A STUDY OF [3] DENDRALENE, 
ITS SYNTHESIS AND APPLICATIONS 

by 

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To my parents and my sister for their continuous support
DECLARATION

I declare that this thesis is my own composition, that it is a record of the work which has been carried out by myself, and that it has not been submitted in any previous application for a higher degree.

The thesis describes the results of research carried out in the Department of Chemistry, University of Edinburgh, under the supervision of Dr. I. Gosney since 1st October 1986, the date of my admission as a research student.

POST-GRADUATE LECTURE COURSES

The following is a statement of the courses attended during the period of research:

- Organic Research seminars (3 years attendance).
- Current Topics in Organic Chemistry, various lecturers, (15 lectures).
- Strategy of Synthesis, Dr. I. Gosney (5 lectures).
- Structural Elucidation, Dr. D. Leaver (5 lectures).
- Mass Spectrometry, Prof. K.R. Jennings (5 lectures).
- Medicinal Chemistry, Prof. P.G. Sammes, 1988 (5 lectures).
- Medicinal Chemistry, Dr. P. Leeson and Dr. R. Baker, 1989, (5 lectures).
- Recent Advances in Organic Chemistry, various speakers (5 lectures).
- Multipulse n.m.r. Spectroscopy, Dr. I. Sadler (5 lectures).
- Two Dimensional n.m.r. Spectroscopy, Dr. I. Sadler, Dr. R. Baxter and Dr. B. Birdsall (5 lectures).

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ABSTRACT

The synthesis of [3] dendralene [3-methylene-1,4-pentadiene] by chelotropic extrusion of SO$_2$ from 3-vinyl-2,5-dihydrothiophene-1,1-dioxide is reported. The six-step synthesis from butadiene sulphone, a readily available reagent, afforded the triene in ca. 20% overall yield.

Contrary to previous reports [3] dendralene is a stable, easily handled, low-boiling liquid, that can be stored for several months at -30°C in the presence of a radical inhibitor such as galvinoxyl. However, pure samples of [3] dendralene tend to dimerise slowly when left at room temperature. The structural elucidation of this dimer has been determined by derivatisation to an unusual iron dicarbonyl compound.

Spectroscopic investigations into the structure of [3] dendralene itself has shown that it exists in a symmetrical conformation with the external double bonds deviated 25° in and out of the plane. This finding is in conflict with the structure predicted by theoretical calculations which describes [3] dendralene as a trans butadiene with an orthogonal vinyl group twisted 40° out of the plane.

The diene-transmissive nature of [3] dendralene is also investigated by carrying out a number of Diels-Alder cycloaddition reactions with various cyclic and acyclic
dienophiles. Its potential for tandem annulations is illustrated by the selective formation of mono- and bis-adducts as well as mixed bis-compound with a variety of dienophiles.

The cross-conjugating properties of [3] dendralene are further exploited in the area of polymer chemistry. Its incorporation as a cross-linking reagent into polyisoprene caused premature gelling and a general change in the physical properties of the final material. A free radical polymerisation reaction of the precursor, 3-vinyl-2,5-dihydrothiophene-1,1-dioxide, gave rise to a colourless polymer which on heating lost SO$_2$, thereby exhibiting excellent potential for its use as a masked cross-linking copolymer. Other facets of dendralene chemistry including the synthesis of 3-formyl-2,5-dihydrothiophene-1,1-dioxide and [5] dendralene are discussed.
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INTRODUCTION
INTRODUCTION

The following work concentrates on [3] dendralene, the smallest representative of the dendralene group of cross-conjugated molecules. An overview of this type of polyene is given in section A, as well as an outline of the history of the dendralenes in their context as cross-conjugated molecules.

A good deal of the interest in dendralenes lies in their ability to undergo diene-transmissive cycloaddition reactions, thereby making them useful tandem annulating reagents. Perhaps a less ostensible aspect of these cross-conjugated compounds is their use in dye and polymer chemistry. Section B discusses the dendralenes in these roles and highlights some of the noteworthy examples of annulations in the literature.

The synthetic route chosen to prepare [3] dendralene and its derivatives, incorporates thermal extrusion of SO\textsubscript{2} from sulpholene compounds to give substituted butadienes. The preparation of butadienes in this manner is well known, and section C provides a precise for this topic.
INTRODUCTION

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A. DENDRALENES, THE ACYCLIC MEMBERS OF A GROUP OF CROSS-
CONJUGATED POLYENES

Cross-conjugated polyenes are a class of compounds possessing three unsaturated groups, such that two are conjugated to a third centre, but not directly to each other\(^1\). This intrinsic property may be found in the fulvenes (1) and (2) and radialenes (3) and (4) by broadening the definition. Another group of polyenes that exhibit this property and which until only recently have experienced growing attention\(^2\), are the acyclic representatives, dendralenes\(^3\) (5), (6) and (7).
Despite this recent interest, the dendralenes as a collective group have been neglected over the years. Quantum mechanical calculations have been performed on [5] dendralene$^4$ (7), but as yet it has not been prepared. [3] and [4] dendralene (5) and (6) are known, but the extent of their synthetic potential in organic synthesis has not been determined. Furthermore the syntheses of these compounds has been dominated by a mechanistic interest rather than a practical one.

In general the approach to the synthesis of [4] dendralene (6) has relied upon elimination and rearrangement reactions under pyrolytic conditions$^5$. This is evident in the earliest reported preparation of [4] dendralene$^6$ (6), which proceeded through thermolysis of the tetracetate (8) (Scheme 1).

\[ \text{AcO} \begin{array}{c} \text{OAc} \\ \text{AcO} \end{array} \begin{array}{c} \text{OAc} \\ \text{AcO} \end{array} \xrightarrow{\Delta} \begin{array}{c} \text{6} \\ \text{8} \end{array} \]

Scheme 1
In another example, work carried out by Buchan at the University of Edinburgh has shown that (6) can be prepared in almost quantitative yield by SO₂ extrusion from 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane-3,3-dioxide (9); a masked form of [4] dendralene (6) (Scheme 2). This pyrolytic step was achieved using flash vacuum pyrolysis (f.v.p.) at a temperature of 550°C. The technique relies firstly on the volatilization of (9) under high vacuum, which then in a gaseous form passes through the preheated furnace where reaction takes place. The advantages of this method of pyrolysis are that the contact times in the hot stage are small, thus preventing secondary bimolecular reactions, and the resultant products are easily isolated by condensation onto a cold trap. This preparative route to [4] dendralene was found to give a higher purity and product yield than those previously reported.

Scheme 2

\[
\begin{align*}
\text{EtO}_2\text{C} & \quad \text{CO}_2\text{Et} \quad \text{EtO}_2\text{C} \\
\rightarrow & \quad \rightarrow \\
\text{H}_2 & \quad \text{LiAlH}_4 \\
\quad & \quad (\text{CH}_3\text{CO})_2\text{O}
\end{align*}
\]

\[
\begin{align*}
\text{EtO}_2\text{C} & \quad \text{CO}_2\text{Et} \\
\rightarrow & \quad \rightarrow \\
\text{EtO}_2\text{C} & \quad \text{CO}_2\text{Et}
\end{align*}
\]

Scheme 3
[3] Dendralene has also been prepared using the diacetate\(^9\), 3-methylene-1,5-pentadiacetate (12) (Scheme 4). The flow rate through the furnace could be controlled to give either (5) or (13) predominantly. Under optimum conditions (12) was pyrolysed at 485°C over nitrogen and carborundum to give 47% of (5).

$$\text{AcO} \text{AcO} \rightarrow \begin{array}{c}
\text{AcO} \\
\text{OAc}
\end{array} \text{(12)} \quad \text{AcO} + \begin{array}{c}
\text{OAc}
\end{array} \text{(13)} \quad \text{OAc} \text{(5)}$$

Scheme 4

Alternatively, the conversion of 1,2,3-propanetricarboxylic acid (14) into the quaternary ammonium hydroxide (15), followed by a Hofmann elimination to give the triene (5) (Scheme 5), has also been reported\(^10\). The authors do not however give any experimental conditions or yield.
In their continued work with small polyolefinic compounds, Bailey et al. pyrolysed 1,2-di-(acetoxymethyl)-cyclobutane (16) to give amongst other products, a low 2% yield of (5). In a similar experiment the carbonate (17) was subjected to temperatures of 500°C and produced an improved yield of 18% of [3] dendralene (5). Although the authors did not provide an explanation or mechanism for this rearrangement, they noted the absence of any bis-methylenecyclobutane (18) by-product. A possible mechanistic route to (5) might be via an initial cyclobutane ring cleavage to give the diradical intermediate. This is then followed by a 1,3-hydrogen shift as outlined in Scheme 6.
Scheme 6
Once again employing thermolysis, Hopf and Hanno\textsuperscript{12} also reported the preparation of [3] dendralene in an overall 18\% yield. Their procedure incorporated the dimerisation of propargyl bromide in the presence of magnesium metal and copper(I) chloride to give the 1,2-hexadiene-5-yne compound (19). This allene then underwent thermal isomerisation at 550°C to give the acetylenic derivative (20), followed by a Lindlar catalysed hydrogenation of the triple bond, resulting in the formation of [3] dendralene (5) (Scheme 7).

\[
\begin{align*}
2 \text{BrMg} & \quad \xrightarrow{\text{CuCl}} \quad 550^\circ \text{C} \\
\text{(19)} & \quad \xrightarrow{\text{dd}} \quad \\
\text{(20)} & \quad \xrightarrow{\text{dd}} \\
\text{(5)} &
\end{align*}
\]

Scheme 7

The most recently reported synthesis of [3] dendralene by Vdovin et al (Scheme 8), involved the thermal ring opening of 1-vinylcyclobutene at 335°C\textsuperscript{13}. The authors reported 100\% conversion to (5) at this temperature, but
It has already been mentioned that the study and, therefore, the synthesis of the parent compound [3] dendralene (5), has been extremely limited. In spite of this, the literature does show a substantial number of preparations of its derivatives. Many of these are obtained by thermal rearrangements of substituted cyclobutanes involving a 1,5-hydrogen shift and electrocyclic ring opening. One such example is the preparation of derivative (21) from 1,2-diisopropylidene-cyclobutane (22), with thermolysis at 260°C (Scheme 9).
Using a different approach, a simple "ene" reaction was employed in the synthesis of a number of other derivatives. For example, (23) and (24) were prepared from substituted acetylenes and allenes according to Scheme 10.

\[ R = \text{CF}_3, \text{CO}_2\text{Me} \]
The use of a Wittig reaction on ketone derivatives has been successfully employed by several workers\textsuperscript{17}. In particular Bohlman\textsuperscript{18} was able to synthesise some highly conjugated dendralenes using this method (Scheme 11).
The halogenated derivative (25) was prepared by Weyerstahl and workers' in an application of their simple route to halogenated butadienes. The general procedure which is outlined in Scheme 12, required the addition of chlorocarbene to the double bond of a suitable olefin (27) to form the cyclopropane derivative (26). Under thermolytic conditions, (26) underwent an elimination of hydrochloric acid along with a ring opening to give the halogenated butadiene (25). When the olefin (27) is a butadiene, the vinyl substituent is present in the resultant cyclopropane (26) and the butadiene product (25) thus providing a route to halogenated dendralenes.

\[
\begin{align*}
(27) & \rightarrow (26) \rightarrow (25) \\
\text{eg. } R = & \quad C=CH_2 \quad \rightarrow \\
& \quad \text{CH}_3 \\
\end{align*}
\]

Scheme 12
The number of examples of dendralene derivatives and their preparative routes are quite varied. For example, in a completely different approach, a simple Grignard reagent, methylmagnesium bromide was reacted with the carbonyl group of the dienone (28). The alcoholic product was then dehydrated to give the tetramethyl dendralene compound (29) (Scheme 13).

\[ \text{CH}_3\text{MgBr} \rightarrow \text{(29)} \]

One of the most important characteristics of these cross-conjugated dendralenes, is their diene-transmissive nature in cycloaddition reactions. A Diels-Alder reaction becomes diene-transmissive when a cycloaddition transfers the diene to another part of the molecule. This newly formed diene may then take part in a second Diels-Alder reaction (Scheme 14). The recent interest that has been shown in these diene-transmissive dendralenes, stems from their ability to undergo multiple annulations, and therefore their use in organic synthesis.

\[ \text{[4]} \text{dendralene} + \text{[4]} \text{dienophile} \rightarrow \text{[8]} \text{dendralene} + \text{[4]} \text{dienophile} \rightarrow \text{[16]} \text{dendralene} \]

Scheme 14

In the case of [4] dendralene, cycloaddition reactions proceed readily in the presence of suitable dienophiles. Its versatility as an annulating reagent is however
greatly reduced by a lack of regioselectivity. This point is illustrated by work carried out by Roth et al., who showed that SO$_2$ addition to (6) resulted in mono-adducts (30) and (31) (Scheme 15); products of non-regioselective addition.

![Scheme 15](image)

This example highlights the regioselective problems encountered in a single cycloaddition, but the product distribution potentially becomes far more complex if a second addition reaction takes place.

Apart from the regioselectivity, consideration must also be given to the unpredictable reactivity of [4] dendralene (6). A case in point is the reaction of (6) with maleic anhydride, which gave a mixture of the bis- (32) and tris- (33) adducts as identified by mass spectrometry.
In a similar experiment, reaction of (6) with equimolar dimethylacetylenedicarboxylate (DMAD) yielded the bis-adduct (34)\(^7\) (Scheme 16).

These regiospecificity and reactivity problems were in part overcome by using the dimethylene sulphone (9) as a
diene in [4+2] Diels-Alder additions, and Buchan\(^7\) investigated a number of these reactions with a range of dienophiles (Scheme 17). She found that subsequent f.v.p. of the cyclic mono-adduct (35), resulted in the formation of (36) by SO\(_2\) extrusion. Spontaneous electrocyclic ring closure gave reasonable yields of the hexahydronaphthalene derivatives (37).

By analogy [3] dendralene also shows sufficiently high affinity towards dienophiles in cycloaddition reactions. This reactivity is evident in the tendency of (5) to dimerise at temperatures as low as \(-5^\circ\text{C}\). It is, however,
simpler than its tetraene homologue (6), and therefore the range of cycloaddition products should be limited to only the mono- and bis-adducts. The absence of the regiospecificity problems encountered with [4] dendralene, makes [3] dendralene a far more suitable tandem annulating reagent and worthy of detailed examination.

The application of cross-conjugated [3] dendralene derivatives towards diene-transmissive cycloaddition reactions was realised as early as 1951, when Paul and Tchelitcheff prepared the derivative (38). Treatment of (38) with a two molar equivalent of maleic anhydride resulted in the formation of a bis-adduct (39) (Scheme 18).

\[
\text{(38)} + 2X \xrightarrow{\text{maleic anhydride}} \text{(39)}
\]

\[\text{Scheme 18}\]

Reports on the parent dendralene (5), are however limited to only a few examples. Diels-Alder addition of (5) to maleic anhydride and quinone have been carried out
to yield the bis-adducts (40) and (41) respectively. When napthoquinone (42) and decahydroanthracene-1,4-dione (43) were reacted with (5), the hexaphene (44) and octaphene (45) derivatives were isolated in reasonable yields; thus illustrating the applicability of [3] dendralene (5) in the preparation of condensed polynuclear aromatic molecules (Scheme 19).
Scheme 19
The concept of tandem annulations using [3] dendralene shown in these early examples, was not investigated until much later when Tsuge and workers prepared the triene (46) and examined its cycloaddition reactions with several acetylenic$^{23}$ and cyclic$^{24}$ dienophiles (Scheme 20). They realised the potential of this class of polyene in designed organic synthesis but felt the parent compound,
[3] dendralene to be too unstable, and so concentrated on its derivatives.

For example, the activated cross-conjugated triene (47) was investigated<sup>25</sup> and found to exhibit some selectivity towards the formation of mono-adducts when acetylenic dienophiles were used. Cyclic dienophiles on the other hand gave both the mono- and bis-annulated products.

![Dienophile Structures](image)

A more refined derivative (48) which was also prepared by these workers<sup>26</sup> has an ethoxy activating group substituted onto the 2-position. They hoped to induce selectivity towards addition across the activated diene but found addition took place across the unsubstituted diene preferentially. This was attributed to the non-planarity of the cis diene due to the steric bulk of the substituents (Fig. 1).
Another problem encountered with this derivative (48) was thermal lability and a tendency to polymerise. They felt these problems could be overcome using the triene equivalent (49) (Scheme 21) which undergoes cycloaddition prior to dehydrobromination. Formation of the second diene followed by another cycloaddition reaction takes place with acetylenic dienophiles.
This new strategy of Tsuge and workers\textsuperscript{27}, to concentrate on tandem annulating reagents which defer the formation of the second diene, was evident from their preparation and application of (50). This material is in fact the synthetic equivalent of 3-methylene-1,4-pentadiene, [3] dendralene (Scheme 22).
Apart from the diene-tranmissive compounds, the advantages to using other types of tandem annulating reagents in organic synthesis is well recognised. Trost used the bifunctional conjunctive butadiene derivative (51) to alkylate the ketosulphone (52), and this in turn underwent cyclization to (53) to affect the first annulation. A Diels-Alder addition with DMAD or maleimide (Scheme 23) brought about the second annulation.
Another example of tandem annulations using a disubstituted butadiene (54) was provided by Gaoni\textsuperscript{29} who, with a reaction sequence of cycloaddition, debromination and cycloaddition prepared (55) as a double Diels-Alder adduct (Scheme 24).
The 1,3-butadiene derivative (54) was prepared in good yields by a zinc-copper couple debromination of (56), whereas the alternative route occurred with difficulty by extrusion of SO$_2$ from the sulpholene (57) (Scheme 25).
These workers in the course of their investigations have also prepared the novel sulphone (58) by oxidation of 3,4-dimethylenethiolane (59) and debromination of (57). This tetramethylene diradical equivalent undergoes cycloaddition with DMAD and dimethylazidocarboxylate (Scheme 26). Whilst the authors recognised the importance of these sulpholene compounds in cycloaddition reactions, they did not attempt to extrude $\text{SO}_2$ from the adducts (60) or (61) in order to generate the diene for further addition.

In a similar manner to Gaoni's work, Moody and Johnston in 1985 treated the diene (62) with the highly reactive N-phenyl-1,2,4-triazoline-3,5-dione (63) at $-50^\circ\text{C}$, to form the unstable mono-adduct (64). A zinc-copper couple was employed to affect dehydrohalogenation of the diiodo compound (64), thus forming a new diene functionality. This species (65) was further reacted with a number of dienophiles in order to illustrate its tandem annulating ability (Scheme 27).
Scheme 26
The preparation of large polycyclic compounds through multiple annulations has also received much attention. For example, Block and workers\textsuperscript{32} have exploited the Ramberg-Backlund reaction to prepare linear fused carbocycles and polyarene precursors (Scheme 28). In their synthetic route, 1,2-dimethylenecyclohexane (66) was converted to the napthalene derivative (67) by treatment with chloromethyl-1,2-propadienyl sulphone (68). Subsequent sulphonyl chloride elimination from (67) gave the exocyclic butadiene derivative (69). This derivative
(69) then underwent another reaction with (68) and thus the sequence was repeated until the desired number of annihilations had been achieved.

\[ \text{(66)} \quad \text{+} \quad \text{Cl-CH}_2\text{SO}_2\text{H}-\text{C}\equiv\text{C}=\text{CH}_2 \quad \Delta \quad \text{(67)} \]

\[ \text{(66)} \quad \text{Repeat} \quad \text{two steps} \quad \text{(67)} \quad \text{(69)} \]

\[ \text{Scheme 28} \]

Cross-conjugation is a characteristic that is frequently found in pigment and dye chemistry. One such example which incorporates a [3] dendralene type centre is the trinuclear guanidinium cation dye (70); in which the \( \pi \) electrons are delocalized over the system. The overall synthesis of this symmetrical molecule (70), is outlined in Scheme 29 and may be described as a condensation of
formylmalondialdehyde (71) with a three molar equivalent of the heterocyclic imonium salt (72).

\[ \text{CH}_3 \text{I} \text{BF}_4^+ \text{CH}_3 \text{I} \text{BF}_4^+ \]

\[ + \text{CH}_3 \text{CH}_3 2\text{BF}_4^- \]

\[ \text{AcO}_2^-/\text{NaOAc}/100^\circ \text{C} \rightarrow -3\text{H}_2\text{O}, -\text{HBF}_4^- \]

\[ (70) \]

\[ Z = \text{C(CH}_3)_2 \text{, O, Se, S, (CH=CH)} \]

Scheme 29

Compounds having cross-conjugation have found a practical application in polymer chemistry. They enable not only cross-linking but also provides a pendant diene for cycloaddition reactions. The dendralenes have not
remained unnoticed in this area of chemistry, and as early as 1954 Bailey and Economy \textsuperscript{35} prepared the ladder polymer (73) using benzoquinone as a cycloaddend (Scheme 30).

Scheme 30

This concept was later readopted by Bailey and Feinberg \textsuperscript{36} in their preparation of (74) amongst a number of other ladder polymers. The impetus behind this renewed interest was the formation of ladder polymers containing long chained linking sections such as (74); where the napthalene backbone is fused by a 20 membered ring (Scheme 31). These polymers possessed flexibility and solubility
which the small ring linked polymers such as (73) lacked, without losing any stability.

Scheme 31

Thermal homopolymerisation of the dendralene derivative 2,4-dimethyl-3-methylene-1,4-pentadiene (75) has been reported to give a high molecular weight elastomer of approximately 20,000. The versatility of this material was further illustrated when a cycloaddition reaction with tetracyanoethylene (TCNE) gave a polymeric Diels-Alder adduct, which was then used to make a
colourless insoluble film. The monomer (75) was prepared by reacting tetramethyl allene (76) with formaldehyde to give the alcohol (77). Subsequent isomerisation of (77), followed by dehydration gave the dendralene derivative (75) (Scheme 32).

\[
\text{\ce{C=C}} + \text{\ce{HCHO}} \rightarrow \text{\ce{\overset{\text{OH}}{\overset{\text{C(CH}_3)_2\text{OH}}{}}}}}
\]

\text{Scheme 32}

C. SULPHOLENES, A SOURCE OF BUTADIENES

The use of 3-sulpholene as a masked form of 1,3-butadiene is well known, and indeed has been a synthetic tool in organic synthesis for some time. The
versatility of this form of diene generation, stems from an ease of "unmasking" by the loss of SO₂. 3-Sulpholene itself undergoes chelotropic extrusion of SO₂ and 1,3-butadiene will cycloadd in a concerted fashion to give 3-sulpholene. This reversibility has a practical application in that highly reactive dienes may be stored as stable crystalline materials in the sulpholene form, and used as such in cycloaddition reactions. For example benzyne undergoes cycloaddition reactions with cyclic dienes but characteristically shows a lack of reactivity towards acyclic butadienes. This may be explained by an inherent conformational difference whereby the cyclic diene has the rigid cis structure, a necessary requirement for addition to take place. The open chain butadiene on the other hand exhibits conformational mobility. This point is reinforced by the transient nature of benzyne which will decompose if the conditions for cycloaddition are not suitable. The apparent difficulties of trapping benzyne with butadiene were overcome by the concurrent decomposition of benzenediazonium-2-carboxylate and 3-sulpholene (Scheme 33) to give benzyne and butadiene which combine to form 1,4-dihydronaphthalene (78). The authors believe that the addition of benzyne to the butadiene formed in situ, is fast enough for the butadiene to retain the cis conformation.
In another example, the storage problems of the substituted 1,3-butadiene (79), which is reported to be quite unstable, were overcome by converting (79) to the sulpholene compound (80).

Substituted 1,3-butadienes show different reactivities towards $\text{SO}_2$ addition and this observation has been used successfully to separate isomeric materials. Nesbitt et al. in their work with bollworm sex pheromones, were able
to isolate the more potent trans-9,11-dodecadiene-1-yl-acetate (81) from the unreactive cis-isomer, by reaction with SO$_2$ (Scheme 34). The mixture was separated and the pure isolated sulpholene flash distilled to regenerate the trans-isomer.

![Chemical Structure](image)

Scheme 34

The extrusion of SO$_2$ from 3-sulpholene and the reverse reaction, is stereospecific and may be explained by examining the interacting frontier molecular orbitals. In the case of the forward reaction, a simple linear approach is allowed thus permitting orbital overlap to occur on the same face; in a suprafacial fashion. In addition to this, the development of an orbital overlap also requires the movement of orbitals in a disrotatory manner as illustrated in Fig. 2, and it can be seen that the stereochemistry of the reacting butadiene is inherent in the cyclic product.
These fundamental characteristics apply equally well to both the forward and reverse reactions and have been utilized by Bloch to prepare the stereoselective (EE)-1,4-disubstituted diene (82) (Scheme 35), to use in insect pheromone synthesis. The scheme involves in the first step, a stereoselective alkylation of (83) to give the substituted sulpholene (84). A subsequent retro-Diels-Alder and SO₂ extrusion occurs in the one step, yielding the single trans-product (82).
The acidity of the \( \alpha \)-hydrogen in 3-sulpholenes makes them ideally suited to electrophilic addition and thus provides a simple means of derivatising 1,3-butadiene. The previous example outlined in Scheme 35, illustrates this point by the stereoselective substitution of the \( \alpha \)-hydrogen prior to pyrolysis. In work carried out by DiFranacesco\(^44\) this acidity was utilised in the preparation of deuterated Diels-Alder adducts (Scheme 36),
for use in mechanistic studies.

\[
\begin{align*}
\text{SO}_2 + \text{CO}_2\text{CH}_3 & \rightarrow \text{CO}_2\text{CH}_3
\end{align*}
\]

Scheme 36

The total synthesis of dl-estra-1,3,5(10)-triene-17-one (84) has been accomplished by Nicolaou who incorporated a strategy based on the capture of o-quinodimethanes generated by chelotropic extrusion of \(\text{SO}_2\) (Scheme 37). The synthesis relied on the alkylation of the sulphone (85) by the tosylate (86) prior to thermal \(\text{SO}_2\) extrusion.

An interesting example of the utilization of the \(\text{SO}_2/\text{diene}\) reaction is given by Yamada and workers in their preparation of (5E)- and (5Z)-vitamin D\(_3\) 19-alkanoic acids (Scheme 38). Vitamin D\(_3\) (87), when treated with \(\text{SO}_2\) gave both the S and R isomers of the sulpholane adducts (88). The epimeric mixture (88) then underwent a highly regioselective and stereospecific alkylation which resulted in two isomeric products of (89), each having
trans sulpholane substituents. Unexpectedly, desulphorylation of the two isomers of (89) occurred in an antarafacial manner to give (90) as the major product. The author’s suggested explanation for this anomaly is that the steric bulk of the sulpholane ring substituents causes extrusion to take place in a fashion contrary to the selection rules to give the most thermodynamically favoured product (90).
Scheme 38
RESULTS AND DISCUSSION
The use of sulpholene derivatives as precursors to 1,3-butadienes, is a subject which has been covered in Section C of the Introduction. One particular example of their application, of relevance to this work, may be found in the simple preparation of [4] dendralene (6), which requires the thermal extrusion of $\text{SO}_2$ from 6,7-dimethylene-3-thiabicyclo[3.2.0]heptane-3,3-dioxide (9) at 550°C to give the divinyl butadiene derivative (6) in almost quantitative yield (Scheme 39).

![Scheme 39](image)

The success of this pyrolytic step in the synthesis of [4] dendralene (6) provided a priori for a new route to [3] dendralene (5), incorporating the chelotropic extrusion of $\text{SO}_2$ from the sulpholene derivative (91) (Scheme 40).
In order to achieve this new route to [3] dendralene, a synthesis of the precursor (91) was firstly required, and this was accomplished starting from the readily available butadiene sulphone and using the scheme outlined in Section C. A number of alternative less successful routes were also investigated and these are discussed in their relevant Sections A and B.

Once a new route to (5) had been developed, an attempt was made to try to rectify the literature omissions concerning its function as a cross-conjugated diene in Diels-Alder reactions. A general study of the reactivity of [3] dendralene with a number of dienophiles is discussed in Section E, and these reactions were carried out with a view towards eventually inducing mono- and bis-
annulations selectively. A selectivity of this type was considered desirable, as it would enable [3] dendralene to be used as a versatile annulating reagent capable of reacting sequentially with two different dienophiles.

The cross-conjugating characteristics of (5) were further explored for cross-linking properties in polymer chemistry, and this application was extended to include the study of its precursor, the vinyl substituted sulpholene (91). Section H deals with the polymerisation of these compounds and the physical properties of the polymer products.

With the development of a new route to the parent dendralene (5), and some examples of tandem annulations, it was felt that an interesting extension might be to investigate the synthesis and reactivity of some dendralene derivatives. This began with an attempt to design a simple synthetic route, in order to provide a means of customising these dendralene products for use in specific synthesis. The preparation of a carbonyl derivative (168) was proposed, because its potential for modification of the sulpholene ring and vinyl substituent, would eventually lead to the required dendralene precursor. Several strategies to the synthesis of (168), including fused isoxazolines, were investigated and these are covered in Section F.
Although both [4] and [3] dendralene were prepared prior to this work, [5] dendralene (7) remains unknown and its synthesis using SO$_2$ extrusion from sulpholene compounds, presented itself as a challenging extension to the dendralene chemistry investigated so far. Some of the routes attempted unsuccessfully in this work, are discussed in Section G and provide a platform for further study.
RESULTS AND DISCUSSION

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A. ATTEMPTED ROUTE TO [3] DENDRALENE BY METALLATION OF 2,5-DIHYDROTHIOPHENE-1,1-DIOXIDE

The first route to [3] dendralene to be investigated is outlined in Scheme 41, with the initial step being the metallation of 3-bromo-2,5-dihydrothiophene-1,1-dioxide (93). The metallated species (94) could then undergo alkylation, such that the newly introduced alkyl group could be easily converted into a vinyl substituent. For example, reaction with ethylene oxide to yield (95) would enable the hydroxy group to be dehydrated or derivatised for elimination to the alkene substituent (91) (Scheme 41).

![Scheme 41](image-url)
A literature search for 3-halo-3-sulpholene compounds revealed a preparation for 3-chloro-2,5-dihydrothiophene-1,1-dioxide (96). This material (96) was obtained in 25% yield, as one of two isomeric products from a base catalysed elimination of (97) (Scheme 42). The other isomer (98) was formed predominantly in 70% yield.

The bromine analogue (99), however, had not been reported previously and an attempt was therefore made to prepare this compound by dehydrobromination of (100). Base catalysed eliminations with potassium hydroxide, tert-butoxide and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) failed to give the expected product (99). In all cases only the isomer (101) was identified as part of a mixture.
of starting material and 3a,7a-dihydrobenzothiophene-1,1-dioxide (102) (Scheme 43). The formation of this dimer (102), has been reported previously by Bailey and Cummins as the decomposition product of thiophene dioxide (103). Its formation in this work can be explained by a bis-elimination of the dibromo-compound.

\[ \text{Scheme 43} \]

(100) to give thiophene-dioxide (103). In a similar
manner to that found by these early workers\textsuperscript{50}, this unstable material dimerises readily with the extrusion of SO\textsubscript{2} to form (102).

The failure of this material (100) to eliminate across the 3,4-position even as a minor reaction, as found in the chlorinated compound, is not clear. Generally materials were separated by chromatography over silica and isolated fractions examined by n.m.r. spectroscopy. The possibility that silica catalyses the isomerisation of 3-sulpholene to 2-sulpholene cannot be excluded and in hindsight gas chromatography may have been a better method for identifying the product composition. Nevertheless, the predominant formation of \( \alpha,\beta \)-unsaturated sulpholenes is not uncommon and so the isolation of (101) warrents some consideration.

A general preference for \( \alpha,\beta \)-elimination in acyclic derivatives caused by the enhanced acidity of the \( \alpha \)-hydrogen, is believed to arise from a kinetic rather than thermodynamic influence; as base catalysed isomerisation proceeds readily to give the thermodynamically favoured \( \beta,\gamma \)-product\textsuperscript{51}. Cyclic sulphones present a different picture and are primarily dependant on ring substituents and size. The \( \beta,\gamma \)-unsaturated thiacyclohexene-1,1-dioxide (104) predominates over the \( \alpha,\beta \)-compound (105) in a ratio of 97:3. Butadiene sulphone on the other hand (106) exists in an equilibrium of 42:58 % (Fig. 3). The five membered ring sulpholenes
do, however, exhibit very marked substituent effects. The presence of a methyl group favours the $\alpha,\beta$-sulpholene (107) to the extent of 86% and even more apparent is the virtual non-existence of the $\beta,\gamma$-isomer when a hydroxy-substituent is incorporated.

![Chemical structures](image)

It is generally assumed that the addition of bromine to butadiene sulphone (106) gives the trans dibrominated
product (108) (Fig. 4). Subsequent dehydrobromination across the $\beta,\gamma$-position would mean a cis-syn elimination; the least favoured conformation. A trans anti-periplanar conformer is preferred and therefore eliminations across the $\alpha,\beta$-carbons should proceed more readily to give (101). A cis dibromo-compound could undergo anti-elimination equally in the $\alpha,\beta$- or $\beta,\gamma$-position.

As mentioned beforehand the structures of 3,4-dibromo-tetrahydrothiophene-1,1-dioxide was assumed to be the trans isomer (108). This assumption is reasonable based on the accepted mechanism that electrophilic additions of bromine to alkenes proceed through a bromonium ion intermediate. An exception to this general rule, however, was found in the bromination of the bicyclic sulphone\textsuperscript{52}
when a mixture of isomers (110) and (111) were formed (Scheme 44).

These results were explained by the intermediacy of an open cationic species which is stabilised by through-space interaction of the sulphone group (Fig. 5). This allows the bromide ion to attack in either *syn* or *anti* fashion to the sulpholane ring.
Similarly, ring opening of the epoxide (112) using HBr in glacial acetic acid, resulted in 37% yield of the cis diol (113) (Fig. 6). When the same reaction was repeated using aqueous N-bromoacetamide, the usual trans isomer (114) was formed exclusively. This paradoxical behaviour is believed to be the effect of the hydration of the SO₂ in aqueous solution, which effectively diminishes the through-space stabilizing influence of the remote SO₂.
The bromination of butadiene sulphone (106) yields one isomer as determined by $^{13}$C and 'H n.m.r. spectroscopy. Speculation into a similar remote SO$_2$ effect on the bromination of these sulpholenes, prompted an investigation into the identity of this single product (100). Unfortunately, n.m.r. techniques were inadequate for this task and so a crystal structure was taken. This
also proved an inconclusive exercise as the
crystallographic data was distorted by the presence of an
overlapping enantiomeric mixture.

Despite the apparent failure in resolving this
molecule (100) by crystallographic methods, some
interesting structural characteristics were brought to
light. The X-ray crystal data, which was well refined for
the sulphone, C2, C5 and the bromines, showed these atoms
to be in roughly the same plane (Fig. 7). The ambiguity
in the final resolution, however, was due entirely to the
poorly defined C3 and C4 carbon atoms. This inherent
problem may be explained by the presence of enantiomeric
pairs which pack so similarly that they are superimposed
in the one site, and therefore cannot be distinguished by
X-ray crystallography. In order to meet the requirements
mentioned beforehand, where the bromines, C2, C5 and the
sulphone atoms are in the same plane, the average position
between enantiomeric pairs must be in that plane. A trans
structure meets those requirements as illustrated in Fig.
7. This is also true of an eclipsed cis isomer but the
energetic strain of forcing the bromines into an eclipsed
position makes the formation of this isomer unlikely. It
therefore appears that although the crystal structure was
not resolved for (100), the data does support the expected
trans compound (108).
Fig. 7

An alternative approach to this problem was to investigate any change in isomeric ratio when the bromohydrin (115) was prepared using different brominating
reagents and conditions. More specifically could a mixture of cis and trans isomers be detected in an anhydrous environment? Aqueous bromine water$^{53}$ and N-bromoacetamide were reacted with butadiene sulphone (106). The bromohydrin (115) was also prepared from the epoxide and from the nitrate ester$^{54}$. $^{13}$C n.m.r. spectra were obtained for each of the products and these are outlined in Table 1. It can be seen clearly that there are negligible differences in chemical shifts for each bromohydrin, thus indicating that one isomer only is formed in each case, and a reasonable deduction is that the unique isomer is the trans structure (115a).

Table 1 A comparison of $^{13}$C n.m.r. shifts for the bromohydrin (115)

<table>
<thead>
<tr>
<th>Method of Preparation</th>
<th>$\delta$</th>
<th>$C_2$</th>
<th>$C_3$</th>
<th>$C_4$</th>
<th>$C_5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Bromine water (aq)</td>
<td>56.72</td>
<td>47.57</td>
<td>73.46</td>
<td>57.69</td>
<td></td>
</tr>
<tr>
<td>(2) Via the nitrate ester (aq)</td>
<td>56.11</td>
<td>47.60</td>
<td>73.43</td>
<td>57.67</td>
<td></td>
</tr>
<tr>
<td>(3) From the epoxide (anhydr.)</td>
<td>56.76</td>
<td>47.60</td>
<td>73.43</td>
<td>57.71</td>
<td></td>
</tr>
<tr>
<td>(4) N-bromoacetamide (aq)</td>
<td>56.77</td>
<td>47.55</td>
<td>73.45</td>
<td>57.75</td>
<td></td>
</tr>
</tbody>
</table>
It therefore seems that the remote stabilisation by the SO$_2$ group on the unbridged carbocation, exhibited in the bicyclic sulphone (109), is not evident in the monocyclic compound (106). Any through-space effect would in any case be exerted equally on either side of the carbocation due to the conformational mobility of the structure and one would expect nucleophilic attack to result in a 50:50 mixture of cis (115b) and trans (115a) isomers. Clearly the relative stability of the bromonium ion intermediate overrides any influence of the remote SO$_2$ functionality.
B. ATTEMPTED ROUTE TO [3] DENDRALENE VIA DIETHOXY-CARBONYLMETHYL-2,3-DIHYDROTHIOPHENE-1,1-DIOXIDE (116)

A synthesis which used the diethyl malonate derivative (116) as a starting material, was considered a likely route to the vinyl sulphone (91) (Scheme 45).

![Chemical diagram](attachment:chemical_diagram.png)

Scheme 45

The success of the synthesis relied on the isomerisation of (117) to (91) in the final step and was based on the premise that conjugation with the vinylic group would lead to the more favoured product. This is
exemplified in the accompanying isomerisation of the double bond of the thiolate derivative (118) upon oxidation (Scheme 46).

\[ \text{Scheme 46} \]

The literature procedures of Argyl et al., were employed for the preparation of the starting material (116), its subsequent hydrolysis and decarboxylation to the acid (119), and also in the synthesis of the ethyl ester (120a). Their yield of 82% for the preparation of acid (119) was optimised to 94% in this work and a modification of their esterification procedure was required for the reaction to work. The conversion of (119) into the ethyl ester (120a) was accomplished by boiling (119) in ethanol with 20% w/w sulphuric acid. Similarly, the methyl ester (120b) was prepared using methanol and sulphuric acid. Methylation of (119) with diazomethane also gave (120b) in high yields.
The next step in the synthesis involved selective reduction of the ester functionality. Both lithium aluminium hydride and sodium borohydride reducing agents were employed for this task.

Lithium aluminium hydride is often the reagent of choice when reduction of an ester function is required in the presence of an olefin. If, however, the double bond is activated by an adjacent group such as a sulphone, reduction may occur. This was found by Bordwell and McKellin who demonstrated that benzothiophene-1,1-dioxide (121) was reduced slowly by lithium aluminium hydride to 2,3-dihydrobenzothiophene (122) (Scheme 47). When (123) was treated with lithium aluminium hydride, reduction to (122) was rapid. The authors inferred from these results that the double bond is reduced slowly, and prior to the sulphone group.

\[
\begin{align*}
\text{LiAlH}_4 & \quad \text{slow} \\
\text{LiAlH}_4 & \quad \text{fast} \\
(121) & \quad (122) & \quad (123)
\end{align*}
\]

Scheme 47
Treatment of sulpholene (120a) with lithium aluminium hydride also resulted in reduction of the double bond along with the ester group (Scheme 48) to give the alcohol (124).

![Scheme 48]

Table (2) illustrates how a change of reaction conditions resulted in varying product yields, but failed to give the desired sulphone (125). It is also worth noting that reductions carried out in diethyl ether, gave a mixture of starting material (120a) and the fully reduced compound (124) in a ratio of 1:1.8, even when the reaction period was prolonged. In contrast to this, reactions carried out in tetrahydrofuran (THF) resulted in the formation of the fully reduced alcohol (124) as a mixture with other products. No starting material was identified.
It appears that the rate of reduction is enhanced using THF as a solvent. Despite the common usage of lithium aluminium hydride for reductions, there have been only a limited number of reports concerning solvent effects. One example is the conversion of n-octyl iodide into n-octane. When the reaction was carried out in an ethereal solution, 24h was required for a 90% reduction. By comparison, the reduction was complete in a quarter of an hour when THF was used as a solvent, and in monoglyme and diglyme the reaction times were even less.

Table 2 Lithium Aluminium hydride reductions of (120a)

<table>
<thead>
<tr>
<th>Temp.</th>
<th>Time</th>
<th>Solvent</th>
<th>Equiv. of LiAlH₄</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>35°C</td>
<td>3h</td>
<td>ether</td>
<td>4</td>
<td>(120a) &amp; (124)</td>
</tr>
<tr>
<td>66°C</td>
<td>18h</td>
<td>THF</td>
<td>4</td>
<td>(124)* &amp; @</td>
</tr>
<tr>
<td>66°C</td>
<td>4h</td>
<td>THF</td>
<td>12</td>
<td>(124)* &amp; @</td>
</tr>
<tr>
<td>R.Temp.</td>
<td>13h</td>
<td></td>
<td></td>
<td>68%</td>
</tr>
<tr>
<td>35°C</td>
<td>6h</td>
<td>ether⁺</td>
<td>4</td>
<td>(120a) &amp; (124)</td>
</tr>
<tr>
<td>-20°C</td>
<td>2h</td>
<td>THF</td>
<td>1.5</td>
<td>(124) &amp; @</td>
</tr>
</tbody>
</table>

* Major product by n.m.r. spectroscopy.
+ The ester was placed in a soxhlet extraction thimble and LiAlH₄ as a suspension in ether was heated to boiling.
@ Other unassigned products.
These results are consistent with a separated lithium ion pair in THF as illustrated in Fig. 8. In contrast, contact pairs\textsuperscript{58} are described for diethyl ether, which has a poor solvating ability. The solvation of the lithium ion by THF at normal concentrations therefore makes the aluminium hydride ion more accessible and reduction proceeds at a greater rate. This argument may also be extended to include monoglyme and diglyme solvents.

\[
+ \quad \text{Li} \quad \begin{array}{c}
\text{O} \\
\text{R} \\
\text{R} \\
\text{R} \\
\text{R}
\end{array} \quad + \quad \text{AlH}_4
\]

Fig. 8

The increased reaction time from 3h to 6h for the reduction of (120a) using lithium aluminium hydride in ether at 35°C (Table 2), failed to give any significant increase in yield for the alcohol product (124). The ratio of starting material to product in each case can only be explained by a reaction equilibrium, however the extent of this interesting kinetic control cannot be exploited in the light of the present results alone, and
requires further investigation.

As an alternative to lithium aluminium hydride, reductions using sodium borohydride were also investigated. This reagent is far less reactive than its aluminium counterpart and is known to be fairly unreactive towards carboxylic esters. However, if used in a large excess\(^5\)\(^9\), sodium borohydride will reduce carboxylic esters to alcohols and has the advantage of being a mild selective reducing agent in protic solvents.

Table 3 Sodium borohydride reductions of (120a)

<table>
<thead>
<tr>
<th>Temp.</th>
<th>Time</th>
<th>Solvent</th>
<th>Equiv. of NaBH(_4)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>64°C</td>
<td>2h</td>
<td>Methanol</td>
<td>10</td>
<td>(124) &amp; (126)*</td>
</tr>
<tr>
<td>R.Temp.</td>
<td>1h</td>
<td>Methanol</td>
<td>10</td>
<td>(124)* &amp; (126)</td>
</tr>
<tr>
<td>R.Temp.</td>
<td>5h</td>
<td>Ethanol</td>
<td>4</td>
<td>(124)* &amp; (126)</td>
</tr>
<tr>
<td>- 25°C</td>
<td>1h</td>
<td>H(_2)O</td>
<td>3</td>
<td>(120a) 65%</td>
</tr>
<tr>
<td>0°C</td>
<td>1/2h</td>
<td>Ethanol/ Methanol</td>
<td>8</td>
<td>(120a)* &amp; (124)</td>
</tr>
</tbody>
</table>

* Indicates major product by n.m.r. spectroscopy

Unfortunately, reductions of (120a) with sodium borohydride failed to selectively convert the ethyl ester into the desired alcohol (125), but instead the fully reduced material (124) was again isolated. Table 3 summarises the results of a number of reductions carried
out under a variety of conditions. Reductions at -25°C in water using only a 3-fold excess failed to give any reduction at all. When the reaction was carried out at 0°C in a methanol/ethanol solvent mixture, the starting material (120a) was recovered as the major product along with the fully reduced compound (124). It appears that there is no selectivity at all under these conditions between olefinic and ester reductions. Increased temperatures and prolonged reaction times also failed to produce (125) and led to a mixture of (124) and the fused furan derivative (126) (Scheme 49).

\[
\begin{align*}
\text{(120a)} & \quad \xrightarrow{\text{NaBH}_4} \quad \text{(124)} + \text{(126)} \\
\end{align*}
\]

Scheme 49

It was thought that the lack of selectivity of both sodium borohydride and lithium aluminium hydride might be overcome by using the lactone (127). It could be easily prepared from the acid\(^5\) (119) in high yields and reductions using lithium aluminium hydride would result in
the formation of the diol (128) (Scheme 50), thus alleviating the problems of the double bond reduction associated with the ester. Conversion of the diol (128) into the vinyl sulpholene (91) should proceed relatively easily.

Scheme 50
However, attempts to reduce this lactone using lithium aluminium hydride once again resulted in the isolation of (124). Clearly the ring opened carboxylic acid (119) exists to some extent in the reaction mixture and is being reduced by lithium aluminium hydride to (124).
C. PREPARATION OF [3] DENDRALENE FROM BUTADIENE SULPHONE

The preparation of [3] dendralene (5) in ca. 20% overall yield was eventually achieved using the route outlined in Scheme 51; starting from butadiene sulphone (106) which is a readily available cheap reagent.

The most convenient literature preparation of the epoxide (129) was by Sorenson\(^6\) who reacted butadiene sulphone (106) with performic acid. His yield of 30% was optimised to 42% in this work by prolonging the reaction times. However, it was felt that a more efficient preparation was required and with this in mind alternative oxidising agents were investigated. Meta-chloroperbenzoic acid was unsuitable because the starting material, butadiene sulphone (106) was always isolated in addition to the epoxide (129), despite attempts to improve product yields. When peracetic acid was used, once again the starting material (106) and 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide (130) were identified. This sulpholene (130) is formed presumably by the dehydration of the diol (131), and this diol has been reported as the oxidation product when acetic acid is used\(^6\) rather than the expected epoxide (129).
Scheme 51
In view of the lack of success in improving the epoxide product yields using these other reagents, performic acid was adopted as the reagent of choice for the oxidation of butadiene sulphone (106) albeit in low yields.

The next stage of the synthesis required the incorporation of a vinyl group by nucleophilic ring-opening of the epoxide (129) and this was achieved using vinylmagnesium bromide to give (132) in 83% yield. The brown viscous oily product (132) was found to be thermally labile when distillation was attempted. Fortunately it could be used crude, in the following step; an acetylation reaction.

The preparation of acetate (133) from (132) took place at room temperature using an excess of acetyl chloride and triethylamine. The crude brown oily material isolated, was purified by high vacuum sublimation onto a cold
finger. This procedure yielded the acetate (133) as a colourless solid in addition to another acetoxy compound identified as the minor product (134). When the reaction was carried out using 4-dimethylamino.pyridine (DMAP) as an acetylating reagent, the ratio of products (133) to (134) were identical to those in the previous experiment. This suggests that the precursor to (134) was present in the unpurified alcoholic material (132), and its conversion to (134) and may be explained by analysis of the previous vinylation.

The action of the Grignard reagent in this case has been predominantly a nucleophilic attack on the epoxide ring. If vinyl magnesium bromide also acts as a base, and abstracts a proton \( \alpha \) to the sulphone, this would lead to small amounts of the sulpholene (130) which in turn is acetylated. Alternatively, any unreacted epoxide (129) in the Grignard reaction may be hydrolysed in the acidic work-up to give the diol (131), and this diol is in fact
formed when the work-up procedure is carried out in the presence of the epoxide. This material (131) could then undergo base elimination as the hydroxy or acetoxy compound during the basic acetylation procedure. Fortunately, the impurity (134) could be separated from (133) using preparative thin layer chromatography. However, a more effective method of purification of the crude material was by flash chromatography which gave (133) in 61% yield.

As already mentioned in the introduction, f.v.p. is a widely used technique for the thermal elimination of small stable moieties. When the acetate (133) was subjected to f.v.p. at 650°C, acetic acid was eliminated to form only one isomer, the α,β-unsaturated compound (117). This result was somewhat unexpected as it was thought that conjugation with the substituted vinyl group would promote β,γ-elimination as discussed in Section B. Fortunately, (117) could be converted into the desired isomer (91) by the action of DBU at 40°C. Both acid catalysis and the use of Wilkinson’s catalyst failed in this respect.

The subject of β-eliminations of carboxylic esters, which was reviewed by De Puy in the sixties, is fairly well covered in the literature. These reactions generally involve flow pyrolysis techniques which incorporate nitrogen gas and sometimes columns packed with glass helices. Whilst there exists substantial differences in this technique compared to flash vacuum pyrolysis, it is
assumed that the reactions that take place in the gas phase, are of the same type.

The mechanism of carboxylic ester elimination has slowly become established over the last century, and incorporates a number of electronic and steric considerations. Some of these are relevant to the prediction of isomeric distribution and are discussed here as an aid to understanding the predominant formation of the 2-sulpholene (117) compound in this work.

Thermal elimination of a carboxylic ester requires a six-membered transition state generally with a cis co-planar \( \beta \)-hydrogen. If it is assumed that the disubstituted vinyl alcohol (132) and the acetate (133) are in a trans configuration (Fig. 9), these requirements are satisfied by both of the \( \beta \)-protons on the ester. Therefore based on this prerequisite alone, elimination is as likely in either position to give the 2- and 3-sulpholene derivatives (117) and (91).

![Fig. 9](image-url)
Another major consideration to be taken into account is the conjugative stabilization of the alkene product with its adjacent substituents. Once again both the vinyl group and the sulphone in (133) are available for \( \pi \) electron delocalization and the question which must be asked is whether the sulphone exhibits a greater stabilizing effect, or whether it is a matter of the acidity of the proton \( \alpha \) to the sulphone group which promotes this predominant elimination. The literature information on this subject is somewhat speculative. For example, Maccoll showed that the introduction of a \( \beta \)-carbonyl group increased the rate of ester pyrolysis by nearly 100-fold. He inferred that a ratio of conjugated-to non-conjugated products was greater than that expected based solely on \( \pi \) electron stabilizing effects, and that it reflected the acidity of the \( \beta \)-ester proton. Apart from some peripheral interest in the acidity of the \( \beta \)-ester proton, the extent of this effect mechanistically has not been adequately covered in the literature to date. Far more emphasis has been placed on the concept that isomeric distribution is favoured by the product's thermodynamic stability, and this is exhibited through conjugation with the activating group. This had been the general consensus until it was recently questioned by Taylor. He carried out an experimental elimination reaction of 1-(p-anisyl)-3-phenylprop-2-yl acetate (135). The products (136) and (137) were formed in a ratio of
1.1:1.0 (Scheme 52). On comparison of the isomers it is clear that the double bond of structure (136) is conjugated to the anisyl substituent. This isomer is the thermodynamically favoured one rather than (137) where the double bond is conjugated to a phenyl group only. The experimental results show an almost equal ratio for (136) to (137), and Taylor explains this as arising from a dominant kinetic influence. A much higher proportion of (136) would be expected from a thermodynamically controlled reaction.

\[
\begin{align*}
\text{An-CH}_2\text{CH-CH}_2\text{-Ph} & \quad \rightarrow \quad \text{An-CH=CH-CH}_2\text{-Ph} \\
\text{I} & \quad + \\
\text{OAc} & \\
(135) & \\
\end{align*}
\]

These findings support the predominant formation of sulpholene (117) as being the kinetically controlled isomer, when the properties of f.v.p. are considered.
Flash vacuum pyrolysis promotes unimolecular reactions which occur in very short contact times in the furnace, thereby virtually eliminating the possibility of bimolecular and surface catalysis. Furthermore, the fact that this isomer (117) is converted completely to the target sulpholene (91) in the presence of DBU indicates an isomerisation into a more thermodynamically stable material.

Stringent reaction conditions were required for this isomerisation reaction in order to isolate the desired isomer (91) in virtually quantitative yield. Excessive heating, prolonged reaction times or excess DBU resulted in an equilibrium favouring the conversion of (91) to the fully conjugated compound (138). Table 4 which summarises the isomeric ratios obtained by varying the reaction conditions, was used as a guide to the conditions which optimised the formation of (91).
Table 4 A study of the base catalysed isomerisation of vinyl sulphones

<table>
<thead>
<tr>
<th>Equiv. of DBU</th>
<th>Temp</th>
<th>Reaction Time</th>
<th>$^{13}$C n.m.r. isomeric ratio (138):(91):(117)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>65°C</td>
<td>4h</td>
<td>3 : 2 : 0</td>
</tr>
<tr>
<td>0.14</td>
<td>40°C</td>
<td>4h</td>
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</tr>
<tr>
<td>0.14</td>
<td>40°C</td>
<td>9h</td>
<td>Trace : 1 : 0</td>
</tr>
<tr>
<td>0.19</td>
<td>40°C</td>
<td>26h</td>
<td>1 : 6 : 0</td>
</tr>
<tr>
<td>0.09</td>
<td>40°C</td>
<td>24h</td>
<td>0 : 2 : 1</td>
</tr>
<tr>
<td>0.09</td>
<td>40°C</td>
<td>48h</td>
<td>1 : 2 : 1</td>
</tr>
<tr>
<td>0.05</td>
<td>17°C</td>
<td>90h</td>
<td>0 : 1 : 2</td>
</tr>
<tr>
<td>0.55</td>
<td>55°C</td>
<td>48h</td>
<td>4 : 1 : 0</td>
</tr>
<tr>
<td>0.38</td>
<td>24°C</td>
<td>24h</td>
<td>3 : 1 : 0</td>
</tr>
<tr>
<td>0.10</td>
<td>40°C</td>
<td>36h</td>
<td>0 : 1 : 1</td>
</tr>
<tr>
<td>0.13*</td>
<td>40°C</td>
<td>24h</td>
<td>0 : 1 : 0</td>
</tr>
</tbody>
</table>

These conditions provided the highest ratio of (91) and were ultimately used to carry out the isomerisation reaction.

The possibility of carrying out the elimination in solution was also considered using the tosyl derivative (139). This was prepared by heating (132) and p-toluene-sulphonyl chloride in pyridine to 60°C for 4.5h, although these conditions afforded only 11% yield of (139) (Scheme 53). Even when the reaction was tried at 0°C for 72h and 16°C for 72h, no tosylation took place and the starting
materials were recovered. A one-pot tosylation/elimination and possible isomerisation occurred when the alcohol (132), tosyl chloride and pyridine were heated to boiling. Under these conditions, the vinyl sulphone (91) was isolated in 7% yield after chromatography. It was interesting to note that the $\beta,\gamma$-isomer had been formed in solution in the absence of the $\alpha,\beta$-unsaturated sulpholene, which is in marked contrast to the gas phase pyrolysis of the carboxylic ester (133). To determine whether pyridine could have played a role in the isomerisation, (117) was heated to 60°C in pyridine for 6.5h. No isomerisation was detected, and so the reaction was repeated in boiling pyridine. At these high temperatures isomerisation did take place but it is still unclear whether elimination proceeds to give an $\alpha,\beta$-unsaturated isomer which then undergoes isomerisation to the $\beta,\gamma$-compound, or if the $\beta,\gamma$-product is formed directly.

\[ \text{HO} \begin{array}{c} \text{C}_5\text{H}_5\text{N} / \text{TsCl} \\ \text{60°C} \end{array} \begin{array}{c} \text{TsO} \\ \end{array} \begin{array}{c} \text{S} \\ \end{array} \begin{array}{c} \text{O}_2 \\ \end{array} \begin{array}{c} \text{139} \\ \end{array} \begin{array}{c} \text{C}_5\text{H}_5\text{N} / \text{TsCl} \\ \text{115°C} \end{array} \begin{array}{c} \text{S} \\ \end{array} \begin{array}{c} \text{O}_2 \\ \end{array} \begin{array}{c} \text{91} \\ \end{array} \begin{array}{c} \text{Scheme 53} \\ \end{array} \]
The mechanism behind these eliminations provides some stimulating speculation. However, as a step in a synthetic route to [3] dendralene, they suffer from a number of disadvantages. The products (139) and (91) are difficult to isolate due to the highly impure interactable materials which are also formed during the reaction. Furthermore, the elimination of tosylate from (139) requires temperatures which approach those of SO$_2$ extrusion in sulpholene derivatives, and this may account for the extremely low product yields. Whilst these solvent phase eliminations deserve further investigation, f.v.p. of (133) was adopted as the most efficient and convenient step in the route to the target vinyl sulpholene (91).

The final reaction in the synthetic strategy required chelotropic extrusion of SO$_2$ from (91). This took place readily using f.v.p. at 550°C and resulted in the formation of [3] dendralene (5), along with a small amount of a polymeric material. A subsequent flash distillation of the mixture gave pure [3] dendralene (5) as determined by high resolution $^1$H n.m.r., as a colourless oil in 87% yield. It became apparent that the triene (5) was far more stable than the literature had previously indicated$^2$; to the extent that it could be stored at -30°C for several months in the presence of a free radical inhibitor such as galvinoxyl. However, problems were encountered when [3] dendralene was left at room
temperature for any length of time. In the presence of galvinoxyl, self-cycloaddition occurred and this is discussed in Section E. In the absence of this free radical inhibitor, the triene (5) formed a brown interactable oily material which was presumably the product of its homopolymerisation.
The dendralenes are quite unique in their acyclic cross-conjunctive nature, and the study of their conformational structure from an experimental point of view, is an area that has only recently gained some interest. A number of spectroscopic analyses of [4] dendralene were carried out in these laboratories\textsuperscript{68}, but their structural assignments have been conflicting. On the other hand, [3] dendralene has remained somewhat neglected in this respect, and it was felt that further research into its conformation was warranted. Because of the structural similarities of the dendralene homologues, a study into [3] dendralene might also solve some of the anomalies that had developed with [4] dendralene.

The most sterically stable conformation of [4] dendralene is thought to be one where interaction between the endo-hydrogen is minimal and indeed a structure of this type has been proposed by Hopf\textsuperscript{2} (Fig. 10).

\begin{center}
\textbf{Fig. 10}
\end{center}
This non-planarity has been supported by U.V. spectral data whereby the absorption maximum for [4] dendralene (6) ($\nu_{\text{max}}$ 216.5) and 1,3-butadiene ($\nu_{\text{max}}$ 217) are almost identical, and suggests a conformation that consists of two individual butadiene units. Henry has expanded on this idea by describing (6) as two butadiene units in a trans-orthoganol arrangement, with a dihedral angle of 80.60° between the two planes and supported this proposal with ab initio quantum mechanical calculations (Fig. 11).

![Fig. 11]

Henry also compared the proton n.m.r. spectra of isoprene with [4] dendralene and found a similarity in their coupling constants. Furthermore, the ionization potentials, Raman and infrared spectral data of [4] dendralene and 1,3-butadiene were also found to be alike, pointing to the trans-orthoganol structure described above. Electron diffraction analysis however proved to be
the exception by conflicting with the theoretical calculations. The structure derived from electron diffraction data was consistent with the X-ray structure for the pentalene system, illustrated in Fig. 12.

As mentioned earlier, these discrepancies have remained unresolved and it was thought that some insight into this problem might be found from a study of the lower homologue [3] dendralene (5). Current literature regarding the structure although sparse, does tend to support a non-planar conformer. Ab initio calculations by Norinder\textsuperscript{70} have described the structure of [3] dendralene as having primarily a cis-trans arrangement as opposed to cis-cis or trans-trans (Fig. 13). More precisely, it is believed to exist as a trans butadiene
moiety with an orthogonal vinyl substituent that is twisted 40° (Fig. 14). Whilst the author concedes a planar structure would achieve stability through maximum p-orbital overlap, calculations show that the steric hindrance between hydrogens, makes the non-planar structure energetically favoured.
Hopf\textsuperscript{2} also proposed a twisted structure for [3] dendralene (5) based on both the steric interaction of the endo-hydrogens and on U.V. data. The absorption maximum for [3] dendralene (\(\nu_{\text{max}} 224\))\textsuperscript{8,9} and 1,3-butadiene (\(\nu_{\text{max}} 217\))\textsuperscript{69} are so similar they too suggest related structures. More importantly, however, was the reasoning that \(\nu_{\text{max}}\) for [3] dendralene was lower than that expected for a fully conjugated material, and is explained as a loss of p-orbital interaction due to a non-planarity.

A comparison of the proton n.m.r. data for [3]- and [4] dendralene\textsuperscript{68} together with the substituted butadiene; isoprene\textsuperscript{68} is given in Table 5. It can be seen that very little difference exists in the coupling constants, particularly between [3] dendralene and isoprene.

Table 5 A comparison of proton-proton n.m.r. coupling constants

<table>
<thead>
<tr>
<th></th>
<th>(2J)</th>
<th>(3J)</th>
<th>(4J)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1,1)</td>
<td>(5,6)</td>
<td>(4,6)</td>
</tr>
<tr>
<td>Isoprene</td>
<td>1.70</td>
<td>1.25</td>
<td>10.76</td>
</tr>
<tr>
<td>[4] dendralene</td>
<td>2.33</td>
<td>1.51</td>
<td>10.51</td>
</tr>
<tr>
<td>[3] dendralene</td>
<td>1.78</td>
<td>1.51</td>
<td>10.89</td>
</tr>
</tbody>
</table>
Table 6 illustrates a similar comparative study of the coupled $^{13}$C n.m.r. spectra of [3] dendralene and isoprene. The assignment of the coupling constants for isoprene were based on a carbon-hydrogen correlation which was carried out to distinguish between the two CH$_2$ resonances, A and B. This in turn enabled the coupled carbon-hydrogen spectra to be interpreted. As it can be seen from Tables 5 and 6, very little difference in coupling constant values are observed between isoprene and [3] dendralene, and this also suggests a related butadiene type conformation for the triene for (5).

Table 6 A comparison of carbon-proton one bond coupling constants

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(B, H$_1$ and H$_1$')</td>
<td>156</td>
<td>158</td>
</tr>
<tr>
<td>(C, H$_4$)</td>
<td>153</td>
<td>154</td>
</tr>
<tr>
<td>(A, H$_5$ or H$_6$)</td>
<td>159</td>
<td>159</td>
</tr>
<tr>
<td>(A, H$_5$ or H$_6$)</td>
<td>155</td>
<td>155</td>
</tr>
</tbody>
</table>
The structural question was far from resolved when a Raman and infrared spectra was obtained by Dr. Stephen Cradock at the University of Edinburgh. The experimental data is given in detail in the experimental section but several points should be highlighted. There is a definite distinction between the polarised and non-polarised absorbances, which is indicative of a structure possessing some degree of symmetry. This is strikingly evident in the c=c stretch at 1600-1650 cm\(^{-1}\) which exhibits a depolarised band at the highest frequency, a strongly polarised band and a weakly polarised band. These are assigned to the three c=c stretching modes and are consistent with a two fold axis of symmetry (Fig. 15). The results of these studies have given rise to the structure described by Fig. 16, which approaches co-planarity by having a dihedral angle of approximately 25° either sides of the central double bond. This angle is the deviation necessary to bring the endo-hydrogens 2Å apart (the sum of Van der Waals radii), and only reduces the conjugation to a factor of 0.9. A structure such as that given in Fig. 14, consisting of a planar butadiene and a twisted vinyl substituent would result in a loss of p-orbital overlap to a factor of 0.5.

$\nu_{c=c}$

Polarised

Fig. 15

1700  1500  1300

units cm$^{-1}$
It now appears that the conflicting structural elucidation problems between the theoretical calculations and the electron diffraction results for [4] dendralene, have not been resolved through the study of [3] dendralene. Once again theoretical calculations are not in agreement with the experimental results. The interpretation of the Raman spectra dismisses any possibility of conformational planarity and yet a comparison of the n.m.r. spectra for (5) and isoprene, shows remarkably similar couplings. Theoretical calculations are also at odds with the Raman spectroscopic results and it therefore seems that before
any conclusions can be drawn, additional experimental information is required. For example, an electron diffraction study of [3] dendralene or microwave analysis. Maybe then the structures of these interesting polyenes can be solved.
E. CYCLOADDITION REACTIONS OF [3] DENDRALENE

1. Preparation of Mono- and Bis-adducts of [3] Dendralene

As previously discussed in the Introduction, [3] dendralene and indeed the dendralenes as a class of compounds, possess cross-conjugation which enables them to participate in diene-transmissive multiple annulations (See Scheme 14). The extent of these reactions has not been examined and the study of [3] dendralene in this role, is limited to only a few examples. An obvious need existed to look further into this type of reaction using a range of dienophiles.

To date only the bis-adducts\textsuperscript{8} of the parent [3] dendralene and several ladder polymers\textsuperscript{3,6} have been reported and details of these can be found in the Introduction, Section B. In order to expand the scope of these reactions, [3] dendralene was reacted with 2 molar equivalents of the highly dienophilic 4-phenyl-1,2,4-triazoline-3,5-dione (63) to give the bis-adduct (140) in 21\% yield (Scheme 54).

A similar reaction of (5) with maleimide (141) also yielded a bis-adduct in 65\% yield, in a highly stereoselective manner. The product was found to be only the one isomer (142), having two fused maleimide rings on opposite faces of the napthalenic ring and the ring fusion proton, \textit{anti} to the adjacent maleimide ring.
The structural elucidation of (142) was not a simple task, and required the use of COSY and NOE n.m.r. techniques. Fig. 17 illustrates the expanded 2-dimensional COSY spectrum of the aliphatic protons, along with their assignments. A more detailed interpretation of the H-H correlation may be found in the experimental section. Whilst the COSY experiment was necessary to interpret the proton spectra, in order to determine the stereochemistry of the structure, NOE experiments were required. These were carried out by Dr. Ian Sadler on a number of proton resonances and the
Fig. 17
Table 7  A study of the NOE effects in (142)

<table>
<thead>
<tr>
<th>Proton irradiated</th>
<th>Enhancement</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6a</td>
<td>6A</td>
<td>6B</td>
<td>5</td>
<td>10A</td>
<td>10B (3a &amp; 4A)</td>
<td>10a</td>
<td>9a</td>
</tr>
<tr>
<td>10a</td>
<td>½%</td>
<td>1⅔%</td>
<td>1⅔%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10A</td>
<td>9%</td>
<td>1%</td>
<td>⅔%</td>
<td>2%</td>
<td>1⅔%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4B</td>
<td>2⅔%</td>
<td></td>
<td>1%</td>
<td>6%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6a</td>
<td>⅔%</td>
<td>4%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9a</td>
<td>4%</td>
<td></td>
<td>1⅔%</td>
<td>3%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

enhancements observed, are given in Table 7. Evidence supporting the structure (142) was obtained directly by the irradiation of H$_{10a}$. This led to an enhancement of H$_{10b}$ and H$_{10A}$ suggesting these protons are on the same face. Similar irradiation of H$_{9a}$ resulted in a 3% enhancement of H$_{10B}$ and only 1⅔% of H$_{10A}$, indicating the bridging protons H$_{6a}$ and H$_{9a}$ to be on the oppositive face to H$_{10A}$. 
In conjunction with the n.m.r. spectral investigations, a computer aided molecular modelling program called Alchemy II was employed. This package, supplied by Tripos and Associates Inc., allows the 3-dimensional construction of molecular structures. Its options include bond length and bond angle variations, and the co-ordinates may also be modified to obtain the lowest energy geometries. In order to simplify the task of using the Alchemy II program, the four possible diastereomeric cycloadducts (142)-(145) were carefully considered.
Structures (142) and (143) were then selected as the isomers most likely to be formed. This was based on the absence of the pronounced steric interaction, which is experienced by the maleimide rings of structures (144) and (145). With the aid of molecular modelling, the conformation of minimum energy was determined and the bond angles of these conformers were used to estimate coupling constants from a Karplus curve. Table 8 summarises these constants for the theoretical structures (142) and (143) and compares them with the actual coupling constants for the isolated material. On examination of Table 8, it can be seen that these values are very similar for the theoretical structure (142), and those obtained experimentally. On the other hand, (143) does not correlate as well with the experimental values and it is apparent from these results that the molecular modelling has supported the spectroscopic assignments of the product (142). However, it should be noted that the modelling program and the COSY experiment were not sufficient alone to ascertain the structure of (142) and an NOE experiment was necessary.
Table 8 Comparison of theoretical and experimental coupling constants in Hz.

<table>
<thead>
<tr>
<th>Coupled Proton</th>
<th>10A</th>
<th>10B</th>
<th>6B</th>
<th>6A</th>
<th>9a</th>
<th>6a</th>
<th>4B</th>
<th>4A</th>
<th>3a</th>
<th>10a</th>
<th>5</th>
</tr>
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<tbody>
<tr>
<td>10A (i)</td>
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<td>2.2</td>
<td>9.7</td>
<td>15</td>
<td>2.4</td>
<td>2.2</td>
<td>9.7</td>
<td>15</td>
<td>2.4</td>
<td>2.2</td>
<td>9.7</td>
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<td>(ii)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10B</td>
<td>6</td>
<td>7.6</td>
<td>9.7</td>
<td>14</td>
<td>2</td>
<td>0.6</td>
<td>0.3</td>
<td>6</td>
<td>2</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>6B</td>
<td>2</td>
<td>0.6</td>
<td>0.3</td>
<td>6</td>
<td>9.5</td>
<td>5.7</td>
<td>7.6</td>
<td>0.8</td>
<td>9.7</td>
<td>5.7</td>
<td>7.6</td>
</tr>
<tr>
<td>6A</td>
<td></td>
<td>6</td>
<td>9.5</td>
<td></td>
<td>3.8</td>
<td>9</td>
<td>6</td>
<td>6</td>
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<td>9</td>
</tr>
<tr>
<td>9a</td>
<td>2</td>
<td>2.2</td>
<td>0.8</td>
<td>9.7</td>
<td>6</td>
<td>3.8</td>
<td>6</td>
<td>6</td>
<td>9</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>6a</td>
<td>2</td>
<td>6.6</td>
<td>9.7</td>
<td>0.6</td>
<td>0.3</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>9</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>4B</td>
<td>4</td>
<td>4.2</td>
<td>9</td>
<td>7.4</td>
<td>7.5</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>5</td>
<td>5.5</td>
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<tr>
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<td>7.4</td>
<td>7.5</td>
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<td>9</td>
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<tr>
<td>3a</td>
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<td>9</td>
<td>9</td>
<td>9</td>
<td>5</td>
<td>5.5</td>
<td>9</td>
</tr>
</tbody>
</table>

(i) Experimental coupling constants  
(ii) Coupling constants for structure (142)  
(iii) Coupling constants for structure (143)  
* Where large differences in coupling between (i) and (ii) exist.
The pronounced stereoselectivity experienced in the aforementioned Diels-Alder addition, has also been found using other [3] dendralene type compounds. For example the isomers (146a) and (146b) were isolated as the only stereoisomers of the cycloaddition reaction between the dendralene (147) and maleimide (141) when the reaction was carried out at room temperature (Scheme 55).

This remarkable stereoselectivity was explained by a preferred "endo type" addition which experienced a lower energy to that for the exo-transition state; due to secondary orbital interactions. Furthermore, cycloaddition of the second maleimide, which took place exclusively on the side opposite to the first maleimide ring, was attributed to the interaction of the cyclohexyl hydrogens as indicated in Fig. 18.
It has already been mentioned in the Introduction how Bailey and Economy reacted [3] dendralene with maleic anhydride to afford the bis-adduct (40). The corresponding reaction of (5) with 2 molar equivalents of benzoquinone was also found to give the bis-adduct (41). However, when the reaction was repeated in this work using an equimolar amount of benzoquinone, the crude mono-adduct (148) was isolated in 90% yield. In another experiment (148) and (41) were formed as a mixture when the reaction was carried out in a sealed tube at 60°C. The results of these reactions show how careful control of the conditions can lead to a predetermined selectivity, and this was put to use by preparing the mono-adduct (148) and then reacting it with N-phenyl-1,2,4-triazoline-3,5-dione (63).
Scheme 56
The product of this cycloaddition was the mixed bis-adduct (149) (Scheme 56).

A similar selectivity was exhibited by the cycloaddition of (5) to DMAD. The reaction was carried out with both an equimolar amount, as well as an excess of dienophile at 60°C for 5h and 36h, respectively. In each case only the mono-adduct (150) was formed in 80% yield. It was only when the reaction was carried out in a sealed tube at 70°C for 72h that the bis-adduct (151) could be isolated.

Tetracyanoethylene (TCNE), which is known to be a reactive dienophile, was treated with (5) and formed only the mono-adduct (152) in 92% yield after purification. The failure of this adduct to undergo a second Diels-Alder addition is not clear; although steric factors may be responsible (vide infra). By comparison, maleic anhydride which has been shown to be less reactive than TCNE with a number of dienes, forms the bis-adduct readily. Furthermore DMAD which also is considerably less reactive than TCNE, also undergoes a double cycloaddition. Despite the failure of the mono-adduct (152) to react with a second equivalent of TCNE, it did undergo cycloaddition with the very reactive triazoline dione (63) to form the tricyclic compound (153). This does suggest that cyclic dienophiles are significantly more reactive towards bis-annulation in this case, than the acyclic olefins.
Tsuge and workers\textsuperscript{24} also experienced this lack of reactivity towards bis-annulation with acyclic dienophiles, particularly when they reacted an excess of DMAD with the dendralene (154) in boiling benzene. They isolated a complex mixture of regioisomers and mono- and bis-annulated adducts; partly and fully aromatised (Scheme 57).

\begin{equation}
\text{Scheme 57}
\end{equation}
The inherent selectivity found in [3] dendralene towards some dienophiles, makes this polyene extremely useful in organic synthesis. It allows not only the formation of varied mono- and bis-adducts but also incorporates a significant degree of versatility into the cycloaddition reaction. This apparent selectivity towards the first addition may be explained to some extent by a frontier molecular orbital approach.

Since Woodward and Hoffmann publicised their rules for pericyclic reactions, the frontier orbital theory has been used to explain many of the chemical and stereochemical properties of [4+2] cycloaddition reactions. The theory is concerned only with the interaction of the reacting orbitals of the diene and dienophile. For example the highest occupied molecular orbital (HOMO) of butadiene and the lowest unoccupied molecular orbital (LUMO) of ethylene and vice versa (Fig. 19). It can be seen that this reaction is symmetry allowed because the combination involves orbitals of the same sign. The general concertedness of these reactions means that the stereochemical characteristics of the reactants are handed down to the resultant products.

The influence of activating substituents on both the diene and dienophile was realised as the "Alder rule" in the fifties and is marked by an increase in reaction rate when the dienophile contains electron-withdrawing groups. In terms of an FMO approach, the effect of adding
a withdrawing substituent lowers the energy of both the HOMO and LUMO. On the other hand, an electron-donating substituent raised the HOMO and LUMO energies, whereas conjugating substituents raise the HOMO energy and lowers the LUMO. The rate of reaction is increased when $E_{\text{LUMO}} - E_{\text{HOMO}}$ is smallest. This can be most easily illustrated

**Butadiene**

Fig. 19
in Fig. 20 which compares the energy difference between butadiene and substituted alkenes. It is clear that electron-withdrawing groups on the dienophile bring the LUMO closer to the diene HOMO and the effect is more pronounced when electron-donating groups are present on the diene. Similarly, electron-donating substituents on the alkene and electron-withdrawing groups on the diene also affect a reduced energy difference; and this is an example of inverse electron demand.

\[ \text{HOMO} \rightarrow \text{LUMO} \]

\[ Z = 'e' \text{ withdrawing} \]
\[ X = 'e' \text{ donating} \]
\[ C = \text{conjugating} \]
Without experimental and theoretical evidence, a study of the HOMO and LUMO interactions between [3] dendralene and the dienophiles described in this work, cannot be realistically carried out. Furthermore, the energy data which is available in the literature would have come from a number of sources and would not provide a suitable basis for comparison. However, even in the absence of quantitative energy values one can detect very definite reactivity trends of these dienophiles. These are listed in order of decreasing reactivity along with their theoretical source in Fig. 21. An examination of this activity series shows a good correlation with the reactivity of [3] dendralene towards annulations experienced in this work. This is particularly evident in the preferential formation of bis-adducts with the more
reactive cyclic dienophiles such as the triazoline compound (63), maleimide (141) and maleic anhydride. Acyclic compounds do not undergo cycloaddition with (5) as readily and benzoquinone which is considered one of the least reactive dienophiles in this series, cycloadds selectively to form mono- or bis-adducts. The exception to this trend is TCNE, which preferentially forms the mono-adduct and may be influenced by factors other than electronic and substituent effects in the second cycloaddition reaction. The possibility of a steric interaction between the incoming TCNE molecule and the mono-adduct (152) was examined using molecular modelling. The results of this study clearly showed the unlikelyhood of the approach of the second dienophile preventing cycloaddition from taking place. Whilst molecular modelling apparently negates steric interactions, these results should not be considered conclusive as the effect of non-bonding interactions may also be a contributing factor. A similar situation has been observed in the reaction of 2,4-dimethyl-3-methylene-1,4-pentadiene (155) with TCNE which gave only the mono-adduct (156) even in the presence of excess reagent (Scheme 58).
The preparation of mixed bis-adducts required firstly the selective mono-annulation of [3] dendralene. This preference for the first cycloaddition may also be explained by a FMO approach. The HOMO and LUMO of a planar [3] dendralene have been calculated by Kahn et al as -195 and 67 kcal mol\(^{-1}\), respectively. When compared to butadiene with a HOMO of -204 and LUMO of 78 kcal mol\(^{-1}\), it can be seen that the effect of the conjugating group is to raise the HOMO and lower the LUMO energies (Fig. 22); thus making the energy gap smaller. When [3] dendralene undergoes the first addition the presence of a vinyl substituent compacts the energy levels resulting in an easier reaction. The conjugative influence is not present in the second cycloaddition and therefore the reaction proceeds at a reduced rate. The formation of the mono-adducts (148) and (150) from quinone and DMAD show that the reactivity of the first cycloaddition is
significantly greater than the second cycloaddition and that the second annulation takes place only in the absence of unreacted [3] dendralene.

Fig. 22

In addition to the Diels-Alder reactions carried out with [3] dendralene, the reactivity of the diene group of the vinyl sulpholene (91) toward annulation was also investigated. It was found that (91) underwent cycloaddition with the highly reactive triazoline dione (63) to afford the tricyclic compound (223) in 64% yield.
However, an attempt to react (91) with maleic anhydride proved to be unsuccessful. Based on these results it would appear that the diene of (91) is relatively unreactive.


It was mentioned earlier that [3] dendralene may be stored at low temperatures in the presence of galvinoxyl, a free radical inhibitor. In sharp contrast, at room temperature dimerisation occurs readily to yield a colourless oil. The presence of a dimeric material was first noted by Bloomquist and Verdol who predicted one of four possible isomers (Fig. 23). However, in the absence of modern spectroscopic techniques they were unable to determine its structure. Until the start of this current work, the structure of the dimer had remained unsolved,
and it was thought that its elucidation would prove to be an interesting problem. The approach that was adopted used the FMO theory to predict the isomeric structure and this was then supported by spectroscopic analysis.

On examination of the interacting frontier orbitals of the four possible isomers (157)-(160), dimers (159) and (160) were selected as being the most likely structures. This was based on the substituent effect of the "dienophile" and may be explained as follows. In the formation of the dimer irrespective of its structure, one
molecule of dendralene acts as a diene and the other as a dienophile. There are two dienophilic possibilities using [3] dendralene. One with a butadiene substituent (a) and (b) or the other with a divinyl substituent (c) and (d) (Fig. 24). Whilst the conjugation provided by a butadiene group compacts the frontier orbital energy, the effect is enhanced in a divinyl substituent and therefore this addition is favoured, leading to products (159) and (160). This reasoning was confirmed from the $^{13}$C n.m.r. data for the isolated dimer. It showed the occurrence of only one product which could only be interpreted as either (159) or (160).

![Fig. 24](attachment:figure24.png)
In order to predict the regiospecificity of the dominant isomer (159) or (160) the orbital coefficients of their frontier orbitals were considered. These coefficients represent a polarization of the orbital which is largely dependent on the substituent.

Fig. 25
The regioselectivity was determined by the interaction of orbitals with the most equivalent coefficients. Fig. 25 shows how the LUMO of the olefin and HOMO of the diene interact to give a para-substituted product and likewise with the LUMO of the diene and the HOMO of the dienophile. If we imagine "c" to be a vinyl group in [3] dendralene it is apparent that the para product is the most likely.

'H N.m.r. spectroscopy was inadequate for the determination of the regio-chemistry due to the close proximity of the aliphatic hydrogens. Because the product was an oil a crystal structure was also ruled out. A crystalline derivative seemed to be a viable alternative and so the dimer was reacted with tricarbonyl(benzylideneactone)iron (161) in an attempt to form the adduct (162) or (163) by an iron carbonyl exchange (Scheme 59). Fairly harsh conditions were required and these involved heating the dimer and (161) in toluene at 55°C for 10h and then to 85°C for a further 18h. Subsequent chromatography of the reaction mixture over silica failed to give the expected iron tricarbonyl complexes (162) or (163). Instead a material that appeared by 13C n.m.r., 'H COSY and NOE experiments to be the iron dicarbonyl complex, was obtained as an orange viscous oil. This interesting result indicated that one of the vinyl substituents had coordinated to the iron as part of a 6π system. On first appearance the prospect of an iron dicarbonyl species such as (164) seemed somewhat surprising in view of the
conformation that the cyclohexene ring must adopt in order to accommodate this structure. However, a Dreiding molecular model using the bond lengths and angles from a similar structure\(^{31}\) (165), showed the formation of this complex (164) to be quite feasible. Furthermore, a comparison of the iron dicarbonyl complex (165) with structure (164) of this work, clearly indicated a number of structural similarities (Fig. 26).
Apart from a complex such as (164) which accepts the 6 \( \pi \) electrons from the one molecule, a dimer is also equally possible. This complex would have the diene of one cyclohexene coordinating to the iron, together with the vinyl substituent of a second molecule in a parallel head to tail type arrangement (Fig. 27).
It still remains unclear whether the complex is monomeric or dimeric in nature. X-ray crystallography would provide the structural details necessary to define the iron complex, but attempts to crystallise the compound have so far met with failure. FAB mass spectrometry was also unhelpful in the detection of the presence of possible dimers.

Returning to the problem of the regiospecificity of the original dendralene dimerisation, it was mentioned earlier that through n.m.r. techniques the iron complex was determined to be (164). Therefore the original dimer must have been the para type compound (159), as predicted by FMO theory. The interpretation of the proton n.m.r. spectrum required a two dimensional COSY which is given in Fig. 28 along with the structural assignments. The
salient points in the interpretation were firstly the unique vinyl group, with characteristic low field chemical shifts. Protons $H_5$ and $H_6$ were outstanding by their complexity such that each proton was part of a four nuclei system. $H_2$ could be distinguished from the other resonances by having two equivalent coupling constants of 15 Hz suggesting a geminal arrangement, and also by having a negligible coupling to $H_3$. These assignments were confirmed and refined by an NOE experiment which is summarised in Table 9. The resonance $H_{6\alpha}$ could be determined by its proximity to $H_C$, and also to $H_{5\alpha}$ to a lesser extent. Similarly, $H_{6\beta}$ was enhanced by irradiating $H_{2\beta}$ indicating the $\beta$ protons are on the same face of the cyclohexane. The vinylic geminal type arrangements of $C_C$, $C_t$, and $B_t$, $B_C$ were also confirmed.
Table 9  Selected proton irradiations for the study of the NOE effect in structure (164)

<table>
<thead>
<tr>
<th>Proton irradiated</th>
<th>Enhancement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>C</td>
<td>2%</td>
</tr>
<tr>
<td>B</td>
<td>2%</td>
</tr>
<tr>
<td>B_t</td>
<td></td>
</tr>
<tr>
<td>C_C</td>
<td></td>
</tr>
<tr>
<td>2β</td>
<td></td>
</tr>
<tr>
<td>2α</td>
<td></td>
</tr>
<tr>
<td>C_t</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

The derivatisation of the dendralene dimer has solved the problems of structural elucidation and brought to light some interesting and unusual aspects of iron carbonyl coordination. In retrospect, it seems possible that additional heating of the reaction mixture to 85°C
may well have promoted the olefinic replacement of the third carbon monoxide moiety. Furthermore, a crystal structure of the iron dicarbonyl molecule would ascertain the monomeric or dimeric nature of the complex, and the formation of suitable crystals may well be a question of alternative reagents and purification procedures. These questions provide a stimulating topic for further investigative research.
F. ATTEMPTED ROUTE TO 3-FORMYL-2,5-DIHYDROTHIOPHENE-1,1-DIOXIDE

The most significant outcome of the aforementioned studies into the properties and reactivities of [3] dendralene, is that these polyenes exhibit appreciable synthetic potential not only to annulate, but to do so selectively. This ability is not restricted to the parent compound (5), and Section B of the Introduction gives several examples where dendralene derivatives have been incorporated into annulation reactions. The preparation of these derivatives is varied, ranging from thermal rearrangements to metal mediated reactions and it appears that to date, a simple general route to these compounds has not been developed. The success of the synthesis of [3] dendralene in this work, which incorporates chelotropic extrusion from the sulpholene material (91), provided the incentive to design a route to dendralene derivatives, using a similar sulpholene precursor (166). Provided this route was simple, and enabled structural variability in the precursor (166), subsequent f.v.p. should yield the desired dendralene (182) (Scheme 60). It is important to note, that this route should have the flexibility to allow for these dendralene compounds to be customised for further use.
In order to prepare a compound such as (166) a number of modifications on the basic sulpholene structure had to be carried out. Firstly, a method was required which enabled the substitution of alkyl groups onto the ring itself. It was thought that this could be achieved by exploiting the acidity of the carbon α to the sulphone group, which in the presence of base undergoes alkylation by substitution. Some examples of this type of reaction have already been given in the Introduction. In addition to a modification of the ring, a method which alters the vinyl substituent was also needed. One possibility was to prepare a carbonyl compound such as (168). The carbonyl group could then be converted to an olefin using a Wittig reaction as outlined in Scheme 61. By utilising this phosphine ylid, the choice of vinyl substituents would be
large enough to ensure versatility in the preparation of the final dendralene derivative (182).

\[
\text{R} \quad + \quad (\text{Ph})_3\text{P} - \text{C} \quad \xrightarrow{\text{f.v.p.}} \quad \text{S} \quad \begin{array}{c}
\text{O} \\
\text{S} \\
\text{O} \\
\text{O}
\end{array}
\]

Scheme 61

Armed with a choice of strategies for modifying the butadiene sulfone, emphasis was placed on the preparation of the carbonyl derivative (168) rather than the alkylation of the sulfophane ring. This was mainly because substitution of alkyl groups onto the ring was a task that could be carried out during the synthesis of the carbonyl compound (168). In addition to this, it was felt that by preparing (168), its subsequent pyrolysis may
yield the carbonyl analogue (167), which is as yet unknown (Scheme 61).

1. Isoxazoline Derivatives

The subject of 1,3-dipolar additions in the preparation of organic compounds is vast, and covers many aspects of mechanistic and synthetic chemistry. Of particular interest to this work, is the role of nitrile oxides in their reactions with dipolarophiles. These compounds exhibit a broad affinity towards olefinic materials and undergo dipolar cycloaddition reaction to form isoxazolines. One example of this type of reaction is the regioselective addition of 2-sulpholene to benzonitrile oxide which affords the fused thienoisoxazoline (169) almost exclusively (Scheme 62).

\[
\begin{align*}
\text{PhNCO} & \quad \xrightarrow{\text{Scheme 62}} \\
\text{Ph} & \\
\text{N} & \\
\text{S} & \\
\text{O} & \\
\text{S} & \\
\text{O} & \\
\text{N} & \\
\text{S} & \\
\text{O} & \\
\text{O} & \\
\text{N} & \\
\text{S} & \\
\text{O} & \\
\end{align*}
\]

(106) \quad (169)

Scheme 62
The heterocyclic isoxazoline ring acts as an intermediate to a range of open chain and cyclic multifunctional compounds. Depending on the choice of reagents, they provide access to \( \gamma \)-amino alcohols, \( \beta \)-hydroxy ketones as well as unsaturated oximes. Their application to natural product chemistry has met with increasing interest over the years and this is particularly evident in the work carried out by Kozikowski. In the continuing study of these heterocycles, Kozikowski and Stein demonstrated their applicability in the construction of the cyclopentanoid, sarkomycin (170). Their synthesis involved the formation of a nitrile oxide by treatment of (171) with para-chlorophenylisocyanate and catalytic triethylamine. The dipolar moiety of (171) then underwent an intramolecular cycloaddition to its olefinic group, thus forming the isoxazoline (172). Reductive cleavage of the N-O bond by hydrogenation over W-2 Raney nickel, gave the \( \beta \)-hydroxy ketone (173). The final step which was the elimination of the hydroxy group, afforded the natural product sarkomycin (170) (Scheme 63).

Another example of the intermediacy of isoxazolines in organic synthesis has been described by Burri et al. in their route to vermiculine. The salient step involved a diisobutylaluminiumhydride (DIBAH) reduction of the
pendant isoxazoline (174), to give a racemic mixture of the ring opened γ-amino alcohol (175) (Scheme 64).

Scheme 64
With this approach in mind a similar strategy was proposed for the preparation of the carbonyl derivative (168). It was thought that a 1,3-dipolar addition of benzonitrile oxide to 3-sulpholene (106) would afford the fused isoxazoline (176). This could then undergo reductive ring cleavage to yield the β-hydroxy ketone (177) and this compound in turn, should lead to the target molecule (168) by elimination of the hydroxy group (Scheme 65). A major advantage of using this route, was the potential to change the ultimate keto-substituent by choosing different nitrile oxides.

![Diagram of the reaction](attachment:reaction_diagram.png)

Scheme 65
The isoxazoline (176a) was successfully prepared as a colourless solid in 29% yield by the 1,3-dipolar cycloaddition of benzonitrile oxide with butadiene sulphone (106). One of the major problems with these 1,3-dipolar additions is the formation of dimeric nitrile oxide by-products (178) and (179) due to the highly reactive nature of these transient dipolar species. In order to minimise the formation of the furoxan (178) and (179), a 3.6 fold excess of butadiene sulphone was employed. In addition to this, a perfusor was used to slowly add a solution of benzohydroximoyl chloride, over a period of 42h to a basic solution of the dipolarophile (106). Both of these measures insured a high local concentration of butadiene sulphone about the nitrile oxide, and by carrying out the reaction in this way, the presence of these dimeric by-products was virtually eliminated.

\[ \text{(178)} \]

\[ \text{(179)} \]
The next step involved the reductive hydrolytic cleavage of the isoxazoline ring and several attempts using acidic palladium on charcoal failed to yield the \( \beta \)-hydroxy ketone (177). Amongst the complex mixture of products which were formed in each case, the \( \gamma \)-hydroxy amine (180) was detected, and a possible explanation may be found by considering the mechanistic aspects of the reaction. In the ring scission route to the \( \beta \)-hydroxy ketone, the N-O bond is firstly cleaved to give the \( \beta \)-hydroxy imine. This unstable compound, in the presence of aqueous acid, is immediately hydrolysed to the ketone. It appears that the hydrogenation of the N-O bond in (176) did not stop at the imine stage but rather was reduced all the way to the amine (Scheme 66). Increasing the acidity of the reaction mixture by replacing boric acid with hydrochloric acid, did not improve the situation.

Scheme 66
An alternative approach to the isoxazoline N-O ring cleavage was developed by Grund and Jager⁸. In their procedure the N-O bond is cleaved by base to give the oxime and this is then converted to the β-hydroxy ketone by titanium (III) chloride. In the application of their route to the preparation of (168) in this work, the isoxazoline (176) was converted into the benzaldoxime (181) in 41% yield by reaction with lithium-diisopropylamide (LDA) (Scheme 67). Subsequent treatment of (181) with a solution of acidic titanium(III) chloride resulted in a highly complex mixture of products. The starting material (181) and the eneone (168) could be detected but only by high resolution mass spectrometry.

Scheme 67
Fairly recently Baraldi and workers reported a smooth cleavage of the N-O bond to give the corresponding β-hydroxy ketone using molybdenum hexacarbonyl. When this reagent was mixed with a two fold excess of the isoxazoline (176) in wet acetonitrile, the eneone (168) was isolated in 36% yield together with unreacted starting material (176). With a large excess of molybdenum hexacarbonyl, total conversion of the starting material occurred to give the eneone (168) and the β-hydroxy ketone (177) (Scheme 67). Purification was carried out over silica and two fractions were isolated. The first band consisted of the dehydrated product (168) and the second band was identified as a mixture of (177) and the eneone (168). It seems that dehydration of (177) occurs to some extent during the purification procedure.

It is apparent from this investigation that the 1,3-dipolar addition of benzonitrile oxide to butadiene sulphone provides a route to fused thienoisoxazolines. Similarly, the carboethoxy isoxazoline (176b) was also prepared in this work in 18% yield. However, the ease of these preparations is severely marred by the ring opening step, which suffers from excessive by-products, making purification difficult and yields low. Perhaps further research into the reductive cleavage of these isoxazolines may lead to some more encouraging results.
2. "Umpolung" Using 1,3-Dithiane

Umpolung reactivity of carbonyl compounds was recognised in the utilization of lithiated 1,3-dithianes (183) which undergo nucleophilic addition as masked acyl anions. The anion (183) which is generated by the action of a strong base such as butyllithium (n-BuLi), is reacted with a suitable alkyl halide to yield an alkylated dithiane derivative (184). In the presence of a second mole of base, the tertiary anion (185) is formed and may then undergo a second nucleophilic addition to give (186) (Scheme 68). The S,S-acetal derivatives can then be converted into a carbonyl compound (187), by hydrolysis with mercury (II)\textsuperscript{[89]}.

![Scheme 68](image-url)
It was hoped that this versatile synthon might provide a simple method of formylating the sulpholane ring as outlined in Scheme 69. According to this scheme, an alkylation reaction by the unsubstituted dithiane anion (184a), should lead to the corresponding alkylated compound (188a), which may then undergo hydrolysis and dehydrobromination to the formyl derivative of (168). Alternatively, the use of a substituted anion (184b) in the first step would ultimately lead to derivatives with keto-substituents.
The results from a number of attempted substitution and addition reactions using the simple dithiane anion (183), is summarised in Table 10 and in Scheme 70. The outstanding feature of these results is that the sulpholane ring introduces a complexity into simple substitution reactions. The presence of an acidic H α to the sulphone group causes the dithianyl anion (183) to act as a base. This arose when the anion was added to 3,4-dibromotetrahydrothiophene-1,1-dioxide (100). The dehydrobrominated material (101) and the thiophene-1,1-dioxide dimer (102) were isolated along with recovered 1,3-dithiane (189) (path a). In addition to these materials a colourless solid with a melting point of 127-128°C was also isolated. The structure of this compound as yet remains unresolved, despite the simplicity of its n.m.r. spectra, and its accurate mass.

Table 10  A summary of products and conditions for the alkylation of the 1,3-dithianyl anion (183)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reaction Time</th>
<th>Reaction Temp.</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>(100)</td>
<td>1h</td>
<td>-5°C</td>
<td>(189)</td>
</tr>
<tr>
<td></td>
<td>65h</td>
<td>0°C</td>
<td>9 : 1 : 2</td>
</tr>
<tr>
<td>(101)</td>
<td>18h</td>
<td>0°C</td>
<td>(189)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 : 2</td>
<td></td>
</tr>
<tr>
<td>(129)</td>
<td>1h</td>
<td>-5°C</td>
<td>(189)</td>
</tr>
<tr>
<td></td>
<td>18h</td>
<td>0°C</td>
<td>13 : 3 : 1</td>
</tr>
<tr>
<td>(129)</td>
<td>5 days</td>
<td>-30°C</td>
<td>(189) : (130)</td>
</tr>
<tr>
<td>(129)</td>
<td>17h</td>
<td>40°C</td>
<td>(130) (X)</td>
</tr>
</tbody>
</table>
Due to the dehydrobromination problems encountered with (100), it was thought that reaction of the anion (183) in a Michael-type fashion with the sulpholene (101) may result in some addition rather than complete elimination. This proved to be incorrect and the dimer (102) was once again isolated (path b). When the epoxide (129) was treated with the dithiane anion, two products were isolated apart from recovered 1,3-dithiane, the eliminated 3-hydroxysulpholene (130) and only 2% of the addition product (188).

A variation of the procedure was to carry out the reaction at -30°C, but this gave mainly the hydroxy sulpholene (130) and starting materials (189). Similarly increasing the temperature resulted in (130) and a significant amount of the aforementioned unidentified product (X).

3. **Nitrile Conversion**

Nitrile compounds are known to undergo reduction to aldimines using DIBAH\(^\text{90}\) which upon work-up give rise to the corresponding aldehydes. As a model, the simple 3-cyanosulpholane (190) was treated with DIBAH to determine whether carbonyl formation could take place.
selectively in the presence of a sulphone group, to give (191) (Scheme 71). Spectroscopic data of the product indicated that the reaction had not proceeded as expected, by the absence of an S=O stretch in the infrared. Similarly, it was clear that conversion had not taken place on the nitrile group because a carbonyl stretch was also absent. From these results it would appear that the thiolane (192) had been formed and that the sulphone group is reduced far more readily than the nitrile. Studies carried out by Gardner and workers support this idea. They found that the reduction of sulpholane over a 72h period at 20-25°C was quite exothermic.

Scheme 71
4. Oxidation of an Allylic Halogen Derivative

Alkenes are known to undergo allylic bromination, and this intrinsic property has been applied to the bromination of the methyl substituted sulpholene (193). Using the method of Krug and Yen, (193) was treated with N-bromosuccinimide and the allylic bromide (194) was formed in reasonable yield of 48% (Scheme 72). It was hoped that this halogenated material (194) could be oxidised to the corresponding carbonyl (168) by using anhydrous trimethylamine oxide. This reagent was selected in preference to other oxidising agents, due to its relatively low temperature requirements. For example, when dimethylsulphoxide is employed, temperatures of 100-160°C are necessary to affect oxidation. These temperatures are high enough to be impractical for sulpholene compounds due to the possibility of thermal extrusion of SO₂.

Scheme 72
Unfortunately an attempted oxidation using trimethylamine oxide failed to give the desired product (168). Instead it led to a 1,4-elimination of hydrogen bromide and yielded (195) in 58% yield (Scheme 73). This structure was confirmed by comparison of the experimental spectral data with that reported by Chou et al. These workers also prepared (195) by treatment of (194) with potassium carbonate. The favoured conjugative elimination over oxidation found in this work is not surprising when the strongly basic character of the polarised oxygen in trimethylamine oxide is considered. The methods available to convert halogenated substituents into carbonyl compounds are quite numerous and despite the failure of trimethylamine oxide in this respect, the oxidative route deserves further investigation.

Scheme 73
Towards the final stages of this work, quite a different approach to the synthesis of (168) was adopted. Preliminary investigations indicated that the ozonolysis of the acetate (133) followed by a reductive work-up using dimethylsulphide\textsuperscript{95}, does result in the formation of the carbonyl derivative (196). Subsequent f.v.p. should affect the elimination of the acetate to give (168) and perhaps extrude SO\textsubscript{2} to give (169), at the same time (Scheme 74). Work in the area is now continuing in these laboratories.

![Scheme 74](image)
To date the interest in the polyene (7) has been primarily theoretical and as yet, it has not been prepared. The syntheses of both [4] and [3] dendralene, which incorporate the chelotropic extrusion of $\text{SO}_2$ as a key step, highlights the prospect of making [5] dendralene (7) by the same methodology. In keeping with the lower homologues, the sulphonene derivative (197) should lose $\text{SO}_2$ on heating to give the corresponding dendralene (7).

![Scheme 75](image-url)
A synthetic route to the precursor (197) was therefore needed and it was thought that this might be achieved through a Wittig reaction with carbonyl compound (198). Not only would (198) serve a synthetic purpose, but a subsequent pyrolysis might provide an interesting analogue of [5] dendralene (199) (Scheme 75). Several different strategies to the formation of (198) were investigated and are discussed in the following text.

1. Metallation of the Sulpholane Ring

Adopting as a first approach a route where the sulpholane ring acts as nucleophilic species (Scheme 76), an attempt was made to prepare the metallated sulpholane (200). According to this scheme, a two molar excess of this organometallic compound (200) could undergo addition to phosgene to form the protected carbonyl derivative (201). A subsequent deprotection and elimination should yield the target molecule (198). In the initial step, the hydroxy group of (115) was protected as the trimethylsiloxy derivtive (202) by reaction with bis(trimethylsilyl)acetamide (203). The resultant silyl derivative (202) was found to be moisture sensitive and underwent hydrolysis in air to give back the hydroxy species (115). Accordingly, reactions and storage were carried out under an atmosphere of dry argon or nitrogen. Attempts to metallate this material to form (200) using
Scheme 76
magnesium failed despite the use of techniques such as ultrasound\textsuperscript{96} and catalytic Red-Al. Alternatively, when lithium metal was used, a mixture of elimination products (130) and (204) were formed. Clearly the lithium metal abstracts the acidic proton in preference to the bromine atom, thwarting attempts to prepare (200).

2. **Alkylation of the Sulpholane Ring by Activated Methylenes**

It was thought that with the apparent difficulty of placing a negative charge on the $\beta$-carbon of the sulpholane ring, an alternative approach might be to create an electron deficient $\beta$-carbon instead. This type of positive polarization may be found in the oxide carbon of (129), and its electrophilic addition to an activated methylene should result in the desired alkylation of the sulpholane ring. With this approach in mind, a number of acidic methylene reagents were investigated.

(i) **Alkylation with monoethyl malonate**

Diethyl malonate (205) was considered to be a suitable reagent because it has two acidic protons enabling successive additions. Thus, by reaction of (205) with a two molar excess of epoxide (129), a feasible framework for the target molecule (197), may be outlined (Scheme 77).
The classical malonic ester synthesis which involves alkylation by diethyl malonate coupled with a thermal decarboxylation and esterification, can be circumvented by using a simple procedure reported by McMurry and Musser. Their method which involves an alkylation of the halide (206) with the monoethyl malonate anion (207), and a subsequent decarboxylation to give the ester (208), takes place in the one step (Scheme 78). It was thought that this simple alkylation procedure might be incorporated into a complete synthesis of [5] dendralene. The proposed route, which is outlined in Scheme 79, would involve the reaction of a two molar equivalent of epoxide (129) with
Scheme 78

CO₂Li
| Li-C₇H₂-CO₂Et + R-X → R-C₇H₂-CO₂Et

Scheme 79

2 X

→

S₅O₂

S₅O₂

→

S₅O₂

→

S₅O₂

→

S₅O₂

→

S₅O₂

(207)

(206)

(208)

(129)

(207)

(209)

(210)

(7)

(197)
the monoethyl malonate anion (207), to form the bis-sulpholane (209). The ester function of (209) could then be reduced to give the triol (210). In order to aid elimination, the hydroxy group could be converted into an ester and subsequent thermolysis should yield the target precursor (197) or the dendralene (7).

When the first step of Scheme 79 was attempted; viz the addition of the malonate anion (207) to (129), only the hydroxy sulpholene (130) was formed. Clearly, the anion (207) acts as a base to abstract the highly acidic sulpholane α-hydrogen.

A modification to this procedure would be to attempt a Michael addition using the acetyl derivative (211) as the acceptor. This material (211), which is prepared in 88% yield by a one step acetylation and dehydrobromination of (115) using acetyl chloride and triethylamine (Scheme 80),
would serve a dual function. Firstly by protecting the hydroxy proton, and secondly by providing an activated double bond for the Michael reaction. This line of study is worthy of further investigation.

(ii) **Alkylation with nitromethane**

Nitromethane was considered a suitable alternative to the malonate compound. This was partly due to its high acidity despite having only one activating group, and also because of the potential to convert the nitro group into a carbonyl compound using a Nef reaction. The first reaction that was attempted using this reagent, involved the epoxide (129), nitromethane and sodium ethoxide as the base. Unfortunately, this led only to an addition of the ethoxide ion to (129) to form (212), rather than the nitro sulpholene (213) (Scheme 81). A similar situation has been reported by Motherwell et al.\(^8\). They encountered an epoxy ring opening of 3,4-epoxy-3-methyltetrahydro thiophene-1,1-dioxide (214) by an ethoxide ion, and this led to the substituted compound (215).
Michael reactions of nitromethane to sulpholene compounds akin to those described in this work, have been carried out by Argyl et al. In the light of their investigations it was hoped that addition of nitromethane to the activated double bond of an excess of (130), might result in the formation of (216). This compound could then be converted to (198) or [5] dendralene (7) according to Scheme 82. Indeed Argyl and workers found that the
Scheme 82

Scheme 83
formation of (217) took place using an equimolar concentration of (218) and the nitroparaffin (Scheme 83).

A number of different attempts to prepare these nitro compounds (216), such as varying the base, the concentrations, and extending the reactions times, met with limited success. In general, isolated materials were complex mixtures of products or simply starting materials. For example, in keeping with the procedure given\(^4\), when (130) was treated with an ion exchange resin at a concentration of 100g/mole, equimolar nitromethane and heated to boiling for 170h, only the starting material was recovered in 91\% yield. On the other hand, a 20-fold excess of nitromethane and a 700g/mole equivalent of catalyst resulted in a complex mixture of products, including the starting material (130). Similarly, when only two equivalents of sodium ethoxide was employed, along with a 20-fold excess of nitromethane, a mixture of 6 products was obtained. Purification on a Chromatatron using silica gel resulted in the isolation of a two-product mixture with very similar RF values. Analysis by \(^{13}\text{C}\) n.m.r. spectroscopy indicated a mixture of cis- and trans-isomers (Fig. 29). These findings were further substantiated by the inclusion of chromium(III) acetylacetone, a relaxation agent which permits the quantitative assignment of peak intensities. From the
peak integrals, a product ratio of 1:0.6 was evident pointing to an isomeric mixture. A high resolution mass spectra of the material showed a molecular ion peak corresponding to the loss of NO$_2$ from (213). Whilst these spectral details indicate an isomeric mixture of (213a) and (213b), a full characterisation of the products is still required. Unfortunately time did not permit these detailed studies to be carried out. However, one conclusion which may be drawn, is that the simple product isolation found by Argyl and workers$^{54}$ is not reproduced here. They encountered no major problems and were able to isolate pure products in reasonable yields. No mention of the possibility of isomers or the acidity effect of the hydroxy proton was made, and it appears that the difficulties found in this work must be inherent in the Michael acceptors used.

![Fig. 29](image-url)
Despite this lack of success, an endeavour was made to prepare the Michael adduct by using a phase-transfer catalyst. A report by Belsky claims that Michael additions carried out in aprotic solvents, can be catalysed by potassium fluoride and 18-crown-6-ether. In an attempt to apply Belsky's findings, a phase-catalysed reaction of (130) with nitromethane in acetonitrile was carried out. Unfortunately this failed to give the desired product (213) and only starting materials were isolated. Similarly, when tetra-butylammonium fluoride was used as a phase transfer catalyst, once again only the starting materials were recovered.

3. Preparation of Sulpholane Fused Acetal Compounds

During the course of the aforementioned investigations into [5] dendralene (7), two fairly interesting acetal derivatives were prepared. Compound (219) was formed during an attempt to prepare the alcohol (130). This sulpholene derivative (130) is normally prepared by pyridine-promoted elimination of hydrogen bromide from the bromohydrin (115). In an attempt to carry out the elimination using Amberlite IRA-400(OH), a basic ion exchange resin in acetone, the acetal (219) was isolated as a colourless crystalline compound. A possible mechanism is given in Scheme 84 and relies on the exchange resin being sufficiently basic to abstract the hydroxy proton. The key steps involve a nucleophilic attack by
the oxy-anion (220) at the electron deficient carbon of the solvent acetone, to form an intermediary hemiacetal (221). This is then followed by an intramolecular Michael addition.

Scheme 84

Unexpectedly, acetal formation was also dominant in another experiment where derivatives (222a) and (222b) were formed as the result of an unsuccessful attempt to
generate an acetyl anion. A mixture of the epoxide (129), acetaldehyde and LDA were stirred at -75°C for 0.5h then at room temperature for a further 1 hour. Subsequent work-up and sublimation gave a mixture of the acetals (222a) and (222b). A similar mechanism to that outlined in Scheme 84 is proposed whereby the epoxide (129) in the presence of LDA undergoes an eliminative ring-opening. Subsequent non-stereoselective attack by the oxygen anion at the electropositive acetaldehyde carbonyl, followed by ring-closure onto the activated double bond, gives rise to the two isomers of (222) (Scheme 85).
Scheme 85
H. THE ROLE OF [3] DENDRALENE AND ITS SYNTHETIC PRECURSOR (91) IN POLYMER CHEMISTRY


As mentioned in the Introduction, one of the salient features of the cross-conjugated dendralenes is their usefulness, as cross-linking agents in polymer chemistry. Their incipient high-degree of unsaturation provides a mechanism for free radical, anionic and cationic polymerisation as well as Diels-Alder cycloaddition reactions.

Indeed work carried out by Shepard et al\textsuperscript{102} has capitalised on these properties. His patented investigation of polyesters is concerned with the cross-linking aspect of polymer chains through Diels-Alder additions and in particular, the use of [3] dendralene with its diene functionality to react with unsaturated sections in the polymer. Although the cross-linking of these materials usually employs ethylenic copolymers which function through a free radical mechanism, there are a number of problems associated with this method. For example, oxygen inhibits the curing process of the material leading to non-uniformity. This may also occur with the introduction of metal impurities which promote premature curing. In addition to material defects, the high volatility of the ethylenic copolymers causes potential toxicity and fire hazards. The utilization of
[3] dendralene to create three dimensional properties through cycloadditions alleviates these problems, and is easily initiated thermally. Furthermore, the authors believe their thermoset materials have not only a greater flexibility and extensibility, but by regulation of the initial monomer and reagent concentrations, they achieve a wider range of polymeric materials.

More recently [3] dendralene has been incorporated into a polymer film[103], by plasma-induced polymerisation. The film which exhibits hydrophilic properties is formed on the surface of the optical product. This method of homopolymerisation apparently overcomes the problem of forming an oily gelatinous polymer, previously encountered by Blume[32]. The number of examples where [3] dendralene is involved in polymer chemistry is limited, and to date has been restricted to homopolymerisation or Diels-Alder reactions. In this work, attention was focussed on using [3] dendralene as a copolymer possessing cross-linking properties, and it was proposed that its incorporation into a growing polyisoprene chain should markedly change the physical properties of the polymer by including a 3-dimensional component.

Polyisoprene, the natural constituent of Hevea rubber, has been a topic of interest for more than a hundred years, and as a consequence has been studied extensively. Isoprene undergoes polymerisation with a number of alkali metals and alkali metal alkyl catalysts which differ in
their mode of polymerisation. For example, the use of lithium metal results in the formation of between 93-95% cis-1,4 head-to-tail addition\(^\text{104}\) (Fig. 30). On the other hand vanadium tri- and tetra-chlorides are capable of converting isoprene into essentially the trans polymer. The well known trialkylaluminium-titanium trichloride, Ziegler-Natta catalysts, also play an important role in the regularity of polymerisation giving only cis addition of 96% 1,4- and 4% of the 3,4-product.

\[ \text{Li} \quad \text{cis-1,4} \rightarrow \text{Li} \quad \text{trans polymer} \]

Fig. 30

Not only does the type of initiator effect the outcome of the polymer, but the concentration is also important. In general, higher concentrations lead to lower molecular
weight polymers. Temperature also plays a role in determining the molecular weight distribution.

Therefore, in order to analyse the cross-linking properties of [3] dendralene, a meticulously prepared polyisoprene control was required. This took place by polymerising isoprene at 40°C for 24h, using butyllithium in hexane as the initiator. The resultant material, a fairly non-viscous oil, was judged by n.m.r. spectroscopy to be a mixture of 67% 1,4-cis, 27% trans and 6% 1,2-addition. The incorporation of 3.5% of [3] dendralene into the mixture, under identical conditions gave a gel within one hour of reaction. This material was not only insoluble in hydrocarbon and chlorinated solvents, but attempts to dissolve them, resulted in considerable swelling of the polymeric material. This feature is characteristic of highly cross-linked polymers. It therefore seems that from a physical point of view, the evidence suggests that [3] dendralene has copolymerised as expected. However, substantial chemical data to support this assumption, has not been found due to a number of inherent problems. The insolubility of the material was the major drawback making structural elucidation by n.m.r. spectroscopy impossible. It was hoped that the original oxidative double bond cleavage method which was employed to determine the composition of natural rubber, might be applied in this case. Several attempts using phase-transfer catalysts with potassium permanganate failed to
oxidise this material, due to the total insolubility of the polymer. Ozonolysis was not tried as it was felt that the extent of oxidation could not be controlled making the range of products too vast to accurately quantify the extent of dendralene incorporation. Whilst infrared techniques have been used in the past to determine the nature of polyisoprene, spectra are normally poorly resolved and are used comparatively for pre-defined absorbances. It would be a difficult exercise to locate the absorbances specific for cross-linked hydrocarbons especially in such low concentrations. A pyrolysis/GC at 550°C on a KCl modified alumina column was carried out by Mr. K. Oliver at the BP laboratories in Sunbury. This thermolytic technique, gave detailed finger prints of the most volatile pyrolysates from samples of polyisoprene and isoprene impregnated with [3] dendralene. Both of these materials exhibited almost identical programs, and these are illustrated in Fig. 31, along with the major pyrolysate assignments and the experimental conditions. Pyrolysis GC/MS also showed very similar spectra with the exception of one small peak at scan 267 (Fig. 32). If [3] dendralene cross-linking is present in the polymer, the pyrolysate might be expected to contain a component of molecular weight 160, indicative of the fragment given in Fig. 33. A peak at scan 267 albeit extremely small, does correspond to a molecular weight of 160 and suggests some incorporation of [3] dendralene into the polymer.
Pyrolysis/GC at 550°C

Analysis Name:
POLY(ISOPRENE (A)).

Fig. 31

Analysis Name:
POLY(ISOPRENE + DENDRALENE (B)).
2. Polymerisation of 3-vinyl-3-sulpholene (91)

The presence of a pendant diene within a polymer chain is a desirable property and Union Camp Corporation have amply demonstrated this point by making commercially available the polymer of 2,6-dimethyl-2,4,6-octatriene (Fig. 34), otherwise called poly(alloocimen). This reactive hydrocarbon polymer copolymerises to produce sections of polymer with diene substituents. These dienes may then undergo cross-linking by either free-radical or by cycloaddition reactions. In a situation where [3] dendralene is incorporated into a free radical initiated...
polymer chain, such as polyisoprene, cross-linking takes place there and then. This concurrent cross-linking is not always required, and many applications exist where curing takes place at a later date. One example is the previously mentioned thermoset polyesters¹⁰² (see Section H 1).

![Chemical Structures](image)

**Fig. 34**

By exploring the free radical polymerisation of the dendralene precursor (91), it was found that of the possible 1,4- or 1,2-additions this monomer underwent significant 1,2-addition across the vinyl substituent leaving the butadiene sulphone group intact (Fig. 35).
Fig. 35
The polymerisation itself required a relatively large concentration of $\alpha,\alpha'$-azo-isobutyronitrile (AIBN) initiator and fairly lengthy reaction times. Nevertheless, a colourless polymer was isolated in 82% yield. The material was sparingly soluble in deuterated dimethyl sulphoxide and despite the poor resolution of its resultant n.m.r. spectrum it was clear that a mixture of 1,4- and 1,2-addition products were present. This was substantiated by a thermal analysis of the polymeric material run by Dr. E. Gimzewski on a Perkin Elmer TGA7 FTIR instrument at BP. The thermogram in Fig. 36 shows polymer weight loss (the solid line) as a function of temperature, in addition to the rate of weight loss (the dashed line). It is evident that the rate maximum occurs at approximately 184°C and that the original weight of the polymeric material decreases by 40% between 25°C and 225°C. The gaseous pyrolysate was examined at 170°C and exhibited large absorbances at 1344 and 1376 cm$^{-1}$ (Fig. 37), corresponding to $SO_2$ extrusion from the pendant butadiene sulphone side chains, and that these side chains are the result of 1,2-polymer addition. Using this information and the weight loss measurements from the thermogram, the amount of 1,2-addition is calculated to be roughly 85% of the total polymer and is clearly favoured over the 1,4-addition product.
Fig. 36

Fig. 37
This result is encouraging if (91) is to be used as a cross-linking agent. It means that with a tendency to polymerise by 1,2-addition, its copolymerisation will result in a material containing a significant number of these pendant butadiene sulphone substituents. They could then be converted when convenient, into butadiene groups by thermal extrusion of $SO_2$, thus providing a mechanism for cross-linking. Apart from adding a three dimensional component to the polymer, this type of diene may also be used to introduce a specific physical property into the resultant polymer. For example, reaction with antioxidants would provide a means of uniformly preserving the polymer, rather than simply protecting the exposed areas. So far this investigation has only covered the homopolymerisation of sulpholene (91), and clearly a continued line of research would be to actually incorporate (91) into a polymeric material as a copolymer. In view of the practical and possibly commercial potential of this compound (91) in polymer synthesis, and its tremendous scope, further investigation in this area is definitely warranted.
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1. Preparation of

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2. Preparation of

\[ \text{R is } (CO_2H) \quad \text{R’ is } H \] 183

3. Preparation of

\[ \text{R is } (CO_2Et) \quad \text{R’ is } H \] 184

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6. Preparation of 

7. Reduction of 

C. PREPARATION OF [3] DENDRALENE STARTING FROM 2,5-DIHYDROTHIOPHENE-1,1-DIOXIDE 

1. Preparation of 
   (a) using meta-chloroperbenzoic acid  
   (b) using peracetic acid  
   (c) using performic acid  

2. Preparation of
3. Preparation of

\[
\begin{aligned}
\text{AcO} & \quad \text{S} \\
\text{O}_2 & \quad \text{O}_2
\end{aligned}
\]

(a) using acetyl chloride 193
(b) using DMAP 195

4. Preparation of

\[
\begin{aligned}
\text{S} & \quad \text{O}_2
\end{aligned}
\]

195

5. Attempted isomerisation of

\[
\begin{aligned}
& \quad \text{If}
\end{aligned}
\]

(a) with Wilkinson's catalyst 196
(b) with acid catalyst 196

6. Isomerisation of

\[
\begin{aligned}
& \quad \text{TsO}
\end{aligned}
\]

197

7. Preparation of

\[
\begin{aligned}
\text{Tso} & \quad \text{S} \\
\text{O}_2 & \quad \text{O}_2
\end{aligned}
\]

198

8. Preparation of

\[
\begin{aligned}
\text{S} & \quad \text{O}_2
\end{aligned}
\]

from 199

9. FVP of

\[
\begin{aligned}
& \quad 
\end{aligned}
\]

200
D. CYCLOADDITION REACTIONS

1. Preparation of

2. Reaction of [3] dendralene with $2 \times$ Ph-N=N-Ph

3. with $2 \times$ H-N

4. with $2 \times$ O

5. with $2 \times$ CO$_2$Me

6. with $\equiv$ 205

7. with $\equiv$ 206

8. with $\equiv$ 207
9. Preparation of

10. Preparation of


12. Derivatisation of

(a) Preparation of

(b) Reaction of

E. ATTEMPTED PREPARATION OF 3-FORMYL-2,5-DIHYDROTHIOPHENE-1,1-DIOXIDE, AS A ROUTE TO [3] DENDRALENE DERIVATIVES

1. Via isoxazolines

(a) Preparation of α-benzaldoxime

(b) Preparation of benzhydroxamic chloride

(c) Cycloaddition of

(i) to PhC=\text{N}–\text{O}
E. Cont’d.

(c) cont’d.

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(ii) 222
2. (b) Cont’d.

(iii)

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(b) Attempted oxidation of

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1. Preparation of

2. Attempted metallation of

3. Preparation of

4. Preparation of
F. Cont'd.

5. Reaction of \textit{"} with nitromethane 229

\[
\text{\begin{center}
\begin{tikzpicture}
\node (OAc) at (0,0) {$\text{OAc}$};
\node (S) at (0,0) {$\text{S}$};
\node (O2) at (0,0) {$\text{O}_2$};
\end{tikzpicture}
\end{center}}
\]

6. Preparation of 229

7. Preparation of monoethyl malonate 230

8. Reaction of \textit{"} with

\[
\text{\begin{center}
\begin{tikzpicture}
\node (O) at (0,0) {$\text{O}$};
\node (S) at (0,0) {$\text{S}$};
\node (O2) at (0,0) {$\text{O}_2$};
\end{tikzpicture}
\end{center}}
\]

9. Reaction of nitromethane with \textit{"} 232

10. Reaction of acetaldehyde with \textit{"} 233

G. POLYMERS 234

1. Polymerisation of

\[
\text{\begin{center}
\begin{tikzpicture}
\node (S) at (0,0) {$\text{S}$};
\node (O2) at (0,0) {$\text{O}_2$};
\end{tikzpicture}
\end{center}}
\]

2. Polymerisation of isoprene 235

Symbols and Abbreviations

mol; mmol  moles; millimoles
ml; l      millilitres; litres
g; mg      gram; milligram
M          mol dm$^{-3}$
m.p; b.p   melting point; boiling point
Sublm.     sublimation
decomp.    decomposition
h; min; s  hours; minutes; seconds
Lit.       literature
conc.      concentrated
vol.       volume
Temp.      temperature
R.Temp.    room temperature
t.l.c.     thin layer chromatography
FAB        fast atom bombardment
NOAB       3-nitrobenzylalcohol
CI          chemical ionization
EI         electron impact
f.v.p.     flash vacuum pyrolysis
m/z        mass to charge ratio
M$^+$      molecular ion mass
calc.      calculated molecular ion mass
exp.       experimentally found molecular ion mass
n.m.r.     nuclear magnetic resonance
COSY coupling correlated spectroscopy
NOE nuclear Overhauser effect
DEPT distortionless enhancement by polarisation transfer
Q quaternary carbon atom
δ chemical shift
ppm parts per million
J spin-spin coupling constant
s; d; t; q; m singlet; doublet; triplet; quartet; multiplet
c; b; dist; p complex; broad; distorted; pair
decpl. decoupling
irrad. irradiation
A; B geminal protons may be assigned as A or B
e; a equitorial; axial
O; M; P ortho; meta; para
IR Infrared
"max maximum wave number
δs; ω; τ; p scissoring; wagging; twisting; rocking
'r as; 's stretching asymmetrical and symmetrical
liq. cap. film. liquid capillary film
liq. film liquid film
v/v volume to volume
New compounds have been named in accordance with the IUPAC rules of nomenclature (1957) where possible.
Purification and Techniques

1. General Purification

(i) Purification and drying of solvents and gases

Commercially available AR solvents were used when high purity was required and these were normally dried with 4A molecular sieves. Pyridine was dried over potassium hydroxide pellets as was triethylamine. 'Super dry' methanol and ethanol were obtained using the procedure outlined in Vogel and stored over 4A sieves. Benzene, toluene and diethyl ether (ether) were dried over sodium wire and tetrahydrofuran (THF) was purified by distillation from sodium and benzophenone indicator under a nitrogen atmosphere. Dry heptane and hexane were obtained by distillation from calcium hydride also under nitrogen. The purification of chloroform was achieved using the method outlined in Vogel and involved shaking chloroform with half its volume of water five to six times. This was followed by drying over calcium chloride and then distillation. The purified chloroform was stored in the dark.

Drying of organic extracts was achieved using anhydrous drying agents by allowing the extract and drying agent to stand for at least 1/2 h. The drying agent was then filtered and the solvent evaporated in vacuo. Products that were not isolated from organic extracts were left on a high vacuum pump for several hours to remove
traces of solvent and water.

Gases such as argon and nitrogen were dried through a series of dreschel vessels in the gas line containing sulphuric acid, calcium chloride granules and self-indicating silica.

(ii) Chromatographic techniques
a. Thin layer chromatography

Analytical t.l.c. was carried out on plastic backed Kieselgel 60 GF 254 silica plates with U.V. indicator. When the material was not sensitive to U.V. light, plates were developed in an iodine bath and the presence of amine functionalities were detected using a ninhydrin spray.

For preparative t.l.c. glass backed plates 20 x 20 cm, 1.00 mm thickness, were coated with Kieselgel GF 254 from Fluka and a usual loading of 20-30 mg of material was used. The plates were developed in a suitable solvent system, allowed to dry and the bands detected by U.V. absorption. The appropriate bands were then scraped from the plates and the adsorbed silica added to methanol. Filtration of the silica left the compound of interest dissolved in the methanol filtrate and this was then evaporated in vacuo.

A chromatatron, which is supplied by Harrison Research, was also employed for thin layer chromatography. The circular plates were coated with Kieselgel GF 245 to a thickness of 1.0 mm and the bands were detected by U.V.
light as they moved through the plate. The fractions were collected accordingly and the solvent then evaporated to give the isolated material.

b. **Dry flash chromatography**

Both Kieselgel 60 (230-400 mesh) silica from Merk and silica (60-120 mesh) from Fisons were used with water pump vacuums of 20-30 mm Hg.

c. **Flash chromatography**

Mixtures were separated on either Sorbsil 40/60 flash silica from May and Baker, Kieselgel 60 or Kieselgel G254 (t.l.c. silica). Air pressures of 10-15 psi were employed for flash chromatography grades of silica. When t.l.c. silica was used, greater pressures of about 30 psi were required to achieve a flow of 50 ml/min and the columns were made especially to withstand these higher pressures. For air sensitive materials, nitrogen gas was used and solvents were transferred with the aid of a double ended needle. Subsequent evaporation of the solvent in vacuo took place in a shlenk tube.

d. **Soxhlet extraction**

Some solids were found to be fairly insoluble in common solvents and were purified by soxhlet extraction. This involved placing the material in a soxhlet thimble where it could be continuously dissolved into the boiling
solvent. When most of the material had been removed from the thimble, the solution was cooled and the purified material precipitated out.

2. **General Techniques**

(i) **Cyloaddition reactions**

Diels-Alder addition reactions were generally carried out in a sealed carius tube\(^{107}\) that had been pre-rinsed with a galvinoxyl solution, ca. 5 mg in 25 ml of acetone, and dried in a stream of air.

(ii) **Flash vacuum pyrolysis**

A diagram depicting a standard flash vacuum pyrolysis apparatus is given in Fig. 38 and the pyrolysis procedure is as follows. A liquid or solid sample is placed in the inlet tube and the apparatus is evacuated using an Edwards high capacity rotary oil pump to pressures of 0.001 to 0.02 mm Hg. The inlet tube is sufficiently heated by means of Kugelrohr oven to allow volatilization of the sample. The gaseous material then passes through a preheated Stanton Redcroft LM8 100 furnace, which utilises a Pt/Pt 13% Rh thermocouple located at the centre of the furnace. The pyrolysate is finally condensed onto a liquid nitrogen cooled trap. When flash distillation of the pyrolysate is required, another trap is placed in sequence and the first trap is allowed to warm to room
temperature while the more volatile components condense onto the second trap which is liquid nitrogen cooled. On completion of the pyrolysis, the apparatus is flooded with nitrogen gas and the traps allowed to reach room temperature before they are exposed to the air. The pyrolysate is then removed by dissolving it into a suitable solvent.

Fig. 38
3. **Analytical Techniques**

(i) **Melting point determination**

Routine melting points were determined using a Gallenkamp melting point apparatus. For new compounds and for the determination of sublimation points, a Reichart hot stage microscope was employed. These melting points are uncorrected.

(ii) **Elemental analysis**

Micro-analysis for carbon, hydrogen and nitrogen were carried out by Mrs. E. McDougal using a Carlo Erba elemental analyser, model 1160.

(iii) **Infrared**

Infrared spectra were recorded on a Perkin Elmer 781 instrument. Samples were generally run neat as thin films or as a nujol mull on sodium chloride plates. Samples which were run as KBr plates are indicated as such in the experimental section. All infrared spectra were referenced to polystyrene 1603 cm$^{-1}$, and their wavenumbers have been corrected accordingly.

(iv) **Nuclear magnetic resonance**

Proton and $^{13}$C n.m.r. spectra that were recorded on the 80 MHz Bruker WP 80 and the 200 MHz Bruker WP 200 instruments, were operated by Ms. H. Grant and Mr. J. Miller. Those obtained on a Bruker WH 360 were operated
by either Dr. D. Reed or Dr. I. Sadler. Dr. J. Bales, Dr. J. Boyle and Ms. S. Mercer recorded proton and \textsuperscript{13}C n.m.r. spectra on both a Bruker AM 250 and JEOL GX 400 instrument. Chemical shifts are reported in parts per million and are referenced to the deuterated solvent used. All \textsuperscript{13}C n.m.r. are broad band decoupled unless otherwise stated.

(v) \textbf{Mass spectrometry}

Low resolution EI mass spectra were recorded by Ms. E. Stevenson on an AEI MS-902 instrument, whereas high resolution EI and FAB mass spectra were obtained on a Kratos MS-50 spectrometer operated by Mr. A. Taylor. CI and ICMS mass spectra were obtained using a Kratos MS-80, operated by Mr. A. Chandler.

\* \textsuperscript{13}C n.m.r. spectra 200 MHz, 250 MHz and 400 MHz refers to the Bruker WP 200, AM250 and JEOL GX 400 instruments.
A. ATTEMPTED METALLATION OF 3-BROMO-2,5-DIHYDROTHIOPHENE-1,1-DIOXIDE

1. Preparation of 3,4-Dibromotetrahydrothiophene-1,1-dioxide

The method of Bailey and Cummins\textsuperscript{50} was used. 2,5-Dihydrothiophene-1,1-dioxide (88.6 g, 0.75 mol) was heated with stirring in dry chloroform (125 ml) to boiling. Dry bromine (120 g, 95 ml) in chloroform (95 ml) was then added in ten equal portions over 7 h. After the final addition, the reaction mixture was stirred a further 2 h and then left to stand overnight. Filtration of the mixture gave colourless crystals of 3,4-dibromotetrahydrothiophene-1,1-dioxide (179 g, 86%) m.p. 144-146°C, sublim. 135°C (lit.\textsuperscript{50}, 141.0-141.8°C).

2. Attempted Dehydrohalogenation of 3,4-Dibromotetrahydrothiophene-1,1-dioxide

(a) With potassium hydroxide

3,4-Dibromotetrahydrothiophene-1,1-dioxide (1.1 g, 3.9 mmol) and potassium hydroxide (0.28 g, 5.0 mmol) in methanol (25 ml) was stirred and heated for 48 h to 60°C. The solvent was then removed in vacuo and the residue dissolved in toluene (5 ml). Separation by dry flash chromatography using a gradient elution of ethyl acetate/toluene, resulted in the recovery of the starting material 3,4-dibromotetrahydrothiophene-1,1-
dioxide (0.25 g, 22%) and 3-bromo-2,3-dihydrothiophene-1,1-dioxide (0.12 g, 16%) as confirmed by n.m.r. spectroscopy.

(b) With 1,8-diazabicyclo[5.4.0]undec-7-ene

3,4-dibromotetrahydrothiophene-1,1-dioxide (2.2 g, 7.7 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.5 g, 10 mmol) was heated to boiling in dry acetone (30 ml) for 72 h. The reaction mixture was added to silica gel 60-120 mesh (37 g), the solvent removed under reduced pressure and the adsorbed silica then washed with an ethyl acetate/toluene, (30:50) mixture (5 x 80 ml). T.l.c. of the crude material indicated three products. These were separated by flash chromatography using Kieselgel 60 and eluting with ethyl acetate/hexane, (50:50). The fractions were collected, examined by n.m.r. and found to contain the starting material, 3,4-dibromotetrahydrothiophene-1,1-dioxide, 3-bromo-2,3-dihydrothiophene-1,1-dioxide and the dimer 3a,7a-dihydrobenzothiophene-1,1-dioxide. The dimer was identified by $^{13}$C n.m.r. spectral comparison (CDCl$_3$, 200 MHz, DEPT) $\delta$[ppm]: 140.09 C2, 131.91 C3, 126.75 and 122.23 C7 and C6, 122.12 C5, 115.43 C4, 58.01 C7a, 39.10 C3a.

3. Preparation of 3-Bromo-4-hydroxytetrahydrothiophene-1,1-dioxide

(a) With bromine water

Using the method of Ellis and Sammes, bromine
(19 g, 0.12 mol) and 2,5-dihydrothiophene-1,1-dioxide (12 g, 0.10 mol) were allowed to stand for 4 days at 4-5°C in water (2.5 l). The solid formed, was filtered and recrystallised after a hot filtration, from methanol to give (8.71 g, 41%) of 3-bromo-4-hydroxytetrahydrothiophene-1,1-dioxide as colourless crystals m.p. 189-190°C (lit., 189-190°C).

(b) Via the nitrate ester

The method of Argyl et al. was employed. This involved firstly passing a stream of air over a reservoir of bromine and water (7 g in 9 ml) and then into a chilled solution of 2,5-dihydrothiophene-1,1-dioxide (10 g, 8.4 mmol) in 40% aqueous nitric acid (100 ml). This was continued for 4h and the precipitate filtered to give the nitrate ester, 3-bromo-4-nitratetetrahydrothiophene-1,1-dioxide as a colourless solid (6.0 g, 30%); m.p. 94-96°C (lit., 94-95°C). Subsequent boiling in water for 2h did not give the clean hydrolysis as indicated in the literature, but rather a mixture of products as indicated by 13C n.m.r. spectroscopy. The nitrate ester, 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide as well as the bromohydrin, 3-bromo-4-hydroxytetrahydrothiophene-1,1-dioxide were identified. (CD3SOCD3, 200 MHz, DEPT) δ[ppm]: 47.54 C3, 56.11 C2, 57.67 C5, 73.41 C4.

(c) From the epoxide

A similar procedure to that outlined by Cameron was used. To an ice chilled solution of 3,4-epoxytetrahydro-
thiophene-1,1-dioxide (0.2 g, 1.5 mmol) in glacial acetic acid (10 ml), was slowly added a solution of hydrogen bromide 45% in glacial acetic acid (0.13 g, 1.6 mmol). This was stirred for 20 min at 0°C and then a further 4 h at room temperature. The precipitate was filtered and washed with water to give (0.25, 78%) of 3-bromo-4-hydroxytetrahydrothiophene-1,1-dioxide m.p. 189-192°C (lit.109, 189-190°C); 13C n.m.r. (CD3SOCD3, 200 MHz, DEPT) δ[ppm]: 47.60 C3, 56.74 C2, 57.71 C5, 73.43 C4.

(d) With aqueous N-bromoacetamide

Using a similar procedure to that outlined by Cameron108, a solution of N-bromoacetamide (0.55 g, 4.7 mmol) in acetone (5 ml) was added to 2,5-dihydrothiophene-1,1-dioxide (0.50 g, 4.3 mmol) in 10 ml of acetone/water (4:1). The mixture was stirred at room temperature for 5 days. The acetone was removed in vacuo and water (25 ml) added to the residue. This was extracted into ethyl acetate (5 x 20 ml) and the extracts combined and dried over anhydrous magnesium sulphate. Subsequent solvent evaporation in vacuo gave a colourless crystalline material 3-bromo-4-hydroxytetrahydrothiophene-1,1-dioxide (0.43 g, 46%) m.p. 186-194°C (lit.109, 189-190°C); 13C n.m.r. (CD3SOCD3, 200 MHz, DEPT) δ[ppm]: 47.60 C3, 56.76 C2, 57.72 C5, 73.43 C4.
B. ATTEMPTED ROUTE TO [3] DENDRALENE VIA 3-DIETHOXY-CARBONYLMETHYL-2,3-DIHYDROTHIOPHENE-1,1-DIOXIDE

1. Preparation of 3-Diethoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide

Preparation of the title compound was carried out using the method of Argyl et al.\textsuperscript{54}. 3,4-Dibromo-tetrahydrothiophene-1,1-dioxide (3.48 g, 0.12 mol) was added slowly to a cooled solution of sodium (5.75 g, 0.25 mol) and diethyl malonate (43.75 g, 0.27 mol) in ethanol (375 ml). The mixture was allowed to stand at room temperature for 115h and was then filtered to give 3-diethoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide (26.4 g, 70%) as colourless crystals m.p. 68-69\degree C (lit.\textsuperscript{54}, 74-75\degree C); \textsuperscript{13}C n.m.r. (CDCl\textsubscript{3}, 200 MHz) \delta[ppm]: 12.35 (CH\textsubscript{3}), 38.00 C3, 50.59 C2, 53.31 (CH) 61.28 (OCH\textsubscript{2}), 131.85 C4, 140.12 C5, 166.65 (CO).

2. Preparation of 3-Carboxymethyl-2,3-dihydrothiophene-1,1-dioxide

Using a modification of the procedure by Argyl et al.\textsuperscript{54}, 3-diethoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide (20.0 g, 64 mmol) in 15\% hydrochloric acid (150 ml) was refluxed over 16h. Solid sodium bicarbonate was added to the reaction mixture until a pH of 8 was obtained. The solution was then continuously extracted into ether over 4h. The ether extract was discarded and the aqueous phase reacidified to pH 1-2 with aqueous
hydrochloric acid. The mixture was continuously extracted into ether for a further 48h. Removal of the solvent under high vacuum gave 3-carboxymethyl-2,3-dihydrothiophene-1,1-dioxide (10.5 g, 94%) as colourless crystals m.p. 124-126°C from ethyl acetate, (lit.\textsuperscript{54}, 122-124°C); \textsuperscript{13}C n.m.r. (CD\textsubscript{3}OD, 200 MHz, DEPT) δ[ppm]: 35.26 C3, 36.59 C2, 52.51 (CH\textsubscript{2}), 130.94 C4, 142.62 C5.

3. Preparation of 3-Ethoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide

The method of Argyl et al\textsuperscript{54} was employed. 3-Carboxymethyl-2,3-dihydrothiophene-1,1-dioxide (3.97 g, 23 mmol) and conc. sulphuric acid (0.75 g) was heated to boiling in dry ethanol (120 ml) for 84 h. Solid sodium bicarbonate (0.64 g) was then added, and the solvent removed under vacuum leaving a colourless oil. This was distilled to give (3.64 g, 80%) of 3-ethoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide b.p. 225°C, 0.4 mm Hg, (lit.\textsuperscript{54}, 163°C, 0.1 mm Hg); \textsuperscript{1}H n.m.r. (CDCl\textsubscript{3}, 80 MHz) δ[ppm]: 1.19 (3H, t, (CH\textsubscript{3}) J 7Hz), 2.54(2H, bd, H\textsubscript{1}, J\textsubscript{1} 8Hz), 2.96(1H, dist.t, H\textsubscript{3}, J 8Hz), 3.29-3.50(2H, m, H\textsubscript{2}), 4.09(2H, q, (OCH\textsubscript{2}),J 7Hz); \textsuperscript{13}C n.m.r. (CDCl\textsubscript{3}, 200 MHz, DEPT) δ[ppm]: 13.91 (CH\textsubscript{3}), 35.49 C3, 37.87 (H\textsubscript{2}), 52.27 C2, 60.91 (OCH\textsubscript{2}), 131.99 C4, 141.87 C5.
4. Preparation of 3-Methoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide

(a) Using diazomethane

To an ice cooled solution of diazald (3.21 g, 15 mmol) in ether (45 ml), was added potassium hydroxide (0.4 g, 7 mmol) in ethanol (10 ml). The resultant diazomethane was distilled and added slowly to a chilled solution of 3-carboxymethyl-2,3-dihydrothiophene-1,1-dioxide (0.5 g, 2.8 mmol) in 13 ml of a (1:4) ethanol/ether mixture. This was stirred for 1h and then allowed to stand at room temperature overnight. The solvent was removed in vacuo, and the resultant oily solid was dissolved into methanol and purified with flushing through a 60-120 mesh silica packed column. Evaporation of the solvent in vacuo yielded (0.46 g, 85%) of 3-methoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide m.p. 52-53°C; (Found C 43.3%, H 5.27%, C7H10O4S; requires C 44.2%, H 5.29%); \(^1^H\) n.m.r. (CD\(_3\)OD, 200 MHz) \(\delta\) [ppm]: 2.46-2.58 (2H, ABX, (CH\(_2\)), \(J_{gem}\) 16Hz, J 8Hz, J 6Hz), 2.81-3.05 (1H, dist.d, H\(_2\), J\(_2\), 9Hz), 3.30-3.62 (2H, cm, H\(_2\) and H\(_3\)), 3.70 (3H, S, (CH\(_3\))), 4.71-4.81 (2H, m, H\(_4\) and H\(_5\)); \(^{13}\)C n.m.r. (CD\(_3\)OD, 200 MHz) \(\delta\) [ppm]: 35.24 C3, 36.59 (CH\(_2\)), 50.52 (CH\(_3\)), 52.51 C2, 131.01 C4, 142.33 C5, 170.82 (CO); m/z 190 (M \(^+\)), 159 (M-OCH\(_3\))\(^+\), 126 (M-SO\(^+\)).

(b) Using acidified methanol

3-Carboxymethyl-2,3-dihydrothiophene-1,1-dioxide (0.5 g, 2.8 mmol) in methanol (30 ml) and conc. sulphuric
acid (0.125 g) was heated to boiling for 96h. Solid sodium bicarbonate (0.1 g) was then added and the solvent removed in vacuo giving an oil (0.59 g). The crude material later solidified to yield 3-methoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide, as identified by n.m.r. spectroscopy.

5. Reduction of 3-Ethoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide

A number of reductions were carried out under various conditions and these are outlined in Table 2 and Table 3 of the Results and Discussion, Section B. An example of the procedure employed for reductions with lithium aluminium hydride and sodium borohydride is given below.

(a) Using lithium aluminium hydride

Anhydrous conditions were required for this reaction. To a suspension of lithium aluminium hydride (0.22 g, 6 mmol) in dry THF (8 ml), was added dropwise a solution of 3-ethoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide (0.39 g, 2 mmol) in THF (5 ml). The reaction mixture was heated to boiling for 4h, then allowed to stand overnight at room temperature. Water (0.2 ml), then 15% sodium hydroxide (0.2 ml), followed by water (0.2 ml) were added. The fine white solid was filtered and the solvent evaporated from the filtrate in vacuo. Distillation gave a colourless oil (0.12 g, 68%) of 3-(2'-hydroxyethyl)-tetrahydrothiophene-1,1-dioxide b.p. 190°C, 0.8 mm Hg;
(Found C 43.8%, H 7.48%, C₆H₁₂O₃S, requires C 43.8%, H 7.36%); $\nu_{\text{max}}$ 3440 (OH), 1300 and 1145 (SO₂), 1120 cm⁻¹ (C-O); 'H n.m.r. (CDCl₃, 80 MHZ) δ[ppm]: 1.25-1.85(2H, m, H₁, J₁,₂ 6Hz), 1.90-3.37(8H, cm, H₂, H₃, H₄ and H₅), 3.50-3.75(2H, t, H₂', J₁',₂', 6Hz); ¹³C n.m.r. (CDCl₃, 200 MHz) δ[ppm]: 28.88 Cl', 33.66 C₃, 36.65 C₄, 51.81 C₅, 56.59 C₂, 59.78 C₂', m/z 147(M-OH⁺), 134(M-CH₂O⁺).

(b) Using sodium borohydride

3-Ethoxycarbonylmethyl-2,3-dihydrothiophene-1,1-dioxide (0.3 g, 1.5 mmol) in dry methanol (15 ml) was added slowly to sodium borohydride (0.55 g, 15 mmol). The mixture was refluxed for 2h and water (20 ml) was then added. Most of the methanol was removed by evaporation in vacuo and a further 20 ml of water was added. The solution was extracted with methylene chloride (5 x 20 ml) and the extracts combined and dried over anhydrous magnesium sulphate. Subsequent evaporation of the solvent in vacuo gave a brown oil (145 mg). Preparative thin layer chromatography over silica, eluting with ether/acetone (50:50) resulted in the isolation of 3-(2'-hydroxyethyl)-tetrahydrothiophene-1,1-dioxide (41 mg, 25%) and (29 mg, 11%) of tetrahydrothieno[3,4-d]-1-oxole-5,5-dioxide as a colourless solid m.p. 83-85°C $\nu_{\text{max}}$ 1300 and 1145 (SO₂), 1100 cm⁻¹ (R-O-R); 'H n.m.r. (CDCl₃, 200 MHZ) δ[ppm]: 1.73-1.99(1H, m, H₃A), 2.19-2.37 (1H, m, H₃B), 2.86-2.92(1H, m, H₄A), 3.01-3.14(1H, m, H₂A), 3.16-3.43(3H, m, H₄B and H₆), 3.77-3.86(1H, m, H₂A),
3.99-4.10 (1H, m, H₂B), 4.56-4.65(1H, m, H₆A); ¹³C n.m.r. (CDCl₃, 200 MHz, DEPT) δ[ppm]: 31.46 C3, 38.55 C3a, 54.03 C4, 55.87 C6, 67.48 C2, 77.61 C6a; m/z 162(M⁺), Calc. 162.0351; exp. 162.0345, dev. 3 ppm.

A different work-up procedure was employed for reactions carried out at room temperature or less. A two molar excess of 15% hydrochloric acid is added and most of the solvent is evaporated under vacuum. Water is then added and the mixture extracted into methylene chloride as outlined in the above procedure.

6. Preparation of Tetrahydrothieno[3,4-d]-1-oxole-2(3H)-one-5,5-dioxide

Using the procedure outlined by Argy1⁵⁴, 3-carboxymethyl-2,3-dihydrothiophene-1,1-dioxide (3.3 g, 19 mmol) was heated to boiling in water for 3 days. On cooling a colourless solid precipitated. This was filtered and dried over anhydrous magnesium sulphate to give tetrahydrothieno[3,4-d]-1-oxole-2(3H)-one-5,5-dioxide (3.1 g, 95%) m.p. 160-162°C (lit.⁵⁴, 160-162°C); ¹³C n.m.r. (CD₃SOCD₃, 200 MHz, DEPT) δ[ppm]: 32.84 C3a, 33.87 C3, 53.11 and 53.20 C4 and C6, 76.99 C6a.

7. Reduction of Tetrahydrothieno[3,4-d]-1-oxole-2(3H)-one-5,5-dioxide with Lithium Aluminium Hydride

The reaction conditions were varied and these are outlined in Table 11. A general procedure was employed
and is described as follows. To a suspension of lithium aluminium hydride (0.36 g, 9.3 mmol) in dry THF (15 ml) under an atmosphere of nitrogen, was added the lactone tetrahydrothieno[3,4-d]-1-oxole-2(3H)-one-5,5-dioxide (0.31 g, 1.8 mmol), and it was noted that a gas presumed to be hydrogen was given off. The mixture was stirred at room temperature for 2h. Water (0.3 ml), 15% sodium hydroxide (0.3 ml) and then water (0.9 ml) were added consecutively and the suspension then filtered. Evaporation of the solvent from the filtrate in vacuo resulted in a pale coloured oil, which was distilled to give 3-(2′-hydroxyethyl)-tetrahydrothiophene-1,1-dioxide (0.19 g, 59%) b.p. 190°C, 0.8 mm Hg.

Table 11  Lithium aluminium hydride reduction of the lactone (127)

<table>
<thead>
<tr>
<th>Excess</th>
<th>Temp.</th>
<th>Time</th>
<th>Solvent</th>
<th>of AlH₄</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>64°C</td>
<td>7h</td>
<td>THF +</td>
<td>4 fold</td>
<td>(124) (63%)</td>
</tr>
<tr>
<td></td>
<td>Room Temp.</td>
<td>2h</td>
<td>THF</td>
<td>10 fold</td>
<td>(124) (59%)*</td>
</tr>
</tbody>
</table>

(124) Fully reduced compound, 3-(2′-hydroxyethyl)-tetrahydrothiophene-1,1-dioxide.

* After distillation.
C. PREPARATION OF 3,3-DENDRALENE STARTING FROM 2,5-DIHYDROTHIOPHENE-1,1-DIOXIDE

1. Preparation of 3,4-Epoxytetrahydrothiophene-1,1-dioxide
(a) Using meta-chloroperbenzoic acid

A solution of 2,5-di hydrothiophene-1,1-dioxide (1.0 g, 8.5 mmol) and 85% meta-chloroperbenzoic acid (1.7 g, 8.5 mmol) in ethyl acetate (40 ml) was heated to boiling for 48h. The solution was washed with 10% sodium thiosulphate (50 ml), 5% sodium bicarbonate (25 ml) and brine solution (25 ml). The ethyl acetate was then evaporated in vacuo and the residue dried under high vacuum to give a brown oil (0.8 g) shown by $^{13}$C n.m.r. spectroscopy to be a mixture of the starting material, 2,5-di hydrothiophene-1,1-dioxide and 3,4-epoxytetrahydrothiophene-1,1-dioxide in a ratio of approximately 4:1, $^{13}$C n.m.r. (CD$_3$SOCD$_3$, 200 MHz, DEPT) $\delta$[ppm]: 55.18 (CH$_2$), 124.72 (CH) butadiene sulphone; 51.90 (CH), 53.26 (CH$_3$) epoxide.

(b) Using peracetic acid

A solution of 2,5-di hydrothiophene-1,1-dioxide (0.9 g, 7.6 mmol) and 30% hydrogen peroxide (4.2 ml, 37 mmol) in
acetic acid (25 ml), was warmed to 50°C for 4 days. A saturated solution of sodium bicarbonate was then added until the solution was neutral ca. 10 ml. The solution was extracted into ethyl acetate (4 x 40 ml) and the combined extracts were washed again with dilute sodium bicarbonate solution. Water and ethyl acetate were then removed in vacuo. The resultant brown oil (0.3 g) was shown by n.m.r. to be a mixture of 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide, 13C n.m.r. (CD3SOCD3, 200 MHz, DEPT) δ[ppm]: 56.48 C2, 67.11 C3, 132.32 C4, 142.88 C5 and the starting material 2,5-dihydrothiophene-1,1-dioxide; 55.15 (CH2), 124.72 (CH) in a ratio of approximately 1:3.

(c) Using performic acid

A modification on the method of Sorrenson\textsuperscript{60} was employed. To an ice cooled solution of 2,5-dihydrothiophene-1,1-dioxide (85 g, 0.72 mol) in 98% formic acid (425 ml), was added 30% hydrogen peroxide (107 g). The mixture was allowed to stand at room temperature for 45 days. A starch iodide paper test for peroxides proved negative, and ca. 80% of the solvent was evaporated in vacuo. The solid was filtered, washed with water and dried to give (39.2 g, 42%) of 3,4-epoxytetrahydrothiophene-1,1-dioxide as colourless plates m.p. 160-163°C, from ethyl acetate (lit.\textsuperscript{60}, 159.5-160°C, from acetone); 13C n.m.r. (CD3SOCD3, 200 MHz, DEPT) δ[ppm]: 51.93 (CH), 53.30 (CH2).
2. Preparation of 3-Hydroxy-4-vinyltetrahydrothiophene-1,1-dioxide

A standard preparation of vinyl magnesium bromide was employed and this is outlined by Seyforth\textsuperscript{110}. A three-necked round bottom flask equipped with a dry ice condenser was used, and the entire procedure was carried out in anhydrous conditions under nitrogen. To magnesium turnings (3.6 g, 0.15 mole) in dry THF (40 ml) was added ca. a 1 ml portion of the freshly distilled vinyl bromide (31.4 g, 0.30 mol) in THF (10 ml). A crystal of iodine and one drop of methyl iodide were required to initiate the reaction. Once the reaction had started the rest of the vinyl bromide solution was added at rate sufficient to maintain gentle boiling along with a further (40 ml) of dry THF. The entire mixture was then added over 15 min to a stirred solution of 3,4-epoxytetrahydrothiophene-1,1-dioxide (10 g, 0.075 mol) in dry THF (35 ml). The cloudy suspension was heated to boiling for 1h and on cooling poured into crushed ice (500 ml) containing conc. sulphuric acid (100 ml). The THF was removed \textit{in vacuo} and the residue extracted continuously with methylene chloride. Evaporation \textit{in vacuo} of the solvent and a thorough drying of the residue with a vacuum pump resulted in a brown oil (10.13 g, 83\%) of 3-hydroxy-4-vinyltetrahydrothiophene-1,1-dioxide. Attempts to distill the oil resulted in charring, decomp. 110°C, 0.2 mm Hg; \textit{v}_\text{max} 3480 (OH), 1300 and 1115 (SO\textsubscript{2}), 1640 (C=C), 1000 and 920 cm\textsuperscript{-1} \omega
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(CH₂); 'H n.m.r. (CDCl₃, 200 MHz) δ[ppm]: 3.08-3.37 (6H, cm, H₂, H₅, H₄ and OH), 4.54-4.57 (1H, m, H₃), 5.25- 5.29 (2H, m, vinyl (CH₂)), 5.89 (1H, ddd, vinyl (CH), Jcis 10.4Hz, Jtrans 16.8Hz, J(CH), 4 6Hz); '³C n.m.r. (CDCl₃, 200 MHz, DEPT) δ[ppm]: 44.03 C₄, 52.32 C₅, 61.19 C₂, 70.58 C₃, 118.91 vinyl (CH₂), 133.27 vinyl (CH); m/z 162(M⁺), 118 (M-C₂H₄OH⁺), 98(M-SO₂⁺), 54(C₄H₆⁺), Calc. 162.0351, exp. 162.0351, dev., 0 ppm.

3. Preparation of 3-Acetoxy-4-vinyltetrahydrothiophene-1,1-dioxide

(a) With acetyl chloride

The acetylation method of Trahanovsky¹¹¹ was used. To a stirred solution of 3-hydroxy-4-vinyltetrahydrothiophene-1,1-dioxide (6.2 g, 38 mmol) and triethylamine (18.5 g, 180 mmol) in dry THF (40 ml), was slowly added a solution of acetyl chloride (6.9 g, 88 mmol) in THF (10 ml). The mixture was stirred at 20°C for 3h. Water (60 ml) was then added and most of the THF removed in vacuo. The residue was extracted into methylene chloride (5 x 30 ml), the extracts combined and dried over anhydrous magnesium sulphate. Removal of the solvent in vacuo left a brown oil (10.1 g). This was sublimed onto a cold finger at 100°C, 0.2 mm Hg, to yield a colourless solid (4.61 g) which showed two spots on t.l.c. Using preparative t.l.c. with silica plates and eluting with hexane/ethyl acetate (1:1), the two products were
separated to give (80%) 3-acetoxy-4-vinyltetrahydrothiophene-1,1-dioxide as colourless crystals m.p. 110-112°C from ethyl acetate (Found C 47.1%, H 5.95%, C₇H₁₂O₄S; requires C 47.1%, H 5.88%); \( \nu_{\text{max}} \) 1750 (CO), 1305 and 1125 (SO₂), 1230 (C=CO-O), 1025 and 940 cm⁻¹ \( \omega \)(CH₂);

\(^1\)H n.m.r. (CDCl₃, 200 MHz) \( \delta \)[ppm]: 2.08(3H, s, (CH₃), 3.21-3.39(5H, m, H₁, H₅, H₄), 5.19(1H, d, vinyl (CH₂), Jtrans 17Hz), 5.24(1H, d, vinyl (CH₂), Jcis 11Hz), 5.47-5.51(1H, m, H₃), 5.68-5.85(1H, m, vinyl (CH); \(^{13}\)C n.m.r. (CDCl₃, 200 MHz) \( \delta \)[ppm]: 20.25 (CM₃), 43.75 C4, 52.75 C5, 58.41 C2, 71.66 C3, 118.80 vinyl (CH₂), 131.75 vinyl (CH), 169.36 (CO); m/z 204(M⁺), 161(M-CH₃CO⁺), 140(M-SO₂⁺), 86(M-C₄H₆SO₂⁺); Calc. 204.0456, exp. 204.0454, dev. 1 ppm; and 20% of 3-acetoxy-2,3-dihydrothiophene-1,1-dioxide m.p. 111-113°C from ethyl acetate (lit.¹⁰⁰, 111.5-112.5°C), (Found C 40.9%, H 4.57% C₆H₈O₂S; requires C 40.9%, H 4.55%); \( \nu_{\text{max}} \) (KBr) 1740 (CO), 1295 and 1105 (SO₂), 1620 (C=C), 1415 \( \delta \)S (CH₃), 1380 \( \delta \)as (CH₃), 1240 cm⁻¹ (C=CO-O); \(^1\)H n.m.r. (CDCl₃, 200 MHz) \( \delta \)[ppm]: 2.11(3H, s, (CH₃), 3.14-3.22(1H, q, H₂, Jgem 14Hz, J₁,₂,₃ 3Hz), 3.64-3.75(1H, q, H₂, Jgem 14Hz, J₂,₃,₄ 7Hz), 5.86-5.93(1H, m, H₃), 6.70-6.84(2H, pd, H₄ and H₅, J₄,₅ 6Hz); \(^{13}\)C n.m.r. (CDCl₃, 200 MHz) \( \delta \)[ppm]: 20.51 (CH₃), 53.96 C2, 68.84 C3, 135.55 C4, 136.25 C5; m/z 176(M⁺), 134(M-CH₃CO⁺), 116(M-CH₂CO₂H⁺), Calc. 176.0143, exp. 176.0138, dev. 3 ppm.

A separation was carried out by flash chromatography
over Sorbsil 40/60 silica, using a gradient elution of petroleum ether 40-60°C and ethyl acetate, giving (4.72, 61%) of the title compound.

(b) Using 4-dimethylaminopyridine and acetic anhydride

A solution of acetic anhydride (0.43 g, 4.2 mmol), triethylamine (0.53 g, 5.3 mmol) and 4-dimethylaminopyridine (0.09 g, 0.07 mmol) in dry chloroform (15 ml) was stirred for 12h at 18°C under nitrogen. The reaction mixture was then washed with 10% citric acid solution (20 ml), water (10 ml) and the chloroform removed in vacuo. The resultant brown material was sublimed at 100°C, 0.3 mm Hg to give a colourless solid (0.31 g). H n.m.r. indicated a mixture of 3-acetoxy-4-vinyltetrahydrothiophene-1,1-dioxide and 3-acetoxy-2,3-dihydrothiophene-1,1-dioxide, in a ratio of (4:1).

4. Preparation of 3-Vinyl-2,3-dihydrothiophene-1,1-dioxide

F.v.p. [60°C, 660°C, 1.3 x 10^{-2} mm Hg] of 3-acetoxy-4-vinyltetrahydrothiophene-1,1-dioxide (37 mg, 0.18 mmol) gave a pale yellow oil shown by n.m.r. spectroscopy to be only one product. Acetic acid was removed under high vacuum and sublimation at 38°C, 0.7 mm Hg resulted in 3-vinyl-2,3-dihydrothiophene-1,1-dioxide as an oily colourless solid (15 mg, 54%) (Found C 49.7%, H 5.86%, C_{6}H_{8}O_{2}S; required C 49.9%, H 5.59%); \nu_{\text{max}} 1300 and 1140 (SO_{2}), 995 and 890 vinyl (CH), 1640 vinyl (C=C), 1600 cm^{-1}
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(C=C); 'H n.m.r. (CDCl₃, 200 MHz) δ[ppm]: 2.95(1H, dd, H₂, Jₜₜ 13.6Hz, Jₜᵢ 8.3Hz), 3.41(1H, dd, H₂', Jₜₜ 13.6Hz), 3.73-3.77(1H, m, H₃), 5.14-5.23(2H, m, vinyl (CH₂), Jₜₜ 17.1Hz, Jₜᵢ 9.9Hz), 5.73(1H, ddd, vinyl (CH), Jₜₜ 17.1Hz, Jₜᵢ 9.9Hz, J(CH), 7Hz), 6.59-6.64(2H, m, H₄ and H₅, J₄,₅ 6.6Hz); ¹³C n.m.r. (CDCl₃, 200MHz, DEPT) δ[ppm]: 42.62 C₃, 53.28 C₂, 118.15 vinyl (CH₂), 131.61 vinyl (CH), 135.15 C₄, 141.40 C₅, m/z 144 (M⁺), 96(M-SO⁺), 54(C₄H₆⁺), Calc. 144.0245, exp. 144.0236, dev. 6 ppm.

5. Attempted Isomerisation of 3-Vinyl-2,3-dihydrothiophene-1,1-dioxide

(a) With Wilkinson’s catalyst

A solution of 3-vinyl-2,3-dihydrothiophene-1,1-dioxide (139 mg, 1 mmol) and tris(triphenylphosphine)rhodium(I) chloride in chloroform (20 ml), were heated to boiling for 4h. The solvent was then removed in vacuo and ethanol (7 ml) added to the residue. The solid material was filtered and the solvent evaporated in vacuo from the filtrate to affect the recovery of the starting material, 3-vinyl-2,3-dihydrothiophene-1,1-dioxide (130 mg, 94%).

(b) With acid catalysis

A solution of 3-vinyl-2,3-dihydrothiophene-1,1-dioxide (99 mg, 0.7 mmol) and anhydrous oxalic acid (14 mg, 0.2 mmol) in dry ethanol (20 ml), was stirred at 35°C for
4h under nitrogen. The ethanol was then evaporated under vacuum and methylene chloride (5 ml) added to the residue. The oxalic acid precipitate was filtered and when the solvent was evaporated in vacuo from the filtrate, a brown oily residue was left (154 mg). This was shown by n.m.r. spectroscopy to be the starting materials, 3-vinyl-2,3-dihydrothiophene-1,1-dioxide and oxalic acid.

6. Isomerisation of 3-Vinyl-2,3-dihydrothiophene-1,1-dioxide

Reaction conditions were varied in order to optimize the formation of 3-vinyl-2,5-dihydrothiophene-1,1-dioxide and these are given in Section C, Table 4, of the Results and Discussion. Based on these results, the experimental procedure that was employed for this reaction is given below.

To 3-vinyl-2,3-dihydrothiophene-1,1-dioxide (1.37 g, 9.5 mmol) in dry THF (60 ml) was added 1,8-diazabicyclo-[5.4.0]undec-7-ene (190 mg, 1.2 mmol). The solution was stirred at 40°C for 24h. Ethyl acetate (40 ml) was added, and then half of the solvent evaporated under reduced pressure, at room temperature. This step was repeated and the resultant solution washed with 5% hydrochloric acid (25 ml), then brine solution (30 ml) and finally water (20 ml). Ethyl acetate was removed in vacuo at room temperature and the resultant 3-vinyl-2,5-dihydrothiophene-1,1-dioxide was dried on a high vacuum pump to
leave colourless crystals (1.08 g, 79%) which were purified by sublimation at 38°C, 0.77 mm Hg; m.p. 75-76°C (Found C 50.2%, H 5.72%, C₆H₈O₂S; requires C 49.9%, H 5.59%); \( \nu_{\text{max}} \) 1300 and 1123(SO₂), 1640(C=C), 1025 and 925 cm⁻¹ vinyl (CH); \(^1\)H n.m.r. (CDCl₃, 200 MHz) \( \delta \text{[ppm]}: \)

3.82-3.92(4H, m, H₂ and H₅), 5.13(1H, d, vinyl (CH₂), Jₜrans 17Hz), 5.31(1H, d, vinyl (CH₂), Jₜcis 11Hz), 5.92-5.96(1H, m, H₄), 6.42(1H, dd, vinyl (CH), Jₜcis 10Hz, Jₜrans 17Hz); \(^{13}\)C n.m.r. (CDCl₃, 200 MHz, DEPT) \( \delta \text{[ppm]}: \)

54.65 C₂, 57.19 C₅, 118.32 vinyl (CH₂), 121.08 C₄, 132.37 vinyl (CH); FAB-glycerol, m/z (M+1⁺), Calc. 145.0323, exp. 145.0323, dev. < 1 ppm.

7. Preparation of 3-(para-toluenesulphonyl)-4-vinyltetrahydrothiophene-1,1-dioxide

A solution of 3-hydroxy-4-vinyltetrahydrothiophene-1,1-dioxide (0.16 g, 1 mmol) and para-toluenesulphonyl chloride (0.38 g, 2 mmol) in dry pyridine (8 ml) was stirred under nitrogen at 60°C for 4h. The mixture was poured into 5% V/V sulphuric acid and crushed ice solution (150 ml) and then extracted into methylene chloride (4 x 20 ml). The combined extracts were dried over magnesium sulphate and the solvent evaporated in vacuo to afford a brown oil (0.1 g). Purification by dry flash chromatography with Kieselgel 60, and a gradient elution of ethyl acetate/hexane; resulted in colourless crystalline prisms (33 mg, 11%) of 3-(para-toluenesulphonyl)-4-vinyltetrahydrothiophene-1,1-dioxide m.p.
134-135°C from chloroform/hexane (Found C 49.2%, H 5.11%, C\textsubscript{13}H\textsubscript{11}O\textsubscript{5}S\textsubscript{2}; required C 49.4%, H 5.09%); \(\nu_{\text{max}}\) 1300, 1225 and 1180 (SO\textsubscript{2}) and (SO\textsubscript{3}), 903 cm\(^{-1}\) aromatic (CH); \(^1\)H n.m.r. (CDCl\textsubscript{3}, 200 MHz) \(\delta\) [ppm]: 2.45 (3H, s, (CH\textsubscript{3})), 3.15-3.35 (5H, m, H\textsubscript{2}\textsubscript{1}, H\textsubscript{5} and H\textsubscript{6}), 5.12-5.21 (3H, m, H\textsubscript{3} and vinyl(CH\textsubscript{2})), 5.58-5.72 (1H, m, vinyl(CH)), 7.33-7.37 (2H, dist.d, m(CH), J 9Hz), 7.73-7.79 (2H, dist.d, o(CH), J 9Hz and fine para coupling); \(^{13}\)C n.m.r. (CDCl\textsubscript{3}, 200 MHz, DEPT) \(\delta\) [ppm]: 21.58 (CH\textsubscript{3}), 44.73 C4, 52.51 C5, 58.49 C2, 78.31 C3, 120.09 vinyl (CH\textsubscript{2}), 127.83 (CH), 129.99 (CH), 130.86 vinyl (CH); FAB-glycerol m/z (M+1\(^+\)) Calc. 317.05173, exp. 317.05171, dev. < 1 ppm.

8. Preparation of 3-Vinyl-2,5-dihydrothiophene-1,1-dioxide from 3-(para-toluenesulphonyl)-4-vinylthiophene-1,1-dioxide

To 3-hydroxy-4-vinylthiophene-1,1-dioxide (0.39 g, 2.4 mmol) in dry pyridine (5 ml) was added para-toluene-sulphonyl chloride (0.94 g, 5 mmol) in dry pyridine (5 ml). The mixture was heated to boiling for 2 h under an atmosphere of dry nitrogen, allowed to cool and then poured into a 3% V/V sulphuric acid and crushed ice solution (150 ml). The aqueous mixture was then extracted into methylene chloride (4 x 10 ml) and the extracts combined and dried over anhydrous magnesium sulphate. Evaporation of the solvent under vacuum gave a dark oily
solid which was purified using chromatotron chromatography and elution with ether. The resulting colourless solid (23 mg, 7%) was found to be 3-vinyl-2,5-dihydrothiophene-1,1-dioxide which was sublimed at 40°C, 0.1 mm Hg, m.p. 75-76°C.

9. Flash Vacuum Pyrolysis of 3-Vinyl-2,5-dihydrothiophene-1,1-dioxide

All pyrolysis glassware was rinsed with a solution of galvinoxyl ca. 5 mg in acetone (25 ml) and dried in a stream of air. F.v.p. [40°C, 550°C, 5 x 10⁻³ mm Hg] of 3-vinyl-2,5-dihydrothiophene-1,1-dioxide (0.60 g, 7.5 mmol), followed by flash distillation of the pyrolysate into a second liquid nitrogen cooled trap, resulted in the isolation of 3-methylene-1,4-pentadiene as a colourless oil (0.29 g, 87%) b.p. 50°C (lit. 8, 32°C, 200 mm Hg); IR (liq. cap. film) ν_max 3087 and 3004 ν(CH), 2975, 2920, 1970, 1825, 1792, 1715, 1630 and 1606 ν_as(C=C), 1585, 1572 shoulder, 1425 and 1383 δ_S(CH), 1292 δ_S(CH), 1070, 1039, 989 and 919-910 ω(CH₂) 897, 760, 745, 695, 620, 500, 372 cm⁻¹; ν_max (gas) 3085 ν(CH), 2990, 2920, 1835, 1804, 1631 and 1590 ν_as(C=C), 1425 and 1380 δ_S(CH₂), 1272 ρ(CH), 1058, 1039, 988 and 910 ω(CH₂), 897, 760, 753, 615, 505, 365 cm⁻¹; Raman (liq. film) ν_max 3085 ν(CH), 3004 ν(CH), 1645 1630p 1620p 1606 and 1580p ν(C=C), 1430p and 1418p δ_S(CH₂), 1290p 1258p ρ(CH), 1185 ν(C=C), 1072p and 1045 ρ(CH₂), 990p, 938, 910p, 890p ω(CH₂), 810, 780p τ(CH₂),
760, 735, 712 $\tau$(CH$_2$), 640, 542p, 496, 415, 360, 310, 250 cm$^{-1}$ (bands marked p were polarised then depolarised); $^1$H n.m.r. (CDCl$_3$, 360 MHz) $\delta$(ppm): 5.12-5.17(2H, d, fs, H$_6$, J$_{cis}$ 11Hz, J$_{gem}$ 2Hz), 5.15(2H, s, fs, H$_1$ and H$_1'$), 5.40(2H, dd, H$_5$, J$_{trans}$ 18Hz, J$_{gem}$ 2Hz), 6.45(2H, dd, fine splitting, H$_4$, J$_{trans}$ 18Hz, J$_{cis}$ 11Hz); $^{13}$C n.m.r. (CDCl$_3$, 360 MHz, coupled) $\delta$(ppm): 115.39(tt, B, J$_B$H$_1$ and H$_1'$, 158 Hz), 115.53(dd, A, J$_A$H$_5$ and J$_A$H$_6$ 159Hz and 155Hz), 135.62(m, C, J$_C$H$_4$ 154Hz); the labelling for dendralene may be found in the Results and Discussion, Section D.

D. CYCLOADDITION REACTIONS

1. Preparation of 5,7,9,9a-Tetrahydro-2-phenyl-1H-thieno-[3,4-c][1,2,4]triazolo[1,2-a]pyridazine-1,3-(2H)-dione-8,8-dioxide

The title compound was prepared by leaving 3-vinyl-2,5-dihydrothiophene-1,1-dioxide (184 mg, 1.3 mmol) and 4-phenyl-1,2,4-triazoline-3,5-dione (220 mg, 1.3 mmol in a sealed tube with acetone (12 ml) at 52°C for 6h. The completion of the reaction was indicated by the loss of pink colouration. Evaporation of the acetone in vacuo followed by the addition of diethyl ether ca. 0.5 ml resulted in the formation of a cream coloured solid. This was filtered to yield (260 mg, 64%) of 5,7,9,9a-tetrahydro-2-phenyl-1H-thieno[3,4-c][1,2,4]triazolo[1,2-a]-
pyridazine-1,3-(2H)-dione-8,8-dioxide decomp. 225°C from chloroform/hexane/trifluoracetic acid (Found C 52.6%, H 4.04%, N 13.2%, C_{14}H_{12}N_{3}O_4S: requires C 52.6%, H 4.08%, N 13.2%); r_{\text{max}} 1710 (CO), 1322 and 1135 (SO_2), 710 cm\(^{-1}\) aromatic (CH); 'H n.m.r. (CDCl\(_3\)/CF\(_3\)CO\(_2\)H, 360 MHz) \(\delta\) [ppm]: 3.41-3.53(1H, dd, H\(_9\)A, J\text{gem} 10Hz, J\(_9\)A,\(_9\)a 13Hz), 3.92-4.03(2H, bpd, H\(_5\), J\text{gem} 16Hz), 4.13-4.26(2H, m, H\(_7\)A and H\(_9\)a), 4.46-4.58(1H, dd, H\(_9\)B, J 18Hz, J 1Hz), 4.77-4.89(1H, bt, H\(_9\)B, J\text{gem} 10Hz, J\(_9\)B,\(_9\)a 10Hz), 6.09-6.16(1H, bs, H\(_6\)), 7.38-7.55(5H, m, (Ph)); assignments were made using single frequency spin decoupling of individual proton resonances; decpl. H\(_6\) (H\(_7\)A,H\(_7\)B), H\(_9\)B ((H\(_7\)A H\(_9\)A), H\(_9\)A), H\(_7\)B ((H\(_7\)A H\(_9\)A), H\(_5\) small, H\(_6\)), (H\(_7\)A,H\(_9\)A) (H\(_9\)B, H\(_7\)B,H\(_9\)A), H\(_5\) (H\(_6\)), H\(_9\)A (H\(_9\)B,(H\(_7\)A:H\(_9\)a), H\(_6\) small). ^{13}\text{C} n.m.r. (CDCl\(_3\)/CF\(_3\)CO\(_2\)H, 200 MHz) \(\delta\) [ppm]: 42.92 C5, 53.59 C9a, 55.09 C9, 56.90 C7, 121.09 C6, 126.56 (CH), 126.75 Q C6a, 128.56 (CH), 129.23 (CH), 131.35 Q(CH), 151.59 and 153.71 (CO); m/z 319(M^{+}), 91(C\(_6\)H\(_5\)N^{+}), Calc. 319.0626, exp. 319.0610, dev. 5 ppm.

2. Reaction of [3] Dendralene with 4-Phenyl-1,2,4-triazoline-3,5-dione

A solution of [3] dendralene (65 mg, 0.82 mmol) and 4-phenyl-1,2,4-triazoline-3,5-dione (287 mg, 1.6 mmol) in acetone (8 ml) was heated at 40°C in a sealed tube for 28h. The solvent was then evaporated in vacuo and methylene chloride (5 ml) was added. On standing in the
freezer overnight, a colourless precipitate was formed. This was filtered and the colourless crystals (68 mg, 21%) identified as $5,7,13,13a$-tetrahydro-2,10-diphenyl-1H,9H-$[1,2,4]$triazolo[1,2-a]$[1,2,4]$triazolo[1',2':1,2]$pyridazino-[4,5-c]$pyridazine-1,3,9,11-(2H,10H)-tetrone m.p. 223-225°C from ethanol containing 1% trifluoroacetic acid, (Found C 61.5%, H 4.20%, N 19.7%, $C_7H_{18}N_6O_2$; requires C 61.4%, H 4.18%, N 19.5%); $\nu_{max}$ 1780 and 1700 (CO), 1035 and 1015 cm$^{-1}$ aromatic (CH); $^1$H n.m.r. (CDCl$_3$/CF$_3$CO$_2$H, 200 MHz) $\delta$[ppm]: 3.16-3.27(1H, t, $H_{13}B$, $J_{gem}$ 11Hz, $J_{13,13a}$ 11Hz), 3.91-3.98(1H, d, $H_{7B}$, $J_{gem}$ 13Hz), 4.22-4.39(2H, bpd, $H_5$, $J_{gem}$ 15Hz), 4.54-4.62(1H, m, $H_{13a}$), 4.64-4.71(1H, d, $H_{7A}$, $J_{gem}$ 13Hz), 5.19-5.29(1H, dd, $H_{13A}$, $J_{gem}$ 11Hz, $J_{13A,13a}$ 5Hz), 6.21(1H, bs, $H_5$), 7.36-7.53(10H, m, (Ph)); single frequency decoupling (CDCl$_3$/CF$_3$CO$_2$H, 360 MHz), decpl. $H_5$ ($H_5$, $H_{13a}$ small), $H_{13a}$ ($H_{13a}$), $H_{7B}$ ($H_{7B}$), $H_{13a}$ ($H_{13A}$, $H_{13B}$, $H_{7B}$ and $H_5$ small), $H_5$ ($H_5$, $H_{13a}$ small), $H_{7B}$ ($H_5$, $H_{7A}$), $H_{13B}$ ($H_{13A}$,$H_{13a}$); $^{13}$C n.m.r. (CDCl$_3$/CF$_3$CO$_2$H, 200 MHz) 42.39 C13, 46.08 C5, 48.31 C7, 52.68 C13a, 120.39 C6, 125.37, 125.45, 128.58, 128.61, 129.21 (Ph), 125.95 C6a, 130.22 and 130.43 Q(Ph), 151.33, 151.68, 152.05, 152.41 (CO); m/z 430(M$^+$), 91($C_6H_5N^+$), Calc. 430.1389, exp. 430.1407, dev. 4 ppm.


[3] Dendralene (0.20 g, 2.5 mmol) and maleimide (0.48 g, 5.0 mmol) in THF (15 ml) were heated in a sealed
tube at 70°C for 27h. The colourless precipitated product was filtered and washed with THF to give (0.29 g, 65%) of 3a,4,6,6a,9a,10,10a,10b-octahydroisoindolo[5,6-e]-isonidole-1,3,7,9(2H,8H)-tetrone decomp. 150°C after purification by soxhlet extraction into ethanol, (Found C 61.7%, H 5.31%, N 10.0%, C₁₄H₁₄N₂O₄; requires C 61.3%, H 5.11%, N 10.2%); νmax 3180 (NH), 1700 cm⁻¹ (CO); ¹H n.m.r. (C₅D₅N, 400 MHz) δ[ppm]: 1.77-1.81(1H, bddd, H₄A, Jgem 15Hz, J₄A,₅, 7.5Hz, J₃A,₄a 4Hz), 2.32-2.35(1H, m, H₁₀A), 2.44-2.49(1H, bddd, H₆A, Jgem 14Hz, J₆A,₆a 6.7Hz, J 2.5Hz), 2.55(1H, ddd, H₁₀A, Jgem 14Hz, J₁₀A,₁₀a 5Hz, J₈a,₁₀A 2.4Hz), 2.61(1H, dd, H₄B, Jgem 15Hz, J₃A,₄B 7.4Hz), 2.72(1H, ddd, H₆B, Jgem 14Hz, J₆B,₆a 2Hz), 2.96(1H, ddd, H₁₀B Jgem 14Hz, J₁₀B,₁₀a 14Hz, J₉a,₁₀B 6Hz), 3.06-3.12(2H, m, H₁₀B and H₃a), 3.15-3.19(1H, ddd, H₆a, J₆a,₆a 9.5Hz, J₆a,₆B 6Hz, J₆a,₆B 2Hz), 3.31-3.36(1H, ddd, H₉a, J₆a,₉a 9.5Hz, J₉a,₁₀B 2.4Hz, J₉a,₁₀B 6Hz), 5.64-5.69(1H, m, H₅), 11.07(2H, bps, NH); COSY ¹H n.m.r. (C₅D₅N, 250 MHz) H₄A to (H₄B,H₃A,H₅), H₁₀A to (H₁₀A,H₁₀B,H₁₀B), H₆A to (H₆B,H₆a), H₁₀A to (H₁₀B,H₉a, H₁₀a), H₄B to (H₃a,H₄A), H₆B to (H₆a,H₆A,H₉a small), H₁₀B to (H₁₀A,H₁₀a,H₉a), H₃a and H₁₀b to (H₄B,H₁₀A,H₉a), H₆a to (H₉a,H₆B,H₆a), H₉a to (H₆a,H₁₀B,H₁₀A,H₆B small); ¹H NOE (C₅D₅N, 360 MHz) irradiated H₄A (H₁₀a 1%,H₄B 8%,H₃a and H₁₀b 1%), H₁₀a (H₁₀A 1%,H₃a and H₁₀b 1%,H₄A 1%), H₁₀A (H₄A 1%,H₁₀B 9%,H₃a and H₁₀b 1%,H₉a 1%), H₄B (H₃a and H₁₀b 1%,H₅ 2½%,H₄A 6%), H₁₀B (H₉a 2%), H₆a (H₉a 4%,H₆B 4%,H₆A

The maleic anhydride adduct was prepared using the method of Bailey and Economy. This involved heating a solution of [3] dendralene (20 mg, 0.28 mmol) and maleic anhydride (50 mg, 0.56 mmol) in toluene (12 ml) over a steam bath for 2h. When the mixture was cooled a pale yellow solid fell out of solution. This was filtered and dried to give (71 mg, 92%) of 1,2,3,5,6,7,8,8a-octahydro-1,2,6,7-napthalenetetracarboxylic-1,2;6,7-dianhydride.


[3] Dendralene (55 mg, 0.7 mmol) and dimethyl acetylenedicarboxylate (0.36 mg, 2.8 mmol) in deuterated chloroform (0.5 ml) were heated in a sealed n.m.r. tube to 70°C for 72h. Spectroscopic analysis showed the product to be \(1,4,4a,7\)-tetrahydro-2,3,5,6-tetramethoxycarbonylnapthalene; \(\lambda_{\text{max}}\) 2955 (C=C-H), 1725 (CO), 1648 (C=C), 1260 cm\(^{-1}\) (C-CO-O); \(^1H\) n.m.r. (CDCl\(_3\), 80 MHz) \(\delta\) [ppm]: 2.86-3.07(6H, bs, H\(_1\), H\(_4\) and H\(_7\)), 4.57(OCH\(_3\)) obscured by excess DMAD), 4.82-5.29(1H, m, H\(_{8a}\)), 5.71(1H, bs, H\(_8\)); \(^{13}C\)
n.m.r. \((\text{CDCl}_3, 200 \text{ MHz})\), 27.14 C4, 32.75 C7, 33.68 C1, 34.37 C4a, 51.50 and 52.63 (OCH\(_3\)), 116.43 C8, 129.29 C5, 131.90 C6, 133.33 C3, 133.61 C2, 134.22 C8a, 167.19 and 167.38 (CO); \(m/z\) 364(M \(^+\)), 332(M-CH\(_3\)OH\(^+\)), Calc. 364.1158, exp. 364.1157, dev. < 1 ppm.


A solution of [3] dendralene (0.125 g, 1.6 mmol) and dimethyl acetylenedicarboxylate (0.22 g, 1.6 mmol) in methylene (45 ml) was heated in a sealed tube at 60°C for 5h and then allowed to stand overnight at room temperature. The solvent was removed in vacuo and the unreacted dimethyl acetylenedicarboxylate distilled off at 110°C, 25 mm Hg to give a brown oil identified as 1,2-dimethoxycarbonyl-5-vinyl-1,4-cyclohexadiene, (0.282 g, 80%) \(\nu_{\text{max}}\) 1728 (CO), 1439 \(\delta_{\text{as}}\)(CH\(_3\)), 1270 cm\(^{-1}\) (C-CO-0); \(^1\)H n.m.r. \((\text{CDCl}_3, 200 \text{ MHz})\) \(\delta\) [ppm]: 2.99(4H, bs, H\(_6\) and H\(_3\)), 3.72(OCH\(_3\), obscured by trace DMAD), 4.89-5.03(2H dist.t, vinyl(CH\(_2\)), \(J_{\text{trans}}\) 18Hz, \(J_{\text{cis}}\) 11Hz), 5.63(1H, bs, H\(_4\)), 6.19-6.34(1H, dd, vinyl(CH), \(J_{\text{trans}}\) 18Hz, \(J_{\text{cis}}\) 11Hz); \(^{13}\)C n.m.r. \((\text{CDCl}_3, 200 \text{ MHz}, \text{DEPT})\) \(\delta\) [ppm]: 28.18 C3, 26.34 C6, 51.91 (OCH\(_3\)), 111.90 vinyl(CH\(_2\)), 123.37 C4, 137.41 vinyl(CH), \(m/z\) 222(M \(^+\)), 220(M-2H\(^+\)), 191(M-O\(\text{Me}\)^+), 189((M-2H)-O\(\text{Me}\)^+), 163 (M-CO\(_2\)Me\(^+\)), Calc. 222.08920, exp. 222.0878, dev. 6 ppm.

[3] Dendralene (40 mg, 0.5 mmol) and para-benzoquinone (54 mg, 0.5 mmol) in toluene (14 ml) were stirred on a steam bath for 24h. The solvent was then evaporated to give a brown oil (89 mg, 90%) of 4a,5,8,8a-tetrahydro-7-vinylnapthoquinone. 13C n.m.r. (CDCl₃, 200 MHz, DEPT) δ[ppm]: 23.00 C5, 24.61 C8, 45.94 and 46.09 C4a and C8a, 111.35 vinyl(CH₂), 115.87 vinyl(CH), 125.69 C6, 138.57 and 139.14 C2 and C3.

The reaction was repeated by heating a solution of [3] dendralene (0.14 g, 1.8 mmol), benzoquinone (0.19 g, 1.8 mmol) and benzene (6 ml) in a sealed tube, at 60°C for 26h. The contents were then filtered and the residue evaporated in vacuo to leave a green oily material. This was judged by n.m.r. spectroscopy to be a mixture of the mono- and bis-adducts. Attempts to purify these materials on preparative t.l.c. were unsuccessful due to their decomposition on the plates.


A solution of [3] dendralene (61 mg, 0.76 mmol) and tetracyanoethylene (0.19 g, 1.5 mmol) in methylene chloride (6 ml) was heated in a sealed tube at 50°C for 72h. Most of the solvent ca. 70% was removed in vacuo leaving a brown solid; unreacted tetracyanoethylene, which was then filtered. Subsequent evaporation of the filtrate in vacuo resulted in a solid which was recrystallised from
cyclohexane to yield 4,5-tetracyano-2-vinylcyclohex-1-ene as yellow needles (0.16 g, 92%) m.p. 103-104°C. (Found C 69.2%, H 3.83%, N 27.0%; requires C 69.2%, H 3.85%, N 26.9%); \( \nu_{\text{max}} \) (KBr) 2232 (CN), 1618 (C=C), 998 and 937 cm\(^{-1}\) \( \omega \)(CH\(_2\)); \(^1\)H n.m.r. (CDCl\(_3\), 200 MHz) \( \delta \)[ppm]: 3.25(4H, s, H\(_3\) and H\(_6\)), 5.23-5.34(2H, pd, vinyl(CH\(_2\)), J\(_{\text{cis}}\) 11Hz, J\(_{\text{trans}}\) 17Hz), 5.83(1H, bs, H\(_1\)), 6.32-6.46(1H, dd, vinyl(CH), J\(_{\text{cis}}\) 11Hz, J\(_{\text{trans}}\) 17Hz); \(^13\)C n.m.r. (CDCl\(_3\), 200 MHz, DEPT) 31.22 C6, 32.31 C3, 116.03 vinyl(CH\(_2\)), 119.65 Cl, 135.03 vinyl(CH); m/z 208(M\(^+\)), 182.0682 (M-CN\(^+\)), 180.0553(M-CNH\(_2\)\(^+\)), 156.0620(M-2CN\(^+\)), 154.0546 (M-C\(_2\)N\(_2\)H\(_2\)\(^+\)), Calc. 208.0748, exp. 208.0744, dev. 2 ppm.

9. Preparation of 2,3,5,7,10,10a-Hexahydro-1,3-dioxo-2-phenyl-1H-[1,2,4]triazolo[1,2-a]cinnoline-8,8,9,9-tetracarbonitrile

A solution of 4,5-tetracyano-2-vinylcyclohex-1-ene (38 mg, 0.18 mmol) and 4-phenyl-1,2,4-triazoline-3,5-dione (38 mg, 0.20 mmol) in acetone (5 ml) were heated in a sealed tube at 40°C for 24h. The solvent was evaporated in vacuo leaving a pale brown residue. On addition of chloroform (2 ml) a pale yellow solid precipitated. This was filtered and dried to give (28 mg, 41%) of 2,3,5,7,10,10a-hexahydro-1,3-dioxo-2-phenyl-1H-[1,2,4]triazolo[1,2-a]cinnoline-8,8,9,9-tetracarbonitrile. \(^1\)H n.m.r. (C\(_5\)D\(_5\)N, 200 MHz) \( \delta \)[ppm]: 2.81(1H, dd, H\(_{10A}\), J\(_{\text{gem}}\) 14Hz, J\(_{10A,10a}\) 12Hz), 3.67(2H, bd, H\(_3\)A, J\(_{\text{gem}}\) 14Hz and H\(_5\)A), 4.15(1H, d,
H₂B, J₁₀, J₆, J₉ 14Hz, 4.40(2H, m, H₅B and H₆a), 4.55(1H, dd, H₈B, J₁₀, J₆, J₉ 14Hz, J₁₀, J₆, J₉ 5Hz), 6.41(1H, m, H₆), 7.25-7.46(5H, m, (Ph)); ¹³C n.m.r. (C₅D₅N, 200 MHz) δ[ppm]: 33.26 C10, 36.85 C7, 40.59 C9, 42.18 C8, 42.99 C5, 49.92 C10a, 109.66, 109.72, 110.90, 111.10 CN, 122.72 C6, 125.15, 127.43, 128.69 (Ph), 128.08 C6a, 130.85 Q(Ph); m/z 383(M⁻), 305(M-3CN⁻), 236(M-(CO)NPhCO⁺), 119(C₆H₅NCO⁺), 91(C₆H₅N⁺), Calc. 383.1131, exp. 383.1123, dev. 2 ppm.

10. Preparation of 5,7,7a,11a,12,12a-hexahydro-2-phenyl-1H-benzo[g]-s-triazolo[1,2-a]cinnoline-1,3,8,11-(2H)-tetrone

Benzoquinone (12 mg, 0.11 mmol) in toluene (1 ml) was added to a solution of [3] dendralene (15 mg, 0.18 mmol) in toluene (1 ml) and stirred at 40°C for 36h. The solvent was evaporated under high vacuum and 4-phenyl-1,2,4-triazoline-1,3-dione (19 mg, 0.11 mmol) in acetone (1 ml), was added to the residue. Further stirring at 40°C for 2h, removal of the acetone in vacuo, followed by trituration with diethyl ether resulted in a pale yellow solid which was filtered and dried in vacuo to give (25 mg, 63%) of 5,7,7a,11a,12,12a-hexahydro-2-phenyl-1H-benzo[g]-s-triazolo[1,2-a]cinnoline-1,3,8,11-(2H)-tetrone decomp. 150°C, ¹max 1768 (CO) amide, 1703 cm⁻¹ (CO); H n.m.r. (CDCl₃, 80 MHz) δ[ppm]: 1.10-1.87(3H, cm, H₁ and H₁₂), 2.05-4.67(6H, m, aliphatic H), 5.61-5.91(1H, m, H₆), 6.68-6.79 (2H, m, H₉ and H₁₀), 7.30-7.81(5H, m, (Ph)); ¹³C

A solution of [3] dendralene (75 mg, 1 mmol) in methylene chloride (6 ml) was heated in a sealed tube at 40°C for 4 days. Subsequent removal of the solvent in vacuo at room temperature resulted in a brown oil (72 mg). This was distilled to give a colourless oil 1,1,4-trivinylcyclohex-3-ene (44 mg, 59%) b.p. 30°C, 1mm Hg, (lit.9, 72-74°C, 8mm Hg); 1H n.m.r. (CDCl₃, 80 MHz) δ[ppm]: 1.59-1.76(2H, m, H₆), 2.02-2.27(4H, m, H₂ and H₅), 4.81-5.15(5H, m, vinyl(CH₂) at C₁ and 1H from vinyl(CH₂) at C₄), 5.63-5.95(3H, m, vinyl(CH) at C₁ and 1H from (CH₂) at C₄), 6.33(1H, dd, vinyl(CH) at C₄, Jcis 11Hz, Jtrans 17Hz); 13C n.m.r. (CDCl₃, 200 MHz), δ[ppm]: 21.16 C₆, 31.27 C₂, 34.37 C₅, 41.81 C₁, 110.03 vinyl(CH₂) at C₄, 112.45 vinyl(CH₃) at C₁, 127.17 C₃, 135.36 C₄, 139.41 vinyl(CH) at C₄, 144.06 vinyl(CH) at C₁.

12. Derivitisation of 1,1,4-trivinylcyclohex-3-ene

(a) Preparation of tricarbonyl(benzylideneacetone)iron

The title compound was prepared using the method of Howell112. The entire procedure was carried out under an
atmosphere of dry argon. Benzylideneacetone (2.6 ml, 18 mmol) and diiron nonacarbonyl (6.5 g, 21 mmol) in dry toluene (25 ml) were heated at 55°C for 4h. The mixture was filtered and the solvent removed in vacuo. Flash chromatography on Kieselgel 60 silica eluting with ethyl acetate/toluene (1:9) gave tricarbonyl(benzylideneacetone)iron (2.0 g, 39%) m.p. 82-86°C (lit. 112 88-89°C), \(\text{v}_{\text{max}}\) 1985, 2005, 2065 cm\(^{-1}\) (CO); these infrared absorbances compared favourably with the literature values. 

(b) Preparation of dicarbonyl(1,1,4-trivinylcyclohex-3-ene)iron

The reaction and work-up was carried out in an atmosphere of dry argon. A solution of 1,1,4-trivinylcyclohex-3-ene (44 mg, 0.28 mmol) and tricarbonyl(benzylideneacetone)iron (78 mg, 0.28 mmol) were heated in toluene at 55°C for 10h and then at 85°C for a further 17h. Flash chromatography on Kieselgel 60 of the product using ethyl acetate/toluene (1:9) as the eluent, resulted in an oily orange material (35 mg, 46%) of dicarbonyl(1,1,4-trivinylcyclohex-3-ene)iron. Several attempts to crystallise the amorphous material from toluene/hexane were unsuccessful. \(\text{v}_{\text{max}}\) 1985 and 2003 cm\(^{-1}\) (CO); \(^1\)H n.m.r. (CDCl\(_3\), 360 MHz) \(\delta\) [ppm]: 0.08(1H, s, \(H_3\)), 0.36(1H, d, \(H_{\text{Ct}}\), \(J_{\text{Ct,C}}\) 8Hz), 0.76(1H, d, \(H_{2\alpha}\), \(J_{2\alpha,2\beta}\) 15Hz), 1.24(1H, d, \(H_{2\beta}\), \(J_{2\beta,2\alpha}\) 15Hz), 1.69-1.79(1H, m, \(H_6\beta\)), 1.94-2.04(1H, m, \(H_6\alpha\)), 2.13(1H, d, \(H_{\text{CC}}\), \(J_{\text{CC,C}}\) 7Hz),
2.24(1H, d, H_{Bt}, J_{Bt} B 12Hz), 2.77(1H, d, H_{BC}, J_{BC}, B 8Hz), 2.85-2.94(1H, m, H_{5\alpha}), 2.99-3.06(1H, m, H_{5\beta}), 3.34(1H, dd, H_B, J_B, Bt 12Hz, J_B, BC 8Hz), 4.89(1H, d, H_{At}, J_{trans} 17.4Hz), 4.98(1H, d, H_{AC}, J_{cis} 10.6 Hz), 5.36(1H, dist.t, H_C, J 8Hz), 5.81-5.88(1H, dd, H_A, J_{trans} 1.74Hz, J_{cis} 10.6Hz) COSY and NOE techniques were employed for $^1$H n.m.r. assignments. Details of these experiments, along with the numbering of the structures are given in the Results and Discussion, Section E2. $^{13}$C n.m.r. (CDCl$_3$, 250 MHz) $\delta$(ppm): 26.21 C$_6$, 29.63 C$_2$, 34.27 C$_5$, 34.97 and 42.51 vinyl(CH$_2$) C and B, 38.35 C$_1$, 46.97 and 83.52 vinyl(CH) C and B, 106.10 C$_4$, 111.15 vinyl(CH$_2$) A, 146.43 vinyl(CH) A; FAB-glycerol/NOAB m/z 272(M$^+$), 244(M-CO$^+$), 216(M-2CO$^+$), Calc. 272.04992, exp. 272.04991, dev. < 1 ppm.

E. ATTEMPTED PREPARATIONS OF 3-FORMYL-2,5-DIHYDRO-THIOPHENE-1,1-DIOXIDE, AS A ROUTE TO [3] DENDRALENE DERIVATIVES

1. Via Isoxazolines

(a) Preparation of $\alpha$-benzaldoxime

$\alpha$-Benzaldoxime was prepared using the procedure outlined in Vogel$^{106}$. To a mixture of sodium hydroxide (14 g, 0.35 mol) and benzaldehyde (20 ml, 0.2 mol) in water (40 ml), was added hydroxylamine hydrochloride
(15 g, 0.22 mol) in small portions. The mixture was continuously shaken until the benzaldehyde disappeared and the crystalline oxime derivative was formed. Water was added to give a clear solution and then sufficient solid carbon dioxide to saturate the mixture. This was then extracted into ether, the extracts dried over anhydrous sodium sulphate and the solvent evaporated in vacuo to give solid \( \alpha \)-benzaldoxime (20.64 g, 83%) m.p. 31-33°C (lit., 35°C).

(b) Preparation of benzhydroxamic chloride

A modification on the method of Chiang was employed for the preparation of benzhydroxamic chloride. This involved bubbling chlorine gas through a solution of \( \alpha \)-benzaldoxime (26 g, 0.17 mol) in chloroform (400 ml) at -5°C. The solution went from blue to green to yellow, and was then flushed with nitrogen gas. The solvent was removed in vacuo and the resultant oily solid left in the freezer for several days with ca. 5 ml of petroleum ether 40-60°C. The colourless solid was then filtered and recrystallised from chloroform/petroleum ether 40-60°C to give (5.14 g, 20%) of benzhydroxamic chloride m.p. 49-51°C (lit., 50-51°C).

(c) 1,3-Dipolar addition of 2,5-dihydrothiophene-1,1-dioxide

(i) To benzonitrile oxide

A solution of benzhydroxamic chloride (1.27 g, 8.2 mmol) in dry benzene (45 ml) was added over a period
of 42h, using a perfusor, to a solution of 2,5-dihydrothiophene-1,1-dioxide (3.54 g, 30 mmol) and triethylamine (0.85 g, 8.2 mmol) in dry benzene (200 ml). The addition was carried out in anhydrous conditions using an atmosphere of dry argon. When the addition was complete, the triethylamine hydrochloride salt was filtered and washed with small quantities of benzene. The filtrate was then evaporated to dryness in vacuo and the solid residue washed with methylene chloride (5 x 10 ml), then water (2 x 10 ml) and finally dried to leave a colourless solid (0.55 g, 29%) of 3a,4,6,6a-tetrahydro-3-phenylthieno[3,4-d]isoxazole-5,5-dioxide m.p. 193-194°C from ethanol (Found C 55.5%, H 4.57%, N 5.84%, C_{11}H_{11}NO_3S; requires C 55.7%, H 4.64%, N 5.91%); υ_max (KBr) 1332 and 1117 (SO_2), 771 cm⁻¹ (CH); ¹H n.m.r. (C_5D_5N, 80 MHz) 3.85-3.96 (4H, cm, H₂ and 6) 4.73-5.06 (m, H₃a obscured by H₂O peak), 5.06-5.92 (1H, 6 peaks, H₃a), 7.36-7.49 (3H, m, m and p(CH)), 7.81-7.92 (2H, m, o(CH)) ¹³C n.m.r. (C_5D_5N, 200 MHz, DEPT), 46.82 C₃a, 59.97 C₄, 54.42 C₆, 79.23 C₆a, 126.81, 128.81, 130.19 (Ph); m/z 237(M⁺), 119(C₆H₅CNO⁺), 103(C₆H₅CN⁺), 91(C₆H₅⁺), Calc. 237.0459, exp. 237.0460, dev. < 1 ppm.

(ii) To carboethoxyformanitrile oxide

A solution of triethylamine (0.52 g, 5 mmol) in dry benzene (45 ml) was added to a solution of 2,5-dihydrothiophene-1,1-dioxide (2.4 g, 20 mmol) and ethyl chlorooximidoacetate (0.78 g, 5 mmol) in benzene (100 ml) at
40°C. The addition took place under anhydrous conditions and at a rate of 3 ml/h using a perfusor. When the addition was complete, the solid triethylamine salt was filtered and the filtrate evaporated to dryness in vacuo. Ethanol (25 ml) was added to the solid residue and the insoluble material filtered. The filtrate was allowed to stand overnight and a colourless crystalline material was formed. This was filtered, dried in vacuo and identified as (0.22 g, 18%) of 3a,4,6,6a-tetrahydro-3-carboethoxythieno[3,4-d]isoxazole-5,5-dioxide m.p. 131-132°C from ethanol (Found C 41.2%, H 4.82%, N 6.17%, C₈H₁₁NO₅S, requires C 41.2%, H 4.72%, N 6.00%); ¹H n.m.r. (C₅D₅N, 200 MHz) δ[ppm]: 1.33(3H, t, (CH₃)), 3.69-3.88(4H, cm, H₄ and H₆), 4.34(2H, q, (CH₂)), 4.69-4.78(1H, m, H₃a), 5.76-5.86 (1H, m, H₆a); ¹³C n.m.r. (C₅D₅N, 200 MHz) δ[ppm]: 12.83(CH₃), 46.27 C₃a, 50.57 C₄, 53.69 (OCH₃), 54.82 C₆, 61.28 C₆a, 151.28 C₃, 159.27 (CO); m/z 233(M⁺), 188(M-OCH₂CH₃⁺), 169(M-SO₂⁺), Calc. 233.0358, exp. 233.0363, dev. 2 ppm.

(d) Ring Opening of 3a,4,6,6a-tetrahydro-3-phenylthieno-[3,4-d]isoxazole-5,5-dioxide

(i) With palladium on charcoal

A solution of 3a,4,6,6a-tetrahydro-3-phenylthieno[3,4-d]isoxazole-5,5-dioxide (39 mg, 0.16 mmol), boric acid (61 mg, 0.98 mmol) and 5% palladium on charcoal ca. 16 mg in 15 ml of methanol/water (5:1) was stirred under hydrogen at 3 psi for 68h. The catalyst was then filtered
through celite and the filtrate evaporated in vacuo. Separation firstly by preparative thin layer chromatography using ethyl acetate/cyclohexane (3:1) as the eluent, followed by a further separation of the first band eluting with ethyl acetate/acetone (3:1), resulted in the isolation of 4-benzylamine-3-hydroxy-tetrahydrothiophene-1,1-dioxide. 

\[ r_{\text{max}} \] 3640 (OH), 2940 (NH$_2$), 1128 and 1302 cm$^{-1}$ (SO$_2$); 'H n.m.r. (CDCl$_3$, 80 MHz) 1.99-3.63(7H, cm, (2.30, bs, NH$_2$)), 4.41(1H, d, J 5Hz), 4.71(1H, m, H$_3$), 7.08-7.52 (5H, m, (Ph)); total aliphatic to aromatic protons (5:10); after D$_2$O shake (5:7); 'C n.m.r. (CDCl$_3$, 200 MHz), 47.21 C4, 48.56 C5, 56.42 C1', 61.98 C2, 71.66 C3, 125.25 o(CH), 125.71 QC, 127.92 p(CH), 129.03 m(CH), m/z 241(M$^+$), 148(M-C$_2$H$_5$SO$_2$), 106(PhCHNH$_2$), Calc. 106.06577, exp. 106.0661, dev. 3 ppm; Calc. 241.0774, exp. 241.0798, dev. 10 ppm.

(ii) With lithium diisopropylamide

Ring opening of the thienoisoxazoline was achieved using the method of Grund and Jäger. A solution of lithium diisopropylamide was prepared by adding n-butyllithium (0.51 ml, 1.3 M) to diisopropylamine (61 mg, 0.6 mmol) in dry THF (2 ml) whilst stirring under argon between -20° to -30°C. The reaction mixture was then cooled to -78°C and 3a,4,6,6a-tetrahydro-3-phenyl-thieno[3,4-d]isoxazole-5,5-dioxide (100 mg, 0.4 mmol) in dry THF (8 ml) was added. After stirring for 1½h the reaction was allowed to warm to room temperature and was
then stirred for a further hour. Glacial acetic acid (80 mg) was added and the solution washed with saturated sodium chloride solution (20 ml), then extracted with methylene chloride (3 x 10 ml). Subsequent preparative thin layer chromatography, eluting with ethyl acetate/cyclohexane (3:1) gave the starting material 3a,4,6,6a-tetrahydro-3-phenylthieno[3,4-d]isoxazole-5,5-dioxide (11 mg, 26%) as confirmed by n.m.r. spectroscopy and 2,5-dihydro-3-thienyl phenyl ketone oxime,1,1-dioxide (17 mg, 41%) \( \text{max} \ 3440 \text{ (OH)}, \ 1322 \text{ and} \ 1135 \text{ cm}^{-1} \text{ (SO}_2\text{)}; \) \(^1H\) n.m.r. (CDCl\(_3\), 80 MHz) \( \delta[ppm] \): 3.87(2H, ABX m, H\(_5\), \( J_{4,5}\) 3Hz), 4.19(2H, AB q, H\(_2\), \( J_{2,4}\) 2Hz), 6.06(1H, m, H\(_4\), \( J_{4,5}\) 3Hz, \( J_{2,4}\) 2Hz), 7.24-7.65(5H, m, (Ph)), (oxime proton in baseline); \(^13C\) n.m.r. (CDCl\(_3\), 200 MHz) 55.10 C2, 56.89 C5, 126.84 C4, 127.91 (CH), 128.59 (CH); 129.68 C3, 129.96 (CH), 133.62 Q(Ph), 152.86 (oxime); m/z 237(M \( ^+ \)), 103(C\(_6H_5CN^+\)), 77(C\(_6H_5^+\)), Calc. 237.0460, exp. 237.0455, dev. 2 ppm.

(e) Preparation of 2,5-dihydrothiophene-1,1-dioxide-3-phenone

(i) Using titanium(III) chloride

2,5-Dihydro-3-thienyl phenyl ketone, oxime, 1,1-dioxide was prepared according to the procedure described in the previous section. A modification of the work-up procedure was necessary however, and this is described as follows: After acidification with glacial acetic acid,
the mixture was washed with saturated sodium chloride solution (20 ml) and the aqueous layer discarded. The resultant organic phase was dried over anhydrous sodium sulphate and the solvent evaporated in vacuo to give a pale yellow solid. This was washed under suction with chloroform and the remaining colourless crystals shown by n.m.r. spectroscopy to be the starting material 3a,4,6,6a-tetrahydro-3-phenylthieno[3,4-d]isoxazole-5,5-dioxide (32 mg, 27%). The filtrate was then evaporated to dryness in vacuo leaving the crude α-enoxime (86 mg, 73%) as a brown oil. 2,5-Dihydro-3-thienyl phenyl ketone, oxime, 1,1-dioxide was then dissolved into N,N-dimethylformamide (2 ml) and added to 15% hydrochloric acid (2 ml) and 15% of titanium(III) chloride solution (2 ml), according to method of Grund and Jäger\(^8\). The mixture was stirred overnight under argon. Water (15 ml) was then added, and the reaction mixture extracted into methylene chloride (3 x 10 ml). The extracts were combined, dried over anhydrous magnesium sulphate and the solvent evaporated in vacuo to leave a brown oil (75 mg). The oil was flushed through a keiselgel 60 silica dry flash chromatography column, eluting first with cyclohexane and then ethyl acetate. The ethyl acetate fractions were shown by t.l.c. to consist of many compounds. The presence of 2,5-dihydro-3-thienyl phenyl ketone, oxime, 1,1-dioxide and 2,5-dihydrothiophene-3-benzophenone-1,1-dioxide could only be determined by high resolution mass spectrometry; m/z
Calc. 237.0459, exp. 237.0507, C_{11}H_{11}NO_{3}S, dev. 2 ppm;
Calc. 222.0351, exp. 222.0362, C_{11}H_{10}O_{3}S, dev. 5 ppm,
105(C_{6}H_{5}CO^+), 77(C_{6}H_{5}^+).

(ii) Using molybdenum hexacarbonyl

The method of Baraldi was employed. A solution of
3a,4,6,6a-tetrahydro-3-phenylthieno[3,4-d]isoxazole-5,5-
dioxide (141 mg, 0.59 mmol) and molybdenum hexacarbonyl
(85 mg, 0.32 mmol) in acetonitrile containing one drop of
water (10 ml) was refluxed for 2½h. On completion of the
reaction, the mixture was filtered through celite and the
solvent evaporated in vacuo. The brown residue was
separated firstly by preparative t.l.c. eluting with ethyl
acetate/hexane (1.8:1) to give the first band, the
isoxazoline starting material (77 mg, 55%). The second
band an impure orange oily substance, was identified as
2,5-dihydrothiophene-1,1-dioxide-3-phenone, (47 mg, 36%)
ν_{max} 1648 (CO), 1679 ν(C=C), 1312 and 1125 cm^{-1} (SO_2); ^1H
n.m.r. (CDCl_3, 80 MHz) δ[ppm]: 4.04-4.19(4H, m, H_2 and
H_5), 6.86(1H, m, H_4), 7.45-7.79(5H, m, (Ph)); ^13C n.m.r.
(CDCl_3, 200 MHz, DEPT) δ[ppm]: 55.32 and 57.95 C2 and C5,
128.37, 128.63 and 128.96 (Ph), 134.56 C4; m/z 222(M^{+}),
105(C_{6}H_{5}CO^+), Calc. 222.0351, exp. 222.0348, dev. 1 ppm.

The procedure was repeated using a solution of
isoxazoline (92 mg, 0.4 mmol) and molybdenum hexacarbonyl
(121 mg, 0.43 mmol) in acetonitrile (20 ml) containing
0.5 ml of water. This was heated to 45°C for 5h. When
analytical t.l.c. indicated an incomplete conversion, a
further (100 mg, 0.35 mmol) of molybdenum hexacarbonyl was added along with (1.5 ml) of water in acetonitrile (20 ml). The solution was heated to boiling for a further 3h and consequently went black. The crude material was separated on the chromatotron using a gradient elution of hexane/ethyl acetate. Two bands were separated, the first consisting of the eneone 2,5-dihydrothiophene-1,1-dioxide-3-phenone as an orange oil (22 mg, 25%) and the second band (44 mg) appeared to be two products with very similar RF values. This fraction was repurified by chromatotron using the same solvent system, giving once again the eneone and 3-hydroxy-tetrahydrothiophene-1,1-dioxide-4-phenone as a colourless solid m.p. 162-165°C ν max 3460 (OH), 1688 (CO), 1305 and 116 cm⁻¹ (SO₂); 'H n.m.r. (CDCl₃, 80 MHz) δ [ppm]: 3.04-4.48 (6H, m, H₂, H₅, H₄ and (OH)), 4.77-5.01 (1H, m; H₃), 7.24-7.75 (3H, m, m and p (CH)), 7.85-8.06 (2H, m, o (CH)); ¹³C n.m.r. (CDCl₃, 200 MHz, DEPT) 50.69 C₄, 52.53 C₅, 56.72 C₂, 69.11 C₄, 128.32, 128.69, 128.96, 129.10 (Ph); m/z 240(M⁺), 133(C₄H₅SO₃¹⁺), 105(C₆H₅CO¹⁺), 77(C₆H₅⁺).

2. Via 3-(1,3-Dithianyl)-4-hydroxytetrahydrothiophene-1,1-dioxide

(a) Preparation of the dithiane anion

The carbanion was prepared using the method of Corey and Seebach. 1,3-Dithiane (0.90 g, 7.5 mmol) was dissolved into dry THF (60 ml) and cooled to -30°C under
an atmosphere of argon. A 1.5 M solution of n-butyllithium (4.83 ml, 7.5 mmol) was added slowly at a rate of 3.5 ml/min. The reaction mixture was stirred at -20°C for 1h.

(b) Reactions of the 1,3-dithiane anion

(i) With 3,4-dibromotetrahydrothiophene-1,1-dioxide

3,4-Dibromotetrahydrothiophene-1,1-dioxide (2.29 g, 8.3 mmol) in dry THF (25 ml) was cooled to -5°C. A THF solution of the 1,3-dithiane anion (60 ml, 0.125 M) was added slowly, and the reaction mixture stirred under nitrogen at -5°C for 1h. After standing at 0°C for 65h, the reaction mixture was poured into water (300 ml) then acidified to pH 4 with aqueous hydrochloric acid. The aqueous mixture was extracted into cyclohexane (5 x 30 ml) followed by washing with 3% sodium bisulphite (50 ml), 5% potassium carbonate (20 ml) and water (40 ml). Subsequent drying of the organic extract with anhydrous potassium carbonate and evaporation of the solvent in vacuo gave a green oil (0.83 mg). This was separated using flash chromatography with Kieselgel 60 silica and gradient elution of hexane/ethyl acetate. 1,3-Dithiane (0.25 g, 27%) was recovered as well as 3,4-dibromotetrahydrothiophene-1,1-dioxide (65 mg, 3%). The dimer of thiophene-1,1-dioxide, 3a,7a-dihydrobenzothiophene-1,1-dioxide was also formed (36 mg, 5%) as well as a colourless solid (56 mg) m.p. 127-128°C. This material had an accurate mass indicating a formula of C$_3$H$_{12}$O$_6$S$_2$ but
has not yet been characterised.

When the reaction was carried out at room temperature for 1h subsequent work-up resulted in a 93% recovery of 1,3-dithiane.

(ii) With 3-bromo-2,3-dihydrothiophene

Completely anhydrous conditions and an atmosphere of nitrogen was employed. To a solution cooled to -5°C of 3-bromo-2,3-dihydrothiophene-1,1-dioxide (1.47 g, 7.5 mmol), in dry THF (20 ml), was added a solution of the prepared 1,3-dithiane anion (60 ml, 0.125 M). The reaction was stirred at 0°C for 18h. Saturated ammonium chloride (10 ml) was then added and most of the solvent evaporated in vacuo. Water (20 ml) was added and the aqueous layer extracted into methylene chloride (4 x 20 ml). The combined extracts were dried over anhydrous magnesium sulphate and removal of the solvent in vacuo resulted in a brown oil (1.57 g). This was shown by n.m.r. spectroscopy to be a mixture of the recovered 1,3-dithiane, 3a,7a-dihydrobenzothiophene-1,1-dioxide in a ratio of (1:2), and the unknown material which was described in the previous section.

(iii) With 3,4-epoxytetrahydrothiophene-1,1-dioxide

A suspension of the epoxide (0.2 g, 1.5 mmol) in dry THF (10 ml) was cooled to -5°C. The dithiane anion in THF (1.1 ml, 1.6 M) was added and the reaction stirred for 1h at -5°C and then for 18h at room temperature. The entire mixture was poured into water (60 ml) and acidified with
with aqueous hydrochloric acid to pH6. Extraction into ethyl acetate (3 x 20 ml), followed by drying over anhydrous magnesium sulphate, and finally evaporation of the solvent in vacuo left a pale yellow solid (0.23 g). This was separated by flash chromatography using Kieselgel GF 245 and a gradient elution of ethyl acetate and petroleum ether 40-60°C. Three main fractions were taken and these were identified by n.m.r. spectroscopy as the 1,3-dithiane starting material (40 mg, 26%), 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide (11 mg, 6%) and 3-(1,3-dithanyl)-4-hydroxytetrahydro-thiophene-1,1-dioxide (9 mg, 2%).

\[^1\text{H}\] n.m.r. (CDCl\(_3\), 400 MHz) \(\delta\)[ppm]: 1.86-2.14(2H, ABM m, H\(_5\)'), 2.71-2.97(4H, m, H\(_4\)' and H\(_6\)'), 3.11(1H, s, OH, loss of signal in D\(_2\)O), 3.12-3.29(2H, m, H\(_5\)'), 3.42-3.43(2H, m, H\(_2\)'), 4.24(1H, d, H\(_3\)'), 4.63-4.69(1H, m, H\(_3\)'), assignments were made using single frequency decoupling techniques. \[^13\text{C}\] n.m.r. (CD\(_3\)COCD\(_3\), 400 MHz) [ppm]: 26.48 C5', 30.36 C4, 30.95 C4' and C6', 48.12 C2', 57.35 and 57.62 C2 and C5, 73.45 C3.

The procedure was repeated with a modification that allowed the reaction to stand at -30°C for 5 days. The work-up which was described in the previous section, followed by n.m.r. spectral analysis indicated a mixture of 1,3-dithiane, 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide and 3,4-epoxytetrahydrothiophene-1,1-dioxide in a ratio of approximately (5:1:2).

Another attempt at the addition reaction was tried and
this involved heating the mixture to 40°C for 17h. The resultant colourless material was shown by n.m.r. spectroscopy to be 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide and the major product was the unknown material also isolated in section b(i) and b(ii).

3. Conversion of 3-Cyanotetrahydrothiophene-1,1-dioxide

3-Cyanotetrahydrothiophene-1,1-dioxide (80 mg, 0.55 mmol) was dissolved in dry THF (8 ml) and cooled to -78°C under nitrogen. Diisobutylaluminium hydride solution was added (3.2 ml, 1.0 M) over 15 min and the reaction stirred for 4h. This was followed by an addition of methanol (0.5 ml) in 1 ml of THF and then a water/methanol mixture (0.2 ml in 5 ml). T.l.c. indicated the formation of one product. The solution was flushed through a silica column and the solvent evaporated in vacuo to leave a pale brown oil (49 mg). Infrared spectroscopy indicated the formation of 3-cyanotetrahydrothiophene by the loss of (SO₂) absorbances and the absence of a carbonyl stretch.

4. Attempted Preparation of 3-Formyl-2,3-dihydrothiophene-1,1-dioxide from the Allylbromide

(a) Preparation of 3-bromoethyl-2,3-dihydrothiophene-1,1-dioxide

Using the procedure of Krung and Yen⁹¹ a solution of 3-methyl-2,5-dihydrothiophene-1,1-dioxide (2.0 g,
15 mmol), N-bromosuccinamide (2.6 g, 15 mmol) and benzoylperoxide (0.2 g, 0.8 mmol) in chloroform (35 ml), was stirred at 75°C for 26 h under nitrogen gas. After cooling, the succinamide was filtered and the filtrate evaporated in vacuo to a third of the original volume. The residue was left in the freezer overnight and the precipitated material was refiltered. Evaporation of the filtrate to dryness, yielded a pale yellow solid identified as 3-bromoethyl-2,5-dihydrothiophene-1,1-dioxide (1.5 g, 48%), m.p. 83-86°C from ethanol (lit. 91, 87-88°C).

(b) Attempted oxidation of 3-bromoethyl-2,3-dihydrothiophene-1,1-dioxide

The procedure of Franzen 92 was employed for this reaction and the work was carried out by J. Grzybowski. Trimethylamine N-oxide (0.42 g, 5.6 mmol) was pre-dried according to the cited literature method, and then dissolved into dry chloroform (5 ml). The solution was slowly added over a 21 h period to a solution of 3-bromoethyl-2,5-dihydrothiophene-1,1-dioxide (0.6 g, 2.8 mmol) in chloroform (5 ml). After heating the mixture to boiling for 50 min and then cooling, 0.5 M sulphuric acid (3 ml) was added. The chloroform layer was then removed, washed with water (5 ml) and with 2 M sodium bicarbonate solution (5 ml). Drying of the chloroform extract over anhydrous sodium sulphate followed by evaporation of the
solvent in vacuo gave a pale brown oil identified as 3-methylene-2,3-dihydrothiophene-1,1-dioxide by comparison of spectroscopic data. $^9\text{max} 1560, 1400, 1130 \text{ cm}^{-1}$, $^1H$ n.m.r. (CDCl$_3$, 200 MHz) [ppm]: 3.81(2H, s, H$_2$), 5.40(2H, ps, methylene), 6.48(1H, d, H$_4$, $J_{4,5} 6.5\text{Hz}$), 6.92(1H, d, H$_5$, $J_{4,5} 6.5\text{Hz}$); $^{13}C$ n.m.r. (CDCl$_3$, 200 MHz, DEPT) $\delta$[ppm]: 52.37 C2, 117.00 (CH$_2$), 135.58 C4, 138.77 C5.

F. PROPOSED ROUTES TO [5] DENDRALENE

1. Preparation of 3-bromo-4-trimethylsiloxytetrahydrothiophene-1,1-dioxide

A suspension of 3-bromo-4-hydroxytetrahydrothiophene-1,1-dioxide (0.54 g, 2.5 mmol) and bis(trimethylsilyl)acetamide (0.9 ml, 3.6 mmol) in methylene chloride (3 ml) was stirred under argon at room temperature for 1h. During this time, the bromohydrin dissolved. The solvent was then evaporated in vacuo and the unreacted bis-(trimethylsilyl)acetamide distilled off at 65°C, 0.6 mm Hg, to leave 3-bromo-4-trimethylsiloxytetrahydrothiophene-1,1-dioxide as colourless crystals (0.62, 88%) m.p. 60-62°C from hexane under argon (Found C 29.6%, H 5.28%, C$_7$H$_{13}$BrO$_3$Si, requires C 29.3%, H 5.26%); $^\text{max} 1323$ and 1110 (SO$_2$), 1258 (Si-CH$_3$), 1057 cm$^{-1}$ (Si-O-C); $^1H$ n.m.r. (CDCl$_3$, 80 MHz) $\delta$[ppm]: 0.11(9H, s, (CH$_3$)); 2.87-3.89(4H, cm, H$_5$ and H$_2$), 4.27(1H, dd, $J 12.6\text{Hz}, J 6.4\text{Hz}, H_4$),
4.57(1H, dd, H₃, J 10.5Hz); ¹³C n.m.r. (CDCl₃, 200 MHz, DEPT) δ[ppm]: -0.28 (CH₃), 46.01 C4, 57.34 and 58.06 C2 and C5, 74.46 C3; FAB-glycerol m/z (M+1) Calc. 286.97732, exp. 286.97733; dev. < 1 ppm.

It was found that this material was air sensitive resulting in the hydrolysis of the trimethylsiloxy group.

2. Attempted Metallation of 3-Bromo-4-trimethylsiloxytetrahydrothiophene-1,1-dioxide

3-Bromo-4-trimethylsiloxytetrahydrothiophene-1,1-dioxide (0.2 g, 0.7 mmol) and lithium metal (10 mg, 1.4 mmol) in dry hexane (5 ml) was stirred at room temperature under argon for 3h. Water (5 ml) was added cautiously and the aqueous layer removed. The hexane solution was dried over anhydrous magnesium sulphate and the solvent evaporated to dryness in vacuo to leave an oily residue. This was shown by n.m.r. spectroscopy to be 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide and 3-trimethylsiloxy-2,3-dihydrothiophene-1,1-dioxide.

3. Preparation of Tetrahydro-2,2-dimethylthieno[3,4-d]-1,3-dioxole-5,5-dioxide

A solution of 3-bromo-4-hydroxytetrahydrothiophene-1,1-dioxide (0.24 g, 1.1 mmol) and Amberlite IRA-400(OH) ion exchange resin (0.7 g) in acetone (15 ml), was heated to boiling for 3 days. The catalyst was filtered through celite and the filtrate evaporated to
dryness in vacuo to give an oily colourless solid (0.12 g). This was judged by n.m.r. spectroscopy to be a mixture of 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide and tetrahydro-2-methylthieno[3,4-d]-1,3-dioxole-5,5-dioxide in a ratio of (1:7) respectively; m.p. 94-96°C; νmax 1275 (SO₂), 1120 and 1110 cm⁻¹ (SO₂) and (C-O-C); ⁱH n.m.r. (CD₃COCD₃, 200 MHz) δ[ppm]: 1.32(3H, d, (CH₃), J 0.6Hz), 1.47(3H, d, (CH₃), J 0.6Hz), 3.19(2H, d with fine coupling, H₄A and H₆A, Jgem 14Hz), 3.39(2H, ddd, H₄B and H₆B, Jgem 14Hz, J₄B,₃a and J₆B,₆a 4.5Hz, J₄B,₆a and J₆B,₃a 1.8Hz), 5.04(2H, dist.ddd, H₃a and H₆a, J₆a,₃a and J₃a,₄B 4.5Hz, J₆a,₄B and J₃a,₃a 1.8Hz); ¹³C n.m.r. (CD₃SOCD₃, 200MHz) δ[ppm]: 24.04 and 25.85 (CH₃), 54.32 C6 and C4, 74.01 C6a and C3a, 109.73 C2; m/z 191(M-1⁺), Calc. 191.0378, exp. 191.0375, dev. 2 ppm, 177(M-CH₃⁺), calc. 177.0221, exp. 177.0217, dev. 2 ppm.

4. Preparation of 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide

Using the method O.E. Van Lohuizen⁷⁰ a solution of 3-bromo-4-hydroxytetrahydrothiophene-1,1-dioxide (0.75 g, 3.5 mmol) and pyridine (0.55 g, 7 mmol) in acetone (15 ml) was heated to boiling for 22h. On cooling the solid pyridine hydrobromide was filtered and the filtrate basified to PH8 with aqueous potassium hydroxide. The solvent was then removed under high vacuum and the residue dissolved into acetone (15 ml). Unreacted starting
material and the potassium salt was then filtered and the solvent removed from the filtrate in vacuo to leave a colourless oil (0.45 g). This was distilled to give (0.31 g, 69%) of 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide b.p. 175°C, 0.5 mm Hg (lit. 101°C, 0.3 mm Hg); 'H n.m.r. (CD$_3$COCD$_3$, 400 MHz) δ[ppm]: 3.01(1H, dd, H$_2$A, J$_{2A,2B}$ 13.8Hz, J$_{2A,3}$ 3.8Hz), 3.63(1H, dd, H$_2$B, J$_{2B,2A}$ 13.8Hz, J$_{2B,3}$ 7.7Hz), 5.14-5.17(2H, ddd, H$_3$, J$_{2B,3}$ 7.7Hz, J$_{2A,3}$ 3.8Hz, J$_{3,4}$ 1.6Hz, bs, OH), 6.83(2H, m, H$_4$ and H$_5$, J$_{4,5}$ 7Hz); 'C n.m.r. (CDCl$_3$, 400 MHz) δ[ppm]: 56.80 C$_2$, 68.19 C$_3$, 133.30 C$_4$, 141.16 C$_5$.

5. Reaction of 3-Hydroxy-2,3-dihydrothiophene-1,1-dioxide with Nitromethane

A solution of 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide (0.22 g, 1.5 mmol) and nitromethane (90 mg, 1.5 mmol) in boiling ethanol (15 ml), was stirred with Amberlite IRA-400(OH) (0.15 g) for 170h. The solvent was then evaporated in vacuo and a soxhlet extraction of the residue with water gave (0.20 g, 91%) of the recovered starting material 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide as identified by n.m.r. spectroscopy.

6. Preparation of 3-Acetoxy-2,3-dihydrothiophene-1,1-dioxide

To a stirred solution of 3-bromo-4-hydroxytetrahydrothiophene-1,1-dioxide (1.04 g, 4.7 mmol) and triethylamine
(7.1 ml, 51 mmol) in THF (40 ml) and under an atmosphere of dry argon, was slowly added a solution of acetyl chloride (1.5 ml, 21 mmol) in THF (5 ml). After the addition was complete, the reaction mixture was stirred at 30°C for 41h. A 5% citric acid solution (50 ml) was then added and the mixture extracted into methylene chloride (4 x 25 ml). The extracts were combined and the solvent removed in vacuo leaving a solid residue. The material was then washed with ethyl acetate and filtered to give 3-acetoxy-2,3-dihydrothiophene-1,1-dioxide (0.52 g, 88%) m.p. 110-112°C (lit. 101, 111.5-112.5°C).

7. Preparation of Monoethyl Malonate

Part (a) Monoethyl malonate was prepared using the method of Strube116. To a stirring solution of diethyl malonate (7.2 g, 4.5 mmol) in absolute ethanol (30 ml) was added potassium hydroxide (2.5 g, 4.5 mmol) in ethanol (30 ml) over 1h. The mixture was stirred a further 2h then allowed to stand overnight. On the following day a hot filtration was carried out and the filtrate allowed to stand in an ice bath to facilitate precipitation. The potassium ethyl malonate was filtered, washed with ether and then dried to yield a colourless crystalline solid (4.3 g, 56%).

Part (b) The potassium salt (4.3 g, 2.5 mmol) in water (5 ml) was cooled to 5°C and concentrated hydrochloric acid (2.2 ml) added using a dropping funnel
over 30 min The solid potassium chloride was filtered and washed with ether. When the aqueous layer of the filtrate was washed with more ether (3 x 10 ml) and the organic extracts combined, drying over anhydrous magnesium sulphate and finally evaporation under high vacuum left monoethyl malonate as a colourless oil (1.8 g, 55%) b.p. 90°C, 0.5 mm Hg (lit. 147°C, 21 mm Hg).

8. Reaction of 3,4-Epoxytetrahydrothiophene-1,1-dioxide with Monoethyl Malonate

The procedure used was by McMurry and Musser and the reaction was carried out under anhydrous conditions, using an atmosphere of argon. To a solution of diisopropylamine (0.4 ml, 3.0 mmol) in dry THF (1 ml) at -78°C, was added n-butyllithium (1.8 ml, 1.6 M) followed by monoethyl malonate (0.19 ml, 1.5 mmol). The reaction mixture was allowed to warm to 0°C and hexamethylphosphoramide (0.4 ml) and a solution of the epoxide (0.2 g, 1.5 mmol) in dry THF (10 ml) was added. After stirring for 3 days at room temperature followed by boiling overnight, the mixture was poured into water (25 ml) and extracted into ethyl acetate (4 x 15 ml). The extracts were combined and dried over anhydrous magnesium sulphate. Evaporation of the solvent under vacuum gave a brown oily material; (0.14 g, 70%) of 3-hydroxy-2,3-dihydrothiophene-1,1-dioxide. The aqueous phase was continuously extracted with ethyl acetate and 13C n.m.r. spectroscopy of the organic extract showed the
original aqueous layer to contain a complex mixture of compounds and more of the above-mentioned elimination product.

9. Reaction of 3,4-Epoxytetrahydrothiophene-1,1-dioxide with Nitromethane

Anhydrous conditions and an atmosphere of argon was used for this reaction. To a -5°C stirred suspension of the epoxide (0.2 g, 1.5 mmol) and nitromethane (92 mg, 1.5 mmol) in ethanol (14 ml) was slowly added sodium ethoxide in ethanol solution (8 ml, 0.19 M). The reaction mixture was warmed to 30°C and stirred for 15h. The work-up involved adding the entire solution to 100 ml of crushed ice containing 10% hydrochloric acid (10 ml). The aqueous solution was then extracted into methylene chloride (3 x 25 ml) and the extracts combined. Drying over anhydrous magnesium sulphate followed by evaporation of the solvent under high vacuum afforded a dark red oil (0.27 g) shown by n.m.r. spectroscopy to be predominantly 3-ethoxy-4-hydroxytetrahydrothiophene-1,1-dioxide; \( \delta_{\text{max}} \) 3480 (OH), 1300 and 1102 cm\(^{-1}\) (SO\(_2\)); \(^1\)H n.m.r. (CD\(_3\)COCD\(_3\), 400MHz) \( \delta \) [ppm]: 0.73-0.91 (3H, m, (CH\(_3\))), 2.68-3.16 (4H, m, H\(_2\) and H\(_5\)), 3.31 (OH, loss of peak in D\(_2\)O), 3.90 (1H, m, H\(_3\)), 4.32 (1H, m, H\(_4\)); \(^13\)C n.m.r. (CD\(_3\)COCD\(_3\), 400 MHz) \( \delta \) [ppm]: 15.19 (CH\(_3\)), 54.79 (OCH\(_2\)), 57.56 C2, 58.35 C5, 71.72 C4, 77.82 C3; CI(NH\(_3\)) m/z 198 (M+NH\(_4^+\)), 153 ((M+NH\(_4^+\))-OCH\(_2\)CH\(_3^+\)) 136 ((M+H)-OCH\(_2\)CH\(_3^+\)), M+NH\(_4^+\) calc.
1. Reaction of 3,4-Epoxytetrahydrothiophene-1,1-dioxide with Acetaldehyde

To a solution of acetaldehyde (132 mg, 3 mmol) in dry THF (5 ml) was added lithium diisopropylamide in cyclohexane (1.5 ml, 1.5 M). The mixture was stirred at -75°C under nitrogen for 30 min and 3,4-epoxytetrahydrothiophene-1,1-dioxide (0.2 g, 1.5 mmol) in dry THF (20 ml) was then added. After stirring for 1h at room temperature an addition of glacial acetic acid (0.5 ml in 5 ml THF) was made. Approximately half of the THF was then removed in vacuo at room temperature. Methylene chloride (20 ml) was then added, followed by a brine solution (25 ml). The organic layer was removed and the brine solution washed with methylene chloride (2 x 20 ml). The extracts were combined, dried over anhydrous magnesium sulphate and the solvent evaporated in vacuo to leave a brown oil. This was heated to 105°C, 0.25 mm Hg and resulted in a pale yellow crystalline material subliming onto the receiving flask. Recrystallisation from carbon tetrachloride gave (83 mg, 31%) the two isomers of tetrahydro-2-methylthieno-[3,4-d]-1,3-dioxole-5,5-dioxide as colourless plates m.p. 72-74°C (Found C 40.9%, H 5.41%, C_{6}H_{10}O_{4}S, requires C 40.4%, H 5.62%); r_{max} 1316 (SO_{2}), 1135 and 1110 cm^{-1} (SO_{2}) and (C-O-C); 'H n.m.r. (CDCl_{3}, 400 MHz) δ[ppm]: 1.33 and 1.41(3H, pd, (CH_{3}), J(CH_{3})_{2} , 5Hz), 3.23-3.41(4H, m, H_{4})
and H₆), 4.76(1H, t, H₃a and H₆a, isomer A, J 3Hz), 4.98-5.03(1H, m, H₆a, H₃a isomer B on H₂ isomer A), 5.43(1H, q, H₂ isomer B, J₂(CH₃) 5Hz), ¹³C n.m.r. (CDCl₃, 400 MHz) δ[ppm]: 19.25 and 19.57 (CH₃), 54.71 and 55.17 C6 and C4, 74.67 and 75.15 C3a and C6a, 102.14 and 102.99 C2, both ¹H and ¹³C n.m.r. indicate a 1:1 ratio of isomers; m/z ICMS (M-H⁺), Calc. 177.02216, exp. 177.02166, dev. 3 ppm, (M-CH₃⁺), Calc. 163.00651, exp. 163.00582, dev. 4 ppm.

G. POLYMERS

1. Polymerisation of 3-Vinyl-2,3-dihydrothiophene-1,1-dioxide

3-Vinyl-2,5-dihydrothiophene-1,1-dioxide (0.1 g, 0.7 mmol) was freshly purified by sublimation and dissolved into pre-distilled ethyl acetate (1.0 ml) along with α,α'-azoisobutyronitrile (11 mg, 0.07 mmol). The solution was degassed, sealed in a glass vial under nitrogen and then heated to 50°C for 5 days. The polymeric material was then filtered and dried to afford (82 mg) of colourless polymer; υmax 1306 and 1123 cm⁻¹ (SO₂); ¹H n.m.r. (CD₃SOCD₃, 400 MHz) δ[ppm]: 1.28(1.5H, s, terminal(CH₃)), 3.81(4H, bs, H₂ and H₅), 5.56(0.31H, bs, olefinic from A), 5.73(0.69H, bs, olefinic from B). The terminal (CH₃) suggests an approximate chain length of 9
monomer units. $^{13}$C n.m.r. (CD$_3$SOCD$_3$, 400 MHz) $\delta$(ppm): 26 C3A, 33 C6B, 54 and 55 C2 and C5 of A and B, 120 C3B, 133 C6A, 139 C4 of A and B. Both the $^1$H and $^{13}$C n.m.r. spectra were extremely broad and integrations are approximate. 'A' refers to the 1,4-addition polymer and 'B' to the 1,2-addition polymer. m/z CI(NH$_3$), 102(M+NH$_4^+$), 96(M+NH$_4^+$), 85(M+H$^+$), 79(M+H$^+$); EI 84, 78, 66, 63.

2. Polymerisation of Isoprene

Isoprene was flash distilled from sodium (20% dispersed in light oil) under vacuum prior to use. The entire procedure was carried out under inert anhydrous conditions. To a solution of isoprene (2.63 ml, 26 mmol) in dry heptane (3.3 ml) was added n-butyllithium in hexane (0.07 ml, 1.5 M). The apparatus was sealed and kept at 40°C for 24h. On cooling the resultant oily product was poured into a solution containing hydroquinone (80 mg in 10 ml of methanol) and the suspension coagulated. The solvent was then decanted, and the polymeric material washed with more methanol before drying in a vacuum oven at 40°C. The resultant polyisoprene was isolated as a pale viscous oil (0.4 g, 22%); $^1$H n.m.r. (CDCl$_3$, 400 MHz) $\delta$(ppm): 1.58(24H, s, (CH$_3$), trans A and B), 1.62 (8H, (CH$_3$) cis B), 1.65(84H, (CH$_3$) cis A), 2.04(158H, other aliphatic protons), 4.70(5H, bd, H$_{\text{i}}$, B), 5.11(40H, m, H$_3$ cis and trans A). 'A' represents 1,4-addition and 'B'
1,2-addition. Assignments by $^{13}$C n.m.r. and $^1$H n.m.r. were based on literature values\textsuperscript{118} and the isomeric ratios were determined to be cis 1,4-addition 67%, trans 1,4-addition 27% and 1,2-addition 6%. $^{13}$C n.m.r. (CDCl\textsubscript{3}, 400 MHz) $\delta$[ppm]: 16.01(CH\textsubscript{3}) trans A, 18.69 (CH\textsubscript{3}) B, 23.50 (CH\textsubscript{3}) cis A, 26.47 C4 cis A, 26.55 C4 trans A, 28.89 C4 B, 32.27 C1 cis A, 40.11 C1 trans A, 47.81 C3 B, 124.28 C3 trans A, 125.09 C3 cis A, 135.14 and 135.25 C2 cis and trans.


To freshly distilled isoprene (2.63 ml, 26 mmol) and [3] dendralene (75 mg, 0.9 mmol) in dry heptane (3.3 ml) was added n-butyllithium (0.07 ml, 1.5 M) under completely inert and anhydrous conditions. The reaction vessel was sealed and heated to 40°C for lh. The pale gel that had formed, was washed with a hydroquinone solution (80 mg in 10 ml of methanol) and the solvent decanted. The residual polymer was found to be highly insoluble in most common solvents. Thorough drying of the material under high vacuum left a highly elastic colourless material (1.34 g, 72%); $^1$H n.m.r. (CDCl\textsubscript{3}, 400 MHz) $\delta$[ppm]: 1.58(18H, bs, (CH\textsubscript{3}) trans A and B), 1.66(40H, bs, (CH\textsubscript{3}) cis A), 2.02 (74H, other aliphatic protons), 4.70(3H, bd, H\textsubscript{1} B), 5.10 (16H, bs, H\textsubscript{3} cis and trans A); sections of the polymer from 1,4-addition are designated 'A' and sections from
1,2-addition are designated 'B'.
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