylacetic acid (3.00 g.), toluene-p-sulphonic acid (0.42 g.), benzaldehyde (1.23 g.) and benzene (50 ml.) were heated together at reflux for 5 hours, with azeotropic removal of water and under nitrogen. The reaction product was worked up in the usual way and the organic layer dried. Evaporation of the solvent gave the oxathiolan-5-one as a white solid.

Crystallisation from acetone/hexane gave colourless conglomerates, m.p. 96.5 - 97.5°, 94% theor.

Attempted preparation of (XXI) direct from the thiocarbamate (XIX).

Hydrogen chloride gas was passed into a mixture of N-phenyl-S-benzhydrylthiocarbamate-2-carboxylic acid (1.0 g.), glacial acetic acid (2.5 ml.) and benzaldehyde (0.3 g.) at 50° for 5 hours. At the end of this time the reaction product was poured into water, extracted with diethylether and worked up in the usual way. The organic layer was dried and the solvent evaporated to give a semi-solid containing a very small amount of the required oxathiolan-5-one.

Triphenylethylene (XXV).

2,4,4-Triphenyl-1,3-oxathiolan-5-one (1.50 g.) and tris(diethylamino)phosphine (1.23 g.) were heated together under nitrogen at 150 - 160° for 2 hours, by which time monitoring of the i.r. absorption at 1755 cm^{-1} showed the reaction to be complete. T.l.c. (silica gel, benzene) showed a fast-running major component which did not appear to contain sulphur (undeveloped by palladium chloride spray), but which was u.v. active and rapidly developed by iodine. Column chromatography (silica gel, benzene) gave triphenylethylene as a white solid m.p. 67 - 68°, 95% theor. One crystallisation from methanol gave colourless rods m.p. 70 - 71° (lit.[5] 70°); ν_{max}(mull) 3050, 1600, 1495, 1435, 780, 760, 720, 700 cm^{-1}; λ_{max} (EtOH) 298, 228 nm. (ε 20,000 and 18,700) cf lit.[6] λ_{max} (EtOH) 303, 230 nm. (ε 26,900 and 26,900); (M^+) $^m/_e$ = 256.

4,4-Diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-cyclohexane (XXII).

a) Hydrogen chloride catalyst.

Dry hydrogen chloride was passed into a mixture of potassium-2-mercaptodiphenylacetate (1.89 g.), glacial acetic acid (4.0 ml.) and cyclohexanone (0.84 g.) at 55°. After 3.1/2 hours the reaction product was decomposed with ice-water and stored at 0° for 1 hour. The precipitate was collected, worked up in the usual way and dried. Crystallisation from acetone/light petroleum gave the oxathiolan-5-one as colourless rhombs m.p. 82 - 83.5°, 78% theor. (lit.[4] 80 - 82°); ν_{max}(mull) 3050, 1755 s (lactone CO) cm^{-1}; (M^+) $^m/_e$ = 324.

b) Toluene-p-sulphonic acid catalyst.

2-Mercaptodiphenylacetic acid (3.00 g.), toluene-p-sulphonic acid (0.56 g.), cyclohexanone (1.20 g.) and benzene (50 ml.) were heated together at reflux for 7.1/2 hours, with azeotropic removal of water and under nitrogen. The reaction product was worked up in the usual way and the organic layer dried. Evaporation of the solvent gave an off-white solid. Crystallisation from acetone/light petroleum gave the oxathiolan-5-one m.p. 82 - 83°, 83% theor.

c) Boron trifluoride catalyst.

Boron trifluoride gas was passed into a solution of 2-mercaptodiphenylacetic acid (1.89 g.) and cyclohexanone (0.76 g.) in benzene (25 ml.) at 18°. A red oil started to separate soon after the passage of gas was commenced. After one hour the reaction product was decomposed with ice-water, worked up in the usual way, and the

organic layer dried. Evaporation of the solvent gave the oxathiolan-5-one as a white solid m.p. 79 - 81°, 84% theor.

Diphenylcyclohexylidenemethane (XXVI).

Slightly impure 4,4-diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-cyclohexane (0.40 g.) and tris(diethylamino)phosphine (0.35 g.) were heated together under nitrogen at 160°. The temperature was raised to 200° over a period of 5 hours, by which time monitoring of the i.r. absorption at 1755 cm^{-1} showed the reaction to be complete. Column chromatography (silica gel, benzene) gave diphenylcyclohexylidene-methane (the first component off the column) as a white solid m.p. 79 - 80°, 82% theor. Recrystallisation from light petroleum gave colourless rhombs m.p. 83 - 83.5° (lit.[7] 82 - 83.5°); ν_{max}(mull) 3080, 3050, 3025, 2980, 2930, 2855, 1630, 1600, 1490, 1440, 760 cm^{-1}; λ_{max} (EtOH) 245 nm. (ε 14,100) cf. lit.[7] 246 nm. (14,800); τ 8.4 (6H, m), 7.8 (4H, m), 2.8 (10H, m); (M^+) $^m/_e$ = 248.

Pyrolysis of (XXII) in the absence of tervalent phosphine.

4,4-Diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-cyclohexane (439 mg.) was heated to 210° over 15 minutes, evolution of carbon dioxide commencing at about 190°. After 4 hours no oxathiolan-5-one remained, as shown by i.r. monitoring. T.l.c. (silica gel, light petroleum) indicated two major and several minor components. Preparative t.l.c. gave:

COMPONENT 1 (Rf. 0.5), as a colourless oil (100 mg.). T.l.c. now suggested that this contained two products, slightly resolved, but

distinguishable, since one was strongly u.v. active and the other was developed by palladium chloride spray. These two products were not separated. T.l.c. comparison indicated that the first was diphenylcyclohexylidenemethane. T.l.c. behaviour and an extra absorption in the i.r. at 740 cm^{-1} indicated that the second was its thiiran.

COMPONENT 2 (Rf. 0.4), as a white solid (120 mg.) m.p. 89 - 91°. Crystallisation from light petroleum gave colourless rods m.p. 93.5 - 94°, identified as triphenylmethane (m.p., mixed m.p., t.l.c. comparison and i.r.).

Pyrolysis of diphenylcyclohexylidenemethane (XXVI) in the presence of sulphur.

Olefin (297 mg.) and flowers of sulphur (85 mg.) were heated together under nitrogen at 210° for 4 hours. T.l.c. (silica gel, light petroleum) indicated the presence of several products. Preparative t.l.c. gave unreacted olefin (35 mg.), triphenylmethane (65 mg.) and other non-polymeric products (105 mg.).

4,4-Diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-(2'-methylcyclohexane) (XXIII).

a) Hydrogen chloride catalyst.

Dry hydrogen chloride was passed into a mixture of potassium-2-mercaptodiphenylacetate (6.00 g.), glacial acetic acid (12.0 ml.) and 2-methylcyclohexanone (2.47 g.) at 65 - 75°. After 5 hours the reaction product was decomposed with ice-water and extracted with

diethyl ether. The organic layer was worked up in the usual way and dried. Evaporation of the solvent gave an oil, which solidified on standing. The solid was granulated with light petroleum at 0°, collected by filtration and dried, m.p. 66.5 - 68.5°, 74% theor. Recrystallisation from light petroleum gave the mixture of two isomers as colourless conglomerated m.p. 70 - 71.5°; ν_{max} ($CHCl_3$) 1755 s (lactone CO) cm^{-1}; τ 8.9 (ca. 3H, m), 8.3 (ca. 9H, m), 2.5 (10H, m); (M^+) $^m/_e$ = 338, 294. (Found: C, 74.42; H, 6.48; S, 9.41. $C_{21}H_{22}O_2S$ requires C, 74.52; H, 6.55; S, 9.47%).

b) Toluene-p-sulphonic acid catalyst.

2-Mercaptodephenylacetic acid (0.75 g.), toluene-p-sulphonic acid (0.11 g.), 2-methylcyclohexanone (0.34 g.) and benzene (20 ml.) were heated together at reflux with azeotropic removal of water and under nitrogen. Monitoring of the reaction indicated that a reaction time in excess of 24 hours was required, so this procedure was not investigated further.

Diphenyl (2'-methylcyclohexylidene)methane (XXVII).

4,4-Dipenhyl-1,3-oxathiolan-5-one-2-spiro-1'-(2'-methylcyclohexane) (0.60 g.) and tris(diethylamino) phosphine (0.48 g.) were heated together under nitrogen at 215 - 225° for 4 hours, by which time monitoring of the lactone carbonyl absorption showed the reaction to be complete. Column chromatography (silica gel, benzene) gave diphenyl(2'-methylcyclohexylidene)methane (the first component off the column) as a white solid m.p. 68 - 70°, 88% theor.

An analytical sample was obtained by recrystallisation from light petroleum m.p. 73.5 - 74°; ν_{max}(mull) 3080, 3060, 3025, 2960, 2930, 2850, 1600, 1490, 1445, 755 cm^{-1}; λ_{max} (EtOH) 243 nm. (ε 13,300); τ (CCl_4) 8.8 (3H, d, J 15Hz), 8.6 - 7.0 (9H, m), 2.9 (10H, s); (M^+) $^m/_e$ = 262. (Found: C, 91.37; H, 8.31. $C_{20}H_{22}$ requires C, 91.55; H, 8.45%).

4,4-Diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-(2',2',6'-trimethyl-cyclohexane) (XXIV).

A series of experiments was conducted in which the following reaction parameters were investigated, (i) mole ratio of reactants, (ii) mode of addition of reactants, (iii) reaction time, (iv) reaction temperature (v) nature of the solvent system (vi) nature of the acid catalyst. The optimum reaction conditions are described:

Boron trifluoride gas was passed into a solution of 2-mercaptodiphenylacetic acid (644 mg.) and 2,2,6-trimethylcylohexanone (230 mg.) in dichloromethane/hexane at 24.5°. After 2.1/2 hours a further quantity of acid (490 mg.) dissolved in a minimum of dichloromethane was added, and after 4 hours the addition was repeated. After 6 hours excess hexane was added and the passage of gas continued for a further 10 minutes. The upper colourless layer was removed and dichloromethane/hexane added to the red oily residue so that it completely dissolved. The passage of gas was continued and after 1 hour the process of precipitating the red oil and removing the upper layer repeated. The colourless upper layers

were combined, worked up in the usual way and dried. Evaporation of the solvent gave an oil (344 mg.) which when chromatographed (silica gel, light petroleum/benzene 1:1 by volume) gave the required oxathiolan-5-one as a colourless oil (204 mg., 34% theor.), ν_{max} ($CHCl_3$) 1745 (lactone CO) cm^{-1}; τ 9.0 - 7.5 (16H, m), 2.7 (ca. 10H, m); (M^+) $^m/_e$ = 366. A small sample was purified further for analysis. Preparative t.l.c. (silica gel, light petroleum/benzene 1:1) gave a colourless solid m.p. 23 - 26°. (Found: C, 75.59; H, 7.36; S, 8.81. $C_{23}H_{26}SO_2$ requires C, 75.37; H, 7.15; S, 8.74%).

Diphenyl (2',2',6'-trimethylcyclohexylidene)methane (XXVIII).

4,4-Diphenyl-1,3,-oxathiolan-5-one-2-spiro-1'-(2',2',6'-trimethylcyclohexane) (302 mg.) and tris(diethylamino)phosphine (302 mg.) were heated together under nitrogen at 210 - 230° for 4 hours, by which time i.r. monitoring of the lactone carbonyl absorption showed the reaction to be complete. Column chromatography (alumina, light petroleum) gave diphenyl(2',2',6'-trimethylcyclohexylidene)methane, the first component off the column, as a colourless oil (189.7 mg., 79.4% theor.) which started to solidify after standing at 0° for one year; ν_{max}(film) 3080, 3060, 3025, 1600, 1495, 1445, 760 cm^{-1}; λ_{max} (EtOH) 242 nm. (ϵ 12,100); τ 9.1 (3H, s), 8.9 (6H, s and superimposed d), 8.5 (6H, m), 7.7 (1H, m); (M^+) $^m/_e$ = 290. (Found: C, 90.86; H, 9.00. $C_{22}H_{26}$

requires C, 90.98; H, 9.02%).

1,3-Oxathiolan-5-one-2-spiro-1'-cyclohexane (XXX).

Thioglycollic acid (23.35 g.), toluene-p-sulphonic acid (5.00 g.), cyclohexanone (24.75 g.) and benzene (100 ml.) were heated together at reflux for 3 hours, with azeotropic removal of water and under nitrogen. The reaction product was worked up in the usual way and the organic layer dried. Evaporation of the solvent gave an oil (39.5 g.). Distillation under reduced pressure gave one main fraction b.p. 131 - 134°/10 mm., 43% theor. (one experiment only), which solidified on cooling. An analytical sample was prepared by recrystallisation from light petroleum ‡ m.p. 26.5 - 27°; ν_{max} (CCl_4) 2940 s, 2860 s, 1780 s cm^{-1}; τ 8.7 - 7.8 (10H, m), 6.3 (2H, s). (Found: C, 55.62; H, 6.76; S, 18.71. $C_8H_{12}O_2S$ requires C, 55.78; H, 7.02; S, 18.61%).

Pyrolysis of 1,3-oxathiolan-5-one-2-spiro-1'-cyclohexane (XXX).

Oxathiolan-5-one (4.30 g.) and triphenylphosphine (9.79 g.) were heated together under nitrogen at 220° for 1.1/2 hours, by which time i.r. monitoring of the lactone carbonyl absorption showed the pyrolysis to be complete. Gas evolution was observed. Distillation gave no cyclohexylidenemethane, b.p. 103°/760 mm. Distillation at reduced pressure gave one main fraction b.p. 89 - 91°/ 30 mm. (1.89 g.), identified as 1-methylthiocyclohex-1-ene (XXXI), n_D^{27} 1.5249; ν_{max}(film) 3050 w and 1635 w (C = C) cm^{-1};

(‡, dried *in vacuo* at 0°).

τ 8.4 (4H, m), 7.8 (7H, m), 4.6 (1H, bs); (M^+) $^m/_e$ = 128, 113, 81; (lit.[8] b.p. 75.5 - 77°/ 16 mm., n_D^{20} 1.5252).

Pyrolysis of the oxathiolan-5-one in the presence of tris-(diethylamino)phosphine gave no trace of the required olefin.

Attempted removal of sulphur from 4,4-diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-cyclohexane. (XXII).

4,4-Diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-cyclohexane was treated with hexachlorodisilane under a variety of conditions in an attempt to remove sulphur as the first step of the twofold process. No reaction was observed.

2-Bromocyclohexanecarboxylic acid.

Cyclohexanecarboxylic acid (25.1 g.), phosphorus trichloride (0.4 ml.) and bromine (12.2 ml.) were heated together on a steam-bath for 14 hours. Distillation at reduced pressure gave 2-bromo-cyclohexanecarboxylic acid as one main fraction b.p. 142 - 149°/ 7.5 mm., 76% theor., which solidified. (lit.[9] b.p. 120 - 2°/0.7 mm.)

Ethyl-2-bromocyclohexane-carboxylate.

2-Bromocyclohexanecarboxylic acid (16.15 g.), absolute ethanol (12.0 ml.), benzene (19.0 ml.) and concentrated sulphuric acid (0.15 ml.) were heated together at reflux for 6 hours. Distillate (15 ml.) was removed, further absolute ethanol (5.0 ml.) added, and the heating at reflux continued for a further 15 hours. The reaction product was worked up in the usual way, dried, and the solvent

evaporated. Distillation at reduced pressure gave ethyl-2-bromocyclohexane-carboxylate as one main fraction b.p. 90 - 94°/ 4.5 mm., 61% theor. (lit.[10] b.p. 111 - 115°/ 17 mm.)

Attempted preparation of 1,3-thiazolidin-2-imine-4-one-5-spiro-1'-cyclohexane.

a) From 2-bromocyclohexanecarboxylic acid.

2-Bromoacid (1.03 g.), absolute ethanol (5.0 ml.) and thiourea (0.40 g.) were heated together at reflux for 1 hour. Cooling gave colourless crystalline material, which was collected and shown to be thiourea. Evaporation of the filtrate gave 2-bromocyclohexane-carboxylic acid.

b) From ethyl-2-bromocyclohexane-carboxylate.

2-Bromoester (1.17 g.), absolute ethanol (5.0 ml.) and thiourea (o.41 g.) were heated together at reflux for 1 hour. Cooling gave colourless crystalline material, which was collected and shown to be thiourea. Evaporation of the filtrate gave ethyl-2-bromocyclo-hexane-carboxylate.

Cyclohexane-1,1-dithiol.

This compound was prepared according to the method of Mayer,[11] b.p. 82.5 - 85.5°/12 mm. (lit. 84°/12 mm.) Spectral data was in accordance with this structure.

1,3-Dithiolan-4-imine-2,5-bis(spiro-1'-cyclohexane) (XXXV) and 1,3-dithiolan-4-thione-2,5-bis(spiro-1'-cyclohexane) (XXXIV).

A solution of potassium cyanide (2.60 g.) in water (20 ml.)

and dioxan (10 ml.) was added dropwise over 20 minutes to a solution of cyclohexanedithiol (5.92 g.) in dioxan (5 ml.) at 23°, with stirring, and under nitrogen. Monitoring of the reaction by t.l.c. (silica gel, benzene) indicated the formation of two products and suggested that the reaction was complete after 2 hours. After 6 hours the reaction product was poured into water and extracted with chloroform. The chloroform extracts were washed with water and dried. Evaporation of the solvent gave an orange oil (6.32 g.). Column chromatography (silica gel, benzene) of the reaction product (1.92 g. only) gave:

COMPONENT 1 (Rf. 0.8), as an orange solid (0.88 g.). Recrystallisation from light petroleum gave 1,3-dithiolan-4-thione-2,5-bis(spiro-1'-cyclohexane) as orange plates m.p. 53.5 - 54°. ν_{max} (CCl_4) 2940 s, 2865 m, 1455 m, 1165 w, 1120 w, 1065 w, 1040 w, 970 w, 885 m cm^{-1}; λ_{max} (cyclohexane) 321 nm. (ε 10,700); (M^+) $^m/_e$ = 272. (Found: C, 57.41; H, 7.46; S, 35.35. $C_{13}H_{20}S_3$ requires C, 57.36; H, 7.40; S, 35.30%).

COMPONENT 2 (Rf. 0.3), as a colourless solid (0.96 g.) Recrystallisation from light petroleum gave 1,3-dithiolan-4-imine-2,5-bis(spiro-1'-cyclohexane) as colourless needles m.p. 85.0 - 85.5°. ν_{max} (CCl_4) 3400 w, 2940 s, 2865 m, 1600 s, 1450 s, 1230 s, 1070 m, 1020 w, 960 m, 910 m, 900 m, 850 w cm^{-1}; λ_{max} (cyclohexane) 225 nm. (ε 3,300); τ (CCl_4) 8.0 - 6.5 (20H, m), ca. -4.0 (1H, bs, D_2O exchangeable); (M^+) $^m/_e$ = 255. (Found: C, 61.24; H, 8.29; N, 5.38;

S, 25.19. $C_{13}H_{21}NS_2$ requires C, 61.12; H, 8.29; N, 5.48; S, 25.10%.)

Treatment of (XXXV) with hydrogen sulphide.

Hydrogen sulphide gas was passed into a solution of 1,3-dithiolan-4-imine-2,5-bis(spiro-1'-cyclohexane) (60 mg.) in dioxan (0.3 ml.)/water (0.1 ml.) at 18° for 30 minutes, by which time the solution had changed from colourless to orange. Water was added, the product extractedwith chloroform, and the chloroform extracts dried. Chromatography (silica gel, benzene) gave 1,3-dithiolan-4-thione-2,5-bis(spiro-1'-cyclohexane) (26 mg.) (t.l.c. comparison and i.r.) and starting material (38 mg.).

Attempted preparation of (XXXIV) direct from cyclohexanone.

Attempts to prepare 1,3-dithiolan-4-thione-2,5-bis(spiro-1'-cyclohexane) direct from cyclohexanone, potassium cyanide and hydrogen sulphide gas, in dimethylformamide or methanol/water, with or without added morpholine were unsuccessful.

Treatment of (XXXIV) with tris(diethylamino)phosphine.

1,3-Dithiolan-4-thione-2,5-bis(spiro-1'-cyclohexane) (201 mg.) and tris(diethylamino)phosphine (603 mg.) were heated together under nitrogen at 190° for 2.1/4 hours. T.l.c. (silica gel, light petroleum or benzene) indicated that there was no reaction. Column chromatography gave no bis-cyclohexylidene.

2-Hydrazinopropionic acid.

This compound was prepared according to the method of Carmi, Pollak and Yellin,[12] with one modification, namely, ion exchange

was carried out on Amberlite IR 4B(OH) resin. Recrystallisation from water/ethanol gave colourless needles m.p. 184 - 184.5° (lit. 182°).

2-(Benzalhydrazino)propionic acid (XL).

2-Hydrazinopropionic acid (501 mg.), absolute ethanol (10 ml.) and benzaldehyde (526 mg.) were shaken together for 4.1/2 hours at 21°, after which time the alcohol was evaporated, diethyl ether added, and the solution dried. Evaporation of the solvent gave the hydrazone as a white solid, which crystallised from ethanol/ light petroleum as colourless needles, m.p. 102 - 105°, 69% theor. An analytical sample was prepared by further recrystallisation, m.p. 110 - 112°. ν_{max}(mull) 3220 m (NH), 2500 w (carboxylic OH), 1710 s and 1240 s (carboxylic acid) cm^{-1}; τ 8.5 (3H, d, J 8Hz); 5.75 (1H, q, J 8Hz), 2.7 - 2.2 (8H, m, 6H after D_2O exchange), (M^+) $^m/_e$ = 192. (Found: C, 62.22; H, 6.48; N, 14.31. $C_{10}H_{12}N_2O_2$ requires C, 62.48; H, 6.29; N, 14.58%).

Oxidative cyclisation of (XL) with lead tetra-acetate.

A solution of 2-(benzalhydrazino)propionic acid (102 mg.) in dichloromethane (5.0 ml.) was added dropwise over 45 minutes to a stirred suspension of lead tetra-acetate (0.40 g.) and calcium carbonate (0.50 g.) in dichloromethane (5.0 ml.), at 0° and under nitrogen. The solution was then allowed to warm to 19° over a period of 45 minutes. Water (10 ml.) was added, and the solids removed by filtration through a bed of Celite. The organic layer

was separated, worked up in the usual way, and dried. Evaporation of the solvent gave an unstable oil (45 mg.); ν_{max} (CCl_4) 1770 cm^{-1}, attributed to the required cyclised product. The product could not be crystallised and was unstable to chromatography.

2-(Cyclohexylidenehydrazino)propionic acid (XLII).

2-Hydrazinopropionic acid (201 mg.), absolute ethanol (5.0 ml.) and cyclohexanone (197 mg.) were shaken together for 14 hours at 20°. Evaporation of the solvent gave the hydrazone as a white solid which crystallised from ethanol/light petroleum as colourless needles, m.p. 119.5 - 120°, 74% theor; ν_{max} ($CHCl_3$) 3375 m (NH), 1710 s (carboxylic CO); τ 8.6 (3H, d, J 8Hz), 8.3 (6H, m), 7.8 (4H, m), 6.1 (1H, q, J 8Hz), 2.25 (2H, m, both D_2O exchangeable). (Found: C, 58.90; H, 8.72; N, 15.04. $C_9H_{16}N_2O_2$ requires C, 58.67; H, 8.75; N, 15.21%).

Attempted oxidative cyclisation of (XLII) with activated manganese dioxide.

Oxidation of 2-(cyclohexylidenehydrazino)propionic acid with activated manganese dioxide in dichloromethane at 21° gave several products. The required oxidatively cyclised product was not present, since the i.r. spectrum of the reaction product showed no absorption above 1710 cm^{-1}.

2-Bromo-2-methylpropionic acid.

Isobutyric acid (88.1 g.), phosphorus trichloride (2.0 ml.) and bromine (62 ml.) were heated together on a steam bath for 23 hours.

Distillation at reduced pressure gave one main fraction b.p. 139 - 143°/85 mm., 80% theor., which solidified. (lit.[13] b.p. 115°/24 mm.).

2-Hydrazino-2-methylpropionic acid.

This compound was prepared according to the method of Carmi, Pollak and Yellin,[12] with one modification, namely ion exchange was carried out on Amberlite 120 (H) resin. Recrystallisation from water/ethanol gave colourless clusters m.p. 226 - 227°, 224° after sublimation at 125°/10^{-4} mm. (lit. m.p. 238 - 240°).

2-Methyl-2-(4'-methylcyclohexylidenehydrazino)propionic acid (XLIII).

2-Hydrazino-2-methylpropionic acid (2.37 g.), absolute ethanol (50ml.) and 4-methylcyclohexanone (2.59 g.) were shaken together for 12 hours at 18°. The solid was removed by filtration, washed thoroughly with light petroleum and dried at 40° in vacuo to give the hydrazone as colourless needles m.p. 157 - 158°, 71% theor. An analytical sample was prepared by sublimation, m.p. 155-156°; ν_{max}(mull) 1610 s and 1370 s (ionised carboxyl group) cm^{-1}; τ 9.1 (3H, d, J 6Hz), 8.65 (6H, s), 8.5 - 7.0 (ca. 9H, m), 2.5 (2H, bs, both D_2O exchangeable). (Found: C, 62.17; H, 9.22; N, 13.00. $C_{11}H_{20}N_2O_2$ requires C, 62.23; H, 9.50; N, 13.20%).

Oxidative cyclisation of (XLIII) with lead tetra-acetate.

A solution of lead tetra-acetate (0.90 g.) in dichloromethane (10 ml.) was added dropwise over 10 minutes to a stirred solution of 2-methyl-2-(4'-methylcyclohexylidenehydrazino)propionic acid (423 mg.)

in dichloromethane (20 ml.), at -15° and under nitrogen. The solution was stirred for a further 5 minutes, after which hexylene glycol (1.0 ml.) was added. The solution was stirred for a further 2 minutes, after which saturated sodium bicarbonate solution (20 ml.) was added and the solution stirred at - 5° for 5 minutes. Any solid present was removed by filtration before the organic layer was separated, washed once with cold water, and dried at 0°. Evaporation of the solvent at 0° gave an unstable straw-coloured oil (349 mg.) which did not crystallise; $\nu_{max}(CHCl_3)$ 1740 s cm^{-1}, attributed to the required cyclised product.

Pyrolysis in diethylphthalate at 255°.

The straw-coloured oil (330 mg.) in diethylphthalate (2.5 ml.) was added dropwise over 5 minutes to stirred diethylphthalate (5.0 ml.) at 255° and under nitrogen. The escaping gases were condensed at -76°. T.l.c. examination of the pyrolysis residue and the condensed vapours showed no olefinic products.

Oxidative cyclisation of (XLIII) with diethylazodicarboxylate.

A solution of diethylazodicarboxylate[14] (344 mg.) in dichloromethane (10 ml.) was added to a stirred solution of 2-methyl-2-(4'-methylcyclohexylidenehydrazino)propionic acid in dichloromethane (20 ml.), at 0° and under nitrogen. The solution was stored at 0° for 17 hours, after which the solid was removed by filtration and the filtrate evaporated to yield a semi-solid (510 mg.); ν_{max}(film) 1735 s cm^{-1}.

2-Hydrazinocyclohexanecarboxylic acid.

2-Bromocyclohexanecarboxylic acid (3.70 g.), absolute ethanol (15 ml.) and a large excess of 98% hydrazine hydrate were heated together at reflux for 3 days, after which the solvent and excess hydrazine hydrate were evaporated and the residual viscous oil stored at 0° for one week. The solid was removed by filtration, washed with ethanol and dried, m.p. 205 - 208°. (Result of one experiment). Recrystallisation from aqueous ethanol gave colourless rods m.p. 208.5 - 209.5 (decomp.). An analytical sample was prepared by sublimation at 125°/10^{-3} mm., m.p. 205 - 206°; ν_{max}(mull) 1570 s (ionised carboxyl group) cm^{-1}. (Found: C, 53.06; H, 8.71; N, 17.63. $C_7H_{14}N_2O_2$ requires C, 53.14; H, 8.92; N, 17.71%).

2-(Benzalhydrazino)cyclohexanecarboxylic acid.

2-Hydrazinocyclohexanecarboxylic acid (159 mg.), absolute ethanol (5 ml.) and benzaldehyde (113 mg.) were shaken together for 2.1/4 hours at 23°. Any solid was removed by filtration and the solvent evaporated to give the hydrazone as a white solid, which crystallised from ethanol/light petroleum as long colourless needles m.p. 127 - 129°, 56% theor. An analytical sample was prepared by further recrystallisation m.p. 138 - 140°; $\nu_{max}(CHCl_3)$ 1710 s (carboxyl CO); τ 8.4 (6H, m), 8.0 (4H, m), 2.7 - 2.2 (8H, m, 6H after D_2O exchange); (M^+) $^m/_e$ = 246. (Found: C, 68.20; H, 7.18; N, 11.34. $C_{14}H_{18}N_2O_2$ requires C, 68.27; H, 7.37; N, 11.37%).

2-(Cyclohexylidenehydrazino)cyclohexanecarboxylic acid (XLV).

2-Hydrazinocyclohexanecarboxylic acid (207 mg.), absolute ethanol (7.5 ml.) and cyclohexanone (135 mg.) were shaken together for 18 hours at 22°, after which more ketone (29 mg.) was added, and the shaking continued for a further 3 hours. The solid was removed by filtration, thoroughly washed with light petroleum and dried. Recrystallisation from ethanol gave the hydrazone as long colourless needles m.p. 176° (sealed tube), 66% theor; ν_{max}(mull) 1600 s (ionised carboxyl group) cm^{-1}; τ 8.6 - 7.6 (20H, m), 2.6 (2H, bs, both D_2O exchangeable). (Found: C, 65.36; H, 9.05; N, 11.56. $C_{13}H_{22}N_2O_2$ requires C, 65.51; H, 9.31; N, 11.76%).

Oxidative cyclisation of (XLV) with lead tetra-acetate.

A suspension of 2-(cyclohexylidenehydrazino)cyclohexanecarboxylic acid (235 mg.) in dichloromethane (10 ml.) was added over 1 minute to a stirred suspension of lead tetra-acetate (0.68 g.) and calcium carbonate (1.0 g.) in dichloromethane (5 ml.), at -15° and under nitrogen. The reactants were stirred at this temperature for a further 5 minutes before being allowed to warm to 0° over 30 minutes. Saturated sodium bicarbonate solution (20 ml.) was added and the solids removed by filtration through a bed of Celite. The organic layer was separated, washed once with cold water and dried at 0°. Evaporation of the solvent at 0° gave an off-white solid (171 mg.), which was thermally unstable, but could be crystallised from diethyl ether/light petroleum at low temperature

as colourless plates, decomposing noticeably at 60°, solution being complete at 90°; $\nu_{max}(CCl_4)$ 2950 s, 2870 s, 2120 w (keten), 1750 s (lactone CO), 1595 w (N = N), 1450 m, 1140 m, 1100 m cm^{-1}. Pyrolysis at 100°.

The crystalline product (23 mg.) was pyrolysed at 100° under nitrogen for 30 minutes. The oily residue (11 mg.) was found to contain no bis-cyclohexylidene (t.l.c. comparison with authentic). Pyrolysis in refluxing toluene.

Crystalline product (16 mg.), dissolved in toluene (0.5 ml.), was added dropwise to refluxing toluene, under nitrogen. After 30 minutes the pyrolysis was stopped. The solution contained no bis-cyclohexylidene (t.l.c. comparison).

2-Bromo-2-ethylbutyric acid.

2-Ethylbutyric acid (116 g.), phosphorus trichloride (2.0 ml.) and bromine (62 ml.) were heated together on a steam bath for 21 hours. Distillation at reduced pressure gave one main fraction b.p. 133 - 137°/19 mm., 93% theor.

2-Hydrazino-2-ethylbutyric acid.

This compound was prepared according to the method of Carmi, Pollak and Yellin[12], with one modification, namely ion exchange was carried out on Amberlite 120 (H) resin. Recrystallisation from water/ethanol gave colourless rods m.p. 215° (sealed tube), 223 - 224° after sublimation (lit. 225°).

2-Ethyl-2-(4'-methylcyclohexylidenehydrazino)butyric acid (XLIV).

2-Hydrazino-2-ethylbutyric acid (4.39 g.), absolute ethanol (20 ml.) and 4-methylcyclohexanone (3.69 g.) were shaken together for 15 hours at 21°. The solvent was evaporated to give a viscous oil, which crystallised from light petroleum as colourless needles m.p. 80 - 82°, 87% theor. An analytical sample was prepared by further recrystallisation m.p. 82 - 82.5°; ν_{max}($CHCl_3$) 1725 s, (mull) 1600 s cm^{-1}. (Found: C, 65.14; H, 9.97; N, 11.58. $C_{13}H_{24}N_2O_2$ requires C, 64.97; H, 10.07; N, 11.66%).

Oxidative cyclisation of (XLIV) with lead tetra-acetate.

Oxidative cylisation of 2-ethyl-2-(4'-methylcyclohexylidene-hydrazino)butyric acid (492 mg.) with lead tetra-acetate (1.34 g.) at -15° (by the procedure described for the oxidation of the hydrazone (XLV), except that the hydrazone was added as a solution in dichloromethane) gave an unstable oil (395 mg.) which did not crystallise; ν_{max}(film) 1750 s, 1595 w cm^{-1}, attributed to the required cyclised product.

Pyrolysis in refluxing collidine.

The oil was added dropwise to refluxing collidine under nitrogen. After 15 minutes the solution was cooled and poured into cold dilute hydrochloric acid. The acid solution was extracted with diethyl ether, the organic layer worked up in the usual way, and dried. Evaporation of the solvent gave a straw-coloured oil. ν_{max}(film) 1740 m, 1715 s cm^{-1}.

2-Ethyl-2-(3'-cholestanylidenehydrazino)butyric acid (XLVII).

2-Hydrazino-2-ethylbutyric acid (0.587 g.), absolute ethanol (20 ml.) and cholestanone[15] (1.159 g.) were heated together at reflux under nitrogen for 6 hours. The solvent was evaporated, the residue dissolved in dichloromethane and the solution washed with water to remove any unreacted hydrazino acid before drying. Evaporation of the solvent gave the hydrazone as a foam, which crystallised from light petroleum as colourless conglomerates. The crystals were dried in vacuo at 40°, m.p. 122 - 125°, 76% theor. An analytical sample was prepared by further recrystallisation m.p. 128 - 131°; $[\alpha]_D$ + 31° ($CHCl_3$); ν_{max}($CHCl_3$) 1730 s (carboxyl CO), (mull) 1620 s (ionised carboxyl group) cm^{-1}; τ envelope (ca. 56H), ca. -3.1 (2H, broad, both D_2O exchangeable); (M^+) $^m/_e$ = 514. (Found: C, 76.81; H, 11.20; N, 5.21. $C_{33}H_{58}N_2O_2$, requires C, 76.99; H, 11.36; N, 5.44%).

5,5-Diethyl-Δ^3-1,3,4-oxadiazin-6-one-2-spiro(3'-cholestane) (XLVIII).

A solution of lead tetra-acetate (1.33 g.) dissolved in dichloromethane (15 ml.) was added dropwise over 10 minutes to the hydrazone (XLVII) (1.55 g.) in dichloromethane (80 ml.), at -18° and under nitrogen. The solution was stirred for a further 4 minutes at this temperature before cold saturated sodium bicarbonate solution (75 ml.) was added, and the mixture stirred at 0° for a few minutes. Any solid present was removed by filtration through a bed of Celite before the organic layer was separated, washed once

with cold water, and dried at 0°. Evaporation of the solvent at 0° gave a white solid (1.46 g.) which was stored at 0°. This solid was unstable to heat or chromatography and could not be purified by recrystallisation alone. Purification of the azo-lactone was achieved by gel-filtration (Sephadex LH20, tetrahydrofuran, u.v. monitoring), m.p. 88 - 91°, 64.3% theor. An analytical sample was prepared by slow evaporation of a chloroform/methanol solution, as colourless needles m.p. 95 - 96° (solution with evolution of gas), $[\alpha]_D$ + 14° (tetrahydrofuran); $\nu_{max}(CHCl_3)$ 1740 s (lactone CO), 1590 w (N = N) cm^{-1}; λ_{max} (tetrahydrofuran) 368 nm. (ε 130). (Found: C, 77.51; H, 10.93; N, 5.32. $C_{33}H_{56}N_2O_2$ requires C, 77.29; H, 11.00; N, 5.46 %).

Pyrolysis of (XLVIII).

5,5-Diethyl-Δ^3-1,3,4-oxadiazin-6-one-2-spiro(3'-cholestane) (31 mg.) was pyrolysed at 105 - 110° for 50 minutes. The volatile diethylketen was flushed from the pyrolysis vessel by a stream of nitrogen and trapped in chloroform at -76°. The chloroform solution showed ν_{max} 2100 s (keten) cm^{-1}. After adding absolute ethanol (3 drops) the chloroform solution showed ν_{max} 1720 (ester CO) cm^{-1}.

Ethyl-2-ethylbutyrate was prepared from 2-ethylbutyric acid, ethanol and sulphuric acid catalyst, and shown to be identical with the ester from the trapping experiment (i.r. and g.l.c.).

The pyrolysis residue (27 mg.) was essentially pure cholestanone (m.p., mixed m.p., i.r. and t.l.c. comparison). Preparative t.l.c.

and subsequent mass spectral examination of the other trace products did not show any of the required olefin, $^{m}/_{e}$ = 440. In a second pyrolysis experiment the azo-lactone (98 mg.) was pyrolysed at 115° for 8 minutes and the diethylketen trapped with an ethereal solution of cyclohexylamine. The amide precipitated as a white solid, which was collected and dried (29.5 mg.). Crystallisation from ethyl acetate gave long colourless needles m.p. 125.5 - 126.5° (sealed tube) and identical with an authentic sample of N-cyclohexyldiethylacetamide (m.p., mixed m.p., i.r. and t.l.c. comparison).

N-cyclohexyldiethylacetamide (LI).

A solution of 2-ethylbutyric acid (5.8 g.) in tetrahydrofuran (50 ml.), with triethylamine (5.1 g.) was cooled to 0° and a solution of ethylchloroformate (5.4 g.) in tetrahydrofuran (10 ml.) added with stirring. After stirring at 0° for 20 minutes a solution of cyclohexylamine (5.3 g.) in tetrahydrofuran (25 ml.) was added, and the stirring continued for 2 hours at 0°, then for 12 hours at 20°. The solid was removed by filtration and the solvent evaporated from the mother-liquor. The residue was dissolved in dichloromethane, worked up in the usual way, and dried. Evaporation of the solvent gave a white solid (8.4 g.), which was chromatographed (silica gel, ethyl acetate/benzene 1:3) to give the pure amide. An analytical sample was prepared by recrystallisation from ethyl acetate, as long colourless needles m.p. 126-126.5° (sealed tube), $\nu_{max}(CHCl_3)$ 3450 (NH) 1655 s and 1520 s (amide I and II bands) cm^{-1},

(M^+) $^m/_e$ = 197. (Found: C, 72.76; H, 11.84; N, 7.04. $C_{12}H_{23}NO$ required C, 73.04; H, 11.75; N, 7.10 %).

The pyrolysis residue (79 mg.) was once again shown to be cholestanone, with no trace of the expected olefin.

Photolysis of (XLVIII).

5,5-Diethyl-Δ^3-1,3,4-oxadiazin-6-one-2-spiro-(3'-cholestane) (48 mg.) was photolysed in cyclohexane (15 ml.) using a medium-pressure mercury arc lamp and pyrex apparatus at 19°. The photolysis was monitored by observing the disappearance of the u.v. absorption at 368 nm. and was complete in 90 minutes. The extrusion of carbon dioxide during the photolysis was illustrated by passing a slow stream of nitrogen through the apparatus and into lime-water; the precipitate was readily discernible. Evaporation of the solvent gave a solid (45 mg.) which crystallised from chloroform/ethylacetate as colourless conglomerates (43 mg.) m.p. 210 - 212°, and was identified as the unsymmetrical azine derived from cholestanone and 3-pentanone (XLIX), $[\alpha]_D$ + 58° ($CHCl_3$) ; ν_{max} ($CHCl_3$) 1635 s cm^{-1}. (A mixed m.p. with cholestanoneazine m.p. 208 - 209° gave a depression of 13°). (Mass measurement on the molecular ion = 468.44238. Mass calculated for $C_{32}H_{56}N_2$ = 468.44433). The absence of ions above the molecular ion confirmed that no symmetrical cholestanoneazine was present.

Cyclohexanoneazine.

A solution of 98% hydrazine hydrate (6.2 g.) in ethanol (15 ml.) was added dropwise over 20 minutes to a solution of cyclohexanone

(25.0 g.) in ethanol (60 ml.) at reflux. The heating was continued for 3 hours, after which the solution allowed to stand at 17° for 16 hours. The solvent was evaporated, the residue poured into water (150 ml.), the azine extracted with diethyl ether, and the organic layer dried. Evaporation of the solvent gave an oil, which crystallised from light petroleum as an off-white solid, m.p. 32 - 32.5°, 74 % theor., (lit.[13] m.p. 33°).

1,3,4-Thiadiazolidin-2,5-bis(spiro-1'-cyclohexane)(LII).

a) From cyclohexanone.

At first this compound was prepared from cyclohexanone, hydrazine hydrate and hydrogen sulphide gas, according to the method of Rühlmann,[16] m.p. 98° when pure.

b) From cyclohexanoneazine (cyclohexanone as solvent).

Hydrogen sulphide gas was passed into a solution of cyclohexanone-azine (4.0 g.) dissolved in cyclohexanone (5.0 g.) for 3 hours, by which time i.r. monitoring of the azine absorption at 1640 cm^{-1} showed the reaction to be complete. Cold water (200 ml.) was added, the solid collected by filtration, dried, and shown to be identical with the authentic thiadiazolidine (i.r., n.m.r. and t.l.c. comparison), m.p. 89 - 90°, 74% theor.

c) From cyclohexanoneazine (4-methylcyclohexanone as solvent).

The last experiment was repeated substituting 4-methylcyclohex-anone as solvent. No incorporation was observed, as shown by an n.m.r. study of the final thiadiazolidine.

d) From cyclohexanoneazine (acetone/benzene as solvent, and using an atmospheric pressure hydrogen sulphide apparatus).

A hydrogenation apparatus, with facilities for shaking, was converted for use with hydrogen sulphide gas. A solution of cyclohexanoneazine (2.51 g.) in acetone/benzene 1:1 by volume (9.1 g.) absorbed 537 ml. of gas at 17°/767 mm. in 170 minutes, compared with 170 ml. of gas for a'solvent only'experiment. Evaporation of the solvent gave the thiadiazolidine as a white solid m.p. 91 - 93°, 100% theor.

Δ^3-1,3,4-Thiadiazolin-2,5-bis(spiro-1'-cyclohexane) (LIII).

a) By lead tetra-acetate oxidation of (LII).

Powdered calcium carbonate (6.0 g.) was suspended in light petroleum (b.p. 60 - 80°) and lead tetra-acetate (6.0 g.) added. The suspension was stirred at 0° for 15 minutes and a solution of the thiadiazolidine (LII) (2.0 g.) in light petroleum (b.p. 60 - 80°) (100 ml.) added dropwise over 45 minutes, maintaining the temperature at 0°. The reactants were allowed to warm to 18° and stirred for a further 1.1/2 hours before saturated sodium bicarbonate solution (80 ml.) was added, and the mixture stirred for 20 minutes. The solids were removed by filtration through a bed of Celite, the organic layer separated, worked up in the usual way, and dried. Evaporation of the solvent at < 45° gave the thiadiazoline as an off-white solid m.p. 65 - 70°, 99% theor. An analytical sample was prepared by recrystallisation from light petroleum, m.p. 80 - 81°

(sealed tube); ν_{max}(KBr) 1575 m (N = N) cm^{-1}; λ_{max} (EtOH) 325 and 286 nm. (ε 225 and 330 respectively.) (Found: C, 64.09; H, 8.79; N, 12.60; S, 14.54. $C_{12}H_{20}N_2S$ requires C, 64.22; H, 8.99; N, 12.49; S, 14.30%).

b) By D.D.Q. Oxidation of (LII).

A solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.30 g.) in diethyl ether (75 ml.) was added dropwise over 35 minutes to a stirred solution of the thiadiazolidine (LII) (0.25 g.) in diethyl ether (10 ml.) at 0°. After 30 minutes the solution was allowed to warm to 17° and stirred for a further 30 minutes. The product was washed several times with saturated sodium bisulphite solution, then with saturated sodium bicarbonate solution, and finally with water, before drying. Evaporation of the solvent gave the thiadiazoline as an off-white solid m.p. 76 - 79.5°, 91% theor.

Bis-cyclohexylidene.

a) Using Triphenylphosphine.

The thiadiazoline (LIII) (1.225 g.) and triphenylphosphine (1.577 g.) were heated together on a steam bath for 2 hours. The product was chromatographed (alumina, light petroleum b.p. 60 - 80°) to give bis-cyclohexylidene as a white solid m.p. 53 - 54°, 75% theor. (lit.[13] 53 - 54°); τ 8.7 - 8.4 (12H, m), 8.0 - 7.7 (8H, m); (M^+) $^m/_e$ = 164.

b) Using Tris(diethylamino)phosphine.

Similarly, tris(diethylamino)phosphine gave bis-cyclohexylidene

as a white solid m.p. 53.5 - 54.5°, 77% theor.

Bis-cyclohexylidene from cyclohexanoneazine, without purification of the intermediates.

Bis-cyclohexylidene was obtained in an overall yield of 73% theor. from cyclohexanoneazine when the reaction sequence was repeated without purification of the intermediates.

Photolysis of (LIII).

The thiadiazoline (354 mg.) was photolysed in cyclohexane (60 ml.) using a medium-pressure mercury arc lamp and pyrex apparatus, under an atmosphere of nitrogen at 19°. The photolysis was monitored by t.l.c. and found to be complete in 24 hours, after which time a deposit of elemental sulphur was present inside the photolysis vessel. The solvent was evaporated and the residue chromatographed (alumina, benzene). The major product was cyclohexanoneazine, 52% theor. (t.l.c. and i.r. comparison with authentic). The non-polar material contained some thiiran (t.l.c. and i.r. comparison of isolated material with authentic), but no bis-cyclohexylidene.

2-Methylcyclohexanoneazine.

A solution of 2-methylcyclohexanone (15.3 g.) in n-butanol (35 ml.) was heated at reflux and 98% hydrazine hydrate (3.4 g.) added dropwise over 15 minutes. The heating was continued for 20 hours, after which the solution was allowed to stand at 21° for 24 hours. The solvent was evaporated, and the residue poured

into water. The azine was extracted with diethyl ether, and the organic layer dried. Evaporation of the solvent and distillation of the residue at reduced pressure gave one main fraction b.p. 128 - 130°/0.5 mm., 52 % theor., which solidified; ν_{max}(film) 1640 s cm^{-1}; τ 8.7 - 7.1 (18H, m), 8.8 (6H, d); (M^+) $^m/_e$ = 220.

Attempted 1,3,4-thiadiazolidin-2,5-bis[spiro-1'-(2'-methylcyclohexane)] (LV).

Hydrogen sulphide was bubbled through a solution of 2-methylcyclohexanoneazine (0.5 g.) in acetone/benzene 1:1 by volume (1.5 g.) at 20° for 3 hours, replacing the evaporated solvent as necessary. None of the required thiadiazolidine was formed under these conditions (i.r. monitoring).

Benzalazine.

A solution of benzaldehyde (54.0 g.) in ethanol (120 ml.) was heated at reflux and a solution of 98% hydrazine hydrate (12.5 g.) in ethanol (30 ml.) added dropwise over 20 minutes. The heating was continued for 3 hours, after which the solution was allowed to cool. Benzalazine crystallised as long colourless needles, which were collected and dried m.p. 95°, 75 % theor. (lit.[13] m.p. 93°).

Attempted 2,5-diphenyl-1,3,4-thiadiazolidine (LVI).

Attempts to add hydrogen sulphide to benzalazine using acetone as solvent, at temperatures of 15 , 0 , -20 , -35 and -75° were unsuccessful. No trace of the required thiadiazolidine was observed. Starting material was recovered from each experiment.

The stability of Δ^3-1,3,4-thiadiazolin-2,5-bis(spiro-1'-cyclohexane) (LIII) to hydrogen sulphide.

Hydrogen sulphide was bubbled through a solution of the thiadiazoline (0.5 g.) in benzene (6 ml.) at 21° for 2 hours. Monitoring by i.r. showed that there was no reaction.

Attempted oxidation of 1,3,4-thiadiazolidin-2,5-bis(spiro-1'-cyclohexane) (LII) with milder oxidising agents.

a) Flowers of sulphur.

Thiadiazolidine (0.73 g.), flowers of sulphur (2.70 g.), collidine (1.0 ml.) and benzene (15 ml.) were stirred together at 20° for 66 hours. Monitoring by t.l.c. (silica gel, benzene/ethyl acetate 1:1) showed that there was no reaction. Increasing the reaction temperature led to thermal decomposition of the thiadiazolidine.

b) Oxygen.

Oxygen was bubbled through a solution of the thiadiazolidine (0.5 g.) in cyclohexane (20 ml.) at 19° for 2 hours. Monitoring by t.l.c. and i.r. showed that a small amount of thiadiazoline was being formed, but that the major product was cyclohexanoneazine.

c) Diphenyldisulphide.

The thiadiazolidine was not oxidised to the required thiadiazoline by diphenyldisulphide under a variety of conditions.

Attempted 3-acetyl-2,5-diphenyl-1,3,4-thiadiazolidine (LXIII).

A solution of benzalazine (1.0 g.), acetic anhydride (3.0 g.)

and acetone (4.0 g.) was left to stand at 20° for 18 hours. Evaporation to dryness gave unreacted benzalazine.

Hydrogen sulphide was bubbled through a solution of benzalazine (2.0 g.) in acetic anhydride (6.0 g.) and acetone (8.0 g.) at 20° for 6.1/2 hours. Evaporation of the acetone and acetic anhydride gave an oil, which partially solidified when stored at 0°. The solid was collected (0.5 g.). Crystallisation from benzene gave colourless needles m.p. 124° (decomp.). T.l.c. indicated that the solid was a single non-sulphur containing product (undeveloped by palladium chloride spray). The absence of sulphur was confirmed by a negative Lassaigne test. The solid was not investigated further. T.l.c. indicated that the mother liquor contained several products, none of which were developed by palladium chloride spray.

An attempt at preparing a suitably 3-substituted thiadiazolidine by passing hydrogen sulphide gas into a solution of benzalazine (0.5 g.) in methylal (5.0 g.) in the presence of boron trifluoride etherate (0.2 g.) at 0° gave a mixture which did not afford any useful product.

p-Methoxybenzylhydrazine.

This compound was prepared according to the method of Biel[17] from p-methoxybenzylchloride[18] and hydrazine hydrate. Distillation at reduced pressure gave one main fraction b.p. 128 - 129°/2.8 mm. which solidified (lit. b.p. 106°/0.45 mm.).

Attempted preparation of 3-substituted-1,3,4-thiadiazolidines from p-methoxybenzylhydrazine.

a) Butyraldehyde (0.72 g.), ethanol (10 ml.) and glacial acetic acid (2 drops) were heated together at reflux under nitrogen. After 1 hour p-methoxybenzylhydrazine (0.75 g.) was added. After 3 hours anhydrous sodium sulphide (0.8 g.) was added. The heating was continued for a further 18 hours. Monitoring by t.l.c. (silica gel, benzene/ethyl acetate 5:1) indicated the formation of one major product, which was isolated by preparative t.l.c. Lassaigne test S -ve; (M^+) $^m/_e$ = 260. This product was not investigated further.

b) Under identical conditions, or in the presence of collidine, only one equivalent of cyclohexanone added to p-methoxybenzylhydrazine, and no sulphur-containing products were observed.

c) Hydrogen sulphide was bubbled through a solution of p-methoxybenzylhydrazine (1.53 g.) and cyclohexanone (1.96 g.) in triethylamine (10 ml.)/benzene (25 ml.) at 20° for 7 hours. The solvents were evaporated and the residue examined. T.l.c. (silica gel, benzene) indicated one non-polar sulphur-containing product (developed by palladium chloride spray), which was isolated by column chromatography. Crystallisation from ethanol gave 1,2,4-trithiolan-3,5-bis(spiro-1'-cyclohexane) (XVII) as colourless conglomerates m.p. 50 - 52°, ca. 25% theor., and identical with an authentic sample (mixed m.p., t.l.c. and i.r. comparison).

d) The required thiadiazolidine was not formed when p-methoxybenzylhydrazine, cyclohexanone, potassium hydrogen sulphide and triethylamine were stirred together at 20°. A small amount of 1,2,4-trithiolan-3,5-bis(spiro-1'-cyclohexane) was indicated by t.l.c. (silica gel, benzene).

Attempted direct 1,4-addition of sulphur across azines.

a) Flowers of sulphur.

Cyclohexanoneazine (0.80 g.), flowers of sulphur (0.40 g.), pyridine (0.5 ml.) and benzene (15 ml.) were heated together at reflux under an atmosphere of nitrogen for 44 hours. Monitoring by t.l.c. (silica gel, benzene or benzene/ethyl acetate 1:1) indicated that several products were slowly being formed, none of which corresponded to the required thiadiazoline, thiiran, or olefin.

b) Atomic sulphur.

Attempts to add atomic sulphur (generated in situ from hydrogen sulphide and sulphur dioxide) to cyclohexanoneazine or benzalazine gave none of the required products.

1,1'-Azo-bis(1-chlorocyclohexane) (LXVII).

This compound was prepared by low temperature chlorination of cyclohexanoneazine according to the procedure of Malament and Mcbride[19] and did not require further purification.

1,1'-Azo-bis(1-cyclohexanenitrile) (LXVIII).

The dichloroazoalkane (LXVII) (1.3 g.) was added portionwise over 45 minutes to a vigorously stirred solution of sodium cyanide

(0.8 g.) in water (4.0 ml.), acetone (8.0 ml.) and methanol (8.0 ml.) at 21°. The solution was stirred for a further 2 hours before water (100 ml.) was added and the precipitate collected and dried, m.p. 110 - 113°, 67% theor. Crystallisation from ethanol gave the dinitrile as colourless plates m.p. 112 - 114° (decomp.), (lit.[20] 113.5 - 115.5°).

Attempted preparation of Δ^3-1,3,4-thiadiazolin-2,5-bis(spiro-1'-cyclohexane) from (LXVII) and sodium sulphide.

The dichloroazoalkane (1.3 g.) was added portionwise over 30 minutes to a vigorously stirred solution of sodium sulphide hydrate (5.1 g.) in water (4.0 ml.), acetone (8.0 ml.) and methanol (8.0 ml.). The colour change indicated a fast reaction and consequently the solution was only stirred for a further 30 minutes before water (100 ml.) was added. There was no precipitate, consequently the solution was saturated with sodium chloride and extracted with diethyl ether. The organic layer was dried, and evaporation of the solvent gave a golden oil (1.1 g.). T.l.c. (silica gel, benzene or benzene ethyl acetate 1:1) and i.r. showed that the oil was a mixture of cyclohexanoneazine and cyclohexanone. There was no trace of the required thiadiazoline or of any starting material. A variety of solvent systems were tried, and the results have been summarized (Table 1).

In the final experiment on this table t.l.c. (alumina, light petroleum) indicated the formation of the required thiiran (LIV).

Chromatography gave essentially pure thiiran ca. 10% theor., which was identical with an authentic sample (comparative t.l.c. and i.r.).

TABLE 1.

Sodium Sulphide	Solvent System (V/V)	°C	Major Products
anhydrous	water, acetone, methanol (1/2/2)	21	azine, ketone
anhydrous	water, acetone, methanol, triethylamine (1/2/2/2)	20	azine, ketone
anhydrous	water, acetone, methanol, collidine (1/2/2/2)	19	ketone
anhydrous	water, acetone, collidine (1/2/2)	19	ketone
anhydrous	glyme	18	azine, starting material
hydrate	water, glyme (1/1)	18	azine, ketone
hydrate	water, dimethylformamide (1/4)	22	azine
anhydrous	water, collidine (1/4)	19	several products
anhydrous	collidine	55	starting material
hydrate	collidine	95	thiiran (ca. 10%)

The stability of Δ^3-1,3,4-thiadiazolin-2,5-bis(spiro-1'-cyclohexane) (LIII) to sodium sulphide.

A solution of sodium sulphide hydrate (2.4 g.) in water (5 ml.) was added to a solution of the thiadiazoline (238 mg.) in

dimethylformamide. A further quantity of dimethylformamide (10 ml.) was added, and the solution allowed to stand at 20° for 1 hour. Water (40 ml.) was added, the solution extracted with diethyl ether, and the organic layer dried. Evaporation of the solvent gave unreacted thiadiazoline (235 mg.)

Attempted preparation of Δ^3-1,3,4-thiadiazolin-2,5-bis(spiro-1'-cyclohexane) from (LXVII) and a) hydrogen sulphide or b) potassium hydrogen sulphide.

a) Hydrogen sulphide.

Hydrogen sulphide gas was passed into solutions of the dichloroazoalkane in triethylamine or triethylamine/acetone at 19° for several hours. No reaction was observed in either experiment.

b) Potassium hydrogen sulphide.

Dichloroazoalkane (1.0 g.), potassium hydrogen sulphide (6 g.) and collidine (20 ml.) were stirred together at 30° for 24 hours. Monitoring by t.l.c. (silica gel, benzene) showed no trace of the required thiadiazoline, thiiran , or olefin.

Attempted preparation of Δ^3-1,3,4-thiadiazolin-2,5-bis(spiro-1'-cyclohexane) via 1,1'-dibromoazoalkanes.

Attempts to isolate the 1,1'-dibromoazoaklane (LXX) from the bromination of cyclohexanoneazine with bromine or dioxandibromide gave unstable, moisture-sensitive oils.

A solution of anhydrous dioxandibromide[21] (2.50 g.) in dioxan (30 ml.) was added dropwise over 30 minutes to a solution of

cyclohexanoneazine (1.99 g.) in dioxan (15 ml.) at 10°, with stirring. When the addition was complete anhydrous sodium sulphide (2.7 g.) was added and the mixture stirred at 19° for 24 hours. The reaction was monitored by removing samples, working up with water, and examining the diethyl ether extracts by t.l.c. and i.r. There was no trace of the three required products.

The reaction between disulphur dichloride and cyclohexanoneazine.

A solution of disulphurdichloride (1 equivalent) in dichloromethane was added dropwise to a well-stirred solution of cyclohexanoneazine at various temperatures. Intractable gums were obtained in each experiment.

The reaction between 2,4-dinitrobenzenesulphenylchloride and cyclohexanoneazine.

A solution of 2,4-dinitrobenzenesulphenylchloride (1.18 g.) in dimethylformamide (20 ml.) was added dropwise over 2 minutes to a stirred solution of cyclohexanoneazine (0.96 g.) in dimethylformamide (5 ml.) at 0°. The solution was allowed to stand at 0° for 3 days. The reaction was monitored by removing samples, working up with water, and examining the diethyl ether extracts by t.l.c. and i.r. Several products were formed including 2,4-dinitrobenzenedisulphide. Starting azine was present, even after 3 days.

Treatment of acetophenoneazine with potassium thiocyanate.

Acetophenoneazine (476 mg.), potassium thiocyanate (325 mg.), trimethylamine hydrochloride (487 mg.) and tetrahydrofuran (10 ml.) were stirred together at 20° for 3 days. Monitoring by t.l.c. indicated that there was no reaction. Work up with water and extraction with diethyl ether gave acetophenoneazine.

Treatment of cyclohexanoneazine with potassium selenocyanate.

Cyclohexanoneazine (978 mg.), potassium selenocyanate (730 mg.) trimethylamine hydrochloride (1.0 g.) and methanol (20 ml.) were stirred together at 19° for 18 hours. Monitoring by t.l.c. indicated that there was no reaction. The solution was heated at reflux under an atmosphere of nitrogen for 4 hours. T.l.c. indicated that there was no reaction, and work up with water gave cyclohexanoneazine.

Treatment of cyclohexanoneazine with sodium in tetrahydrofuran†

Clean pieces of sodium (0.275 g.) were added to a solution of cyclohexanoneazine in tetrahydrofuran (50 ml.), and the mixture stirred vigorously at 20° for 2 hours. There was no colour change and the sodium did not dissolve. Consequently, the mixture was heated at reflux for 1 hour, but there was still no reaction.

Treatment of cyclohexanoneazine with lithium-ethylamine, and quenching of the dianion with a) water b) methyliodide c) an alkylthioamine.†

Anhydrous ethylamine (ca. 25 ml.) was distilled from potassium

(† all operations carried out under dry argon).

hydroxide pellets into a dry flask. Freshly cut pieces of lithium (ca. 0.40 g.) were added, and the mixture stirred vigorously. After 1 hour the lithium had dissolved and the solution was dark blue. This lithium-ethylamine complex was added dropwise to freshly distilled ethylamine at -76°. There was no decolouration.

Formation of the dianion.

The lithium-ethylamine complex was prepared as described above and added dropwise to a solution of dry cyclohexanoneazine (1.011 g.) in freshly distilled ethylamine (ca. 25 ml.) at -76°. Each drop was rapidly decolourised, but after approximately two equivalents had been added the decolouration suddenly became very slow. The addition was halted at this stage, and in successive experiments the dianion was quenched with water, methyl iodide and an alkylthioamine:

a) Water.

Water (3 ml.) was added dropwise at -76° and the product allowed to warm to 20°. The ethylamine was allowed to evaporate. The residue was extracted with diethyl ether and the organic layer dried. Evaporation of the solvent gave essentially pure cyclohexanoneazine, 100% theor. (comparative t.l.c. and i.r.)

b) Methyl Iodide.

Excess methyl iodide was added dropwise at -76° and the product allowed to warm to 19°. The ethylamine was allowed to evaporate. Water (20 ml.) was added to the residue and the product extracted with diethyl ether. The organic layer was washed once with water and dried. Evaporation of the solvent gave an oil

which was shown to be predominantly 2-methylcyclohexanoneazine (t.l.c., i.r., n.m.r., and m.s. comparison with authentic). A high resolution u.v. spectrum did not indicate the presence of any material containing the (-N=N-) chromophore.

c) N,N'-Thiobisdiethylamine.[22]

Alkylthioamine (1.2 g.) was added dropwise at -76° and the product allowed to warm to 20°. The ethylamine was allowed to evaporate. Water (20 ml.) was added to the residue and the product extracted with diethyl ether. The organic layer was washed once with water and dried. Evaporation of the solvent gave an oil containing mainly cyclohexanoneazine. A high resolution u.v. spectrum did not indicate the presence of any material containing the (-N=N-)chromophore.

Treatment of cyclohexanoneazine with lithium-naphthalene reagent.[4]

Clean pieces of lithium (0.36 g.) were added to a solution of dry naphthalene (6.62 g.) in tetrahydrofuran (50 ml.) and the mixture stirred vigorously. After 3.1/2 hours all of the lithium had dissolved. This reagent was added dropwise to a stirred solution of cyclohexanoneazine (1.41 g.) in tetrahydrofuran (20 ml.) at -19° until there was a permanent green colouration. Methyl iodide (2 ml.) was added and the product allowed to warm to 19°. The solvent was evaporated and water (20 ml.) added. The product was extracted with diethyl ether and the organic layer dried. Evaporation of the solvent gave an oil which partially crystallised. T.l.c. indicated two major components, which were separated by chromatography.

The first was identified as naphthalene (comparative t.l.c. and i.r.) The second was in fact a mixture of cyclohexanoneazine and 2-methylated cyclohexanoneazines (comparative n.m.r. and m.s.). Several minor components were present.

3-pentanonehydrazone.

3-Pentanone (10.0 g.) was added dropwise over 15 minutes to 49% hydrazine hydrate (160 ml.), with stirring at 19°. After a further 15 minutes the solution was saturated with sodium chloride and extracted with diethyl ether. The organic layer was washed once with water and dried. Evaporation of the solvent gave the hydrazone as a colourless liquid (10.4 g.); ν_{max}(film) 3450 s, 3300 s, 1640 broad, 840, 800, 740 cm^{-1}; τ 9.0 (6H, t, J 7Hz), 7.9 (4H, q, J 7Hz), 5.0 (2H, bs, both D_2O exchangeable).

The formation of Δ^3-1,3,4-thiadiazolines from hydrazones via substituted diazomethanes and thiocarbonyl compounds.

a) Attempted oxidation by iodine, and displacement of the intermediate iodide with sodium sulphide.

Iodine was rapidly decolourised when added dropwise to a vigorously stirred mixture of sodium sulphide in tetrahydrofuran/triethylamine at -18°. The reaction was repeated in the presence of 3-pentanonehydrazone (2.0 g.). Iodine (1.5 equivalents) was added dropwise over 2 hours, and the mixture stirred at -18° for a further 2 hours. The solvent was evaporated and the residue extracted

with diethyl ether. Evaporation of the solvent gave slightly impure 3-pentanoneazine (2.2 g.) (i.r. comparison with authentic sample).

b) Attempted oxidation with sulphur.

3-Pentanonehydrazone (2.0 g.), benzene (20 ml.), triethylamine (5 ml.) and flowers of sulphur (2.0 g.) were stirred together at 21° for 24 hours. Monitoring by t.l.c. did not indicate the formation of any sulphur containing products. Evaporation of the solvent gave a mixture of 3-pentanonehydrazone, 3-pentanoneazine, and sulphur.

c) Attempted reaction of diphenyldiazomethane with β-phenylethylthionbenzoate.

Benzophenonehydrazone was prepared according to the method of Barton[23] and oxidised to diphenyldiazomethane with mercuric oxide.[24]

A solution of diphenyldiazomethane (97 mg.) in diethyl ether (3 ml.) was added to a stirred solution of the thione-ester (117 mg.) in dry diethyl ether (3 ml.) at 24° in the dark. The solution became colourless after several days. Evaporation of the solvent gave an oil which contained a large proportion of unreacted thione-ester (t.l.c. and i.r. comparison). Preparative t.l.c. (silica gel, benzene) gave β-phenylethylthionbenzoate (101 mg.).

<u>The preparation of diazoalkanes.</u>

The Reaction of Benzophenonehydrazone with:

a) Cookson's Reagent.

A solution of 4-phenyl-1,2,4-triazoline-3,5-dione (0.85 g.) in benzene (40 ml.) was added dropwise over 45 minutes to a stirred solution of benzophenonehydrazone (1.12 g.) in benzene (20 ml.) at 0°. The reagent was immediately decolourised on addition indicating that diphenyldiazomethane was not being formed. The solvent was evaporated, diethyl ether (25 ml.) added, and the solid collected and dried (0.74 g.). The i.r. spectrum of this solid was identical with a standard spectrum of 4-phenyl-1,2,4-triazolidine-3,5-dione. The filtrate was evaporated to give a solid which crystallised from ethyl alcohol as long colourless needles m.p. 164 - 165°, identical with an authentic sample of benzophenoneazine (m.p., mixed m.p., and i.r. comparison).

The reaction was repeated in the presence of triethylamine (10 ml.), but no diphenyldiazomethane was formed.

b) Dibenzoyl peroxide.

A solution of recrystallised dibenzoylperoxide in chloroform was added dropwise over 30 minutes to a stirred solution of benzophenonehydrazone in chloroform, at 20°. No colouration was observed. Collidine (2 ml.) was added after 5 minutes and the addition continued, but no colouration occurred. After 24 hours t.l.c. (silica gel, benzene/ethylacetate 1:1) indicated that the benzophenonehydrazone had not reacted.

c) Picryl azide.

A solution of picrylazide (66 mg.) in benzene (3 ml.) was added dropwise over 18 minutes to a stirred solution of benzophenonehydrazone (52 mg.) in benzene (5 ml.) at 18°. The solution was stirred for a further 15 minutes. There was no colour change. After 24 hours t.l.c. (silica gel, benzene)indicated the formation of one major product, which was isolated by preparative t.l.c. (85 mg.). Crystallisation from ethanol gave long orange needles m.p. 198 - 199.5°, identical with an authentic sample of benzophenone-2,4-6-trinitrophenylhydrazone (m.p., mixed m.p., comparative t.l.c. and i.r.).

Benzophenone-2,4,6-trinitrophenylhydrazone (LXXX).

A solution of picrylchloride (122 mg.) and benzophenonehydrazone (98 mg.) in triethylamine (1 ml.) and ethanol (5 ml.) was heated at reflux for 1 hour. The product was poured into water (50 ml.), the solid collected, and recrystallised from ethanol to give long orange needles m.p. 198.5 - 199.5°; ν_{max} ($CHCl_3$) 3250 w, 1620 s, 1595 m, 1555 m, 1340 s, 1300 m, cm^{-1} (Found: C, 56.09; H, 3.27; N, 17.39. $C_{19}H_{13}N_5O_6$ requires C, 56.02; H, 3.22; N, 17.19%).

d) Lead tetra-acetate in triethylamine.

A solution of lead tetra-acetate (889 mg.) in dichloromethane (5 ml.) was added dropwise over 45 minutes to a stirred solution of benzophenonehydrazone (295 mg.) in dichloromethane (4 ml.) and triethylamine (5 ml.), at -20°. The immediate appearance of a

crimson colour indicated the formation of diphenyldiazomethane. The solution was allowed to warm to 20°, the solid removed by filtration, and the organic layer washed with water and dried. Evaporation of the solvent gave diphenyldiazomethane as a crimson solid, 100% theor., and identical with a sample prepared by mercuric oxide oxidation (comparison of i.r. spectra).

Cyclohexanoneazine/sulphur dioxide autoclave experiments.

A series of experiments was conducted in which liquid sulphur dioxide (15 - 20 ml.) was injected into an autoclave containing cyclohexanoneazine (19.2 g.) at -70°, under an atmosphere of nitrogen. The autoclave was sealed and heated at various temperatures. The effect of adding pyrogallol or triethylamine was also investigated.

The tars were extracted with diethyl ether and the extracts examined using column chromatography and preparative t.l.c. In no case was bis-cyclohexylidene, the episulphone (LXXXII) or the azo-sulphone (LXXXI) observed.

In one experiment, where pyrogallol (0.4 g.) had been added, the autoclave heated to 140° over 2.1/2 hours (20 atmospheres) and then allowed to cool, almost pure 1,2,3,4,5,6,7,8-octahydrodibenzothiophene m.p. ca. 26° (0.62 g.) was isolated; Lassaigne test S +ve, N -ve; ν_{max}(film) 1300 w, 1240 w, 1115 m, 1030 m, 760 m, 740 m cm^{-1}; λ_{max} (EtOH) 241 nm. (ε 6,700); (M^+) $m/_e$ = 192, (M + 1) and (M + 2) confirmed $C_{12}H_{16}S$. (lit.[25] m.p. 31°, λ_{max}(EtOH) 243 mm. (ε 6,900).

Treatment of 3-pentanonehydrazone with sulphoxylic acid.

3-Pentanonehydrazone (3.0 g.) was added dropwise to a stirred solution of sulphoxylic acid [prepared according to the method of Goehring[26] by acid hydrolysis of N,N'-thiobisdiethylamine (5.7 g.)] at 0°. After 15 minutes the solution was extracted with diethyl ether, the organic layer worked up in the usual way and dried. Careful evaporation of the solvent gave 3-pentanone (i.r. comparison).

Treatment of 3-pentanonehydrazone with sodium sulphoxylate.

Addition of sodium sulphoxylate(prepared by base hydrolysis of monosulphurdichloride[27]) to 3-pentanonehydrazone under a variety of conditions gave 3-pentanone and/or 3-pentanoneazine.

Δ^3-1,3,4-Thiadiazolin-1-oxide-2,5-bis(spiro-1'-cyclohexane) (LXXXIV).

Δ^3-1,3,4-Thiadiazolin-2,5-bis(spiro-1'-cyclohexane) (9.60 g.), glacial acetic acid (75 ml.), dichloromethane (40 ml.) and 100 volume hydrogen peroxide (10.0 ml.) were stirred together at 20° for 20 hours, by which time t.l.c. monitoring (alumina, benzene/acetone 50:1) indicated that the reaction was complete. The organic layer was separated, worked up in the usual way, and dried. Evaporation of the solvent gave essentially pure azo-sulphoxide as a white solid m.p. 144 - 145°, 96% theor., which crystallised from diethyl ether as long colourless needles m.p. 146 - 147° (decomp.), 94% theor.; ν_{max}(nujol) 1570 m, 1040 s cm^{-1}. (Found: C, 59.96; H, 8.38; N, 11.70; S, 13.14. $C_{12}H_{20}N_2OS$ requires C, 59.96; H, 8.39; N, 11.66; S, 13.34%).

Pyrolysis of the azo-sulphoxide (LXXXIV).

a) In the absence of tervalent phosphine.

Azo-sulphoxide (490 mg.) was pyrolysed at 160° under an atmosphere of nitrogen. Initially the solid melted and turned green, whereupon a vigorous evolution of gas occurred. The pyrolysis was stopped after 34 minutes and the residue chromatographed (silica gel, light petroleum). Olefinic material (42 mg.) containing some bis-cyclohexylidene (t.l.c., i.r. and n.m.r. comparison with authentic sample) was isolated.

b) In the presence of triphenylphosphine.

Azo-sulphoxide (480 mg.) and triphenylphosphine (614 mg.) were heated together at 140° under an atmosphere of nitrogen for 30 minutes, after which the product was chromatographed. Essentially pure bis-cyclohexylidene was isolated, ca. 11% theor.

Photolysis of the azo-sulphoxide (LXXXIV).

Azo-sulphoxide (321 mg.) was photolysed in cyclohexane (80 ml.) using a medium-pressure mercury arc lamp and pyrex apparatus, under an atmosphere of nitrogen at 19°. The photolysis was monitored by t.l.c. (alumina, benzene) and was found to be complete in 150 minutes. The solvent was evaporated and the residue chromatographed. Olefinic material (14 mg.) containing traces of bis-cyclohexylidene (t.l.c. comparison with authentic sample) was isolated. The major product was cyclohexanoneazine, 54% theor., (t.l.c. and i.r. comparison with authentic sample).

Δ^3-1,3,4-Thiadiazolin-1,1-dioxide-2,5-bis(spiro-1'-cyclohexane) (LXXXI).

Azo-sulphoxide (LXXXIV) (2.30 g.), dichloromethane (50 ml.) and 5N. peracetic acid (6.25 ml.) were stirred together at 21° for 48 hours, after which a further quantity of peracid (0.50 ml.) was added and the stirring continued for 4 hours, whereupon monitoring of the reaction by t.l.c. (alumina, benzene) indicated that the reaction was complete. The product was poured into water, the organic layer separated, worked up in the usual way,, and dried. Evaporation of the solvent gave essentially pure azo-sulphone as a white solid ± m.p. 141 - 143°, 98% theor. An analytical sample was prepared by chromatography (alumina, light petroleum)and crystallisation from light petroleum, as colourless plates m.p. 146 - 147° (sintering 132°); ν_{max} (nujol) 1310 m, 1130 m cm^{-1}; λ_{max}(cyclohexane) 366 nm. (ϵ 140). (Found: C, 56.10; H, 7.78; N, 10.72; S, 12.40. $C_{12}H_{20}N_2O_2S$ requires C, 56.19; H, 7.86; N, 10.93; S, 12.51%).

Pyrolysis of the azo-sulphone (LXXXI).

Azo-sulphone (192 mg.) was pyrolysed under an atmosphere of nitrogen. Gas evolution did not become apparent until the temperature had risen to 205° (over 14 minutes). The pyrolysis was stopped after a further 30 minutes, by which time the temperature had risen to 230°. Chromatography (silica gel, light petroleum) gave essentially pure bis-cyclohexylidene, 12% theor., (t.l.c., i.r. and n.m.r. comparison with authentic sample).

(± a mixed m.p. with the azo-sulphoxide gave a depression of 25°.)

Photolysis of the azo-sulphone (LXXXI).

Azo-sulphone (194 mg.) was photolysed in cyclohexane (50 ml.) using a medium-pressure mercury arc lamp and pyrex apparatus, under an atmosphere of nitrogen at 19°. The photolysis was monitored by observing the disappearance of the u.v. absorption at 366 nm., and was complete in 30 minutes. The solvent was evaporated and the residue chromatographed (alumina; benzene). No olefinic material was observed, but cyclohexanoneazine, ca. 18% theor., was isolated (t.l.c. and i.r. comparison with authentic sample).

Attempted reduction of the azo-sulphone (LXXXI) with hexachlorodisilane.

Azo-sulphone (131 mg.), benzene (2.0 ml.) and hexachlorodisilane (0.6 ml.) were heated together at reflux under an atmosphere of nitrogen for 18 hours. The product was cautiously decomposed with water and the solid removed by filtration. The organic layer was washed with water and dried. Evaporation of the solvent gave unreacted azo-sulphone.

Attempted preparation of Δ^3-1,3,4-oxadiazolin-2,5-bis(spiro-1'-cyclohexane) (LXXXIX).

Cyclohexanoneazine (1.94 g.) was added to a solution of potassium hydroxide (8.0 g.) in water (4 ml.) and ethanol (25 ml.) at 21° and oxygen bubbled through the solution for 22 hours. Samples were removed at intervals, worked up with water, andthe diethyl ether extracts examined by t.l.c. (silica gel, benzene/ethyl acetate 1:1) and i.r. There was no reaction.

The experiment was repeated, but this time the reactants were heated at reflux and oxygen bubbled through the solution for 4 hours. Monitoring by t.l.c. and i.r. indicated that there was no reaction.

Fluorenone, silver oxide and potassium ferricyanide were also used instead of oxygen, but with the same result.

Ozone was passed through a solution of cyclohexanoneazine (1.44 g.) in anhydrous, methanol (25 ml.). Monitoring by i.r. indicated that oxidation of the azine was complete in 3 hours. The solvent was evaporated, the product worked up with water, and the diethyl ether extract examined. None of the required product was observed.

Attempted preparation of 1,2,4-triazolidin-3,5-bis(spiro-1'-cyclohexane) (XCI).

Cyclohexanoneazine (383 mg.) and sodamide (239 mg.) were stirred together in tetrahydrofuran (10 ml.) for 21 hours. The solvent was evaporated, diethyl ether (10 ml.) added, and the sodamide decomposed by the dropwise addition of water (10 ml.). The organic layer was washed with water and dried. Evaporation of the solvent gave unreacted azine.

Ammonia was bubbled through a solution of cyclohexanoneazine (0.75 g.) in benzene (10 ml.) at 22° for 5 hours. Evaporation of the solvent gave unreacted azine.

Attempted preparation of 4-benzyl-1,2,4-triazolidine-3,5-bis(spiro-1'-cyclohexane).

Cyclohexanoneazine (1.92 g.), benzylamine (1.18 g.), glacial acetic acid (1 drop) and benzene (15 ml.) were heated together at reflux for 25 hours. Monitoring by t.l.c. and i.r. indicated that there was no reaction.

Attempted preparation of 1-p-methoxybenzyl-4-benzyl-3,5-diphenyl-1,2,4-triazolidine.

A solution of p-methoxybenzylhydrazine (1.91 g.) in benzene (6 ml.) was added to a stirred mixture of benzaldehyde (2.65 g.) and anhydrous sodium sulphate (1.0 g.) in benzene (10 ml.) at 0°. The mixture was stirred for 1 hour, after which glacial acetic acid (2 drops) and a solution of benzylamine (1.47 g.) in benzene (5 ml.) were added, and the reactants heated at reflux for 12 hours under an atmosphere of nitrogen. The warm solution was filtered andthe solvent evaporated. Addition of diethyl ether to the residue gave a white solid, which was collected and dried. Crystallisation of this solid from benzene gave benzaldehyde-p-methoxybenzylhydrazone as colourless plates m.p. 111.5° (decomp.), (2.3 g.); ν_{max} ($CHCl_3$) 3400 w (-NH-) cm^{-1}; τ 6.3 (3H, s), 5.7 (2H, s), 3.2 - 2.3 (11H, m, one being D_2O exchangeable); (M^+) $^m/_e$ = 240. (Found: C, 74.76; H, 6.59; N, 11.36. $C_{15}H_{16}N_2O$ requires C, 74.97; H, 6.71; N, 11.66%). Evaporation of the mother liquor gave an oil (2.7 g.) which was the expected Schiff's base, ν_{max} (film) 1645 s (-C=N-) cm^{-1}; (M^+) $^m/_e$ = 195.

Similarly, when the reaction was repeated with cyclohexanone instead of benzaldehyde the corresponding hydrazone and Schiff's base were obtained.

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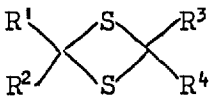
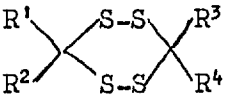
SUPPLEMENT

There are several systems [(I) - (VII)] which have not been mentioned, but which were considered during the course of this work.



(I)



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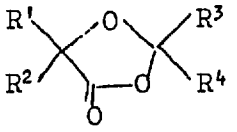

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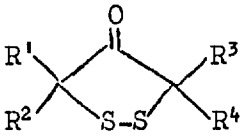

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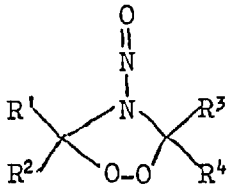

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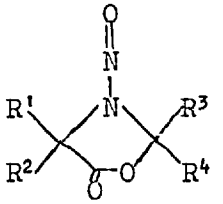


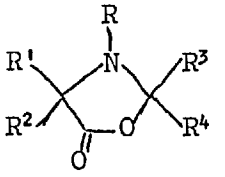
(VI)

(VII)

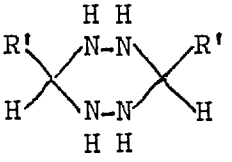
1,3-Dithietans (I) are well-known, although recently doubt has been cast on much of the early work in this field.[1] s-Tetrathianes (II),[2] 1,3-dioxolan-4-ones (III),[3] and 1,2-dithiolan-4-ones (IV)[4] are all well-known.

System (V) is unknown, but in principle might be obtained by treating 1,2,4-dioxazolidines[5] with nitrosyl chloride. System (VI) is unknown, but might be obtained by treating suitably substituted 1,3-oxazolidin-5-ones (VIII)[6] with nitrosyl chloride. System (VII) is unknown, but these compounds might be readily prepared by

controlled oxidation of s-tetrazines (IX).[7] However, 3,3,6,6-tetrasubstituted-s-tetrazines are unknown.

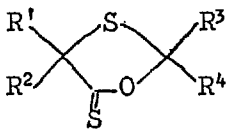


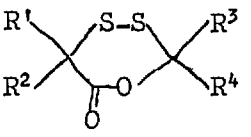
(VIII)

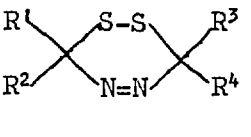


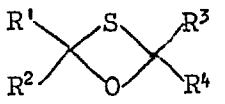
(IX)

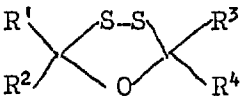
There are many other systems that might be considered (Table 1), and still the list is not exhausted.

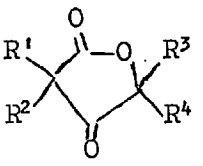


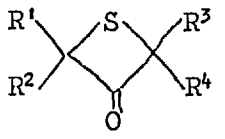


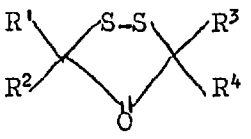


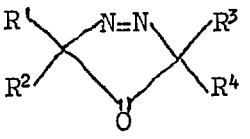


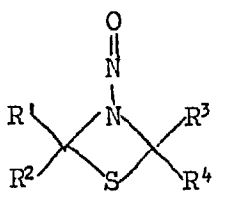












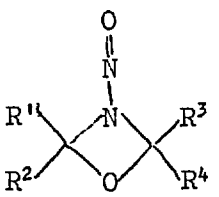


Table 1

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