Peri-substituted dithianaphthalenes as sources of reactive intermediates in organic chemistry

by

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Abstract

This thesis reports the application of 1,8-dithianaphthalenes (peri-substituted dithianaphthalenes) as sources of, and as a means of stabilising, reactive intermediates in organic chemistry.

Three peri-substituted trisulfide-2-oxides (49, 58 and 103) were prepared by reacting 1,8-naphthalene diethiols with thionyl chloride in the presence of pyridine. The trisulfide-2-oxides 49, 58 and 103 were shown to act as sulfur monoxide transfer reagents with dienes. ortho-Substituents on the naphthalene ring increased the rate and lowered the temperature at which SO transfer occurred. Treatment of the resulting sulfoxides under Pummerer conditions afforded the corresponding thiophenes. SO transfer was applied in a formal synthesis of Plavix® and the naturally occurring thioperillene. Mechanistic studies on the SO transfer reaction indicated that the rate-determining step was independent of the diene, and first-order with respect to trisulfide-2-oxide. C-H abstraction from cycloheptatriene suggested formation of triplet SO.

vic-Disulfoxides are reactive intermediates in the oxidation of thiosulfinates to thiosulfonates. The oxidation of 1,8-naphthalene disulfides was investigated. Cyclic voltammetry demonstrated that electron-rich 3,8-dimethoxynaphtho[1,8-cd][1,2]dithiole (87) was easier to oxidise than the parent naphthalene disulfide 50. Treatment of 87 with one equiv. of oxidant resulted in formation of thiosulfonate 206 and disulfide 87, suggesting disproportionation of thiosulfinate 205. Oxidation of t-Bu-substituted disulfide, 3,8-di-tert-butynaphtho[1,8-cd][1,2]dithiole (65), afforded the isolable trans vic-disulfoxide 217. Isomerisation of 217 occurred thermally and photochemically, generating cis vic-disulfoxide 225 and thiosulfonate 224. Complete rearrangement of 217 to the thiosulfonate 224 occurred in refluxing mesitylene, establishing trans-217 as the most stable vic-disulfoxide to date.
Bis(sulfonyl)hydroxylamine 284 is proposed as a potential source of nitric oxide (NO) or nitroxy (HNO). 284 was prepared by formal N-insertion into the S(O)-S(O)₂ bond of sulfinyl sulfone 228, prepared in turn through oxidation of disulfide 50. Bis(sulfonyl)hydroxylamine 284 was found to be stable both thermally and photochemically. Investigations into the oxidation of t-Bu-substituted disulfide resulted in the isolation of sulfinic anhydride, 295, from disulfide 65. Desulfonylation occurred when 295 was heated in H₂O/1,4-dioxane. Deuterium incorporation occurred on running the reaction in D₂O/1,4-dioxane. Refluxing 295 in PhCl resulted in deoxygenation to disulfide 65.
Abbreviations

Å Angström
Ac acetyl
Ad adamantyl
AIBN azobisisobutyronitrile
ap. apparent
aq. aqueous
br broad
Bu butyl
c. concentrated
C Celsius
cat. catalytic
d doublet
DCE 1,2-dichloroethane
DDQ 2,3-dichloro-5,6-dicyanobenzoquinone
DMD dimethyldioxirane
DMF N,N-dimethylformamide
DMI 1,3-dimethyl-2-imidazolidinone
DMPO 5,5-dimethyl-1-pyrroline N-oxide
DMPU 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO dimethylsulfoxide
DPPH 2,2-diphenyl-1-picrylhydrazyl
EDG electron-donating group
EDRF endothelium-derived relaxing factor
EDTA ethylenediamine tetraacetate
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>EI</td>
<td>electron impact</td>
</tr>
<tr>
<td>EPR</td>
<td>electron paramagnetic resonance</td>
</tr>
<tr>
<td>equiv.</td>
<td>equivalent</td>
</tr>
<tr>
<td>ESI</td>
<td>electrospray ionisation</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
</tr>
<tr>
<td>EWG</td>
<td>electron-withdrawing group</td>
</tr>
<tr>
<td>FT-IR</td>
<td>fourier transform infrared</td>
</tr>
<tr>
<td>FVT</td>
<td>flash vacuum thermolysis</td>
</tr>
<tr>
<td>g</td>
<td>gramme(s)</td>
</tr>
<tr>
<td>GST</td>
<td>glutathione S-transferase</td>
</tr>
<tr>
<td>h</td>
<td>hour(s)</td>
</tr>
<tr>
<td>[H]</td>
<td>reduction</td>
</tr>
<tr>
<td>HMBC</td>
<td>heteronuclear multiple bond correlation</td>
</tr>
<tr>
<td>HPLC</td>
<td>high performance liquid chromatography</td>
</tr>
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<td>HMPA</td>
<td>hexamethylphosphoramide</td>
</tr>
<tr>
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<td>high resolution mass spectrometry</td>
</tr>
<tr>
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<td>hard and soft acids and bases</td>
</tr>
<tr>
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<td>heteronuclear single quantum coherence</td>
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<td>IR</td>
<td>infrared</td>
</tr>
<tr>
<td>ISC</td>
<td>inter system crossing</td>
</tr>
<tr>
<td>J</td>
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</tr>
<tr>
<td>L</td>
<td>litre</td>
</tr>
<tr>
<td>m</td>
<td>multiplet</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>$t$</td>
<td>tert</td>
</tr>
<tr>
<td>t</td>
<td>triplet</td>
</tr>
<tr>
<td>TBAB</td>
<td>tetrabutylammonium bromide</td>
</tr>
<tr>
<td>TBAF</td>
<td>tetrabutylammonium fluoride</td>
</tr>
<tr>
<td>TEMPO</td>
<td>2,2,6,6-tetramethylpiperidine 1-oxyl</td>
</tr>
<tr>
<td>TFA</td>
<td>trifluoroacetic acid</td>
</tr>
<tr>
<td>TFAA</td>
<td>trifluoroacetic anhydride</td>
</tr>
<tr>
<td>TGA</td>
<td>thermal gravimetric analysis</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMEDA</td>
<td>tetramethylethylenediamine</td>
</tr>
<tr>
<td>Ts</td>
<td>$p$-toluenesulfonyl</td>
</tr>
<tr>
<td>u</td>
<td>atomic mass unit</td>
</tr>
<tr>
<td>UHP</td>
<td>urea-hydrogen peroxide</td>
</tr>
<tr>
<td>UV</td>
<td>ultraviolet</td>
</tr>
<tr>
<td>vic</td>
<td>vicinal</td>
</tr>
<tr>
<td>vs.</td>
<td>versus</td>
</tr>
<tr>
<td>$v$</td>
<td>frequency</td>
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Chapter One: Sulfur monoxide transfer from
1,8-dithianaphthalene trisulfide-2-oxides
Background and significance

1.1 Sulfur monoxide

Sulfur monoxide (SO) is a reactive diatomic molecule that is isoelectronic with molecular oxygen. The physical properties and thermal decomposition of sulfur monoxide have been reported.\(^1\) SO is an extremely unstable gas and has a half life of 20 ms, undergoing rapid disproportionation in less than one second in the gas phase to \(S_2O\) and \(SO_2\) (scheme 1.1).\(^2\) Disproportionation of \(S_2O\) results in further \(SO_2\) and \(S_3\) formation,\(^3,\,4\) the latter rearranging to the more stable sulfur allotrope \(S_8\).

\[
\begin{align*}
48 \text{SO} & \rightarrow 16 \text{SO}_2 + 16 \text{S}_2\text{O} \\
& \downarrow \\
8 \text{SO}_2 + 8 \text{S}_3 & \rightarrow 3 \text{S}_8
\end{align*}
\]

**Scheme 1.1** Sulfur monoxide breakdown in the gas phase

1.2 Previous sulfur monoxide transfer reagents

There has been substantial interest in uncovering simple chemical processes to produce SO and trap it *in situ*. Dodson and Sauer reported the first SO transfer reagent; they used strained episolfoxide \(1\) to transfer sulfur monoxide to 1,3-dienes to furnish dihydrothiophene \(S\)-oxides in moderate yields (scheme 1.2).\(^5\)

\[
\begin{align*}
\stackrel{\text{toluene, reflux}}{\text{S}} & \rightarrow \text{SO} \\
1 & \rightarrow 2 \quad R = \text{Me}, 21\% \\
& \rightarrow 3 \quad R = \text{Ph}, 25\%
\end{align*}
\]

**Scheme 1.2** SO transfer from ethylene episolfoxide

Saito extended this study by analysing the products from the pyrolysis of episolfoxide \(1\).\(^6\) It was deduced that the reaction proceeded by collapse of the three-membered ring in \(1\) to form ethylene and free SO (scheme 1.2).\(^5\) Characteristic signals of ethylene sulfide and ethylene oxide were absent, and peaks attributed to sulfur monoxide in its triplet ground state were
observed.\textsuperscript{6} This has been supported by recent calculations by Ishikawa which suggest that triplet (\(^3\Sigma^-\)) SO is 20 kcal mol\(^{-1}\) more stable than the singlet (\(^1\Sigma^+\)) form.\textsuperscript{7,8}

Chao and Lemal extensively examined the stereochemistry of the sulfoxides 4-6 of SO transfer to hexa-2,4-dienes (scheme 1.3).\textsuperscript{8,9} Good levels of stereochemical control were observed. It was suggested that singlet SO was initially formed followed by an intersystem crossing to the triplet form, which was the reacting species.\textsuperscript{9}

\[
\begin{array}{ccc}
\text{ethylene} & + & \text{SO} \\
\text{toluene, reflux} & & 0 & 13 & 87 \\
\end{array}
\]

\[
\begin{array}{ccc}
\text{ethylene} & + & \text{SO} \\
\text{toluene, reflux} & & \text{trace} & 95 & 5 \\
\end{array}
\]

\[
\begin{array}{ccc}
\text{cycloheptatriene} & + & \text{SO} \\
\text{toluene, reflux} & & 20 & 61 & 22 \\
\end{array}
\]

Scheme 1.3 SO transfer to hexa-2,4-dienes

Ethylene episulfoxide 1 has been reported to react with trienes by Dodson.\textsuperscript{10} Further evidence for the formation of triplet SO was reported by Dodson. The reaction of ethylene episulfoxide with cycloheptatriene (7) furnished the dimer product 8 in low yield.\textsuperscript{10} This reaction is presumed to occur \textit{via} H-abstraction from 7 by triplet SO followed by dimerisation of the resulting cycloheptatrienyl radical (scheme 1.4).
Although SO was trapped with dienes from episulfoxide 1, the yields were synthetically unsatisfactory. In addition the transfer reagent 1 is inherently unstable due to ring strain, has a bad smell and causes burns to the skin.\textsuperscript{11} Heyke\textsuperscript{12} and Schenk\textsuperscript{13} introduced transition metal-coordinated SO transfer reagents. Trapping experiments in the presence of dienes resulted in comparable yields of sulfoxides (scheme 1.5).

![Scheme 1.4 Dimerisation of cycloheptatriene](image)

In 1970, Chow and co-workers reported a different source of SO.\textsuperscript{14} Disrotatory electrocyclisation of dibenzo\{b,f\}[1,4,6]thiadiazepin-1-oxide (10) leads to the formation of benzo[c]cinnoline (12), elemental sulfur and SO\textsubscript{2}.\textsuperscript{14} Thermal decomposition of 10 in the presence of 2,3-diphenylbutadiene and cycloocta-1,3-diene provided cyclic sulfilene 3 and cyclic sulfoxide 13 in 19% and 30% yields respectively (scheme 1.6).

![Scheme 1.5 Pd coordinated SO transfer reagent](image)

![Scheme 1.6 Thermal decomposition of dibenzo\{b,f\} [1,4,6]thiadiazepin-1-oxide](image)
Harpp and Abu-Yousef introduced an improved source of SO in 1997. Structurally attractive adamantyl-derived episulfoxide 14 was prepared by oxidation of the corresponding episulfide 15. Thermal decomposition of 14 in the presence of dienes 16-19 resulted in good to excellent yields of the corresponding sulfoxides. Reaction conditions were optimised and the best results for sulfoxides 2, 3, 21 and 22 (65-80%) were obtained when using a ratio of 1:3 for SO transfer reagent to diene in refluxing toluene. Reaction times varied between 12 and 36 h (scheme 1.7).

![Scheme 1.7 SO transfer from adamantyl-derived episulfoxide](image)

Although 14 is an effective source of SO, its synthesis is somewhat lengthy. 14 was prepared via electrophilic oxidation of the episulfide 15, which in turn was synthesised from adamantylideneadamantane (20) and a range of sulfenyl chlorides, none of which are commercially available (scheme 1.8).

![Scheme 1.8 Synthesis of episulfoxide 14](image)

SO transfer from the trans stilbene-derived thiirane oxide 23 to diazooalkanes, azides and ylides has been reported (scheme 1.9).
Simpkins furthered the study of this SO transfer reagent by employing 23 in a Rh$_2$(OAc)$_4$ catalysed reaction.\textsuperscript{19, 20} In the absence of the rhodium catalyst no reaction was observed with norbornene 24 or norbornadiene 25. The addition of the Rh$_2$(OAc)$_4$ resulted in the reaction occurring at room temperature and isolation of the desired episulfoxides in moderate yields (scheme 1.10).

It is assumed that rhodium inserts into the C-S bond and that the resulting Rh(SO) complex is the reacting species. The limitation with this method of SO transfer is that it only occurs with strained alkenes 24 and 25.

The thermal breakdown of other strained small ring systems 31\textsuperscript{21} and 33\textsuperscript{22} has been shown to result in loss of SO. Espenson reported the formation of SO from the intermediate sultine 31 formed from the H$_2$O$_2$ oxidation of sulfine 30, catalysed by CH$_3$ReO$_3$ (MTO). Trapping experiments with 2,3-dimethyl-1,3-butadiene resulted in quantitative trapping of sulfur monoxide (scheme 1.11), however the strongly oxidising conditions also resulted in sulfone 32 in addition to 2,5-dihydro-3,4-dimethylthiophene 1-oxide 2.\textsuperscript{21}
Scheme 1.11 Methyltrioxorhenium-catalysed sulfoxidation

The same authors also reported the generation of a structurally interesting platinum complex by insertion of SO into a Pt-Pt bond (scheme 1.12).\textsuperscript{23}

Scheme 1.12 SO insertion into a Pt-Pt bond

Ishii reported \textit{vic}-disulfoxide 33 as a source of SO. Thermal decomposition of 33 in the presence of 2,3-dimethyl-butadiene 16 or thiketone 34 produced sulfilene 2 or thiirane 1-oxide 35 in moderate yields (scheme 1.13), together with (\textit{E})-36, (\textit{Z})-37, \textit{cis}-38, \textit{trans}-39, ketone 40 and thioketone 41.\textsuperscript{22} Thiosulfonates 38 and 39 are a result of SO addition to compound 41.

Scheme 1.13 Thermal breakdown of \textit{vic}-disulfoxide 33

A recent report by Nakayama’s group described the cycloaddition of SO to alkenes and alkynes at room temperature.\textsuperscript{24} The reaction of 3,4-di-\textit{tert}-butylthiophene 1-oxide (42) with dimethyl acetylenedicarboxylate produces bridged bicyclic sulfoxide intermediate 43 which
probably decomposes through extrusion of sulfur monoxide to afford 4,5-di-tert-butylphthalate 44 (scheme 1.14).

\[
\begin{align*}
\text{Scheme 1.14 Room temperature SO release from thiophene 1-oxide 42} \\
\end{align*}
\]

The SO generated in situ from 42 has successfully been trapped with dienes and some strained alkenes and alkynes to provide sulfoxides in poor to modest yields. More interestingly in the presence of cycloheptatriene the product observed was not 7,7'-bicycloheptatriene (8) but sulfoxide 45 (figure 1.1), suggesting formation and trapping of singlet SO.

\[
\begin{align*}
\text{Figure 1.1 1 SO transfer to cycloheptatriene} \\
\end{align*}
\]

Photolysis of structurally fascinating 46 was reported by Morita in 2009 to generate SO.\textsuperscript{25} Irradiation of 1,9-dithiaalkane-bridged thianthrene 10-oxide 46 resulted in inversion of the sulfoxide into the equatorial isomer 47 along with 1,9-dithiabenzo thiophene 48. The reaction was monitored by \textsuperscript{1}H-NMR spectroscopy and it is believed that both 46 and 47 decay to form thiophene 48.Photolysis of 46 in the presence of diene 16 resulted in formation of dihydrothiophene S-oxide 2 in good yield along with thiophene 48 and equatorial sulfoxide 47 (scheme 1.15).

\[
\begin{align*}
\text{Scheme 1.15 Photolysis of SO transfer reagent 46} \\
\end{align*}
\]
1.3 Previous work in the group

In 2001, the Grainger group reported the novel SO transfer reagent 49, exploiting the special reactivity of peri-substituted naphthalene rings. A one-pot synthesis of disulfide 50 was developed starting from 1-bromonaphthalene 51. Lithium-halogen exchange followed by a directed deprotonation and trapping of the dilithio species 52 with elemental sulfur provided disulfide 50 in moderate yields. Reduction of 50 afforded dithiol 53, which was subsequently reacted with thionyl chloride in the presence of pyridine to furnish 1,2,3-trithiaphenalene 2-oxide (49) in good yield along with recovery of naphtho[1,8-cd][1,2]dithiole (50) (scheme 1.16).

![Scheme 1.16 Synthesis of 1,2,3-trithiaphenalene 2-oxide (49)](image)

The crystal structure of 49 has been reported by the Grainger group (figure 1.2).^{27} Peri-strain is evident by expansion of the bond angles at C(1), C(9) and C(8), which are 124.7°, 126.6° and 125.7° respectively. These carbons are sp² hybridised and the ideal bond angles are 120°. Furthermore there is a distortion from planarity of the naphthalene moiety. Dihedral angles at C(1)-C(9)-C(10)-C(4) and C(8)-C(9)-C(10)-C(5) are 1.27° and 2.53° respectively.
SO transfer from trisulfide-2-oxide 49 to a range of dienes in refluxing chlorobenzene has been reported to deliver sulfoxides (2, 3, 21 and 22) in very good yields along with quantitative recovery of the recyclable byproduct disulfide 50 (scheme 1.17).²⁷

![Figure 1.2 X-ray of trisulfide-2-oxide 49](image)

**Scheme 1.17 SO transfer from trisulfide-2-oxide to 1,3 dienes**

The SO transfer reagent 49 can be stored in a refrigerator without decomposition and also has a recyclable byproduct, disulfide 50. SO transfer to cyclic dienes with 49 has yet to be achieved.

1.4 Aims and objectives

The sulfur monoxide transfer reagents surveyed in the literature all result in the formal loss of SO as a result of relief of ring strain or gain of aromaticity. Strain in trisulfide-2-oxide 49 is presumably relieved by the release of sulfur monoxide upon SO transfer and reformation of disulfide 50.

The peri-interaction at the 1,8-positions of naphthalene gives rise to a number of unusual effects due to the close proximity of atoms and/or groups.²⁸ The transannular interaction between sulfur atoms in the 1- and 8-position has been examined by Glass.²⁹-³⁴ Furukawa
demonstrated that tension in 54 could be alleviated by photomediated chalcogen-chalcogen bond formation.\textsuperscript{35, 36} Photomediated extrusion from substituted dithianaphthalenes 54 afforded a range of imine derivatives, olefins, aldehydes and ketones in excellent yields with quantitative recovery of disulfide 50 (scheme 1.18).

![Scheme 1.18 Photomediated extrusion from 1,8-dithianaphthalene 54](image)

The release of ring strain suggested by Furukawa led to the development of trisulfide-2-oxide 49 as a source of SO by the Grainger group.\textsuperscript{27} Trapping experiments demonstrated 49 as an effective source of SO, however transfer occurred close to the temperature where a proposed retrocycloaddition reaction of sulfoxides occurs.\textsuperscript{8, 11}

1,8-bis-Dimethylaminonaphthalene (proton sponge) (55) is a strong base due to the relief of strain upon protonation and/or the strong interaction between the nitrogen lone pairs (scheme 1.19).\textsuperscript{37}

![Scheme 1.19 1,8-bisdimethylaminonaphthalene as a proton sponge](image)

Substitution of groups on the naphthalene moiety has been found to change the basicity of proton sponges, results attributed to both the buttressing effect and electronic factors (figure 1.3).\textsuperscript{38, 39}
Figure 1.3 pKₐ’s of substituted proton sponges

It is feasible that altering the gap between the *peri*-sulfur atoms of 49 will result in a change in strain and as a result may possibly alter the rate and/or temperature at which SO transfer occurs. Novel trisulfide-2-oxides 56-59 are proposed as more strained systems than 49 (figure 1.4). The acenaphthalene-derived trisulfide-2-oxides, 56 and 57, are expected to have an increased distance between the two *peri*-sulfur atoms as a result of the two carbon bridge in the *para peri*-position. As a result of steric buttressing due to the two *ortho tert*-butyl groups, trisulfide-2-oxide 58 is expected to have a decreased distance between the two sulfur atoms. The effect of electron-donating and electron-withdrawing groups on the naphthalene moiety will also be considered. These groups may either assist or impede SO transfer to a diene as the trisulfide-2-oxide breaks down.

Figure 1.4 Proposed strained trisulfide-2-oxides

The exact mechanism of SO transfer from trisulfide-2-oxides to dienes has yet to be determined. Transfer of the sulfur monoxide may occur *via* trapping of “free” SO or a direct (bimolecular) reaction. Attempts will be made to elucidate and propose a plausible mechanism for the transfer of SO.
Results and discussion

1.5 Synthesis of disulfides

The synthesis of trisulfide-2-oxide 49 has already been reported in the group. The first objective was to synthesise disulfide 50. The most common method to produce disulfide 50 is air oxidation of the dithiol 53. The most commonly used method for the synthesis of disulfide 50 was reported by Zweig and Hofmann (scheme 1.20).

![Scheme 1.20 Synthesis of disulfide 50 reported by Zweig and Hofmann](image)

This method uses the inexpensive 8-aminonaphthalene-1-sulfonic acid (61) with sodium disulfide to afford the bis sulfonate 62. Treatment of 62 in the presence of PCl₅ produced naphtho[1,8-cd][1,2]dithiole 1,1-dioxide (63), which in turn is reduced with zinc to disulfide 50, via air oxidation of dithiol 53. This route yielded only traces of dioxide 63 with either PCl₅ or SOCl₂ (2-3%) and was aborted.

The Grainger group reported the one-pot synthesis of disulfide 50 starting from the commercially available 1-bromonaphthalene (51) (scheme 1.16). Two equiv. of n-butyllithium were used to form the thermodynamic dilithio species 52, followed by quenching with elemental sulfur at -20 °C. Preliminary work in the group had shown that use of an activated source of sulfur produced higher yields. Komatsu reported activation of S₈ in a solution of toluene by irradiation with a 500 W halogen lamp. These conditions were
employed for quenching the dilithio species and resulted in a 15-25% yield of the desired product (table 1.1, entry 2). The use of sulfur monochloride ($S_2Cl_2$) as a sulfur quench proved detrimental to the reaction with only a 3% yield of the desired disulfide 50 obtained (entry 4). Utilising recrystallised sulfur (from toluene) afforded the disulfide in highest yield (entry 3).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Sulfur quench of dilithio 52</th>
<th>50 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Elemental sulfur</td>
<td>13</td>
</tr>
<tr>
<td>2</td>
<td>Activated sulfur</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>Recrystallised sulfur</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>$S_2Cl_2$</td>
<td>3</td>
</tr>
</tbody>
</table>

*Table 1.1 Sources of sulfur for quenching dilithio 52*

The synthesis of disulfide 50 has been reported by the Ashe group starting from naphthalene 64 (scheme 1.21). Repetition of these conditions on small scale produced 11% of the desired disulfide 50, however on scale-up the reaction yield diminished to 3%.

![Scheme 1.21 Ashe’s synthesis of disulfide 50 from naphthalene](image)

The spectral data of 1,8-naphthalene disulfide 50 were analysed in order to assign the proton and carbon resonances. Ambiguous spectra were acquired with HMBC experiments due to conjugation of the aromatic system and the long-range coupling present. Instead a simple HSQC (figure 1.5) was obtained alongside a HSQC-$^1J(CC)$-ADEQUATE (figure 1.6), which highlights $^2J$ exclusively. The triplet at 7.27 ppm was assigned H(3) as it shows coupling to both protons H(2) and H(4). Of the 3 quaternary carbons, C(6) was assigned using the HSQC-ADEQUATE as no ortho protons are present (134.7 ppm). C(5) is in a similar environment to C(6) and was assigned as the peak at 135.7 ppm, whereas C(1) is next to the sulfur and is at a higher frequency (144.0 ppm). This is supported by the intensity of C(1).
being double in comparison to other quaternary carbons. The HSQC-ADEQUATE was then used to assign H(2) and H(4), C(5) showed a correlation with the peak at 7.36 ppm which was H(4) and C(1) exhibited a correlation with H(2), the peak at 7.15 ppm. As expected C(3) showed a correlation to both H(2) and H(4). The corresponding carbons were assigned from the simple HSQC.

![Figure 1.5 HSQC of 50](image)

![Figure 1.6 HSQC-^1^J(CC)-ADEQUATE of 50](image)

To explore the steric buttressing effect, 3,8-di-tert-butynaphtho[1,8-cd][1,2]dithiole (65) was prepared by the method reported by Tesmer in 2001 by applying a Friedel-Crafts alkylation on disulfide (scheme 1.22). In this reaction disulfide 50 is heated at 50 °C in the presence of
tert-butylchloride and AlCl$_3$ in nitromethane. The product is then isolated on cooling as an orange precipitate.

![Scheme 1.22 Synthesis of disulfide 65](image)

The quality of the aluminium trichloride was an important factor in maximising yields for this step.$^{42}$ A catalytic amount of freshly opened AlCl$_3$ was added to the reaction mixture, resulting in a purple solution that liberated HCl gas (table 1.2, entry 1). When reactions were left for longer, and/or the quality of the AlCl$_3$ decreased, lower yields were obtained. In an attempt to improve the yield, the reaction mixture was placed in the refrigerator overnight to increase precipitation of 65, however this proved unsuccessful. The reaction was also unsuccessful when the length of the reaction and amount of Lewis acid were varied (entries 2-4). Freshly sublimed AlCl$_3$ has also been employed in the group without success (entry 5). These reactions resulted in a number of products, which proved difficult to separate by HPLC or size exclusion chromatography. Woollins et al. reported that the other major products in this reaction are mono tert-butyl disulfide along with starting material 50.$^{46}$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction time (min)</th>
<th>Molar equiv. of AlCl$_3$</th>
<th>65 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>0.19</td>
<td>48</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>0.50</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>1.00</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>0.19</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>0.19</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 1.2 Reaction conditions for the Friedel-Crafts alkylation of 50

Attention was switched to an alternative set of conditions described by Carpino, who reported the Friedel-Crafts tert-butylation of sulfide 66 (scheme 1.23).$^{47}$ These conditions were used to find a more reliable method for generating disulfide 65.
Scheme 1.21 Friedel-Crafts tert-butylation of phenyl sulfide 66

Refluxing disulfide 50 with 3 equiv. of tert-butylbromide in CH₂Cl₂ for 96 h gratifyingly gave disulfide 65 as the major product after recrystallisation. Further purification of the filtrate by HPLC afforded additional disulfide 65 along with 3,5,8-tri-tert-butyl-naphtho[1,8-cd][1,2]dithiole (68) (scheme 1.24, table 1.3, entry 1).

Scheme 1.24 Improved synthesis of disulfide

A modified procedure with 2 equiv. of tert-butylbromide successfully generated disulfide 65 without depletion in yield through formation of the trialkylated product 68. Recrystallisation of the crude reaction mixture afforded disubstituted disulfide 65 as orange crystals (entry 2).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Molar equiv. of FeCl₃</th>
<th>65 (%)</th>
<th>68 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>44</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>34</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 1.3 Friedel-Crafts alkylation of 50 using FeCl₃

Bridged disulfides 69 and 70 were explored as the distance between the two peri-sulfur atoms is expected to increase as a result of the two carbon bridge in the para peri-position. Synthesis of bridged disulfides 69 and 70 have been reported by Aso⁴⁸ and Meinwald⁴⁹ respectively (scheme 1.25 and 1.26).
The synthesis commenced with regioselective bromination of the commercially available 1,2-dihydroacenaphthylene (73), using NBS, in the peri-positions, as reported by Neudorff (scheme 1.26). The double bond was introduced via DDQ oxidation, as reported by Mitchell, to yield 5,6-dibromoacenaphthylene (72). Although reported to give a 75% yield, only a 28% yield of 72 was achieved after purification (scheme 1.27).

With both dibromo compounds 71 and 72 in hand, attempts to convert them to 1,2-dihydroacenaphtho[5,6-cd][1,2]dithiole (69) and acenaphtho[5,6-cd][1,2]dithiole (70) were carried out. Woolliins’ group has recently synthesised 69 employing conditions reported by Aso using biobeads as a means of purification. The conditions reported by Aso afforded the desired disulfide 69 after separation using biobeads in a 9% yield (table 1.4, entry 1), however this reaction was irreproducible. Attempts to synthesise disulfides 69 and 70 using the conditions reported by Meinwald afforded a mixture of compounds (entries 2 and 3). Using the conditions described by Aso on dibromide 72 were also
unsuccessful (entry 4). Modifying the conditions reported by Meinwald through changing the reaction solvent from THF to Et₂O resulted in a mixture of compounds (entry 5).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting dibromide</th>
<th>Conditions</th>
<th>Result</th>
</tr>
</thead>
</table>
| 1     | 71                | i) n-BuLi (1 equiv.), TMEDA, THF  
|       |                   | ii) S₈  
|       |                   | iii) n-BuLi (1 equiv.), TMEDA, THF  
|       |                   | iv) S₈  
| 2     | 72                | i) n-BuLi (2 equiv.), THF  
|       |                   | ii) S₈  
| 3     | 71                | i) n-BuLi (2 equiv.), TMEDA, THF  
|       |                   | ii) S₈  
|       |                   | iii) n-BuLi (1 equiv.), TMEDA, THF  
|       |                   | iv) S₈  
| 4     | 72                | iii) n-BuLi (1 equiv.), TMEDA, THF  
|       |                   | iv) S₈  
| 5     | 72                | i) n-BuLi (2 equiv.), Et₂O  
|       |                   | ii) S₈  

Table 1.4 Conditions for the attempted synthesis of bridged disulfides 69 and 70

An earlier paper reports unsuccessful attempts at creating the dilithium derivative of 5,6-dibromo-1,2-dihydroacenaphthylene (71). The lithiated species was quenched with D₂O and NMR analysis confirmed that a mixture of both the mono and di-deuterated species were present.

Commercially available 5-bromoacenaphthene (74) was then considered in an attempt to use the conditions exploited for 1-bromonaphthalene (51) to synthesise 69. Remarkably, the product of this reaction was acenaphthylene (75) (scheme 1.28).
The reaction may proceed through a lithium-halogen exchange to form 76, with the lithium in the *peri*-position. 76 is thought to be in equilibrium with 77, where the benzyl position is lithiated. Sulfur quench of 77 followed by aromatisation produces 75 (scheme 1.29). Sulfur and selenium have been reported to dehydrate guaiol and related compounds by the formal loss of $S^{2-}$ or $Se^{2-}$ and have been used in the final steps of natural product synthesis.\textsuperscript{54, 55} Alternatively 75 may arise from the reaction of sulfur with 1,2-dihydroacenaphthylene (73), although this transformation generally requires high temperatures.\textsuperscript{55}

![Scheme 1.28 Attempted synthesis of 68](image)

**Scheme 1.28** Attempted synthesis of 68

Attention turned to 5-bromoacenaphthylene (78) as there are no acidic benzylic protons present. DDQ oxidation of 74 proceeded in moderate yield in refluxing benzene. The product however contained inseparable dibromide 72, as a result of an impurity in the starting material. Conditions analogous to scheme 1.28 were applied to 78, without any success (scheme 1.30).

![Scheme 1.29 Proposed formation of acenaphthylene from 5-bromoacenaphthene](image)

**Scheme 1.29** Proposed formation of acenaphthylene from 5-bromoacenaphthene

![Scheme 1.30 Unsuccessful synthesis of 70](image)

**Scheme 1.30** Unsuccessful synthesis of 70
Disulfide 50 has previously been prepared in the group in 35% yield, starting from 1,8-dibromonaphthalene (79) via the 1,8-diGrignard (scheme 1.31). Attempts to furnish the bridged disulfides 69 and 70 via the bisGrignard, starting from 71 and 72, respectively, resulted in recovery of starting material, implying that the Grignard reagent did not form (table 1.5, entries 1 and 2).

![Scheme 1.31 Synthesis of disulfides via bisGrignard](image)

Disulfides are also synthesised from the reaction of both alkyl and aryl dibromo compounds with sodium disulfide (Na₂S₂). Attempted synthesis of disulfides 69 or 70 using Na₂S₂ as the reagent in DMF resulted in a complex mixture of compounds which could not be purified by column chromatography (entries 3 and 4).

Gamage reported the synthesis of disulfide 50 from 1,8-dichloronaphthalene (80) using sodium disulfide (scheme 1.32). The use of the dichloride derivatives is rationalised by chlorine being more electronegative than bromine, thus aiding attack of the sulfur nucleophile on the ipso-carbon.

![Scheme 1.32 Synthesis of disulfides via sodium disulfide](image)

5,6-Dichloro-1,2-dihydroacenaphthylene (81) and 5,6-dichloroacenaphthylene (82) were successfully synthesised. Chlorination of 73 with sulfuryl chloride in the presence of catalytic aluminium chloride furnished 5,6-dichloroacenaphthene 81. Oxidation utilising DDQ of 81 resulted in 5,6-dichloroacenaphthylene 82 (scheme 1.33).
The conditions of Gamage were adopted with dipolar aprotic DMPU used as a replacement for the carcinogenic HMPA.\textsuperscript{58} Remarkably, the product obtained from this reaction was 1,2-dihydroacenaphthylene (73) in near quantitative yield (scheme 1.34, entry 5) with none of the desired disulfide 69 observed.

Starting material was recovered when attempting to add sodium thiocyanate\textsuperscript{59} to dichloro compounds 81 and 82 (entries 6-9). When reacting dichloride 81 with sodium benzyl thiolate\textsuperscript{60, 61} a mixture containing the desired disulfide 69 as the major product was obtained (entry 10). However repetition on a larger scale failed to furnish 69. Reaction of dichloride 82 under the same conditions failed to furnish the required disulfide, and starting material was recovered (scheme 1.35, entry 11).

Disulfide 69 was synthesised in low yield. Due to the irreproducibility of this reaction, a number of alternative conditions were attempted to synthesise bridged disulfides 69 and 70 with little success.
Altering the electronics of the naphthalene moiety has also been considered as a means to influence the rate or temperature of SO transfer. It has been reported that mono-bromination of naphthalene-2,7-diol (83) does not give the necessary regiocontrol. Thus the first step was methylation of diol 83 with dimethyl sulfate to furnish 2,7-dimethoxynaphthalene (84) in excellent yields (scheme 1.36).  

![Scheme 1.36 Methylation of dihydroxynaphthalene](image)

Adams et al. reported that mono-bromination of 84 with bromine occurred in the peri position. Efforts to synthesise 1-bromo-2,7-dimethoxynaphthalene with elemental
bromine failed to result in the desired product (scheme 1.37). Instead dibromination occurred in the \textit{peri}-position furnishing 1,8-dibromo-2,7-dimethoxynaphthalene (85) in a 10\% yield along with a 35\% yield of the unwanted regioisomer, 1,6-dibromo-2,7-dimethoxynaphthalene (86). The structure of 86 was confirmed by X-ray crystallography, with bromine reacting at the activated 6-position (figure 1.7).

\begin{center}
\begin{tikzpicture}
\node (A) at (0,0) {\includegraphics[width=0.5\textwidth]{scheme.png}};
\end{tikzpicture}
\end{center}

\textbf{Scheme 1.37} Bromination of 2,7-dimethoxynaphthalene

\begin{center}
\begin{tikzpicture}
\node (A) at (0,0) {\includegraphics[width=0.5\textwidth]{figure.png}};
\end{tikzpicture}
\end{center}

\textbf{Figure 1.7} Ortep view of 86 with ellipsoids drawn at the 50\% probability level

Whiting \textit{et al.} reported regioselective dibromination at the \textit{peri}-positions with the use of NBS and pyridine with both diol 83 and 2,7-diisopropoxynaphthalene.\textsuperscript{62} Bromination of diol 83 using the conditions reported by Whiting was unsuccessful and starting material was recovered. Bromination of 2,7-dimethoxynaphthalene under the same conditions successfully generated the desired product 85. NBS (4 equiv.) and pyridine were heated at reflux forming an orange mixture prior to addition of 2,7-dimethoxynaphthalene. The mixture was then
heated at reflux for a further 9 h (scheme 1.38). The desired compound 85 was isolated in a 41% yield, along with recovered starting material, and no other unwanted regioisomers.

![Scheme 1.38 Synthesis of 1,8 dibromo-2,7-dimethoxynaphthalene (85)](image)

In order to obtain 3,8-dimethoxynaphtho[1,8-\textit{cd}][1,2]dithiole (87) a dilithium-halogen exchange was required. It has been reported that dilithium-halogen exchange can occur on 1,8-dibromonaphthalene derivatives in diethyl ether at room temperature.\(^5\)\(^3\) Reaction of 2 equiv. of \textit{n}-BuLi with dibromide 85 in diethyl ether at room temperature followed by a recrystallised sulfur quench resulted in novel disulfide 87 in 42% yield (scheme 1.39). Disulfide 87 was also obtained from the reaction in THF as the solvent with diminished yields (9%).

![Scheme 1.39 Synthesis of disulfide 87](image)

Along with 87, an electron-rich disulfide, electron-deficient disulfides were also explored.

The nitration of disulfide 50 with the dinitrogen tetroxide (N\textsubscript{2}O\textsubscript{4}) has been reported by Oae to quantitatively yield a mixture of \textit{ortho} and \textit{para} regioisomers.\(^6\)\(^5\) Due to the expense of N\textsubscript{2}O\textsubscript{4} a replacement nitrating agent was sought. Nitration of aromatic sulfide 88 has been reported using a mixture of acetic anhydride and nitric acid (scheme 1.40).\(^6\)\(^6\)

![Scheme 1.40 Aromatic nitration using HNO\textsubscript{3} and Ac\textsubscript{2}O](image)
Disulfide 50 was subjected to the conditions reported by Berlin and resulted in a 15:85 mixture of ortho and para regioisomers, 3-nitronaphtho[1,8-\textit{cd}][1,2]dithiole (90) and 5-nitronaphtho[1,8-\textit{cd}][1,2]dithiole (91), in a combined 37% yield. The regioisomers were separated by HPLC (scheme 1.41).

![Scheme 1.41 Nitration of disulfide 50](image)

The structures of 90 and 91 were confirmed by X-ray crystallography (figure 1.8).

![Figure 1.8 X-ray crystal structures of ortho 90 and para 91](image)

As a result of the disulfide bond in 91 the para nitro group has a larger bond angle, of 122.38°, than the expected angle for an sp² hybridised carbon (120°).

Attempts to nitrate disulfide 50 utilising 2 equiv. of nitric acid to form a disubstituted nitro compound resulted in an insoluble product which could not be identified (scheme 1.42).

![Scheme 1.42 Attempted dinitration of disulfide 50](image)
1.6 Synthesis of trisulfide-2-oxides

The synthesis of cyclic trisulfide-2-oxides from dithiols has been reported using thionyl chloride in the presence of pyridine.\textsuperscript{67,68} Disulfide 50 was reduced in the presence of NaBH\textsubscript{4} to afford the dithiol 53 in quantitative yields. Due to the \textit{peri}-interaction, dithiol 53 oxidised back to disulfide 50 in 3 h in the solid state and was therefore used directly in the condensation step. Initially, the conditions used by Field\textsuperscript{69} and Bartlett\textsuperscript{67} were employed, however yields of 1,2,3-trithiphenalene 2-oxide (49) were low and the recyclable disulfide 50 was recovered in good yield (scheme 1.43, table 1.6, entry 1).

![Scheme 1.43 Synthesis of trisulfide-2-oxide (49)](image)

The Grainger group reported optimised conditions for the synthesis of trisulfide-2-oxide 49 using a slight excess of pyridine (1.15 equiv.) along with dithiol 53 added to thionyl chloride (1.45 equiv.).\textsuperscript{26,27} Applying these conditions successfully produced 49 in superior yield (table 1.6, entry 1) compared to the method described by Field and Bartlett (entry 4). The amount of trisulfide-2-oxide diminished in the absence of pyridine (entry 3). Changing the order of addition of reactants did not increase the yield of the trisulfide-2-oxide (entry 5).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions\textsuperscript{[a]}</th>
<th>49 (%)</th>
<th>50 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SOCl\textsubscript{2} (1.00 equiv.), pyridine (1.00 equiv.), Et\textsubscript{2}O</td>
<td>29</td>
<td>53</td>
</tr>
<tr>
<td>2</td>
<td>SOCl\textsubscript{2} (1.45 equiv.), pyridine (1.15 equiv.), Et\textsubscript{2}O</td>
<td>60</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>SOCl\textsubscript{2} (1.00 equiv.), Et\textsubscript{2}O</td>
<td>23</td>
<td>58</td>
</tr>
<tr>
<td>4</td>
<td>SOCl\textsubscript{2} (1.00 equiv.), pyridine (2.00 equiv.), Et\textsubscript{2}O</td>
<td>20</td>
<td>58</td>
</tr>
<tr>
<td>5\textsuperscript{[b]}</td>
<td>SOCl\textsubscript{2} (1.45 equiv.), pyridine (1.15 equiv.), Et\textsubscript{2}O</td>
<td>18</td>
<td>55</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]} pyridine and dithiol added to SOCl\textsubscript{2}

\textsuperscript{[b]} SOCl\textsubscript{2} added to pyridine and dithiol

\textbf{Table 1.6} Conditions employed for the synthesis of trisulfide-2-oxide 49 from dithiol 53

27
The mechanism proposed in scheme 1.44 may explain the reformation of disulfide 50. Grainger and Procopio proposed that pyridine activates the thionyl chloride, forming the activated pyridinium species 92. The dithiol 53 is then believed to react with 92 to form 93, along with pyridinium chloride, which is observed as a precipitate. The second thiol group present in 93 has two possible reaction pathways it can follow (a or b); reaction pathway a is where the thiol reacts with the sulfinyl sulfur to produce trisulfide-2-oxide 49. In pathway b, the thiol in 93 reacts with the peri-sulfenyl sulfur to produce the by-product, disulfide 50. This pathway also suggests that sulfur monoxide is produced in the reaction; attempts to trap the SO at room temperature by addition of butadiene 16 in the reaction failed to result in formation of sulfoxide 2.

Scheme 1.44 Competition between trisulfide-2-oxide and disulfide formation
In an attempt to improve the yield of this reaction to favour formation of the trisulfide-2-oxide, alternative methods of generating 49 were explored. Nakayama has reported the reduction of dithiete 94 using Super-Hydride® and condensing the dithiolate 95 with SOCl₂ to give 96 in low yields (scheme 1.45). Unfortunately Super-Hydride® failed to reduce the S-S bond in disulfide 50 resulting in recovery of starting material.

\[
\text{Ad} \quad \begin{array}{c}
\text{S} \\
\text{S}
\end{array} \quad \text{LiEt₃BH} \\
(2 \text{ equiv.}) \quad \begin{array}{c}
\text{S} \\
\text{S}
\end{array} \quad \text{SOCl₂} \\
\text{S} \quad \begin{array}{c}
\text{S} \\
\text{O}
\end{array}
\]

**Scheme 1.45 Reduction of 94 using Super-Hydride®**

The same authors, and later Ogawa, revealed that dithiolates can be protected with dialkyl tin dichlorides to fashion stannoles and subsequent reaction with SOCl₂ formed the trisulfide-2-oxides in improved yields (scheme 1.46).

\[
\begin{array}{c}
\text{Ad} \\
\text{Me₂SnCl₂}
\end{array} \quad \begin{array}{c}
\text{S} \\
\text{SnMe₂}
\end{array} \quad \text{SOCl₂} \\
\text{S} \quad \begin{array}{c}
\text{S} \\
\text{O}
\end{array} \\
\text{S} \quad \begin{array}{c}
\text{S} \\
\text{O}
\end{array} \quad \text{37%}
\]

**Scheme 1.46 Synthesis of trisulfide-2-oxide 96 via 1,2-dithiastannole 97**

Reduction of disulfide 50 with NaBH₄ followed by reaction with Bu₂SnCl₂ provided a mixture of stannole 98 and disulfide 50. Attempts to isolate the stannole by column chromatography were unsuccessful as the stannole decomposed to the starting disulfide 50. Instead intermediate stannole 98 was not isolated and the crude mixture was reacted with SOCl₂ to obtain trisulfide-2-oxide 49 in a 26% yield along with disulfide 50 in a 50% yield (scheme 1.47).
In 2003, Yip reported the use of 1,8-naphthalene dithiolate 99 to form copper complexes in a one-pot synthesis from disulfide 50.72 These conditions were employed and dithiolate 99 was condensed with SOCl₂ to generate 20% of trisulfide-2-oxide 49, with recovery of 80% of disulfide 50 (scheme 1.48).

Alterating the thionating agent by replacement of the chlorines on thionyl chloride for imidazole groups was also considered (figure 1.9). The reagent was prepared according to the reported method.73 Unfortunately using the optimised conditions reported by Grainger27 (table 1.6, entry 4) resulted exclusively in disulfide. This suggested that thionyl diimidazole 100 was not synthesised or that the dithiol 53 did not react with 100.
A literature procedure reported the reaction of thiophenol with 100 in the absence of additional base. Attempts to repeat this reaction failed to give any acyclic trisulfide-2-oxide, therefore it was concluded that the desired thionyl diimidazole 100 was not produced.

With optimisation for the synthesis of naphthalene trisulfide-2-oxide 49 complete, disulfides 65 and 87 were subjected to these conditions. Reduction of disulfide 65 with excess lithium aluminium hydride generated the desired 2,7-di-tert-butynaphthalene-1,8-dithiol (101) in near quantitative yield, as reported by Tesmer (>99%).

Condensation of dithiol 101 with SOCl₂ resulted in 4,9-di-tert-butyl-1,2,3-trithiophenalene 2-oxide (58). Purification of 58 proved to be difficult using silica, however the use of Florisil® provided pure trisulfide-2-oxide 58 in a 13% yield, along with 87% of recovered starting material 65 (scheme 1.49).

The lower yield of 58 may be rationalised by considering the mechanism suggested in scheme 1.44. The buttressing effect of the ortho tert-butyl groups may make pathway b favoured over pathway a, as a result of the thiol lone pair being in closer proximity to the other peri-sulfur atom.

Reduction of disulfide 87 with NaBH₄ afforded 2,7-dimethoxynaphthalene-1,8-dithiol (102) in quantitative yield as an unstable, white, crystalline solid. The unstable dithiol 102 oxidised back to disulfide 87 in the solid state in 2 h. Treatment of the crude dithiol 102 with SOCl₂ in the presence of pyridine gratifyingly afforded 4,9-dimethoxy-1,2,3-trithiophenalene 2-oxide (103) in moderate yield along with recovery of disulfide 87 (scheme 1.50). Rapid purification of trisulfide-2-oxide 103 by column chromatography was important as 103 decomposed to disulfide 87 over time on silica.
1.7 X-ray analyses of trisulfide-2-oxides

The crystal structures of the two novel trisulfide-2-oxides 58 and 103 were obtained to acquire structural information. The X-rays of trisulfide-2-oxides 49, 58 and 103 are shown in figure 1.10 respectively.

All three structures show similarities, with the trithiane-2-oxide ring adopting a non-planar conformation with five atoms almost in the same plane and the sulfinyl sulfur positioned out of the plane. The sulfinyl bond adopts a pseudo axial orientation in 49, 58 and 103. This is probably as a result of stabilisation through overlap of non-bonding electrons on the peri-sulfur atoms with an SO antibonding orbital (anomeric type effect). This stereoelectronic effect has been proposed to contribute to the preference for a sulfinyl group to adopt an axial orientation in six-membered rings containing an adjacent heteroatom next to sulfur. The X-ray crystal structures for five-membered ring containing trisulfide-2-oxides have been reported, where the S-O bond also adopts a pseudo axial orientation (figure 1.11).
The bond and torsion angles in the X-ray of 58 suggest more strain is present in 58 compared to 49. Strain in the system is evident by the peri-sulfur atoms deviating on either side of the naphthalene moiety and the central sulfur atom to a larger degree (torsion angles C(10)-C(9)-C(1)-S(1), 159.6° and C(10)-C(9)-C(8)-S(2), 163.8° respectively) compared to 49 (table 1.7). The bond angles at C(1), C(9), and C(8) are 122.7°, 126.1° and 119.2° respectively. These angles are smaller compared to trisulfide-2-oxide 49, presumably due to the buttressing effect. Strain is also evident by distortion of the naphthalene ring from planarity (torsion angles C(1)-C(9)-C(10)-C(4), 6.33° and C(8)-C(9)-C(10)-C(5), 6.52° respectively). The bond angles at C(2) and C(7) are also enlarged to 125.0° and 124.3° respectively. The buttressing of the tert-butyl groups is apparent as the distance between the two peri-sulfur atoms in 58 is 3.038 Å, compared to 3.096 Å in trisulfide-2-oxide 49.

The X-ray of 103 indicates strain is present but to a lesser extent compared to 49. Analogous to the previous X-rays, bond angles around C(1), C(9) and (8) are larger than the expected 120° (table 1.7). The peri-sulfur atoms are essentially co-planar with the naphthalene ring, similar to 49. Overall, the structure of trisulfide-2-oxide 103 was comparable to trisulfide-2-oxide 49 and thus it was a good example to directly compare whether the electronic properties of the naphthalene moiety had an effect on SO transfer.
The axial and equatorial conformations of 49 are related by either pyramidal inversion of the sulfinyl group or inversion of the trithiane ring. In general pyramidal inversion of the sulfinyl group does not occur at room temperature. Only one set of signals was observed by variable temperature NMR experiments on cooling from room temperature to -80 °C. This suggests that one conformation was present in solution (figure 1.12), although it is not clear to what extent the two conformations would vary.
1.8 Sulfur monoxide transfer experiments

The successful synthesis of trisulfide-2-oxides 49, 58 and 103 allowed SO transfer experiments with dienes to be undertaken. Compounds 58 and 103 were investigated to establish whether altering the naphthalene moiety would change the temperature and/or rate at which trisulfide-2-oxides act as SO transfer reagents. It was also noted that naphtho[1,8-cd][1,2]dithiole 1-oxide 107 was a by-product from the thermolysis of 49.26 The precaution of degassing the solvent by bubbling through argon resolved this problem.

Previous work in the group showed that the unsubstituted trisulfide-2-oxide transferred SO to dienes at reflux in chlorobenzene.26, 27, 42 Indeed refluxing trisulfide-2-oxide 49 in chlorobenzene for 10 h proved to be the most effective method for obtaining sulfoxides in good yields (table 1.8, entry 1). Running the reaction at a higher concentration led to a lower yield of 2 (entry 2). At lower temperatures of 80 °C and 110 °C yields, of both the sulfoxide 2
and recovered disulfide 50 diminished and the reaction times were considerably longer (entries 3 and 4).

![Chemical structures and reaction scheme]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Trisulfide-2-oxide (10 equiv.)</th>
<th>Time (h)</th>
<th>Solvent</th>
<th>Temperature (°C)</th>
<th>Sulfoxide 2 (%)</th>
<th>Disulfide 50 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>10</td>
<td>PhCl</td>
<td>132</td>
<td>91</td>
<td>50 98</td>
</tr>
<tr>
<td>2[b]</td>
<td>49</td>
<td>10</td>
<td>PhCl</td>
<td>132</td>
<td>75</td>
<td>50 86</td>
</tr>
<tr>
<td>3[c]</td>
<td>49</td>
<td>168</td>
<td>PhH</td>
<td>80</td>
<td>55</td>
<td>50 85</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>23</td>
<td>PhMe</td>
<td>110</td>
<td>73</td>
<td>50 95</td>
</tr>
<tr>
<td>5</td>
<td>58</td>
<td>8</td>
<td>PhCl</td>
<td>132</td>
<td>99</td>
<td>65 96</td>
</tr>
<tr>
<td>6</td>
<td>103</td>
<td>5.5</td>
<td>PhCl</td>
<td>132</td>
<td>96</td>
<td>87 92</td>
</tr>
<tr>
<td>7</td>
<td>58</td>
<td>36.5</td>
<td>PhH</td>
<td>80</td>
<td>93</td>
<td>65 94</td>
</tr>
<tr>
<td>8</td>
<td>103</td>
<td>42</td>
<td>PhH</td>
<td>80</td>
<td>92</td>
<td>87 93</td>
</tr>
</tbody>
</table>

[a] Reactions run at 0.01 M.
[b] Reaction run at 0.1 M.
[c] 8% yield of trisulfide-2-oxide 49 was recovered.

Table 1.8 SO transfer experiments of 49, 58, and 103 at different temperatures

The temperature at which SO transfer occurred from trisulfide-2-oxides 58 and 103 was also investigated. When substituted trisulfide-2-oxides 58 and 103 were heated in refluxing chlorobenzene, reaction times decreased, with trisulfide-2-oxide 103 reacting in 5.5 h (entries 5 and 6). These encouraging results suggested that SO transfer could occur at lower temperatures. Gratifyingly, in refluxing benzene SO transfer occurred with significantly enhanced yields and reaction times in comparison with naphthalene trisulfide-2-oxide 49, albeit in slightly lower yield compared to refluxing chlorobenzene (entries 7 and 8).
The enhanced rate at which trisulfide-2-oxides 58 and 103 transfer SO to dienes in comparison to 49 is noteworthy. X-ray analysis of 58 suggests more strain is present than the parent trisulfide-2-oxide 49, as distortion of the naphthalene ring away from planarity is evident from the dihedral angles (table 1.7). The X-ray of 103 conversely does not suggest additional strain compared to 49, and suggests the increased rate of SO transfer is a result of an electronic rather than a steric effect.

Despite successfully transferring SO to dienes with trisulfide-2-oxides 49, 58 and 103, 49 was the most effective SO transfer reagent in refluxing chlorobenzene. For this reason, trisulfide-2-oxide 49 was successfully reacted with other dienes 17-19 (scheme 1.51, table 1.9).

![Scheme 1.51 Thermal decomposition of 49 in the presence of 1,3 dienes.](image)

It was noticed that excess diene was necessary for effective SO transfer to occur. In the case of isoprene (18), a large excess of diene was required due to the volatility of 18 (entry 1). In the case of myrcene (19), the ratio of diene was explored and good yields of sulfoxide 22 were obtained when the reaction was reacted with excess diene (entry 2). Yields were lower when SO transfer reactions were employed with an equimolar amount of diene (entry 3). However the use of excess trisulfide-2-oxide provided sulfoxide 22 in a good yield (entry 4). Fewer equivalents of diene were also utilised for the reaction with diphenylbutadiene 17 to obtain sulfoxide 3 in good yields (entry 5).
<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>49: Diene ratio</th>
<th>Time (h)</th>
<th>Sulfoxide (%)</th>
<th>49 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>1:10</td>
<td>6</td>
<td>21 66</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>1:2.5</td>
<td>6</td>
<td>21 87</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>19</td>
<td>1:1</td>
<td>6</td>
<td>22 39</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>19</td>
<td>2.5:1</td>
<td>6</td>
<td>22 85</td>
<td>97</td>
</tr>
<tr>
<td>5</td>
<td>17</td>
<td>1:2.5</td>
<td>5.75</td>
<td>3 65</td>
<td>92</td>
</tr>
</tbody>
</table>

Table 1.9 Thermal decomposition of 49 in the presence of 1,3 dienes.

SO transfer to cyclic dienes to produce cyclic sulfoxides has been previously reported, albeit in moderate yields.\textsuperscript{14, 24} Reaction of trisulfide-2-oxide 49 with cyclooctadiene failed to result in any sulfoxide product 13 (scheme 1.52).

Scheme 1.52 Unsuccessful SO transfer to 1,3 cyclooctadiene

SO transfer from episulfoxide 23 to a variety of ylides has been reported.\textsuperscript{18} The reaction of trisulfide-2-oxide 49 with ylide 110 was therefore investigated. Reaction of 9-bromofluorene 108 with PPh\textsubscript{3} gave (9H-fluoren-9-yl)triphenylphosphonium bromide (109), which upon treatment with aqueous ammonium hydroxide afforded the stable fluoren-9-ylidene-triphenyl-\(\kappa^5\)-phosphane (110).\textsuperscript{80, 81} The formation of 110 was confirmed by the synthesis of 9-ethylidene-9H-fluorene (111).\textsuperscript{82} Trisulfide-2-oxide 49 was refluxed in chlorobenzene in the presence of ylide 110 for 2 h to give a mixture of compounds (scheme 1.53).
After separation of disulfide 50, HPLC analysis confirmed a mixture of two compounds in a 1:1 ratio, and purification revealed one of the compounds to be fluoren-9-one (112). The other fraction was a single peak by HPLC but NMR showed it to be a mixture of compounds, one of which was tentatively assigned as fluorenethione-S-oxide (113) based on the infrared stretches of the C=S=O group at 1120 and 1018 cm\(^{-1}\), and by mass spectrometry. Unfortunately the other product was unidentifiable as only multiplets in the aromatic region were observed which also overlapped with signals for protons in sulfine 113. Fluorenone 112 is a known compound resulting from the breakdown of 113, thought to form via a three-membered oxathiirane with loss of sulfur producing ketone 112 (scheme 1.54).

The oxidation of trisulfide-2-oxides has been investigated by Harpp and it is proposed that electrophilic oxidation occurs at the sulfenyl sulfur (scheme 1.55). Oxidation of 114 resulted in thiosulfonate 116 in good yields, providing evidence for the formation of vic-disulfoxide 115, which rapidly rearranges to tert-butylsulfenic tert-butylsulfonic

---

**Scheme 1.53 SO transfer to ylide 110**

**Scheme 1.54 Decomposition of fluorenlylidesulfine 113**
thioanhydride (116) (see Chapter 2 for a discussion ofvic-disulfoxides and their rearrangement).

\[ \text{114} \xrightarrow{\text{DMD}} \text{115} \xrightarrow{} \text{116} 85\% \]

**Scheme 1.55 Oxidation of trisulfide-2-oxide 114**

Efforts to transfer SO to dienes were also explored by oxidation of 49 to possibly form the intermediate vic-disulfoxide 117, which could fragment to thiosulfinate 107 and SO as reported by Furukawa on similar 1,8-dithianaphthalene systems.\(^{35, 36}\) Trisulfide-2-oxide 49 was treated with either DMD or mCPBA at -78 °C warming in the presence of diene 16, however no desired sulfoxide 2 was observed (table 1.10). The isolated products were disulfide 50 and monoxide 107 (entries 1 and 2). The formation of these products could possibly be explained by a competition between different pathways and relative rates of oxidation (scheme 1.56). If vic-disulfoxide 117 is formed, it has two different rearrangement pathways a and b. Path a ultimately results in loss of SO\(_2\) and formation of disulfide 50, and route b produces thiosulfinate 107 via loss of SO. Oxidation of disulfide 50, pathway c, must also be considered as a means to produce monoxide 107.

\[ \text{49} \xrightarrow{[\text{O}]} \text{117} \]

\[ \text{SO}_2 \xrightarrow{a} \text{50} \]

\[ \text{SO} \xrightarrow{b} \text{107} \]

**Scheme 1.56 Oxidation of 49 to release SO**
<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxidant (equiv.)</th>
<th>Conditions</th>
<th>49 (%)</th>
<th>50 (%)</th>
<th>107 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mCPBA (1)</td>
<td>16 (10 equiv.), CH$_2$Cl$_2$, -78 °C → rt, o/n</td>
<td>30</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>DMD (1)</td>
<td>16 (10 equiv), CH$_2$Cl$_2$, -78 °C → rt, o/n</td>
<td>22</td>
<td>40</td>
<td>37</td>
</tr>
</tbody>
</table>

Table 1.10 Oxidation of trisulfide-2-oxide

The isomerisation of trisulfide-2-oxide 118 to 1-oxide 119 under photolytic conditions has been reported by Sato (scheme 1.57).\(^6\)

![Scheme 1.57](image)

Scheme 1.57 Photomediated isomerisation of trisulfide-2-oxide 118

Isomerisation of trisulfide-2-oxide 49 was investigated under photolytic conditions. The UV absorptions of trisulfide-2-oxide 49 and disulfide 50 were recorded, and both show similar absorbances in the visible region. Irradiation of trisulfide-2-oxide 49 at room temperature in the presence of diene 16 resulted in formation of sulfoxide 2 and disulfide 50 (scheme 1.58).

![Scheme 1.58](image)

Scheme 1.58 Photoinduced SO transfer at room temperature

Three separate light sources were employed to transfer SO to diene 16 and although reaction times for the breakdown of trisulfide-2-oxide 49 were improved, yields of the resultant sulfoxide 2 were somewhat lower compared to thermolysis of 49 (table 1.11). Sulfoxide 2 was found to be photostable under these conditions.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions[\textsuperscript{[a]}]</th>
<th>2 (%)</th>
<th>50 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>125 W medium pressure Hg lamp, pyrex filter, 1 h</td>
<td>36</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>500 W halogen lamp, 1 h</td>
<td>48</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>300 W UV sunlamp, 2 h</td>
<td>55</td>
<td>93</td>
</tr>
</tbody>
</table>

\[\text{[a] all reactions were run in 0.01 M PhCl in the presence of diene 16 (10 equiv.) at rt}\]

**Table 1.11** Photomediated SO transfer from trisulfide-2-oxide 49 at rt

Under photolytic conditions cyclooctadiene again failed to produce any of the expected sulfoxide adduct 13 (scheme 1.59).

![Scheme 1.59 Attempted photomediated SO transfer to cyclooctadiene](image)

### 1.9 Mechanistic studies of SO transfer

At the outset of this work, the mechanism of SO transfer from 49 to dienes was not known. There are many possible rate-determining steps (r.d.s.) for SO transfer and some possible routes are proposed in scheme 1.60. Pathway a is direct reaction of the diene with 49, route b illustrates the release of “free” SO, which rapidly reacts with a diene providing a sulfoxide. Path c involves initial rearrangement of 49 to 120, which is then able to react with the butadiene to furnish the sulfoxide. Alternatively 120 may be an intermediate in the release of SO from 49 (path d).
Scheme 1.60 Possible SO transfer pathways of trisulfide-2-oxide 49 to diene 16

The thermal decomposition of acyclic trisulfide-2-oxides has been examined in detail by Field and Harpp (scheme 1.61).

Scheme 1.61 Thermal decomposition of acyclic trisulfide-2-oxides

The proposed mechanism suggests initial heterolytic bond fission of 114. An oxygen transfer affords 1,2-di-tert-butyldisulfane and compound 121 following reaction with another molecule of 114. 1-tert-Butyl-2-(tert-butylsulfinyloxy)disulfane (121) is then believed to decompose immediately to an equimolar mixture of trisulfide 122 and SO₂.
Nakayama studied the thermal decomposition of cyclic trisulfide-2-oxide $^{123}$ (scheme 1.62). $^{70}$ It is proposed that homolytic cleavage of the weak S-S(O) bond forms biradical $^{124}$ which upon extrusion of SO forms $^{125}$.

![Scheme 1.62 Thermal decomposition of cyclic trisulfide-2-oxides](image)

Kinetic investigations were undertaken for the reaction of trisulfide-2-oxide $^{49}$ with 2,3-dimethylbutadiene (16) (scheme 1.63). As diene 16 was used in a large excess for the SO transfer, reactions were run under pseudo first order conditions. $^{87, 88}$ HPLC was used as the method for monitoring the reaction as the reactants and products of the reaction had different retention times. Unfortunately chlorobenzene co-eluted with the reactants, and for this reason the reaction was screened in other solvents (xylenes and anisole) at the boiling point of chlorobenzene (132 °C). Octane, a UV inert solvent, was used to monitor appearance and disappearance of starting materials by HPLC analysis.

![Scheme 1.63 SO transfer to diene 16](image)

The rate equation for the reaction under consideration is

$$\text{Rate} = - k \left[49\right]^a \left[16\right]^b$$  \hspace{1cm} \text{Equation 1.1}

If the initial concentration of the reactant 16 is much larger than that of 49, the concentration of 16 will not change appreciably during the course of the reaction. The concentration of the reactant in excess will remain effectively constant. Thus the rate’s dependence on 49 can be isolated and the rate law can be re-written as:
\[
\frac{d[49]}{dt} = \text{Rate} = -k'[49]^\alpha, \quad \text{where } k' = k[16]^\beta \quad \text{Equation 1.2}
\]

Integration of equation 1.2 results in the integrated rate law, which can then be rearranged into the form \(y = mx + c\) (equation 1.4).

\[
[49] = [49]_o e^{-k't} \quad \text{Equation 1.3}
\]

\[
\ln [49] = \ln [49]_o - k't \quad \text{Equation 1.4}
\]

where \(k = \text{rate constant}, k' = \text{observed rate constant}, t = \text{time}, [\ ] = \text{concentration}, [\ ]_o = \text{initial concentration}, \alpha \text{ and } \beta \text{ are the reaction order with respect to substrate.}

Characteristic kinetic plots resulted in distinctive lines depending on the order of the reaction.\(^87\), \(^88\) A plot of concentration vs. time results in a straight line for a \(0^{th}\) order reaction with respect to substrate. A straight line is observed for a reactant that is \(1^{st}\) order by plotting \(\ln \text{concentration vs. time}\) and a \(2^{nd}\) order by a plot of \(1/\text{concentration vs. time}\) (figure 1.13).

Initially SO transfer reactions were carried out by varying the concentration of the trisulfide oxide, whilst keeping the concentration of the diene constant. A straight line plot was observed when plotting \(\ln \text{concentration vs. time}\), consistent with that of a \(1^{st}\) order reaction in trisulfide-2-oxide. The gradient of the \(\ln [49]\) vs. time plot (figure 1.14) provided the observed rate constant, \(k'\) (table 1.12). The observed rate constants remained constant over a varied concentration indicating a \(1^{st}\) order breakdown for trisulfide-2-oxide.
The order of the reaction with respect to diene was determined by analysis of the rates of reaction when the concentration of the diene was varied whilst the trisulfide-2-oxide concentration was kept constant. With the knowledge that there is a $1^{st}$ order breakdown for trisulfide-2-oxide (i.e. $\alpha = 1$), the order with respect to the diene was calculated using simultaneous equations.

For example, substitution of entries 6 and 7 into equation 1.1 gives the following equations.

**Entry 6:**

\[ [1.19] = - k [0.005]^1 \beta \]  
\[ \text{Equation 1.5} \]

**Entry 7:**

\[ [1.17] = - k [0.005]^1 \beta \]  
\[ \text{Equation 1.6} \]

Rearrangement of equations 1.5 and 1.6 results in equations 1.7 and 1.8:

\begin{align*}
\ln [1.19] &= - \ln k + \ln [0.005] + \beta \ln [0.1] \\
\ln [1.17] &= - \ln k + \ln [0.005] + \beta \ln [0.3] 
\end{align*}

\[ \text{Equation 1.7} \]
\[ \text{Equation 1.8} \]

Subtracting equation 1.8 from 1.7 and making $\beta$ the subject results in the order with respect to the diene to be calculated (equation 1.9).

\[ \beta = \frac{\ln [1.19] - \ln [1.17]}{\ln [0.1] - \ln [0.3]} \approx 0 \]

\[ \text{Equation 1.9} \]
The observed rate constant remained constant within experimental error (table 1.12, entries 4 and 6-9) suggesting that the reaction was 0th order in diene and this did not contribute to the rate-determining step for the reaction. This evidence was furthered when the reaction was run in the absence of diene and the rate constant was the same within experimental error (entry 10).

<table>
<thead>
<tr>
<th>Entry</th>
<th>[49] / M</th>
<th>[16] / M</th>
<th>k' / 10^-4 s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Run 1</td>
</tr>
<tr>
<td>1</td>
<td>0.0080</td>
<td>0.2</td>
<td>1.15 ± 0.25</td>
</tr>
<tr>
<td>2</td>
<td>0.0075</td>
<td>0.2</td>
<td>1.24 ± 0.17</td>
</tr>
<tr>
<td>3</td>
<td>0.0060</td>
<td>0.2</td>
<td>1.23 ± 0.42</td>
</tr>
<tr>
<td>4</td>
<td>0.0050</td>
<td>0.2</td>
<td>1.11 ± 0.10</td>
</tr>
<tr>
<td>5</td>
<td>0.0040</td>
<td>0.2</td>
<td>0.99 ± 0.12</td>
</tr>
<tr>
<td>6</td>
<td>0.0050</td>
<td>0.1</td>
<td>1.19 ± 0.22</td>
</tr>
<tr>
<td>7</td>
<td>0.0050</td>
<td>0.3</td>
<td>1.12 ± 0.11</td>
</tr>
<tr>
<td>8</td>
<td>0.0050</td>
<td>0.4</td>
<td>0.93 ± 0.12</td>
</tr>
<tr>
<td>9</td>
<td>0.0050</td>
<td>0.5</td>
<td>1.05 ± 0.42</td>
</tr>
<tr>
<td>10</td>
<td>0.0060</td>
<td>0</td>
<td>0.98 ± 0.14</td>
</tr>
</tbody>
</table>

Table 1.12 Observed rate constants for the thermal decomposition of trisulfide-2-oxide 49 in the presence of diene 16

The averaged observed rate constant for the disappearance of 49 is 1.16 ± 0.74 × 10^-4 s^-1. The rate constant for the formation of the sulfoxide 2 was calculated to be 1.01 ± 0.62 × 10^-4 s^-1 (table 1.13), which is comparable to the rate of breakdown of 49. With the kinetic results acquired it is possible to state that the r.d.s. of SO transfer from trisulfide-2-oxides does not depend on the presence of the diene (scheme 1.60, path a). Instead, results suggest pathway b or c is the preferred r.d.s.
<table>
<thead>
<tr>
<th>Entry</th>
<th>[49] / M</th>
<th>[16] / M</th>
<th>Run 1</th>
<th>Run 2</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0080</td>
<td>0.2</td>
<td>0.82 ± 0.15</td>
<td>0.99 ± 0.12</td>
<td>0.91 ± 0.20</td>
</tr>
<tr>
<td>2</td>
<td>0.0075</td>
<td>0.2</td>
<td>1.24 ± 0.31</td>
<td>0.83 ± 0.26</td>
<td>1.04 ± 0.40</td>
</tr>
<tr>
<td>3</td>
<td>0.0060</td>
<td>0.2</td>
<td>0.86 ± 0.40</td>
<td>0.88 ± 0.10</td>
<td>0.87 ± 0.42</td>
</tr>
<tr>
<td>4</td>
<td>0.0050</td>
<td>0.2</td>
<td>0.90 ± 0.40</td>
<td>1.13 ± 0.16</td>
<td>1.02 ± 0.43</td>
</tr>
<tr>
<td>5</td>
<td>0.0040</td>
<td>0.2</td>
<td>0.82 ± 0.21</td>
<td>1.24 ± 0.37</td>
<td>1.03 ± 0.43</td>
</tr>
<tr>
<td>6</td>
<td>0.0050</td>
<td>0.1</td>
<td>1.07 ± 0.21</td>
<td>0.88 ± 0.25</td>
<td>0.98 ± 0.32</td>
</tr>
<tr>
<td>7</td>
<td>0.0050</td>
<td>0.3</td>
<td>1.15 ± 0.08</td>
<td>1.10 ± 0.27</td>
<td>1.13 ± 0.28</td>
</tr>
<tr>
<td>8</td>
<td>0.0050</td>
<td>0.4</td>
<td>0.96 ± 0.10</td>
<td>1.14 ± 0.40</td>
<td>1.05 ± 0.41</td>
</tr>
<tr>
<td>9</td>
<td>0.0050</td>
<td>0.5</td>
<td>1.17 ± 0.31</td>
<td>0.97 ± 0.27</td>
<td>1.07 ± 0.41</td>
</tr>
</tbody>
</table>

*Table 1.13* Observed rate constants for the formation of sulfoxide 2 from the reaction of trisulfide-2-oxide 49 in the presence of diene 16.

The study was furthered to determine whether “free” SO was produced in the reaction. Indirect support for the formation of sulfur monoxide was obtained by examining the reaction in the absence of a diene. The decomposition of SO eventually yields sulfur dioxide and elemental sulfur (scheme 1.1).2-4 The vapours of the thermal decomposition of 49 under reflux were tested with wet pH paper and were shown to be acidic, indicating formation of SO2. Additional evidence for the generation of SO was gained when 49 was heated in a sealed tube and then reacted with a theoretical amount of triphenylphosphine needed to form quantitatively triphenylphosphine sulfide 126. An 89% yield of Ph3P=S was achieved, suggesting efficient production of SO (scheme 1.64).

![Scheme 1.64](image)

**Scheme 1.64** Evidence for the formation of SO through the formation of S=PPh3

Evidence for the formation of SO from trisulfide-2-oxide 49 was acquired by IR spectroscopy by means of flash vacuum thermolysis (FVT), in collaboration with Professor Curt Wentrup.
at the University of Queensland, Australia. The IR of the trisulfide-2-oxide 49 was recorded with an SO stretch at 1071 cm\(^{-1}\), and then compared over time with a sample trapped on an argon matrix at 20 K, after gradual heating. Ultimately the characteristic SO stretch for the trisulfide-2-oxide disappeared and a new collection of peaks resulted (figure 1.15), which on careful examination were found to match closely with the peaks of free SO reported at 1137 cm\(^{-1}\) (\(^{32}\)S\(^{16}\)O) and 1126 cm\(^{-1}\) (\(^{34}\)S\(^{16}\)O) by Hopkins and Brown.\(^{89}\)

![Figure 1.15 FVT of trisulfide-2-oxide 49 monitored by infra red spectroscopy to show the developing free SO](image)

A sample of pure 49 was also subjected to Thermal Gravimetric Analysis (TGA) in order to determine the temperature at which SO is expelled from the trisulfide-2-oxide (figure 1.16).

![Figure 1.16 TGA plot of the thermolysis of trisulfide-2-oxide 49](image)
A sharp endotherm was observed on a pure sample of trisulfide-2-oxide at 136 °C indicating that a change had occurred in 49. At this point a loss of 1.8 mg was detected which accounted for the mass of sulfur monoxide from trisulfide-2-oxide 49. The stoichiometry in scheme 1.60 shows that the number of moles of the starting trisulfide-2-oxide should be equimolar with the amount of disulfide 50 and SO released (14.75 mg/238 = 61.97 µmol). According to scheme 1.1, the amount of SO₂ formed will be half of the number of moles of SO developed (61.97 µmol/2 = 30.99 µmol). The theoretical mass loss of SO₂ gas is 1.98 mg (= 30.99 µmol × 64); the observed loss of 1.8 mg is in good agreement with the calculated yield.

Having established that the rate of reaction was independent of diene and sulfoxide 2 was likely formed as a result of trapping of free SO with 16, the mechanism for the decomposition of 49 was addressed. The mechanism of thermal breakdown of both cyclic and acyclic trisulfide-2-oxides has been proposed to occur via homolytic and heterolytic fission respectively.70, 85

The reaction of naphthalene trisulfide-2-oxide 49 in the presence of diene 16 was monitored in a polar protic and a polar aprotic solvent at 132 °C. Qualitatively the rate of thermal decomposition of trisulfide-2-oxide 49 was similar to the rate of breakdown in chlorobenzene. The yields of the resulting sulfoxide 2 were not as high as in chlorobenzene (table 1.14).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>2 (%)</th>
<th>50 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCl</td>
<td>10</td>
<td>91</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>Pentanol</td>
<td>10</td>
<td>86</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>DMF</td>
<td>9.25</td>
<td>95</td>
<td>62</td>
</tr>
</tbody>
</table>

Table 1.14 SO transfer from trisulfide-2-oxide 49 in different solvents

A comparable rate was observed qualitatively in the presence of radical traps (table 1.15), with formation of the disulfide 50 in good yields.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Radical trap (equiv.)</th>
<th>Time (h)</th>
<th>50 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>tert</em>-butylcatechol (1.0)</td>
<td>9.8</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>1, 4 benzoquinone (1.0)</td>
<td>9.9</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>DPPH (2.5)</td>
<td>10</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>TEMPO (2.5)</td>
<td>10</td>
<td>95</td>
</tr>
</tbody>
</table>

Table 1.15 Attempted radical trapping from the decomposition of 49

The rate of thermal breakdown of trisulfide-2-oxide 48 is independent of diene in a range of solvents. Although the rate of reaction of the breakdown of trisulfide-2-oxides in the presence of radical traps is qualitatively the same, it remains inconclusive as to whether or not the reaction proceeds via a radical pathway.

The nature of the SO transferred was also of interest. Nakayama has reported successfully reacting 43 at room temperature with alkenes and alkynes in poor to modest yields (scheme 1.65). This room temperature extrusion is proposed to be concerted and therefore the first example of singlet SO.

The reaction of 49 in the presence of diphenylacetylene (131) failed to give 2,3-diphenylthiirene 1-oxide (136) or benzil (137), a known product of the thermolysis of 136 (scheme 1.66).
Nakayama also showed that the reaction of 43 in the presence of cycloheptatriene resulted in stereoselective formation of sulfoxide 45 (figure 1.1), suggestive of a concerted addition of singlet SO. In comparison, reaction of episulfoxide 1 gave the dimer product 8 indicative of H-abstraction by triplet SO followed by dimerisation of the cycloheptatrienyl radical (scheme 1.4).10 Reaction of trisulfide-2-oxide 49 with excess cycloheptatriene (2.5 equiv.) in refluxing chlorobenzene resulted in dimer 8, along with disulfide 50 and trace amounts of what was presumed to be naphtho[1,8-de][1,2,3]trithiine (138) by 1H-NMR analysis (scheme 1.67).26 As a result it can be concluded that ground state triplet SO is being formed in this process.

Efforts to transfer 3SO to vinyl cyclopropane 140, synthesised from a Wittig reaction with cyclopropyl(phenyl)methanone (139),91 to form the six-membered ring sulfoxide 141 from ring opening of the cyclopropane failed to produce the desired product (scheme 1.68).
The accumulated studies in this section have built a clearer picture of how SO transfer from trisulfide-2-oxide 49 is taking place. The r.d.s. is independent of the diene trap and only involves the decomposition of trisulfide-2-oxide 49. The information obtained does not allow us to unambiguously distinguish between homolytic and heterolytic fission of the S-SO bond, although a concerted pathway is also possible due to the lack of effect of radical traps. Thus the SO formed could be either in the singlet or triplet state. If singlet SO is generated, a rapid intersystem crossing from the singlet to the triplet state and consequent trapping by a diene gives the product sulfoxide via a radical process (scheme 1.69).
### 1.10 Synthesis of thiophenes via sulfoxide dehydration

A simple transformation of 2,3-dihydrothiophene 1-oxide is the dehydration to the corresponding thiophene. The use of anhydrides to initiate the Pummerer reaction is well known.\(^2\) The Pummerer reaction for the formation of thiophenes from 2,3-dihydrothiophene 1-oxides has been reported in the Grainger group.\(^2\) The Pummerer reaction is considered to occur by activation of sulfoxide, followed by dehydration and aromatisation to form the thiophene (scheme 1.70).

**Scheme 1.70** Mechanism of the Pummerer reaction

Acetic anhydride was initially employed for the Pummerer reaction and treatment of diphenyl sulfoxide 3 at reflux for 3 h successfully generated a new white crystalline product confirming previous studies in the Grainger group (scheme 1.71, table 1.16, entry 1). Analysis of the
NMR proved to be difficult as phenyl protons overlapped, however the loss of aliphatic hydrogens was encouraging. $^{13}$C-NMR spectroscopy and mass spectrometry confirmed the assignment as 142. Identical conditions were utilised for sulfoxides 2, 21 and 22. In each case, heating at reflux resulted in decomposition.

Treatment of diphenyl sulfoxide 3 with a slight excess of the more reactive trifluoroacetic acid successfully generated 3,4-diphenylthiophene (142) and decreased the reaction time greatly (table 1.16, entry 5). Dehydration of myrcene adduct 22 with TFAA gave a clean transformation to the naturally occurring thioperillene (143) (scheme 1.71, entry 6), a constituent of hop and rose oil. Isolation of 143 was difficult and the low yield of the reaction is a result of the volatility of 143.

![Scheme 1.71 Thiophene formation from the Pummerer reaction](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Sulfoxide</th>
<th>Conditions</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>Ac$_2$O, 3 h, reflux</td>
<td>142 80</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>Ac$_2$O, 2.5 h, reflux</td>
<td>decomposition</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>Ac$_2$O, 2.5 h, reflux</td>
<td>decomposition</td>
</tr>
<tr>
<td>4</td>
<td>21</td>
<td>Ac$_2$O, 2.5 h, reflux</td>
<td>decomposition</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>TFAA, CH$_2$Cl$_2$, 5 min, 0 °C</td>
<td>142 74</td>
</tr>
<tr>
<td>6</td>
<td>22</td>
<td>TFAA, CH$_2$Cl$_2$, 10 min, 0 °C</td>
<td>143 35</td>
</tr>
</tbody>
</table>

Table 1.16 Formation of thiophenes from dehydration of sulfoxides

Commercially available 1,3-diene, piperine (144), is an extract from black pepper (Piper nigrum). Reaction of trisulfide-2-oxide 49 in refluxing chlorobenzene with piperine directly resulted in thiophene 145 (scheme 1.72).
Scheme 1.72 Reaction of trisulfide-2-oxide 49 with piperine 144

The recovered diene was analysed and shown to be a mixture of three products. Attempted purification of the mixture containing the three compounds by HPLC was unsuccessful and only combinations of two compounds were obtained. However the mass spectrum showed all the fractions to contain the same mass. The double bond isomers of piperine have been isolated and characterised.\(^\text{95}\) The NMR of the mixed fractions showed signals that were distinctive for each isomer. Closer analysis of the mixed fractions allowed tentative assignments by NMR of the double bond isomers to piperine (144), isopiperine (146) and isochavocine (147) (figure 1.17). Attempts to initiate isomerisation of piperine by heating the diene in the presence of thiophenol and dicumylperoxide failed, and starting material was recovered quantitatively.

Direct formation of the thiophene 145 could be explained from an \textit{in situ} dehydration of the sulfoxide intermediate (not observed), possibly promoted by extended conjugation of the product. Alternatively direct formation of thiophene may occur as a result of a transient sulfur species, formed from decomposition of SO, reacting with the diene.\(^\text{96-98}\)
A second example of direct thiophene formation occurred in the formal synthesis of Plavix® (clopidogrel disulfate, 148) (figure 1.18), an oral anti-platelet agent used to inhibit blood clots in coronary artery disease, peripheral vascular disease and cerebrovascular disease.99

![Figure 1.18 Plavix®](image)

A novel synthesis of thiophene 149 was envisaged from dehydration of sulfoxide 150,100 which will be formed from SO transfer with diene 151. A synthesis of diene 151 was forseen from a Wittig reaction of aldehyde 152, which could in turn be synthesised from commercially available alcohol 153 (scheme 1.73).101

![Scheme 1.73 Retrosynthesis of thiophene 149](image)

Alcohol 154 was prepared in moderate yield by N-benzylation, reduction of the pyridinium ring and carbamate protection according to the literature procedure.101 Oxidation of the allylic alcohol 154 using MnO₂ at room temperature resulted in methyl 3-formyl-5,6-dihydropyridine-1(2H)-carboxylate (152) (60%) and recovered starting material (30%).102 Conditions were optimised by refluxing in dichloromethane for 4 h using activated MnO₂ to obtain the desired aldehyde 152 in 78% yield along with recovery of the starting alcohol 154 in 20% yield (scheme 1.74). Wittig methylenation of 152 gave the required diene 151 for the SO transfer experiment in 76% yield (scheme 1.74).103 Refluxing a solution of diene 151 and trisulfide-2-oxide 49 in chlorobenzene directly gave the 6,7-dihydro-4H-
thieno[3,2-c]pyridine-5-carboxylic acid methyl ester (149), along with disulfide 50 and recovered diene 151. Sulfoxide 150, the expected product, was not observed. Optimum conditions required 6 equiv. of trisulfide-2-oxide to yield 73% of the thiophene 149 (scheme 1.74, table 1.17, entry 4). Carbamate deprotection and isolation as the hydrochloride salt in good yield completed a formal synthesis of Plavix® (scheme 1.74).

![Chemical Reaction Diagram]

**Scheme 1.66** Formal synthesis of Plavix®

<table>
<thead>
<tr>
<th>Entry</th>
<th>49 (equiv.)</th>
<th>151 (equiv.)</th>
<th>50 (%)</th>
<th>149 (%)</th>
<th>151 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0</td>
<td>10</td>
<td>94</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
<td>1</td>
<td>100</td>
<td>Trace</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>3.0</td>
<td>1</td>
<td>100</td>
<td>35</td>
<td>19</td>
</tr>
<tr>
<td>4</td>
<td>6.0</td>
<td>1</td>
<td>97</td>
<td>73</td>
<td>25</td>
</tr>
</tbody>
</table>

All reactions were run in refluxing 0.01 M PhCl for 6 h

**Table 1.17** Optimisation for SO transfer to diene 151 in the formal synthesis of Plavix®
Conclusions

Progress has been made in the formation of novel trisulfide-2-oxides. Synthesis and purification of bridged disulfides 69 and 70 have proved troublesome. Disulfides 90 and 91 have been prepared using an alternative to the nitrating agent, N₂O₄, reported in the literature; however separation of the isomers was shown to be difficult.

The synthesis of trisulfide-2-oxides 49, 58 and 103 has been achieved. These compounds are a source of sulfur monoxide and transfer SO in the presence of dienes to produce 2,3-dihydrothiophene 1-oxides thermally. Irradiation of 49 has shown that SO can be transferred at room temperature although yields are not comparable to thermal SO transfer.

Yields of the sulfoxide products 2, 3, 21 and 22 are comparable or better than those described utilising episulfoxides as sulfur monoxide sources, and the recyclable disulfide by-product is obtained in almost quantitative yield. The X-ray of novel trisulfide-2-oxide 58 provides evidence of a strained molecule. Increased rates of SO transfer for trisulfide-2-oxide 58 is possibly due to the buttressing effect of the tert-butyl groups. Increased rates of SO transfer for trisulfide-2-oxide 103 is suggestive of electronic factors participating in the breakdown of 103. In both cases the temperature at which SO transfer occurs has also been lowered without altering the yield of the resulting sulfoxide product 2. However the overall syntheses of 58 and 103 are longer and inferior compared to that of the synthesis of 49 meaning that 49 is still the favoured choice for SO transfer reactions.

Mechanistic studies have shown that the reaction of the trisulfide-2-oxide 49 with diene 16 is 1st order with respect to 49 and independent of the diene. Investigations also suggest that “free” SO results from the breakdown of 49 and it is the triplet ground state that reacts with dienes, although potential radical intermediates have not reacted with radical spin traps. Use of the Pummerer reaction has developed the synthetic utility of the resulting sulfoxides to produce thiophenes, with certain thiophenes forming directly in the SO transfer reactions.
Future work

Further work can be carried out to improve the synthesis and purification of disulfides 69, 70, 90 and 91. Once in hand the corresponding trisulfide-2-oxides can be prepared as described in this chapter. These could then be subjected to SO transfer experiments to investigate the effect of the groups on the rate and temperature of SO transfer.

Extending the conjugation of the aromatic system to 156 should change the chromophore and may hence increase the efficiency of this photomediated SO transfer reaction. In addition by extending the conjugation there should also a larger driving force to regain aromaticity (figure 1.19).

![Figure 1.19 Extending the conjugation of the aromatic system](image)

If the relief of ring strain is the driving force for loss of SO, then it should be possible to alter the design of the 1,8-disubstituted naphthalene ring to transfer other reactive diatomic molecules (e.g. SeO).
Chapter Two: Synthesis and properties of stable \textit{vic}-disulfoxides
Background and significance

2.1 vic-Disulfoxides

The electrophilic oxidation of disulfides has been of interest for many years.\textsuperscript{105-108} The oxidation of disulfide \textsuperscript{157} to thiosulfinate \textsuperscript{158} is well reported in the literature.\textsuperscript{109, 110} The following step however is more contentious; thiosulfonate \textsuperscript{159} is the expected product upon oxidation of thiosulfinate \textsuperscript{158}.\textsuperscript{107, 111, 112} Vic-disulfoxide \textsuperscript{160} (α-disulfoxide) is a proposed intermediate in the electrophilic oxidation of thiosulfinate \textsuperscript{158} to thiosulfonate \textsuperscript{159}.\textsuperscript{113-116} Oxidation is considered to occur at the sulfenyl sulfur, according to HSAB theory, to form vic-disulfoxide \textsuperscript{160} (scheme 2.1).\textsuperscript{117}

\[ \begin{array}{c}
\text{S-S} \\
\text{R R} \\
\text{[O]} \\
\text{157} \\
\text{disulfide} \\
\end{array} \xrightarrow{[\text{O}]} \begin{array}{c}
\text{S-S} \\
\text{O} \\
\text{R R} \\
\text{[O]} \\
\text{158} \\
\text{thiosulfinate} \\
\end{array} \xrightarrow{[\text{O}]} \begin{array}{c}
\text{S-S} \\
\text{O} \\
\text{R R} \\
\end{array} \xrightarrow{[\text{O}]} \begin{array}{c}
\text{2 S-S} \\
\text{O} \\
\text{R R} \\
\end{array} \]

\[ \begin{array}{c}
\text{O} \\
\text{S} \\
\text{S} \\
\text{R R} \\
\text{160} \\
\text{vic-disulfoxide} \\
\end{array} \xrightarrow{2} \begin{array}{c}
\text{O} \\
\text{S} \\
\text{S} \\
\text{R R} \\
\text{161} \\
\text{sulfinyl radical} \\
\end{array} \xrightarrow{2} \begin{array}{c}
\text{O} \\
\text{S-S} \\
\text{O} \\
\text{R R} \\
\text{162} \\
\text{O,S-sulfinyl sulfinate} \\
\end{array} \]

Figure 2.1 Oxidation of disulfides with electrophilic oxidants

Vic-Disulfoxides are known to have low thermal stabilities, which is usually attributed to the weakness of the S-S bond.\textsuperscript{118} Homolytic fission of \textsuperscript{160} forms stabilised sulfinyl radicals which can rapidly recombine in a head-to-tail fashion to form \textit{O,S}-sulfinyl sulfinates \textsuperscript{162}, which are normally not observed. These rearrange to the more thermally stable thiosulfonate \textsuperscript{159}.

Vic-Disulfoxides are one of the most important intermediates in the oxidation of disulfides and are elusive products. Acyclic vic-disulfoxides exhibit limited stability and have only be observed below -40 °C in NMR studies. Freeman reported the first direct evidence of \textit{α}-disulfoxides by low temperature \textsuperscript{1}H-NMR studies of the oxidation of alkyl disulfides.\textsuperscript{119}
Using low temperature NMR spectroscopy, Harpp later identified vic-disulfoxide intermediates in the oxidation of bridged bicyclic thiosulfinate 163 (scheme 2.2).\textsuperscript{105, 106} Electrophilic oxidation of thiosulfinate 163 on the \textit{exo}-face is proposed to form symmetrical vic-disulfoxide 164. An unsymmetrical vic-disulfoxide was also observed in the \textsuperscript{1}H-NMR spectrum, which is envisaged to occur \textit{via} biradical 165. Rotation about one C-S bond, followed by a radical recombination would provide unsymmetrical vic-disulfoxide 168. Thiosulfonate 172 is formed through a rearrangement of \textit{O,S}-sulfenyl sulfinates 170 and 171.

Cyclic vic-disulfoxides 164, 168 and 169 were observed by \textsuperscript{1}H-NMR spectroscopy at 30 °C suggesting that they were more stable than acyclic vic-disulfoxides. These intermediates rearranged to thiosulfonate 172 over time.

In 1999, Nakayama reported the first isolated vic-disulfoxide 174 from the oxidation of tetrathiolane 173 at room temperature (scheme 2.3).\textsuperscript{119}
**Scheme 2.3** First isolated *vic*-disulfoxide 174

*vic*-Disulfoxide 174 showed a high thermal stability compared to that of acyclic *vic*-disulfoxides, which were previously only observed at -40 °C, and bridged *vic*-disulfoxides 164, 168 and 169. However, in solution, *α*-disulfoxide 174 decomposed cleanly to diastereomeric dithiirane 1-oxides 38 and 39, tetrathiolane 173 and elemental sulfur (scheme 2.4).

**Scheme 2.4** Decomposition of 174 at -10 °C

Trapping experiments using butadiene 16 and norbornene 24 gave 175 and 176 respectively following S2O extrusion and subsequent disproportionation products (scheme 2.5).

**Scheme 2.5** Trapping experiments of *vic*-disulfoxide 174

In 2002 Nakayama reported the isolation of *vic*-disulfoxides 179 and 180. Oxidation of trithiolanes 177 and 178 with DMD afforded *α*-disulfoxides 179 and 180 respectively in good yields (scheme 2.6).
Scheme 2.6 Preparation of vic-disulfoxides by oxidation of trithiolanes

Interestingly both oxygen atoms in 180 occupy the equatorial positions so there is no evidence for enhanced stability through overlapping of the one of the lone pairs on sulfur with the antibonding $\sigma^*$-orbital of the S-O bond. The S-S bond length (2.249 Å) in 180 has also increased by almost 10% compared to typical S-S bonds ($\approx 2.05$ Å).\textsuperscript{122} Once more vic-disulfoxides 179 and 180 were stable in the crystalline state but slowly decomposed in a solution of CDCl$_3$.

Treatment of trithiolane 177 with DMD (1.2 equiv.) resulted in a mixture of the axial- and equatorial orientated thiosulfinates 181 and 182 (scheme 2.7).\textsuperscript{121}

Subsequent oxidation of each individual isomer resulted in two different products. Treatment of 181 with 2 equiv. of DMD yielded vic-disulfoxide 179 as a result of oxidation of the sulfenyl sulfur. However 182 required 4 molar equiv. of oxidant to afford 1,1-dioxide 183 which was unstable at room temperature and decomposed rapidly to thioketone 184 (scheme 2.8).\textsuperscript{121} The lower reactivity of 182 was attributed to a lowering of the energy of the lone pair of electrons on the sulfur being oxidised as a result of an anomeric type effect.
Scheme 2.8 Synthesis of dioxides from axial and equatorial thiosulfinates, 181 and 182

The formation of thiketone 184 can be explained in terms of extrusion of SO₂ from 1,1-dioxide 183 or the O,S-sulfenyl-sulfinate 185 (scheme 2.8).

In a later report by the same authors, vic-disulfoxides 186 and 188 were prepared by oxidation of the corresponding sulfides. Isomerisation of 186 and 188 occurred at 298 K in a 95:5 ratio favouring the trans disulfoxide 188 (scheme 2.9). The isomerisation obeyed first order kinetics and was proposed to take place via a biradical mechanism, although the isomerisation was unaffected in the presence of a radical scavenger.

Scheme 2.9 Isomerisation of vic-disulfoxides in solution

Calculations at B3LYP/6-311G(3df)-mix by Jenks modelled both the meso and dl-methyl vic-disulfoxide MeS(O)S(O)Me. The O-S-S-O dihedral angle of 284° for the dl form and 180° for the meso form were reported as the most stable conformation.

In 2004, Ishii obtained the first example of an eclipsed vic-disulfoxide 191. Cycloheptatriene was heated in the presence of S₈O to afford exo monoxide 189 and trisulfide...
Oxidation of 189 with DMD resulted in 7-exo,8-exo disulfoxide 191 as the major product (scheme 2.10). Gradual decomposition of eclipsed vic-disulfoxide 191 in CDCl₃ resulted in the 1,1-dioxide 193.

Further oxidation of cis vic-disulfoxide 191 with 2 equiv. of DMD resulted in thiosulfonate 194 (scheme 2.11).

Ishii reported the first example of a three-membered ring vic-disulfoxide 33 in 2006.²² Oxidation of cis or trans thiosulfinates 38 and 39 with DMD at -20 °C resulted in dithiirane 1,2-dioxide 33 in moderate to good yield (scheme 2.12). X-ray analysis revealed that the S-S bond length of 33 was comparable to other vic-disulfoxide linkages reported.¹¹⁹-¹²¹, ¹²³, ¹²⁴
α-Disulfoxide 33 slowly decomposed in a solution of CDCl₃ at room temperature.²² The outcome of thermolysis of 33 was isomeric sulfines 36 and 37 as the major products, thiosulfinates 38 and 39, ketone 40 and thioketone 41 (scheme 2.13).

Ishii reported the synthesis of vic-disulfoxide 200 by the reaction of di-tert-butyldiazomethane (198) with S₈O to achieve thiosulfinate 199 followed by oxidation using DMD (scheme 2.14).²²⁵

Thermolysis of 200 resulted in the formation of monoxide 199, sulfine 201 and thioketone 202, suggesting a larger activation energy was required for the extrusion of SO to give 201, findings consistent with DFT calculations (scheme 2.15).²²
Platinum insertion into S-S bonds has been studied.\textsuperscript{126-134} The first example of platinum insertion into the (O)S-S(O) bond of \textit{vic}-disulfoxide \textbf{200} was recently reported (scheme 2.16).\textsuperscript{125}

\begin{center}
\textbf{Scheme 2.15} Thermal decomposition of \textit{vic}-disulfoxide \textbf{200}
\end{center}

\begin{center}
\textbf{Scheme 2.16} Platinum insertion into a \textit{vic}-disulfoxide
\end{center}

\textbf{2.2 Aims and objectives}

In general, the low thermal stability of \textit{vic}-disulfoxides has been accredited to the weakness of the (O)S-S(O) bond. The work in this chapter will focus on using the \textit{peri}-interaction in order to increase the strength of the S-S bond by confining the two sulfur atoms to remain in close proximity, thus preventing homolytic fission and rearrangement to the more stable thiosulfonate.

The oxidations of disulfide \textbf{50} and \textit{ortho}-substituted disulfides \textbf{65} and \textbf{87} will be explored (figure 2.1).

\begin{center}
\textbf{Figure 2.1} Proposed disulfides to investigate the oxidation
\end{center}

Naphthelene disulfide \textbf{50} can be easily obtained from oxidation of the corresponding dithiol due to the \textit{peri}-effect, where the two sulfur atoms are closer in proximity than the combined van der Waals radii for sulfur which is 3.70 Å.\textsuperscript{135} The S-S bond length for disulfide \textbf{50},
obtained from X-ray crystallography, is 2.0879 Å, close to the average value for acyclic aromatic disulfides (≈ 2.03 Å). The oxidation of electron rich disulfide 87 will also be explored (figure 2.1).

The X-ray for disulfide 65 has been obtained (S-S 2.0580 Å) and there is a decrease in the S-S bond distance compared to disulfide 50, presumably as a result of steric buttressing from the ortho tert-butyl substituents forcing the sulfur atoms closer together. It was envisaged that this could further disfavour fission of the S-S bond to the sulfinyl radicals, which involves extension of the S-S bond. The oxidations of disulfides 50, 65 and 87 will be probed one oxidation step at a time, applying electrophilic oxidants.
Results and discussion

2.3 Oxidation of naphtho[1,8-cd][1,2]dithiole

The oxides of 50 have already been reported in the literature by Kice, who employed the electrophilic oxidant \textit{mCPBA}.\textsuperscript{137-139} Naphtho[1,8-cd][1,2]dithiole 1-oxide (107) was prepared using this oxidant in dichloromethane in good yield (scheme 2.17, table 2.1, entry 1) and the structure was confirmed by X-ray crystallography (figure 2.2). It was envisaged that if a \textit{vic}-disulfoxide was to form it may not be stable in solution with the \textit{mCBA} formed as a by-product in the reaction. Changing the solvent of the oxidation reaction to diethyl ether resulted in precipitation of thiosulfinate 107 from the solution, however the yield in this case was lower (entry 2).\textsuperscript{140}

\begin{center}
\textbf{Scheme 2.17} Oxidation of disulfide 50 using \textit{mCPBA}
\end{center}

\begin{center}
\textbf{Figure 2.2} X-ray crystal structure of 107. Thermal ellipsoids are drawn at the 50\% probability level
\end{center}

The X-ray structure of 107 shows that two molecules of thiosulfinate are present; this is because disorder is present in the crystal with the sulfinyl group positioned up or down
randomly. In addition the S-S(O) bond length has increased compared to the S-S bond in disulfide 50.

An alternative oxidant used for sulfur oxidations is dimethyldioxirane (DMD) (scheme 2.18).\textsuperscript{141} A solution of DMD was prepared using a modified literature procedure.\textsuperscript{142, 143} Reaction of 50 with one equiv. of DMD resulted in 107 in a lower yield (entry 3).

\[
\text{Scheme 2.18 Oxidation of disulfide 50 using DMD}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxidation conditions</th>
<th>107 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(m\text{CPBA (1.50 equiv.), CH}_2\text{Cl}_2, 0 \degree \text{C}, 2 \text{ h})</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>(m\text{CPBA (1.50 equiv.), Et}_2\text{O, 0 \degree \text{C}, 4 \text{ h}})</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>DMD (1.05 equiv.), Acetone, 0 \degree \text{C}, 1 \text{ h}</td>
<td>72</td>
</tr>
</tbody>
</table>

\textbf{Table 2.1 Preparation of monoxide 107}

Preparation of thiosulfonate naphtho[1,8-cd][1,2]dithiole 1,1-dioxide (63) has been reported by Oae (scheme 2.19)\textsuperscript{65} and Vivarelli (scheme 2.20).\textsuperscript{144}

\[
\text{Scheme 2.19 Oae’s conditions for the oxidation of 107}
\]

\[
\text{Scheme 2.20 Vivarelli’s conditions for the preparation of 63}
\]
Thiosulfonate 63 was prepared using mCPBA with CH₂Cl₂ in place of CCl₄, although this only resulted in a 65% yield of the dioxide after 2 h (table 2.2, entry 1). The second oxidation has a slower rate (5.07 M⁻¹sec⁻¹) compared to the first sulfur oxidation (580 M⁻¹sec⁻¹); therefore the reaction time was extended to 14 h and yields increased correspondingly (entry 2). Starting from disulfide 50 with 2.5 equiv. of mCPBA gave a comparable yield of the desired product (entry 3).

A 95% yield of thiosulfonate 63 was obtained on treating thiosulfinate 107 with 1 equiv. of DMD (entry 4). Reaction of the disulfide 50 with 2.1 equiv. of DMD resulted in only 62% of the desired compound 63 (entry 5), although this may possibly be due to the DMD not having been freshly prepared.

The use of tetrahydrothiopyran-4-one (203) and Oxone® has been exploited for epoxidation of alkenes (scheme 2.21). Oxone® is used to oxidise 203 to epoxide 204.

Oxidation of sulfur using tetrahydrothiopyran-4-one (203) and Oxone® has not been reported, although Oxone® has been employed in sulfur oxidations. The oxidation of disulfide 50 with catalytic 203 and Oxone® yielded 43% of dioxide 63 (scheme 2.22, entry 6).

---

**Scheme 2.21 Oxidation of alkenes using 203 and Oxone®**

**Scheme 2.22 Oxidation of disulfide 50 using 203 and Oxone®**
<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>Conditions</th>
<th>63 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>107</td>
<td>mCPBA (1.10 equiv.), CHCl₃, 2 h, 0 °C</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>107</td>
<td>mCPBA (1.05 equiv.), CH₂Cl₂, 14 h, 0 °C</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>mCPBA (2.50 equiv.), CHCl₃, 14 h, 0 °C</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>107</td>
<td>DMD (1.00 equiv.), acetone, 2 h, 0 °C</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>DMD (2.10 equiv.), acetone, 2 h, 0 °C</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>Oxone®, 203 (0.05 equiv.), NaHCO₃, Na₂.EDTA, MeCN, 3 h, rt, pH 7.0-7.5</td>
<td>43</td>
</tr>
</tbody>
</table>

Table 2.2 Conditions for the preparation of thiosulfonate 63

Thiosulfonate 63 is the product resulting from the oxidation of disulfide 50 with 2 equiv. of oxidant, or from thiosulfinate 107 with 1 equiv. It is clear that the intermediate vic-disulfoxide, if produced, is too unstable to be isolated under the reaction conditions used.

2.4 Oxidation of 3,8-dimethoxynaphtho[1,8-cd][1,2]dithiole

The oxidation of disulfide 3,8-dimethoxy-naphtho[1,8-cd][1,2]dithiole (87) was explored to examine how the ortho methoxy substituents influenced this reaction.

Although not directly related to the chemical oxidation, electrochemical oxidation through cyclic voltammetry was used to explore the ease of oxidation of disulfide 87 compared with the parent naphthalene disulfide 50.

In cyclic voltammetry, the redox process for a compound is electrochemically reversible if the following factors are observed:

- \( I_{p}^{Ox} = I_{p}^{Red} \)
- \( E_{p}^{Ox} - E_{p}^{Red} = 59 \text{ mV/n} \)
- \( E_{p} - E_{p/2} = 59 \text{ mV/n} \)
- \( E_{p}^{Ox} - E_{p}^{Red} \) does not change the scan rate
- \( I_{p}^{Ox} \alpha \text{ scan rate} \)
where $I_p^{Ox} =$ current at the oxidation potential, $I_p^{Red} =$ current at the reduction potential, $E_p^{Ox} =$ oxidation electrode potential, $E_p^{Red} =$ reduction electrode potential and $n =$ number of electrons transferred.

Cyclic voltammetry was carried out on 50 in dichloromethane with 0.1 M $n$Bu$_4$NBF$_4$ as the supporting electrolyte, with a gold working electrode, platinum counter electrode and saturated calomel reference electrode. The oxidation potentials were corrected to saturated calomel electrode (SCE; -0.02 V).

The single electron oxidation of disulfide 50 obeys the criteria described above and is reversible. The first half-wave potential of disulfide 50 occurs at 0.88 V (vs. SCE) in dichloromethane, which was comparable to the values reported in the literature (table 2.3, entries 1-4).$^{40, 48, 147}$

![Figure 2.3 Cyclic voltammogram for the single electron oxidation of disulfide 87 (scan rate = 5 mVs)](image)

Similar conditions were applied for the single electron oxidation of disulfide 87 and again electrochemical reversibility was observed. The half-wave oxidation potential occurred at 0.66 V (vs. SCE) in dichloromethane, lower than 50 (table 2.3, entry 5).
The electrochemical oxidation of disulfide 87 is therefore easier than for 50, presumably as a result of the two ortho methoxy substituents stabilising the radical cation through electron donation.

Table 2.3 Potentials for the single electron oxidations of disulfides 50 and 87

<table>
<thead>
<tr>
<th>Entry</th>
<th>Disulfide</th>
<th>Half wave potential (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>0.88 (vs. SCE)</td>
</tr>
<tr>
<td>2&lt;sup&gt;40&lt;/sup&gt;</td>
<td>50</td>
<td>0.95 (vs. SCE)</td>
</tr>
<tr>
<td>3&lt;sup&gt;147&lt;/sup&gt;</td>
<td>50</td>
<td>0.84 (vs. SCE)</td>
</tr>
<tr>
<td>4&lt;sup&gt;48&lt;/sup&gt;</td>
<td>50</td>
<td>0.68 (vs. Ag/AgCl)</td>
</tr>
<tr>
<td>5</td>
<td>87</td>
<td>0.66 (vs. SCE)</td>
</tr>
</tbody>
</table>

Disulfide 87 was also oxidised with mCPBA in diethyl ether; once more thiosulfonate 206 precipitated from solution in comparable yield (entry 2). The order of addition was varied with disulfide 87 added to mCPBA. The reaction produced thiosulfonate 206, small amounts of novel 3,8-dimethoxy-naphtho[1,8-cd][1,2]dithiole 1,2,2-trioxide (207) and starting disulfide 87 in both dichloromethane and diethyl ether (entries 3 and 4).

The products formed from oxidation of disulfide 87 with 0.5 equiv. of mCPBA were thiosulfonate 206 with recovered starting material. The reaction was repeated with
sub-stoichiometric DMD as the oxidant and identical findings were observed (entries 5 and 6).

NaIO<sub>4</sub><sup>148</sup> and H<sub>2</sub>O<sub>2</sub><sup>146</sup> were also employed in the oxidation of disulfide 87 with thiosulfonate 206 again the product obtained together with disulfide 87 (entries 7 and 8).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>87 (%)</th>
<th>206 (%)</th>
<th>207 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(m)CPBA (1.10 equiv.), CH&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;, 3 h, 0 °C</td>
<td>32</td>
<td>44</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>(m)CPBA (1.10 equiv.), Et&lt;sub&gt;2&lt;/sub&gt;O, 3 h, 0 °C</td>
<td>42</td>
<td>43</td>
<td>-</td>
</tr>
<tr>
<td>3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>(m)CPBA (1.10 equiv.), CH&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;, 3 h, 0 °C</td>
<td>36</td>
<td>37</td>
<td>5</td>
</tr>
<tr>
<td>4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>(m)CPBA (1.10 equiv.), Et&lt;sub&gt;2&lt;/sub&gt;O, 3 h, 0 °C</td>
<td>35</td>
<td>38</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>(m)CPBA (0.50 equiv.), CH&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;, 1 h, -78 °C</td>
<td>71</td>
<td>23</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>DMD (0.50 equiv.), acetone, 0.5 h, -78 °C</td>
<td>68</td>
<td>23</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>NaIO&lt;sub&gt;4&lt;/sub&gt; (1.05 equiv.), H&lt;sub&gt;2&lt;/sub&gt;O/1,4-dioxane, 1 h, 0 °C</td>
<td>39</td>
<td>48</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt; (1.00 equiv.), AcOH, 1 h, rt</td>
<td>37</td>
<td>47</td>
<td>-</td>
</tr>
</tbody>
</table>

[a] Addition of disulfide to oxidant

Table 2.4 Oxidation of disulfide 87

These observations can be explained in terms of the rate of oxidation of disulfide 87 in comparison to thiosulfinate 205 (scheme 2.24). The rate of oxidation to thiosulfinate 205 from disulfide 87 \(k_1\) could be slower than the rate of oxidation from monoxide 205 to thiosulfonate 206 \(k_2\), this differs to what was observed for disulfide 50 by Vivarelli.<sup>144</sup>
Another explanation is the disproportionation of thiosulfinate 205 to disulfide 87 and thiosulfonate 206. Aliphatic thiosulfinates are known to disproportionate, leading to a mixture of disulfides and thiosulfonates (equation 2.1).\textsuperscript{107, 149}

\[
\text{Equation 2.1}
\]

2 RS(O)SR $\rightarrow$ RS(O)\textsuperscript{2}SR + RSSR

The disproportionation reaction of acyclic arene thiosulfinates has been studied by Koch, who proposed a homolytic free radical mechanism including initial S-S bond cleavage (equations 2.2-2.5).\textsuperscript{150}

\[
\text{Equation 2.2}
\]

RSOSR $\rightarrow$ RS(O)$^\ddagger$ + RS$^\ddagger$

\[
\text{Equation 2.3}
\]

2 RS(O)$^\ddagger$ $\rightarrow$ RS(O)-O-SR

\[
\text{Equation 2.4}
\]

RS(O)-O-SR $\rightarrow$ RS(O)\textsuperscript{2}$^\ddagger$ + RS$^\ddagger$ $\rightarrow$ RS(O)\textsuperscript{2}SR

\[
\text{Equation 2.5}
\]

2 RS$^\ddagger$ $\rightarrow$ RSSR

Block\textsuperscript{110} and Kice\textsuperscript{151} have proposed sulfenic acid intermediates to account for the disproportionation of thiosulfinates under acidic conditions (scheme 2.25).

\[
\text{Scheme 2.25 Disproportionation of thiosulfinate}
\]

\[
\text{Scheme 2.24 Rates of oxidation of disulfide 87 vs. thiosulfinate 205}
\]

Although both of these mechanisms are theoretically possible for thiosulfinate 205, they seem unlikely with such a cyclic system.

The reaction of DMD with disulfide 87 was monitored by $^1$H-NMR spectroscopy to see if disproportionation could be observed; the reaction was scanned at -78 °C immediately after the addition of the oxidant and the observed products were disulfide 87 and thiosulfonate 206. The sample was kept at -78 °C and re-scanned 15 min later and the ratio of the products
remained constant, suggesting that the reaction was very quick and if thiosulfinate 205 did not form, it could not be observed by NMR.

Although thiosulfinate 205 could not be isolated, thiosulfonate 206 was prepared in excellent yield by the oxidation of disulfide 87 using 2.2 equiv. of mCPBA (scheme 2.26).

![Scheme 2.26 Preparation of dioxide 87](image)

Given the unusual results obtained in the attempted mono oxidation of disulfide 87, the oxidation of electron-rich aromatic disulfides was further investigated with acyclic systems 208 and 209 to see whether this was a general phenomenon.

Although the oxidation of acyclic disulfide 208 has not been reported in the literature, thiosulfinate 210 has previously been synthesised by preparation of unstable sulfinyl chloride 211 from 1,2-bis(4-methoxyphenyl)disulfane (208) and SO$_2$Cl$_2$ and subsequent reaction with thiol 212 (scheme 2.27). Attempted synthesis of 210 using these conditions was unsuccessful, with only disulfide 208 and thiol 212 recovered.

![Scheme 2.27 Preparation of thiosulfinate 210](image)

Oxidation of disulfide 208 with stoichiometric mCPBA or DMD resulted in 4-methoxy-benzenethiosulfonic acid S-(4-methoxyphenyl) ester (213) and disulfide 208 in approximately equal ratio (scheme 2.28, table 2.5).
Scheme 2.28 Oxidation of disulfide 208

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>208 (%)</th>
<th>213 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mCPBA (1.05 equiv.), CH₂Cl₂, 1 h, -78 °C</td>
<td>43</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>DMD (1.00 equiv.), acetone, 0.5 h, -78 °C</td>
<td>45</td>
<td>47</td>
</tr>
</tbody>
</table>

Table 2.5 Oxidation of disulfide 208

Reaction with equimolar amounts of oxidant resulted in an equal proportion of disulfide 208 and thiosulfonate 213. With 0.5 equiv. of oxidant only a 25% yield of thiosulfonate 213 is produced along with a 75% yield of disulfide 208.

*ortho*-Substituted 1,2-bis(2-methoxyphenyl)disulfane (209) was prepared in 95% yield by oxidation of 2-methoxybenzenethiol (214) with iodine (scheme 2.29).

Scheme 2.29 Synthesis of dithiole 214

Oxidation of disulfide 209 with 1 equiv. of oxidant resulted in formation of thiosulfonate 215 and disulfide 209 (scheme 2.30, table 2.6).

Scheme 2.30 Oxidation of disulfide 209
<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>209 (%)</th>
<th>215 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mCPBA (1.05 equiv.), CH₂Cl₂, 2 h, -78 °C</td>
<td>48</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>DMD (1.00 equiv.), acetone, 10 min, -78 °C</td>
<td>47</td>
<td>47</td>
</tr>
</tbody>
</table>

Table 2.6 Oxidation of bis ortho disulfide 209

These results strongly suggest that disproportionation of acyclic electron-rich aromatic thiosulfinates is occurring readily.

In Chapter 1, it was shown that the oxidation of trisulfide-2-oxide 49 resulted in a mixture of disulfide 50 and thiosulfinate 107 (scheme 1.56). In a final attempt to synthesise thiosulfinate 205, trisulfide-2-oxide 103 was oxidised with 1 equiv. of mCPBA or 1 equiv. of DMD. In contrast to the oxidation of the unsubstituted trisulfide-2-oxide 49, the products obtained were thiosulfonate 206 and disulfide 87 (table 2.7).

![Chemical structures](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>206 (%)</th>
<th>87 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mCPBA (1 equiv.), CH₂Cl₂, -78 °C → rt, o/n</td>
<td>67</td>
<td>31</td>
</tr>
<tr>
<td>2</td>
<td>DMD (1 equiv.), acetone, -78 °C → rt, o/n</td>
<td>63</td>
<td>35</td>
</tr>
</tbody>
</table>

Table 2.7 Oxidation of trisulfide-2-oxide 103

The results from this experiment indicate that 103 is easier to oxidise in comparison to trisulfide-2-oxide 49 as all of the starting material is consumed. The results also support disproportionation of thiosulfinate 205, rather than relative rates of oxidation (scheme 1.56, pathway e), as a mixture of disulfide 87 and thiosulfonate 206 is obtained. However, the lack of a 1:1 ratio of disulfide 87 and thiosulfonate 206 suggests that both pathways a and b compete (scheme 1.56).
2.5 Oxidation of 3,8-di-tert-butyl-naphtho[1,8-cd][1,2]dithiole

A study was undertaken to investigate how the presence of tert-butyl groups (steric buttressing) would affect the stability of vic-disulfoxides upon oxidation of disulfide 65. 3,8-Di-tert-butyl-naphtho[1,8-cd][1,2]dithiole 1-oxide (216) was synthesised in good yields using mCPBA in CH_2Cl_2 (scheme 2.31, table 2.8, entry 1). Oxidation of disulfide 65 with DMD resulted in a slightly lower yield (entry 2).

![Scheme 2.30 Preparation of thiosulfinate 216](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>216 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mCPBA (1.10 equiv.), CH_2Cl_2, 0 °C, 2 h</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>DMD (1.05 equiv.), acetone, 0 °C, 2 h</td>
<td>68</td>
</tr>
</tbody>
</table>

Table 2.8 Oxidation of disulfide 65

The X-ray crystal structure of the thiosulfinate, 3,8-di-tert-butyl-naphtho[1,8-cd][1,2]dithiole 1-oxide (216) is shown in figure 2.4.

![Figure 2.4 X-ray crystal structure of thiosulfinate 216](image)
In the solid state the S-S bond length is 2.0890(9) Å. The sulfur atoms of the dithiolane ring are out of the mean plane of the naphthalene ring (S(1) = 0.407 Å and S(2) = 0.139 Å).

Due to the general instability of vic-disulfoxides, subsequent oxidations were initially performed at -78 °C. To begin with, thiosulfinate 216 was oxidised with mCPBA in diethyl ether to try to avoid exposure of any vic-disulfoxide to the acid byproduct (mCBA) from the oxidant. A product precipitated out of solution and analysis of the solid by ¹H-NMR spectroscopy suggested formation of a vic-disulfoxide (scheme 2.32).

![Scheme 2.32 Synthesis of vic-disulfoxide 217](image)

Although the yield was low, evidence for the formation of the intermediate was encouraging. X-ray analysis confirmed the proposed structure of 3,8-di-tert-butyl-naphtho[1,8-cd][1,2]dithiole 1,2-dioxide (217) and revealed a trans relationship of the two sulfinyl groups (figure 2.5).

![Figure 2.5 X-ray crystal structure of 217. Thermal ellipsoids are drawn at the 50% probability level](image)
In the solid state, the two oxygen atoms occupy pseudoaxial positions on the dithiolane ring. The sulfur atoms of the dithiolane ring are out of the mean plane of the naphthalene ring (S(1) = 0.5 Å and S(2) = 0.372 Å). The S-S bond length is 2.1983(9) Å, which is shorter than any reported vic-disulfoxide in the literature. The dihedral angle between the two sulfinyl oxygen atoms in the dithiolane ring is 174.03°.

It has been reported that vic-disulfoxides are unstable and decompose at room temperature over a short period of time. An NMR sample of trans vic-disulfoxide 217 in CDCl₃ was monitored over a six-month period and no breakdown was observed. A solution of 217 in CH₂Cl₂ was stirred in the presence of both mCBA and benzoic acid to monitor the stability of 217 in order to run the oxidations using different solvents where the resulting acid remained in solution; starting material was recovered without any decomposition observed. Some previous vic-disulfoxides have been reported to be unstable to silica gel chromatography. vic-Disulfoxide 217 was initially purified by recrystallisation from ethyl acetate; however 217 was found to be stable in a solution of ethyl acetate stirred over silica gel for 21 days.

Conditions for the oxidation of thiosulfinate 216 were optimised using both mCPBA in CH₂Cl₂ and DMD to give clean transformations to vic-disulfoxide 217 (table 2.9, entries 1-3). vic-Disulfoxide 217 was also prepared directly from disulfide 65 using 2 equiv. of oxidant (table 2.9, entries 4-6).
<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>Conditions</th>
<th>217 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>216</td>
<td>mCPBA (1.10 equiv.), Et₂O, 0 °C, 2 h</td>
<td>53</td>
</tr>
<tr>
<td>2</td>
<td>216</td>
<td>mCPBA (1.05 equiv.), CH₂Cl₂, 0 °C, 2 h</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>216</td>
<td>DMD (1.05 equiv.), acetone, 0 °C, 30 min</td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>mCPBA (2.10 equiv.), Et₂O, 0 °C, 2 h</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>65</td>
<td>mCPBA (2.10 equiv.), CH₂Cl₂, 0 °C, 2 h</td>
<td>80</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>DMD (2.10 equiv.), acetone, 0 °C, 30 min</td>
<td>92</td>
</tr>
</tbody>
</table>

Table 2.9 Optimisation for the preparation of trans vic-disulfoxide 217

The isomerisation of sulfoxides has been reported in the literature using HCl.\textsuperscript{155, 156} An attempt to isomerise 217 to the cis stereoisomer by the addition of TFA to an NMR sample in CDCl₃ was unsuccessful with only the trans isomer observed over 6 weeks. Isomerisation of sulfoxide 218 with HCl in aqueous 1,4-dioxane has been reported by Mislow (scheme 2.33).\textsuperscript{155}

![Scheme 2.33 Isomerisation of phenyl p-tolyl sulfoxide 218](image)

Treatment of 217 with 4 M HCl in dioxane resulted in clean reduction to the thiosulfinate 216 rather than epimerisation (scheme 2.34).\textsuperscript{155, 156}

![Scheme 2.34 Reduction of trans vic-disulfoxide 217 to thiosulfinate 216](image)
The reduction of sulfoxides by HCl has been reported in the literature and is described in scheme 2.35. Presumably a similar mechanism can operate in the case of 217, although notably the reduction stops at the thiosulfinate stage.

![Scheme 2.35 Mechanism for the reduction of sulfoxides](image)

Block has reported the oxidation of thiosulfinate 220 using both nucleophilic and electrophilic oxidants (scheme 2.36).

![Scheme 2.36 Oxidation of alk(en)yl 1-propenyl disulfide](image)

Oxidation of thiosulfinates to thiosulfonates is thought to occur via oxidation of the sulfenyl sulfur, whereas a nucleophilic oxidant is expected to react on the sulfanyl sulfur. Block proposed electrophilic oxidation of thiosulfinate 220 occurs at the sulfenyl sulfur to form vic-disulfoxide 222, followed by homolytic fission and radical addition to the double bond to form sulfine 223. Nucleophilic oxidation of the same thiosulfinate 220 took place at the sulfanyl sulfur, to produce thiosulfonate 221.

Reactions of nucleophilic oxidants with disulfide 65 were also examined (table 2.10). Reaction of sodium periodate with disulfide 65 resulted in recovered starting material 65,
thiosulfinate 216 and vic-disulfoxide 217 (entry 1), whereas reaction of tetrabutylammonium periodate with disulfide 65 afforded starting disulfide 65 and thiosulfinate 216 (entry 2).\textsuperscript{148, 159}

No reaction occurred when sodium periodate was reacted with thiosulfinate 216, with starting material retrieved in quantitative yield.

KMnO\textsubscript{4} is a stronger oxidant in comparison to the periodate oxidants used. Treatment of disulfide 65 with KMnO\textsubscript{4} resulted in a mixture of products including thiosulfonate 224 and trans vic-disulfoxide 217, depending on the conditions used (entries 3 and 4).\textsuperscript{31, 160}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>65 (%)</th>
<th>216 (%)</th>
<th>224 (%)</th>
<th>217 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaIO\textsubscript{4} (2.10 equiv.), water/1,4-dioxane, 3 days, rt</td>
<td>22</td>
<td>29</td>
<td>-</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>Bu\textsubscript{4}NIO\textsubscript{4} (2.10 equiv.), CHCl\textsubscript{3}, 3 days, reflux</td>
<td>50</td>
<td>49</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>KMnO\textsubscript{4} (2.00 equiv.), MgSO\textsubscript{4} (2.77 equiv.), water/1,4-dioxane, 3 days, rt</td>
<td>40</td>
<td>-</td>
<td>-</td>
<td>44</td>
</tr>
<tr>
<td>4</td>
<td>KMnO\textsubscript{4} (2.00 equiv.), TBAB (0.16 equiv.), CH\textsubscript{2}Cl\textsubscript{2}/H\textsubscript{2}O, 3 days, rt</td>
<td>20</td>
<td>32</td>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 2.10 Oxidation of disulfide 65 with nucleophilic oxidants

2.6 Thermal stability studies

The thermal stability of vic-disulfoxides previously reported in the literature has been determined, with the most thermally stable vic-disulfoxide 33 decomposing when heated at reflux in chloroform.\textsuperscript{124} The thermal stability of a solution of 217 was assessed (scheme 2.37, table 2.11); the temperature was slowly increased until a change was observed by TLC. At 80 °C different oxides were isolated (entry 1).
The analytical data again revealed one new symmetrical product with a mass identical to 217, and was therefore assigned as the cis vic-disulfoxide 225. The second new dioxide was the thiosulfonate 3,8-di-tert-butyl-naphtho[1,8-cd][1,2]dithiole 1,1-dioxide (224). The major product at this temperature was still the trans vic-disulfoxide (entry 1). The X-ray crystal structure of the cis vic-disulfoxide, cis 3,8-di-tert-butyl-naphtho[1,8-cd][1,2]dithiole 1,2-dioxide (225) is shown in figure 2.6.
Figure 2.6 X-ray crystal structure of 225. Thermal ellipsoids are drawn at the 50% probability level

The S-S bond length of cis-225 is 2.2356(9) Å, slightly elongated compared to trans-217 (2.1983(9) Å). This could possibly be due to the dipolar repulsion as a result of the eclipsing nature of the two sulfinyl groups. The dihedral angle between the pseudo axial and pseudo equatorial sulfinyl groups on the dithiolane ring is 29.12°.

The X-ray crystal structure of thiosulfonate 224 was also obtained (figure 2.7).

Figure 2.7 X-ray crystal structure of 224. Thermal ellipsoids are drawn at the 50% probability level
In the solid state, the sulfur atoms of the dithiolane ring are out of the mean plane of the naphthalene ring ($S(1) = 0.305$ Å and $S(2) = 0.172$ Å). The S-S bond length is $2.0764(14)$ Å and is shorter than both vic-disulfoxides.

The temperature was increased further to improve the yield of the rearranged thiosulfonate $224$. When heated at 108 °C, a novel compound was isolated in low yield (entries 2-4). This proved to be the unexpected 3,8-di-tert-butyl-naphtho[1,8-cd][1,2]dithiole 1,1,2-trioxide (226). The structure of 226 was confirmed by X-ray crystallography (figure 2.8).

![Figure 2.8 X-ray crystal structure of 226. Thermal ellipsoids are drawn at the 50% probability level](image)

In the structure of 226 the groups containing sulfur and oxygen are disordered over two positions. The S-S bond length is determined from the major component to be $2.179(4)$ Å.

It is not clear how 226 is formed in this reaction; sulfinyl sulfone 226 and thiosulfonate 224 are thermally stable in chlorobenzene and no disproportionation occurs, implying that 224 is not an intermediate in the development of 226. Reaction mixtures were also degassed to remove all oxygen; however 226 was still obtained in similar quantities. Formation of the six-membered ring intermediate $O,S$-sulfenylsulfinate 227 (figure 2.9), the supposed intermediate in the formation of 224 from 217, was not detected. Total conversion to thiosulfonate 224 was accomplished in refluxing mesitylene in 38 h (entry 6).
Selected bond lengths, bond angles, torsion angles and the distances that the sulfur atoms are out of the mean plane of the naphthalene ring for disulfide 65 and its oxides were compared to the parent naphthalene disulfide 50 and its oxides (tables 2.12 and 2.13). Examination of the X-ray data reveals shorter S-S bond lengths for the tert-butyl derivatives in comparison to the unsubstituted compounds, suggesting a considerable buttressing effect from the ortho tert-butyl substituents. In addition, on increasing oxidation level, there is a general increase in the S-S bond length. The presence of a sulfinyl group leads to longer S-S bonds, which correlates with the usually observed increase in reactivity of these functionalities within organosulfur chemistry of disulfides and their oxides. The longest bonds are accounted for by vic-disulfoxides 217 and 225.
<table>
<thead>
<tr>
<th>Compound</th>
<th>disulfide</th>
<th>thiosulfinate</th>
<th>vic-disulfoxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-S(Å)</td>
<td>2.0879</td>
<td>2.138</td>
<td>2.0890</td>
</tr>
<tr>
<td></td>
<td>[2.096]</td>
<td>[2.141]</td>
<td></td>
</tr>
<tr>
<td>Bond angle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S(1)-C(1)-C(9)</td>
<td>115.03</td>
<td>113.36</td>
<td>113.42</td>
</tr>
<tr>
<td></td>
<td>[114.01]</td>
<td>[116.87]</td>
<td>112.92</td>
</tr>
<tr>
<td>S(2)-C(8)-C(9)</td>
<td>115.11</td>
<td>113.36</td>
<td>111.91</td>
</tr>
<tr>
<td></td>
<td>[117.84]</td>
<td>[114.84]</td>
<td>112.31</td>
</tr>
<tr>
<td>C(1)-C(9)-C(8)</td>
<td>118.65</td>
<td>119.80</td>
<td>120.03</td>
</tr>
<tr>
<td></td>
<td>[117.98]</td>
<td>[119.14]</td>
<td>119.98</td>
</tr>
<tr>
<td>Torsion angle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C(1)-C(9)-C(10)-C(4)</td>
<td>0.70</td>
<td>0.31</td>
<td>-1.20</td>
</tr>
<tr>
<td></td>
<td>[0.30]</td>
<td></td>
<td>-1.48</td>
</tr>
<tr>
<td>C(8)-C(9)-C(10)-C(5)</td>
<td>-179.40</td>
<td>-179.69</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>[-179.00]</td>
<td></td>
<td>-3.23</td>
</tr>
<tr>
<td>Out-of-plane displacement</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>S(1)</td>
<td>-0.0240</td>
<td>0.0841</td>
<td>0.1930</td>
</tr>
<tr>
<td></td>
<td>[-0.0377]</td>
<td></td>
<td>0.4070</td>
</tr>
<tr>
<td>S(2)</td>
<td>-0.0245</td>
<td>-0.0841</td>
<td>0.0640</td>
</tr>
<tr>
<td></td>
<td>[0.0230]</td>
<td></td>
<td>0.1390</td>
</tr>
</tbody>
</table>

[a] The sulfur and oxygen atoms are disordered over two positions in structure 217. The bond lengths, bond angles and torsion angles from the major components have been reported as the minor components could not be determined as accurately due to their low occupancies.

**Table 2.12** Selected lengths (Å) and angles (°) in 1,8-naphthalene disulfide derivatives from X-ray crystallographic analysis (where there are two crystallographically independent molecules the value for the second molecule is given in brackets).
<table>
<thead>
<tr>
<th>Compound</th>
<th>thiosulfonate</th>
<th>sulfinyl sulfone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$^{63}$</td>
<td>$^{136}$</td>
</tr>
<tr>
<td>Bond distance (Å)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S-S</td>
<td>2.1143</td>
<td>2.0764</td>
</tr>
<tr>
<td>Bond angle (°)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S(1)-C(1)-C(9)</td>
<td>116.20</td>
<td>108.97</td>
</tr>
<tr>
<td>S(2)-C(8)-C(9)</td>
<td>113.00</td>
<td>113.79</td>
</tr>
<tr>
<td>C(1)-C(9)-C(8)</td>
<td>119.40</td>
<td>121.22</td>
</tr>
<tr>
<td>Torsion angle (°)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C(1)-C(9)-C(10)-C(4)</td>
<td>-1.30</td>
<td>1.10</td>
</tr>
<tr>
<td>C(8)-C(9)-C(10)-C(5)</td>
<td>179.20</td>
<td>0.54</td>
</tr>
<tr>
<td>Out-of-plane displacement (Å)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S(1)</td>
<td>-0.1180</td>
<td>0.3050</td>
</tr>
<tr>
<td>S(2)</td>
<td>0.1692</td>
<td>0.1720</td>
</tr>
</tbody>
</table>

[a] The sulfur and oxygen atoms are disordered over two positions in structures $^{224}$ and $^{226}$. The bond lengths, bond angles and torsion angles from the major components have been reported as the minor components could not be determined as accurately due to their low occupancies.

Table 2.13 Selected lengths (Å) and angles (°) in 1,8-naphthalene disulfide derivatives from X-ray crystallographic analysis (where there are two crystallographically independent molecules the value for the second molecule is given in brackets).

The stability of cis vic-disulfoxide $^{225}$ was also investigated. NMR experiments revealed that $^{225}$ was stable in a solution of CDCl$_3$ for over six months, and also in the presence of 5 mol% TFA in a solution of CDCl$_3$. The thermal stability of the cis isomer was also investigated (table 2.14). Under analogous conditions, the stability of $^{225}$ appears to be comparable with trans-$^{217}$. At 80 °C small amounts of the trans isomer were isolated, and with increasing
temperature, thiosulfonate 224 and trioxide 226 were also detected. Clean conversion to 224 was achieved in refluxing mesitylene with the rearrangement taking place in a slightly shorter time of 34 h compared to trans-217, possibly owing to the longer and hence weaker S-S bond.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions[a]</th>
<th>217 (%) [b]</th>
<th>225 (%) [b]</th>
<th>224 (%) [b]</th>
<th>226 (%) [b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCl, 80 °C, 38 h</td>
<td>10</td>
<td>75</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>PhCl, 108 °C, 38 h</td>
<td>15</td>
<td>50</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>PhCl, 132 °C, 38 h</td>
<td>20</td>
<td>45</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>mesitylene, 167 °C, 34 h</td>
<td>-</td>
<td>-</td>
<td>93</td>
<td>-</td>
</tr>
</tbody>
</table>

[a] All reactions run as 0.01 M solutions of 226 in degassed solvent.
[b] Isolated yield after column chromatography.

Table 2.14 Thermal rearrangement of cis vic-disulfoxide 225

Clennan has reported the oxidation of disulfides with singlet oxygen produced by photosensitisation (scheme 2.38).\textsuperscript{161,162} The ratio of thiosulfinate to thiosulfonate is strongly solvent dependent with the formation of thiosulfinates favoured in protic solvents.\textsuperscript{161}

\[
\text{R-S-S-R \xrightarrow{\text{O}_2} R-S-S=O + R-S=O}
\]

Scheme 2.38 Oxidation of disulfide with singlet oxygen

Oxygen labelling studies revealed that thiosulfonates are primarily formed by a unimolecular process. Clennan proposed a mechanism involving vic-disulfoxide as an intermediate in the formation of thiosulfonate (scheme 2.39).\textsuperscript{162}
Attempts to synthesise the \( \textit{cis} \ \textit{vic} \)-disulfoxide using this approach were explored as attack of the singlet oxygen occurs in a \textit{syn} fashion. Initially, oxidations were performed on known disulfide 231, which was prepared from 2,2-dimethylpropane-1,3-diol (229) in two steps (scheme 2.40).\textsuperscript{163, 164} Tosylation of diol 229 provided 230 in good yield. Subsequent displacement resulted in a mixture of the desired 4,4-dimethyl-1,2-dithiolane (231) and 5,5-dimethyl-[1,2,3]trithiane (221), which were separable by column chromatography.

A sample of 4,4-dimethyl-[1,2]dithiolane 1,1-dioxide (233) was prepared by \textit{m}CPBA oxidation of disulfide 231 in very good yield so the photooxidation reaction could be monitored (scheme 2.41).
Photooxidation of 231 with oxygen in the presence of methylene blue as the sensitiser in acetone using a 500 W halogen lamp light source provided the expected thiosulfonate 233 in low yield compared to the literature report (84%) (scheme 2.42).  

\[
\begin{align*}
\text{O}_2, \text{hv}, \text{acetone, 2 h} & \rightarrow \quad \begin{align*}
\text{231} & \rightarrow \quad \text{233} \quad 24\% 
\end{align*}
\end{align*}
\]

Scheme 2.42 Photomediated oxidation of dithiolane 231

Identical conditions were employed using the disulfide 65 (table 2.15). Unfortunately attempted oxidation under these conditions did not result in any conversion to the thiosulfinate or thiosulfonate (entries 1-3). Varying the light source to a 400 W medium pressure Hg arc lamp had no effect on the outcome of the reaction (entry 4); starting material was recovered in all cases.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>65 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>O$_2$, hv, acetone, methylene blue, 500 W halogen lamp, 8 h</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>O$_2$, hv, MeOH, methylene blue, 500 W halogen lamp, 8 h</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>O$_2$, hv, PhH, methylene blue, 500 W halogen lamp, 8 h</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>O$_2$, hv, PhH, methylene blue, 400 W medium pressure Hg arc lamp, pyrex filter, 8 h</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2.15 Attempted oxidation using $^1$O$_2$

Clennan has reported the oxidation of aryl sulfides and that oxidation bearing sterically demanding groups is usually low yielding. Oxidation of 65 was unsuccessful presumably due to the steric buttressing of the t-Bu groups.
2.7 Photochemical studies

There is a large thermal barrier for the rearrangement of vic-disulfoxides 217 and 225. Little precedent for the irradiation of vic-disulfoxides exists in the literature; therefore the photochemical stability of the vic-disulfoxides was investigated at room temperature. vic-Disulfoxide 217 decomposed upon irradiation with a 400 W medium pressure Hg arc lamp in degassed chlorobenzene (scheme 2.43).

Scheme 2.43 Irradiation of trans-217 with a 400 W medium pressure Hg arc lamp

Irradiation with a 500 W halogen lamp surprisingly provided isomerisation of vic-disulfoxides within 15 min. Irradiation for longer periods of time resulted in further isomerisation (scheme 2.44, table 2.16).

Scheme 2.44 Photoepimerisation of trans vic-disulfoxide with a 500 W halogen lamp
<table>
<thead>
<tr>
<th>Entry[^a]</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>217 (%)[^b]</th>
<th>225 (%)[^b]</th>
<th>224 (%)[^b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CDCl₃</td>
<td>0.25</td>
<td>84</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>CDCl₃</td>
<td>1</td>
<td>73</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>CDCl₃</td>
<td>2</td>
<td>62</td>
<td>32</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>CDCl₃</td>
<td>4</td>
<td>49</td>
<td>46</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>CDCl₃</td>
<td>17</td>
<td>43</td>
<td>42</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>CDCl₃</td>
<td>44</td>
<td>40</td>
<td>39</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>PhCl</td>
<td>3</td>
<td>48</td>
<td>45</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>PhCl</td>
<td>7</td>
<td>46</td>
<td>46</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>PhCl</td>
<td>14</td>
<td>42</td>
<td>43</td>
<td>9</td>
</tr>
</tbody>
</table>

[^a] Reactions irradiated in 0.01 M solution of 217 in degassed solvent in a water-cooled round bottom flask with a 500 W halogen lamp.

[^b] Isolated yield after column chromatography.

Table 2.16 Photomediated isomerisation of trans vic-disulfoxide 217

The photomediated isomerisation of the trans vic-disulfoxide 217 was also monitored by ¹H-NMR spectroscopy using a water-cooled NMR tube (table 2.17, figure 2.10).

![Figure 2.10 Photoepimerisation of trans vic-disulfoxide in CDCl₃ monitored by ¹H-NMR spectroscopy](image)

Figure 2.10 Photoepimerisation of trans vic-disulfoxide in CDCl₃ monitored by ¹H-NMR spectroscopy
The ratios of the isolated yields were comparable to the ratio of compounds obtained from $^1$H-NMR analysis (scheme 2.45).

![Scheme 2.45 Comparison of isolated yields with NMR yields after irradiation of trans-217 for 4 h](image)

The equilibration provided an approximate 1:1 ratio of trans-217 and cis-225 isomers after approximately 14 h of irradiation, starting from pure 217 or 225, along with small quantities of thiosulfonate 224 (table 2.17, entries 1-6 and 8-10). In the case of the trans isomer, doubling the time of irradiation to 28 h resulted in a 1:1 mixture of the cis and trans isomers along with thiosulfonate (entry 7), suggesting that 224 may be formed from a common intermediate from both the cis and trans isomers at the same rate, as this ratio remains constant. The rearrangement in this case did not produce any sulfinyl sulfone 226, possibly suggesting this formed thermally.

The photoisomerisation was also monitored in polar protic and polar aprotic solvents to establish if solvent effect was a factor in the isomerisation. Isomerisation reactions in all of the solvents were similar with a 1:1 mixture of isomers, 217 and 225, and small amounts of thiosulfonate 224 produced after 14 h (entries 12-34).
<table>
<thead>
<tr>
<th>Entry^[a]</th>
<th>Disulfoxide</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>217 (%)^[b]</th>
<th>225 (%)^[b]</th>
<th>224 (%)^[b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>217</td>
<td>CDCl₃</td>
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<td>40</td>
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</tr>
<tr>
<td>2</td>
<td>217</td>
<td>CDCl₃</td>
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<td>53</td>
<td>43</td>
<td>4</td>
</tr>
<tr>
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<td>217</td>
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<td>51</td>
<td>44</td>
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</tr>
<tr>
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</tr>
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<td>45</td>
<td>46</td>
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</tr>
<tr>
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</tr>
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<td>1,2-DCE</td>
<td>7</td>
<td>51</td>
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</tr>
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<td>225</td>
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<td>55</td>
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<td>5</td>
</tr>
<tr>
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<td>217</td>
<td>MeCN</td>
<td>7</td>
<td>51</td>
<td>44</td>
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</tr>
<tr>
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<td>PhH</td>
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<td>7</td>
</tr>
<tr>
<td>26</td>
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<td>PhH</td>
<td>3</td>
<td>42</td>
<td>54</td>
<td>4</td>
</tr>
<tr>
<td>27</td>
<td>225</td>
<td>PhH</td>
<td>7</td>
<td>45</td>
<td>50</td>
<td>5</td>
</tr>
<tr>
<td>28</td>
<td>225</td>
<td>PhH</td>
<td>14</td>
<td>48</td>
<td>45</td>
<td>7</td>
</tr>
<tr>
<td>29</td>
<td>217</td>
<td>MeOH</td>
<td>3</td>
<td>54</td>
<td>42</td>
<td>4</td>
</tr>
<tr>
<td>30</td>
<td>217</td>
<td>MeOH</td>
<td>7</td>
<td>51</td>
<td>44</td>
<td>5</td>
</tr>
<tr>
<td>31</td>
<td>217</td>
<td>MeOH</td>
<td>14</td>
<td>48</td>
<td>45</td>
<td>7</td>
</tr>
<tr>
<td>32</td>
<td>225</td>
<td>MeOH</td>
<td>3</td>
<td>40</td>
<td>57</td>
<td>3</td>
</tr>
<tr>
<td>33</td>
<td>225</td>
<td>MeOH</td>
<td>7</td>
<td>47</td>
<td>49</td>
<td>4</td>
</tr>
<tr>
<td>34</td>
<td>225</td>
<td>MeOH</td>
<td>14</td>
<td>47</td>
<td>45</td>
<td>8</td>
</tr>
</tbody>
</table>

^[a] All reactions run by irradiation of a 0.01 M solution of 217 or 225 in degassed solvent in a water cooled NMR tube with a 500 W lamp.

^[b] Ratio determined by integration in ^1H-NMR in CDCl₃ after evaporation of reaction solvent.

**Table 2.17** Photomediated epimerisation of *vic*-disulfoxides 217 and 225
2.8 Radical traps and EPR studies

The isomerisation or rearrangement of 217 or 225 is considered to occur either via homolytic or heterolytic fission of the S-S bond (scheme 2.46). The direct formation of cis vic-disulfoxide, via a concerted type rearrangement, is unlikely as the sulfinyl oxygen is unable to access an empty orbital on the adjacent sulfur atom due to the rigidity of the system. Instead it is proposed that homolysis of the S-S bond would occur to give sulfinyl radicals. Rotation about the C-S bond and head-to-head recombination would provide the cis-225.

Sulfinyl radicals are very unstable; they have been reacted with stable nitroxide radicals and have been used for the isomerisation of cis styrene to trans styrene. Both thiyl and sulfonyl radicals have been successfully reacted with radical traps, but there is no
literature evidence for the trapping of sulfinyl radicals with scavengers.\(^{169}\) The isomerisation of *trans* vic-disulfoxide with radical scavengers was studied to determine whether sulfinyl radicals were formed.

*vic*-Disulfoxide 217 was subjected to a range of radical traps (234-241) (figure 2.11) thermally and photochemically, although it was difficult to predict the outcome of these reactions. In all instances the radical scavenger failed to trap any radical (if formed) and the ratio of the products formed remained consistent in nearly all cases (table 2.18).

Irradiation of DPPH (237) in the presence of 217 caused degradation of the radical trap, as reported in the literature (entry 7).\(^{170}\) Treatment of *vic*-disulfoxide 217 with electron-rich and electron-deficient alkenes (239 and 240) resulted in two different outcomes. In the presence of *N*-methylmaleimide (240) isomerisation was observed (entry 15), whilst with 1,1-dimethoxyethene (239), the rearranged thiosulfonate 224 was obtained in a 95% yield photochemically and a 76% yield thermally (entries 13 and 14).

A mechanism for thiosulfonate 224 formation from the reaction of *trans*-217 with 239 is proposed in scheme 2.47. Homolytic bond fission of *vic*-disulfoxide 217 followed by trapping of the resultant radical with 239 results in 242. Si\(^{171}\) at O could possibly occur with the labile C-O bond to form 227, which could then rearrange to 224.
Figure 2.47 Proposed mechanism for the reaction of trans-217 with 239

Attempted double bond migration of methylene cyclopentane (241) to 1-methylcyclopent-1-ene, which is mediated by sulfonyl radicals\(^{172}\) was unsuccessful (entry 16). Irradiation of \(\text{vic-disulfoxide}\) 217 in the presence of \(\text{O}_2\) resulted in the rearranged thiosulfonate 224 exclusively (entry 17).

A possible mechanism for the photoinduced rearrangement to thiosulfonate 224 from \(\text{vic-disulfoxide}\) in the presence of oxygen is proposed in scheme 2.48. Reaction of the sulfinyl radicals with oxygen followed by a rearrangement and extrusion of oxygen could result in thiosulfonate 224.
When *trans* vic-disulfoxide 217 was subjected to an oxygen atmosphere at room temperature in the absence of irradiation, starting material was recovered (entry 18). As rearrangement to thiosulfonate 224 only occurs under photolytic conditions, it could be that singlet rather than triplet oxygen is reacting with *trans*-217, with 217 acting as a sensitisers to promote molecular oxygen to the singlet state.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Radical trap</th>
<th>Conditions</th>
<th>206 (%)</th>
<th>214 (%)</th>
<th>213 (%)</th>
<th>215 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>234</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>44</td>
<td>43</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>234</td>
<td>PhCl, 24 h, 132 °C</td>
<td>46</td>
<td>13</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>235</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>40</td>
<td>40</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>235</td>
<td>PhCl, 24 h, 132 °C</td>
<td>43</td>
<td>12</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>235</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>46</td>
<td>44</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>235</td>
<td>PhCl, 24 h, 132 °C</td>
<td>44</td>
<td>12</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>237</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>237</td>
<td>PhCl, 24 h, 132 °C</td>
<td>42</td>
<td>14</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>238</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>42</td>
<td>40</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>238</td>
<td>PhCl, 24 h, 132 °C</td>
<td>40</td>
<td>13</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>11</td>
<td>238 and bromoadamantane</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>45</td>
<td>43</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>238 and bromoadamantane</td>
<td>PhCl, 24 h, 132 °C</td>
<td>40</td>
<td>15</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>13</td>
<td>239</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>-</td>
<td>-</td>
<td>95</td>
<td>-</td>
</tr>
<tr>
<td>14</td>
<td>239</td>
<td>PhCl, 24 h, 132 °C</td>
<td>-</td>
<td>-</td>
<td>76</td>
<td>-</td>
</tr>
<tr>
<td>15</td>
<td>240</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>44</td>
<td>42</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>16[a]</td>
<td>241</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>49</td>
<td>47</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>17</td>
<td>O₂</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>-</td>
<td>-</td>
<td>90</td>
<td>-</td>
</tr>
<tr>
<td>18</td>
<td>O₂</td>
<td>PhCl, 24 h, 132 °C</td>
<td>46</td>
<td>44</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

[a] Ratio determined by integration in $^1$H-NMR in CDCl₃ after evaporation of reaction solvent.

**Table 2.18 Reaction of trans vic-disulfoxide 217 with radical traps**

105
**vic-Disulfoxide 217** was also reacted in solvents which can act as H-atom donors (table 2.19). Treatment of 217 in these solvents failed to provide any evidence of H-abstraction from the solvent or change the ratio of products obtained by the formation of radicals.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Conditions</th>
<th>217 (%)</th>
<th>225 (%)</th>
<th>224 (%)</th>
<th>226 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>propan-2-ol/PhCl[^a]</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>45</td>
<td>44</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>propan-2-ol/PhCl[^a]</td>
<td>24 h, 132 °C</td>
<td>45</td>
<td>15</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>1,4-cyclohexadiene</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>45</td>
<td>43</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>1,4-cyclohexadiene</td>
<td>24 h, 132 °C</td>
<td>40</td>
<td>13</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>1,3-dioxolane</td>
<td>500 W halogen lamp, MeCN, 7 h, rt</td>
<td>45</td>
<td>42</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>1,3-dioxolane</td>
<td>24 h, 132 °C</td>
<td>45</td>
<td>15</td>
<td>7</td>
<td>5</td>
</tr>
</tbody>
</table>

\[^a\] Equal volume of PhCl added for solubility

**Table 2.19** Isomerisation of trans vic-disulfoxide 217 in different solvents

Although the presence of radical traps did not appear to affect the outcome of the rearrangement experiments, this does not rule out a mechanism involving homolytic fission of the S-S bond.

Electron paramagnetic resonance (EPR) spectroscopy is a technique used for studying chemical species that have one or more unpaired electrons, such as organic and inorganic free radicals. As discussed previously, sulfinyl radicals are very unstable and have not been trapped with radical scavengers, however sulfinyl radicals have been detected by the use of EPR at low temperatures (figure 2.12).\[^{173}\]
EPR was therefore explored as a possible means for detecting small quantities of sulfinyl radicals. Initially, a degassed solution of trans-217 in an EPR tube was placed in a beaker of water and irradiated 15 min. The EPR tube was then placed in the EPR cavity for analysis at a range of temperatures (-173 K → 298 K); unfortunately no evidence of radicals was detected. It was thought that the radicals may not be long-lived and for this reason the reaction set-up was changed so that irradiation of the sample occurred in the cavity and scanned simultaneously. Once again, radicals were not detected, suggesting that either no radical was formed or that homolytic fission may occur but the lifetime of the radical was too short for it to be detected.

Sulfur radicals have been detected using spin traps such as 5,5-dimethylpyrrolidine-1-oxide, DMPO (243) (scheme 2.49). In these situations the radical is not detected on the sulfur atom but on the resulting nitrooxide oxygen radical which is stable and long lived at

\[
\begin{align*}
\text{CH}_3\text{SO}^- & \quad \text{CH}_3\text{CH}_2\text{SO}^- & \quad \text{HOCH}_2\text{CH}_2\text{SO}^- & \quad \text{SO}^- \\
 a(\text{H})/(\text{mT}) & 1.15 & 0.89 & 0.86 & 1.00 \\
 a(2-\text{H})/(\text{mT}) & 0.26 & 0.25 & 0.24 & 0.23 & 0.26 & 0.25 \\
 a(3-\text{H})/(\text{mT}) & \alpha & 0.075 & 0.075 & 0.075 & 0.070 & \alpha \\
 a(4-\text{H})/(\text{mT}) & 0.26 & 0.25 & 0.24 & 0.23 & 0.26 & 0.25 \\
\end{align*}
\]
room temperature. Originally, a three-line spectrum is produced, with coupling of the oxygen-centred radical to the nitrogen \((I = 1, 2nI + 1 = 3)\).

![](image)

**Scheme 2.49** Sulfur centred radicals trapped with DMPO

There is no literature precedent for the spin trapping of sulfinyl radicals due to the instability of the sulfinyl radical.\(^{169}\) For this reason phenyl sulfinyl chloride (245), a known precursor of sulfinyl radical 246, was prepared. Sulfinyl chloride 245\(^{176}\) was unstable and decomposed at room temperature and was thus characterised as 1-(phenylsulfinyl)piperidine 247 (scheme 2.50).\(^{169}\)

![](image)

**Scheme 2.50** Preparation of phenyl sulfinyl radical 246

Chloride 245 was irradiated at low temperature in the EPR cavity in order to obtain a spectrum of the phenyl sulfinyl radical (figure 2.13). A spectrum of 246 was obtained in the absence of a spin trap and was in agreement with the literature.\(^{169}\) In the presence of DMPO, the spectrum for the sulfinyl radical was again observed and no spin-trapped product was detected.
When trans vic-disulfoxide 217 was irradiated in the presence of 243 in degassed PhCl, a six-line spectrum was observed (figure 2.14). The additional peaks are attributed to coupling of the oxygen radical with the β-H, a common feature with DMPO (scheme 2.49).

The spectrum was simulated using Simfonia, with the best fit giving the values, $g = 2.00745$ (corrected to strong pitch), $a(N) = 1.31$ mT and $a(H) = 0.77$ mT. The lineshape is Gaussian and the linewidth is 3.5 G.

Figure 2.14 X-band (9.4336 GHz) EPR spectrum of 0.5 M trans-217 in chlorobenzene at room temperature after photolysis in the presence of 0.1 M DMPO (top) together with a simulation (bottom).
Identical conditions were utilised for the cis vic-disulfoxide and as expected the same six-line spectrum was observed as for trans-217, with identical a values within experimental error (figure 2.15).

The spectrum was simulated using Simfonia, with the best fit giving the values, \( g = 2.00745 \) (corrected to strong pitch), \( a(N) = 1.31 \) mT and \( a(H) = 0.77 \) mT. The lineshape is Gaussian and the linewidth is 3.5 G.

**Figure 2.15** X-band (9.4336 GHz) EPR spectrum of 0.5 M cis-225 in chlorobenzene at room temperature after photolysis in the presence of 0.1 M DMPO (top) together with a simulation (bottom).

With these observations in hand, the variables of the experiment were considered to make sure the nitroxide radical was formed directly from the vic-disulfoxide. Control reactions (irradiation of PhCl, DMPO in PhCl and thiosulfonate 224 in the presence of DMPO in PhCl) failed to produce a spectrum similar to that observed with the vic-disulfoxides, with only a background spectrum observed in each case.

Although there is no evidence for the spin trapping of sulfinyl radicals, other sulfur-centred radicals such as thyl and sulfonyl radicals have been shown to form DMPO adducts. 177 The \( a(N) \) value calculated for the trans and cis vic-disulfoxide is comparable with the literature suggestive of a sulfur-centred radical adding to DMPO (as shown in scheme 2.49). 177
However the $a$(H) coupling calculated for 217 and 225 is much smaller compared to the literature values and so it remains inconclusive whether a sulfinyl radical is formed.

2.9 Attempted amination of vic-disulfoxides

The sulfoximine functionality is highly versatile and is used in building blocks for bioactive molecules and pseudopeptides, chiral auxiliaries for asymmetric synthesis and ligands for enantioselective metal catalysis.\textsuperscript{178, 179} vic-Disulfoxides can be envisaged as precursors to a novel functional group (scheme 2.51), although there is no literature precedent for this functionality.

![Scheme 2.51 Proposed amination of trans-217](image)

Two of the most common ways to prepare sulfoximines are treatment of sulfoxides with hydrazoic acid (HN$_3$) in a Schmidt type reaction, or with $O$-mesitylsulfonylhydroxylamine (MSH) (scheme 2.52).\textsuperscript{180, 181}

![Scheme 2.52 Two possible synthetic routes to sulfoximines](image)

The synthesis of the functional group proposed in scheme 2.53 was initially attempted with MSH, as in the presence of HCl the sulfoxide group was reduced (scheme 2.34). At first, \textit{trans} vic-disulfoxide was stirred in the presence of MSH at room temperature, however the consumption of starting material was not observed (table 2.20, entry 1). The same outcome resulted when the reaction was heated at reflux with excess MSH, with starting material recovered in quantitative yield (scheme 2.53, entry 2).
Efforts to synthesise the sulfoximine functional group from vic-disulfoxide 217 with hydrazoic acid did lead to the oxidation of 217, although the product obtained was the sulfinyl sulfone 226 (scheme 2.54, entry 3). Trioxide 226 was also produced through oxidation of 224 with mCPBA as described in Chapter 3.

Sulfuric acid is known to act as an oxidising agent and therefore could possibly oxidise trans vic-disulfoxide 217 to sulfinyl sulfone 226. Treatment of 217 with sulfuric acid failed to oxidise vic-disulfoxide 217 and resulted in decomposition of trans-217. One possible rationale for the formation of sulfinyl sulfone 226 is that sulfoximine 248 may have formed, but was too unstable and hydrolysed to 226.

Another potential route to sulfoximine 248 is amination of thiosulfinate 216 followed by oxidation (scheme 2.55); however this was unsuccessful with MSH and starting material was recovered (entry 4).
Reaction with the hydrazoic acid mixture resulted in decomposition of thiosulfinate 216 with the reaction mixture turning a deep shade of red (entry 5). Decomposition also resulted when thiosulfinate 216 was stirred in sulfuric acid.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting oxide</th>
<th>Conditions</th>
<th>217 (%)</th>
<th>226 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>217</td>
<td>MSH (2.0 equiv.), CH₂Cl₂, rt, 16 h</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>217</td>
<td>MSH (2.0 equiv.), 1,2-DCE, reflux, 16 h</td>
<td>96</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>217</td>
<td>NaN₃, H₂SO₄, CHCl₃, 0 °C, 15 min</td>
<td>-</td>
<td>57</td>
</tr>
<tr>
<td>4</td>
<td>216</td>
<td>MSH (1.5 equiv.), 1,2-DCE, reflux, 16 h</td>
<td>96</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>216</td>
<td>NaN₃, H₂SO₄, CHCl₃, 0 °C, 15 min</td>
<td>decomposition</td>
<td></td>
</tr>
</tbody>
</table>

Table 2.20 Attempted conditions for the preparation of sulfoximine 248

Amination of trans vic-disulfoxide to the novel functional group in 248 was unsuccessful. Attempts to react thiosulfinate 216 with either MSH or hydrazoic acid resulted in recovery of starting material or decomposition.

2.10 Attempted platinum insertion into vic-disulfoxides

The insertion of platinum into S-S bonds has been investigated.¹²⁶-¹³⁴ The insertion of Pt into a vic-disulfoxide bond has also been reported (scheme 2.16).¹²⁵ Attempted platinum insertion into trans-217 using commercially available Pt(PPh₃)₄ resulted in a mixture of unidentifiable compounds (scheme 2.56).

![Scheme 2.56 Attempted platinum insertion into trans-217](image-url)
Conclusion

The oxidation of disulfides 50, 65 and 87 has been explored. The synthesis of the oxides of naphtho[1,8-cd][1,2]dithiole (50) has been reported in the literature and repeated with optimisation of conditions to improve the yield.

Oxes of disulfide 87 have been prepared. Initially, the oxidation was explored through electrochemistry to understand whether the addition of the ortho methoxy groups has an effect on the oxidation; it was shown that disulfide 87 was easier to oxidise than naphthalene disulfide 50 as it has a lower half-wave potential. Oxidation of disulfide 87 with 1 equiv. of oxidant provided a mixture of disulfide 87 and thiosulfonate 206. The same observation was made when acyclic electron-rich disulfides 208 and 209 were oxidised.

The syntheses and properties of ortho tert-butyl disulfide 65 oxides have been explored. Buttressing by the ortho tert-butyl groups on the naphthalene ring has allowed for the isolation of the peri-substituted vic-disulfoxides, containing the shortest (O)S-S(O) bond reported for this elusive functional group. The trans diastereomer 217 has been synthesised directly through oxidation of the disulfide 65, whereas the cis isomer 225 has been prepared in low yield via thermolysis of 217 or by photoepimerisation of trans-217 at room temperature. The rearrangement experiments have also provided thiosulfonate 224, which was prepared in good yield by heating isomers 217 or 225 in mesitylene at reflux. EPR experiments of vic-disulfoxides 217 and 225 have failed to provide conclusive evidence for the formation of radicals. However, in the presence of a spin trap, DMPO, a six-line signal was been observed and tentatively assigned as a spin trapped product as a result of a sulfinyl radical.
Future work

The oxidative insertion of Pt into the *vic*-disulfoxide can be explored using other Pt sources (scheme 2.57).

![Scheme 2.57 Possible oxidative insertion into *vic*-disulfoxide](image)

*Scheme 2.57* Possible oxidative insertion into *vic*-disulfoxide
Chapter Three: Further oxidations of 1,8-dithianaphthalenes and investigation into a source of nitric oxide
Background and significance

3.1 Nitric oxide

Nitric oxide (NO) is a highly reactive diatomic molecule with a half-life ranging from 6 to 50 seconds.\textsuperscript{182} For many years NO has attracted interest for both its structure and chemistry. NO is prepared commercially by the oxidation of ammonia at high temperatures (750 °C - 900 °C) in the presence of a platinum catalyst (equation 3.1). In the presence of oxygen, nitric oxide is transformed into nitrogen dioxide (equation 3.2).

$$\begin{align*}
4 \text{NH}_3 + 5 \text{O}_2 & \xrightarrow{\text{Pt}} 4 \text{NO} + 6 \text{H}_2\text{O} \\
2 \text{NO} + \text{O}_2 & \longrightarrow 2 \text{NO}_2
\end{align*}$$

Equation 3.1

Equation 3.2

Nitric oxide is an important signalling molecule involved in physiological processes within the body, which can be both beneficial and detrimental. NO has been identified as the endothelium-derived relaxing factor, EDRF, and is biosynthesised within an organism, tissue, or cell from arginine and oxygen by various nitric oxide synthases.\textsuperscript{183} Suitable levels for the production of NO are essential for protecting organs such as the liver from ischemic damage. The endothelium of blood cells employs NO as a messenger to relax the nearby smooth muscle, consequently promoting vasodilation thus allowing greater blood flow. Due to the short half-life in the body and ability to diffuse freely across membranes, nitric oxide is exemplary as a transient paracrine or autocrine messenger molecule.\textsuperscript{184}

3.2 Nitroxyl

Nitroxyl (HNO or NO\textsuperscript{•}) is a reduced form of nitric oxide; the potential pharmacological activity of HNO in relation to NO has recently received much attention.\textsuperscript{185} HNO is a weak acid in solution (pK\textsubscript{a} = 11.4)\textsuperscript{186} and although closely structurally related to NO, HNO (and its deprotonated form, NO\textsuperscript{•}) possesses very distinct chemical properties. HNO is very reactive
and quickly dimerises to hyponitrous acid, H$_2$N$_2$O$_2$, which then dehydrates to nitrous oxide N$_2$O (equation 3.3).

\[
\text{HNO} \xrightarrow{} \text{H$_2$N$_2$O$_2$} \xrightarrow{\text{H}_2\text{O}} \text{N}_2\text{O}
\]

**Equation 3.3**

Nitroxyl has biological activities: it has the ability to act as a powerful cytotoxic agent that instigates double-stranded breaks in DNA, reduction of cellular glutathione,$^{187}$ as well as initiation of smooth muscle relaxation.$^{188}$ HNO was discovered to be a potent inhibitor of thiol-containing enzymes as it favours reactions with thiols, whereas NO prefers to react with radicals.$^{189, 190}$ In biological systems, the two are never seen carrying each other’s functions.$^{191}$ Isomeric hydroxy nitrene, HON, is of importance in atmospheric chemistry, astrophysics and combustion.$^{192}$ Maier reported the characterisation of HON by matrix isolation and IR spectroscopy.$^{193}$

### 3.3 Nitric oxide and nitroxyl donors

Due to the relatively short half-life of NO under physiological conditions and its biological importance as a messenger molecule, a controlled release of NO has been investigated. Figure 3.1 shows some of the current major classes of nitric oxide donors (253-260). Nitrogen-oxygen bonded compounds can decompose, reduce or oxidise to produce nitric oxide.$^{194, 195}$

![Figure 3.1 Major classes of nitric oxide donors](image)
Nitrate \(253,196,197\) nitrosothiol \(254,198\) oxatriazole-5-imine \(255\) and diazetine dioxide \(256\) all produce NO \(via\) a non-enzymatic pathway by reaction with thiols.\(^{194}\) Nitrate \(253\) can also generate NO in the presence of glutathione S-transferase (GST). \(N\)-Nitrosoamine \(257^{199}\) and \(C\)-nitroso \(258\) breakdown to produce nitric oxide photochemically. Hydroxylamine \(259\) can enzymatically generate NO in the presence of \(H_2O_2\) and catalase, whereas hydroxyl urea \(260\) produces nitric oxide by reaction with \(H_2O_2\) and \(Cu^{2+}\) salts, non-enzymatically.

Compounds containing the diazeniumdiolate functional group, such as Cupferron \(261\), and its analogues are one of the most common NO precursors (scheme 3.1).\(^{184,200-202}\) Under atmospheric conditions nitrous oxide is formed from the breakdown of Cupferron, probably as a result of HNO formation, however under physiological conditions NO can be generated \(via\) enzymatic oxidation.\(^{203}\)

\[
\begin{align*}
\text{Cupferron} & \rightarrow 2\text{NO} + 2\text{NH}_3 + \text{H}_2\text{O} \\
261 & \rightarrow 262
\end{align*}
\]

\textbf{Scheme 3.1} Breakdown of Cupferron to form NO

Nitric oxide has also been generated by a photochemical process and photoinduced delivery has been reported as a new controlled method for its release.\(^{204-207}\) Recent advances in this area include the photomediated release of NO from nanoparticles.\(^{208-210}\) Irradiation of small, physiologically stable monolayer diazeniumdiolates produces NO in a controlled manner, making them ideal substrates for biological and pharmaceutical application.\(^{209}\)

The \(N,N\)-bis(arylsulfonyl)hydroxylamine linkage is known in organic chemistry and its reactions and decomposition pathways have been studied for many years.\(^{211-215}\) \(N,N\)-Bis(arylsulfonyl)hydroxylamines are prepared by the reaction of arenesulfinates \(263\) or arene sulfinic chlorides \(65\) with sodium nitrite under acidic conditions (schemes 3.2 and 3.3).\(^{211,216}\)
Scheme 3.2 Preparation of \(N,N\)-bis(arylsulfonyl)hydroxylamine

\[
\begin{align*}
2 \text{PhSOPh} & \stackrel{\text{NaNO}_2, \text{H}^+}{\longrightarrow} \text{PhSO}_3\text{N-PhOH} \\
\text{263} & \quad \text{264}
\end{align*}
\]

Scheme 3.3 Fochi’s synthesis of hydroxylamine from sulfinic chloride

\[
\begin{align*}
\text{PhSO}_2\text{Cl} & \stackrel{\text{NaNNO}_2, \text{H}^+}{\longrightarrow} \text{PhSO}_2\text{N-OH} \\
\text{265} & \quad \text{266}
\end{align*}
\]

In 1996 Balakirev examined the decomposition of \(N,N\)-bis(\(p\)-tolylsulfonyl)hydroxylamine (264) in organic solutions by EPR.\(^{175}\) Radical trapping experiments with nitronyl nitroxide, 267, allowed the kinetics of the decomposition to be studied. It was concluded that NO had formed from the reaction by monitoring the loss of the starting nitronyl nitroxide 267 and the appearance of the imino nitroxide 268, formed as a result of reaction with the NO radical (scheme 3.4).

\[
\begin{align*}
\text{PhPhN}^+\text{N}^\cdot & \quad \stackrel{+ \text{NO}}{\longrightarrow} \text{PhPhN}^-\text{NPh} \\
\text{267} & \quad \text{268}
\end{align*}
\]

Scheme 3.4 EPR evidence for the formation of NO

Nitroxyl is very unstable and dimerises almost immediately, therefore it cannot be stored and must be produced in situ with reactive agents.\(^{185}\) Two of the most studied methods known for the generation of HNO are the photochemical or thermal decomposition of Piloty’s acid (269) or Angeli’s salt (270) (figure 3.2).\(^{190,217}\)
Piloty’s acid (269) only releases nitroxyl under basic conditions (scheme 3.5), decomposition under physiological conditions may release NO.\textsuperscript{188}

\[
\text{269} \quad \text{Piloty's acid} \quad \text{270} \quad \text{Angeli's salt}
\]

**Figure 3.2 Sources of HNO**

At physiological pH, decomposition of Angeli’s salt (270) is initiated by protonation of the dianion to produce nitroxyl (HNO) and nitrite, which possesses its own biological properties (scheme 3.6).\textsuperscript{217,218}

\[
\text{270} \quad \text{273} \quad \text{274}
\]

**Scheme 3.5 Decomposition of Piloty’s acid under basic conditions**

Acyloxy nitroso compounds 275 and 276 release nitroxyl upon hydrolysis (figure 3.3).\textsuperscript{219}

\[
\text{275} \quad \text{276}
\]

**Figure 3.3 HNO donors: acyloxy nitroso compounds**
Oxidation of oxime 277 in the presence of acetic acid furnishes compound 275. Acyloxy nitroso compounds 275 and 276 have been shown to release HNO via hydrolysis and perform in a similar manner to Angeli’s salt but with a lower potency (scheme 3.7).

The formation of nitrous oxide, which indicates the formation of intermediate HNO, from the retro Diels-Alder reaction of N-hydroxyurea-derived 278 was reported by King.\textsuperscript{220, 221} Importantly the discharge of HNO from cycloadduct 278 occurred at biologically relevant temperatures and at neutral pH in the absence of additional reagents, enzymes or catalysts (scheme 3.8).

The same author later reported N-hydroxy sulfonimidamide 281 as a nitroxyl donor.\textsuperscript{222} Reaction of protected N-hydroxy sulfonimidamide 281 with TBAF furnished unstable hydroxylamine 282 which decomposed to sulfinamide 283 and HNO, detected as N\textsubscript{2}O (scheme 3.9). Although 282 is unstable, a new source of HNO was introduced and could be useful in distinguishing the effects of NO from HNO in some systems.
3.4 Aims and objectives

The development of more efficient and controlled methods for NO or HNO release is needed that have fewer side effects.

In Chapter 1, it was shown that trisulfide-2-oxides extrude sulfur monoxide as a result of relief of peri-strain. Based on the same design principle, N-hydroxylamine $284$ is proposed as a source of either nitric oxide (NO), nitroxyl (HNO) or hydroxy nitrene (HON) under appropriate conditions (figure 3.4).

![Figure 3.4 Target molecule](image)

Sulfinyl sulfone $228$ has been prepared by Kice and it has been shown that there is an equilibrium between sulfinyl sulfone $228$ and bissulfinic acid $285$ (scheme 3.10).$^{223}$ Sulfinyl sulfone $228$ can be envisaged as a precursor to the bissulfinic acid $285$, which in turn could be used to prepare hydroxylamine $284$.

![Scheme 3.10 Equilibrium between bissulfinic acid $285$ and sulfinyl sulfone $228$](image)

The aim of this study is to synthesise peri-substituted trioxides $207$, $226$ and $228$ and subject these to the conditions reported by Kice to generate the corresponding bissulfinic acids and hence synthesise peri-substituted bissulfonyl hydroxylamines. The breakdown of $284$ under different conditions can then be investigated.
Results and discussion

3.5 Synthesis of trioxides

Oxidation of thiosulfonates 157 is expected to produce sulfinyl sulfones 286. Two other isomers of this oxidation state exist: sulfinic anhydrides 287, which have been observed and characterised in the literature,114, 224 and O,S-sulfenyl sulfonates 288, which are proposed intermediates in the thermolysis of aryl thiosulfonates (scheme 3.11).107

![Scheme 3.11 The RS₂O₃R isomers](image)

There are many examples of sulfinyl sulfones in the literature,107 including 226 described previously in Chapter 2. The general method for the preparation of sulfinyl sulfones is the treatment of a sulfinyl chloride with a sulfinate salt, or oxidation of thiosulfonates.115, 225 Few examples of sulfinic anhydrides have been reported and are shown in figure 3.5.226, 227 Freeman has detected acyclic sulfinic anhydrides via oxidation of 2-methyl-2-propyl 2-methyl-2-propanethiosulfinate (289) using low temperature NMR spectroscopy, however these were unstable.116

![Figure 3.5 Examples of sulfinic anhydrides 290 and 291](image)

The oxidation of thiosulfonate 63 to sulfinyl sulfone 228 using hydrogen peroxide has been reported by Kice (scheme 3.12).138
Hydrogen peroxide was reacted with dioxide 63 to give the crude disodium salt 292. Work by Kice has shown that the equilibrium between sulfinyl sulfone 228 and bissulfinic acid 285 in a 60% aqueous solution of dioxane favours the trioxide 228 in a three to one ratio (scheme 3.10). Thus, acidification of 292 yielded trioxide 228.

Initially, oxidation using H₂O₂ with dioxide 63 was successful, yielding 45% of 228 (table 3.1, entry 1). However reduced yields were obtained upon repetition of the reaction (entry 2). The H₂O₂ was thought to have decomposed and for this reason the hydrogen peroxide was titrated using a known procedure. Titration of H₂O₂ with KMnO₄ was problematic as the endpoint was difficult to determine; for this reason other oxidants to effect the formation of 228 were screened.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>Conditions</th>
<th>Yield (%)</th>
</tr>
</thead>
</table>
| 1     | 63               | i) H₂O₂ (1.00 equiv.), NaOH (2.05 equiv.), 5 min  
|       |                  | ii) c.HCl  | 228 45    |
| 2     | 63               | i) H₂O₂ (1.00 equiv.), NaOH (2.05 equiv.), 5 min  
|       |                  | ii) c.HCl  | 63 14, 228 19 |
| 3     | 63               | mCPBA (1.30 equiv.), CH₂Cl₂, 2 h, 0 °C | 63 98 |
| 4     | 63               | mCPBA (1.30 equiv.), CH₂Cl₂, 2 h, 0 °C | mixture |
| 5     | 63               | i) UHP (1.00 equiv.), NaOH (2.05 equiv.), 10 min  
|       |                  | ii) c.HCl  | 228 19    |
| 6     | 63               | Oxone®, 203 (0.05 equiv.), NaHCO₃, MeCN/H₂O, 3 h, rt, pH 7-7.5 | 63 96 |
| 7     | 63               | DMD (1.05 equiv.), acetone, 2 h, 0 °C | 63 99 |
| 8     | 63               | NaIO₄ (1.05 equiv.), H₂O/1,4-dioxane, 4 days, rt | mixture |
| 9     | 63               | mCPBA (1.50 equiv.), CHCl₃, 1 day,  
|       |                  | precipitation with hexane | 228 40 |
| 10    | 50               | mCPBA (3.50 equiv.), CHCl₃, 1 day,  
|       |                  | precipitation with hexane | 228 45 |

**Table 3.1** Conditions for the preparation of sulfinyl sulfone 217

In the first instance, oxidation was attempted with mCPBA and results varied, depending on the reaction time (entries 3 and 4). Reaction for 1 h resulted in recovery of dioxide 63. Longer reaction times and excess mCPBA resulted in a mixture of products, which proved difficult to separate. Given that the trioxide was formed using hydrogen peroxide, a peroxide reagent that was easier to handle was sought. Anhydrous urea-hydrogen peroxide (293; UHP) (figure 3.6) is a solid peroxide that can be weighed out accurately and has been used to oxidise sulfi17 des.229

The reaction was carried out in a similar manner to that using H₂O₂, but unfortunately only a 19% yield was achieved (scheme 3.13, entry 5).

![Urea-hydrogen peroxide (UHP)](image)

Figure 3.6 Urea-hydrogen peroxide (UHP)
Tetrahydrothiopyran-4-one (203) and Oxone® were employed, however dioxide 63 was recovered in almost quantitative yield (entry 6).\textsuperscript{145} Gratifyingly, oxidation of 63 using DMD (1.05 equiv.) generated trioxide 228 in 36\% yield (entry 7). The final oxidant screened was sodium periodate, which is known to oxidise sulfur at a slower rate than \textit{m}CPBA. \textit{NaIO}_4 was reacted with dioxide 63 in a mixture of water and dioxane and stirred for several days. A mixture of products was obtained and this method was not pursued (entry 8).

A report by Kice describes the formation of naphtho[1,8-\textit{cd}]1,2-dithiole 1,1,2,2-tetraoxide (294) from dioxide 63 with \textit{m}CPBA (scheme 3.1).\textsuperscript{230}

Following the same procedure but using just 1 equiv. of \textit{m}CPBA successfully produced the trioxide 228 from 63 in a 40\% yield (entry 9). Treatment of disulfide 50 with 3.5 equiv. of \textit{m}CPBA yielded trioxide 228 in a 45\% yield (scheme 3.15, entry 10).

Bissulfone 294 was also prepared in a 45\% yield from thiosulfonate 63 using the procedure reported by Kice in comparable yield (scheme 3.14).
Oxidation of electron-rich disulfide 87 with 3 equiv. of mCPBA resulted in 3,8-dimethoxy-naphtho[1,8-cd][1,2]dithiole 1,2,2-trioxide (207) in reasonable yield (scheme 3.16).

![Scheme 3.15 Synthesis of trioxide 197](image)

The oxidation of disulfide 65 provided vic-disulfoxide 217 which rearranged to thiosulfonate 224 at relatively high temperatures. The oxidation series was extended to study the oxidation of the dioxides reported in Chapter 2. The only example in the literature for the oxidation of a vic-disulfoxide is described in Chapter 2, scheme 2.11. This reaction resulted in the formation of thiosulfonate 194 through the loss of SO₂ followed by oxidation of thiosulfinate 45 (scheme 2.11).²²⁴

The oxidation of thiosulfonate 224 was explored with electrophilic oxidants. Reaction with 1.1 equiv. of mCPBA resulted in the expected sulfinyl sulfone 226 in near quantitative yield (scheme 3.17, table 3.2, entry 1), a product observed and characterised from the thermal rearrangement experiments of vic-disulfoxides 217 and 225, as described in Chapter 2. Sulfinyl sulfone 226 was also obtained when thiosulfonate 224 was reacted with DMD (entry 2).

![Scheme 3.17 Oxidation of thiosulfonate 224](image)

Both cis-225 and trans-217 vic-disulfoxides were individually reacted with 1.05 equiv. of mCPBA resulting in sulfinyl sulfone 226 in very good yields (scheme 3.18, entries 4 and 6). When subjected to DMD, cis vic-disulfoxide 225 required 3 equiv. of oxidant to form sulfinyl sulfone 226, whereas trans-217 required 4 equiv. to form 226 (entries 3 and 5).
Sulfinyl sulfone 226 was synthesised directly from disulfide 65 using 3.5 equiv. of DMD (scheme 3.19, entry 7). Sulfinyl sulfone 226 was also obtained when 3.5 equiv. of \( m\text{CPBA} \) was added dropwise as a solution in dichloromethane to disulfide 65 (entry 8).

Table 3.2 Oxidation to obtain sulfinyl sulfone 226

When \( m\text{CPBA} \) was added portionwise as a solid to disulfide 65 a different product was produced (scheme 3.20). The \( R_f \) of the new product was similar to other oxides and could only be differentiated by visualisation with \( p\)-anisaldehyde.
Scheme 3.20 Oxidation of disulfide 65 to prepare sulfinic anhydride 295

Analytical data and X-ray crystallography confirmed the structure as a rare example of a sulfinic anhydride, 4,9-di-tert-butyl-2-oxa-1,3-dithiaphenalene 1,3-dioxide (295) (figure 3.7).

The major product obtained from this reaction was trans vic-disulfoxide 217.

Figure 3.7 X-ray crystal structure of sulfinic anhydride 295

The bond and torsion angles in the X-ray of 295 suggest the presence of strain in the molecule. Strain in the system is evident by the peri-sulfur atoms deviating on either side of the mean plane of the naphthalene moiety (S(1) = 0.968 Å and S(2) = 0.920 Å). The bond angles at C(1), C(9), and C(8) are 115.32°, 115.46° and 123.04° respectively. These carbons are sp² hybridised and the ideal bond angles are 120°. Strain is also evident by distortion of the naphthalene ring from planarity (torsion angles C(1)-C(9)-C(10)-C(4), 10.87° and C(8)-C(9)-C(10)-C(5), 10.31° respectively).
Attempts to optimise the conditions to improve the yield of the sulfinic anhydride 295 proved futile. *vic*-Disulfoxide 217 was initially believed to be an intermediate in the oxidation to form sulfinic anhydride 295 as this was the other product from the reaction. The formation of sulfinic anhydride 295 may be explained with a Baeyer-Villiger type mechanism on *vic*-disulfoxide (scheme 3.21). *m*CPBA or its acid, *m*CBA, could possibly coordinate to one of the sulfoxides followed by S-S bond migration to form sulfinic anhydride 295.

![Scheme 3.21 Baeyer-Villiger type oxidation to form sulfinic anhydride 295](image)

Harpp reported the formation of *tert*-butyl sulfinic anhydride 291 from the oxidation of thiosulfinate 289 with *m*CPBA. It was suggested that *vic*-disulfoxide 297 was formed, followed by disproportionation of the S-S bond and an oxygen transfer mechanism (scheme 3.22). 227
Attempts to effect the reaction of trans-217 with mCBA in the presence of mCPBA were ineffective with only starting material recovered (table 3.3, entry 1). Vic-disulfoxide 217 was also recovered when oxidised with mCPBA in the presence tosic acid (entry 2). However, reaction of 217 in the presence of BF₃, a Lewis acid, and mCPBA yielded sulfinyl sulfone 226 (entry 3).

Nakayama has reported the isomerisation of thiosulfinate 181 to 182 using Meerwein’s reagent (299) (scheme 3.23).\textsuperscript{123}

Alternatively, Kagan has described the Diels-Alder reaction of cyclopentadiene at low temperatures with activated sulfoxides using Meerwein’s reagent (scheme 3.24).\textsuperscript{231}
Scheme 3.24 Kagan’s activated sulfoxide for the Diels-Alder reaction

Employing 1 equiv. of Meerwein’s reagent 299 in a reaction with trans-217 followed by the portionwise addition of mCPBA generated very small amounts of anhydride 295, along with sulfinyl sulfone 226 as the major product (scheme 3.25, entry 4).

Scheme 3.25 Oxidation of trans-217 assisted by Meerwein’s reagent

The use of excess salt to form the activated sulfoxide, followed by the addition of mCPBA produced the same result within experimental error, suggesting that the amount of Meerwein’s reagent used was inconsequential (entry 5). Activated vic-disulfoxide was destroyed upon attempted isolation.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>217 (%)</th>
<th>295 (%)</th>
<th>226 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mCPBA (1 equiv.), mCBA (1 equiv.), CH₂Cl₂, 10 h</td>
<td>96</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>mCPBA (1 equiv.), tosic acid (1 equiv.), CH₂Cl₂, 18 h</td>
<td>98</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>mCPBA (1 equiv.), BF₃ (1 equiv.), CH₂Cl₂, 3 h</td>
<td>-</td>
<td>-</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>mCPBA (1 equiv.), Meerwein’s reagent (1 equiv.), CH₂Cl₂, 6 h</td>
<td>-</td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>mCPBA (1 equiv.), Meerwein’s reagent (10 equiv.), CH₂Cl₂, 6 h</td>
<td>-</td>
<td>8</td>
<td>92</td>
</tr>
</tbody>
</table>

Table 3.3 Coordinating agents used to promote the formation of sulfinic anhydride 295 from vic-disulfoxide
The results obtained from the oxidation of \textit{trans-217} suggest that only activation using Meerwein’s reagent can produce the sulfinic anhydride \textit{295} and that it possibly may not be an intermediate in the synthesis of anhydride \textit{295}. In addition the yield starting from disulfide \textit{65} is a little bit higher suggesting there may be an alternative pathway involved in the generation of anhydride \textit{295}.

2,2,2-Trifluoroperacetic acid, a more reactive peroxy acid and was prepared \textit{in situ} using with hydrogen peroxide and trifluoroacetic acid (TFA), as reported by Nakayama.\textsuperscript{96} Reaction of TFA with \textit{trans-217} resulted in sulfinyl sulfone \textit{226} in a quantitative yield (scheme 3.26).

\begin{align*}
\begin{array}{c}
\text{S} \hspace{1cm} \text{S} \\
\text{217} \\
\text{O} \hspace{1cm} \text{O} \\
\text{S} \hspace{1cm} \text{S} \\
\text{O} \hspace{1cm} \text{O} \\
\text{O} \\
\end{array}
\end{align*}
\begin{align*}
\overset{\text{TFA (1 equiv.),}}{\text{\text{\quad TFA (1 equiv.),} \
\text{H}_2\text{O}_2 (1.5 equiv.),}} \\
\text{\quad H}_2\text{O}_2 (1.5 \text{ equiv.},) \\
\text{-20}^\circ\text{C} \rightarrow \text{rt}, 14 \text{ h} \\
\end{align*}

\begin{align*}
\begin{array}{c}
\text{O} \hspace{1cm} \text{S} \\
\text{226} \\
\end{array}
\end{align*}

\textit{Scheme 3.26 Oxidation of \textit{trans-217} using 2,2,2-trifluoroperacetic acid}

Reaction of 2.2 equiv. of \textit{mCPBA} added portionwise to thiosulfinate \textit{216} produced the desired anhydride again as the minor product along with the major product \textit{trans-217} (scheme 3.27).

\begin{align*}
\begin{array}{c}
\text{S} \hspace{1cm} \text{S} \\
\text{216} \\
\text{O} \hspace{1cm} \text{O} \\
\text{S} \hspace{1cm} \text{S} \\
\text{O} \hspace{1cm} \text{O} \\
\text{O} \hspace{1cm} \text{O} \\
\end{array}
\end{align*}
\begin{align*}
\overset{\text{\textit{mCPBA} (2.2 equiv.),}}{\text{\text{\quad CH}_2\text{Cl}_2, 16 \text{ h, rt}}} \\
\end{align*}

\begin{align*}
\begin{array}{c}
\text{O} \hspace{1cm} \text{S} \hspace{1cm} \text{S} \\
\text{295} 6\% \\
\text{O} \hspace{1cm} \text{S} \hspace{1cm} \text{S} \\
\text{217} 83\% \\
\text{O} \hspace{1cm} \text{S} \hspace{1cm} \text{S} \\
\text{216} \quad 4\% \\
\end{array}
\end{align*}

\textit{Scheme 3.27 Oxidation of thiosulfinate \textit{216} to prepare sulfinic anhydride \textit{295}}

Both \textit{cis} and \textit{trans vic}-disulfoxides are known to be stable at room temperature thus it is not clear if the disproportionation mechanism proposed by Harpp is followed (scheme 3.22), although it cannot be ruled out. An alternative rationalisation is a competing pathway between formation of anhydride \textit{295} and \textit{trans vic}-disulfoxide \textit{217} (scheme 3.28).
Scheme 3.28 Competing oxidation pathways between formation of anhydride 295 and trans vic-disulfoxide 217

mCPBA could act as an electrophilic oxidant to form trans vic-disulfoxide 217 or as a nucleophilic oxidant and attack the sulfinyl sulfur followed by a migration of the S-S bond to form O,S-sulfenyl sulfinate 227, which could potentially be oxidised to sulfinic anhydride 295. O,S-Sulfenyl sulfinate 227 has three possible pathways. The first is the predicted rearrangement to thiosulfonate 224, however, the formation of 224 was not observed. The second possible route is oxidation of the sulfenyl sulfur on 227 to form sulfinic anhydride 295. The final plausible path is the rearrangement of 227 to form trans-217 and cis-225, however this is unlikely as cis-225 was not observed.

The oxidation of trans vic-disulfoxide 217 with H2O2 and NaOH, forming HOO−, a method reported by Kice for thiosulfonate 63, was also investigated.138 The solvent ratio for equilibrium between the bissulfinic acid 285 and the sulfinyl sulfone 228 was crucial for
favouring the formation of 228 (scheme 3.10). The same solvent mixture was used for the acidification step to try to force the equilibrium towards sulfinyl sulfone 226; however this failed and starting material 217 was recovered (scheme 3.28).

Scheme 3.28 Attempted oxidation of trans-217 with nucleophilic H₂O₂

Use of Meerwein’s reagent 299 in the mCPBA-mediated oxidation of trans-217 resulted in small amounts of the trans anhydride 295. Efforts to oxidise cis vic-disulfoxide 225 utilising these conditions resulted in the generation of sulfinyl sulfone 226 in excellent yields, suggesting that the cis sulfinic anhydride could not be formed in this manner (scheme 3.30).

Scheme 3.30 Oxidation of cis-225 assisted by Meerwein’s reagent 299

In summary, sulfinyl sulfoxides 207 and 228 have been prepared in moderate yields by oxidation of disulfides 87 and 50 respectively. Oxidation of thiosulfonate 224 and vic-disulfoxides 217 and 225 afforded sulfinyl sulfone 226; however electrophilic oxidation of disulfide 65 and monoxide 216 gave a rare example of a sulfinic anhydride, 295 in low yield. The synthesis of 295 has been investigated and it is proposed that 295 is formed in competition with 217.
3.6 Properties of sulfinic anhydride 295

Trioxides 226 and 295 were found to be stable at room temperature in a solution of chloroform. Sulfinyl sulfone 226 was found to be stable to both thermolysis and irradiation with a 500 W halogen lamp, with recovery of starting material in near quantitative yield. Photolysis of \textit{trans} sulfinic anhydride 295 with a 500 W halogen lamp resulted in decomposition and a mixture of unidentifiable compounds. Heating sulfinic anhydride 295 in 1,4-dioxane resulted in slow formation of disulfide 65, with anhydride 295 remaining as the major product (table 3.4, entry 1). When the temperature was increased to refluxing PhCl, disulfide 65 was the major product formed after 14 h (scheme 3.31, entry 2). It is not clear how this remarkable transformation occurs.

\begin{center}
\begin{tikzpicture}
\node at (0,0) {295};
\node at (2,0) {65 72\%};
\draw[->] (0.5,0) -- (2,0);
\end{tikzpicture}
\end{center}

Scheme 3.31 Deoxygenation of sulfinic anhydride 295

Sulfinic anhydride 290 was refluxed in PhCl in the presence of norbornene (24), however oxygen trapped products were not observed (entry 3).

\begin{table}
\centering
\begin{tabular}{llcc}
Entry & Conditions & 65 (%) & 295 (%) \\
\hline
1 & 1,4-dioxane, 70 °C, 17 days & 9 & 85 \\
2 & PhCl, 132 °C, 14 h & 72 & - \\
3 & PhCl, 24 (5 equiv.), 132 °C, 14 h & 75 & - \\
\end{tabular}
\caption{Thermolysis of sulfinic anhydride 295}
\end{table}

A relationship between the sulfinic anhydride 295 and sulfinyl sulfone 226 can be envisaged. Hydrolysis of either 226 or 295 should generate the intermediate bissulfinic acid 305 followed by dehydration to provide the other isomer (scheme 3.32).
Hydrolysis of sulfinyl sulfone 226 in aqueous dioxane failed to provide any of the desired sulfinic anhydride 295 (scheme 3.35); starting material was recovered in a quantitative yield.

When sulfinic anhydride 295 was heated to 70 °C in aqueous dioxane a new product was formed. $^1$H-NMR analysis revealed that 6 protons were present in a symmetrical molecule with 3 different CH environments. The mass spectrum revealed loss of the sulfur and oxygen atoms. The product obtained was 2,7-di-tert-butylnaphthalene (306) in very good yield (scheme 3.34).\(^{232}\)

Desulfonylation of sulfinic acid 307 has been reported in the presence of pyridine, however this has only been described for electron-withdrawing aromatic systems (scheme 3.35).\(^{233}\)
It is proposed that the base deprotonates the sulfinic acid with a loss of sulfur dioxide followed by protonation (scheme 3.36).

The desulfonylation reaction was investigated further by reacting sulfinic anhydride 295 in a 1,4-dioxane/D$_2$O mixture to detect whether deuterium was incorporated in the naphthalene ring. Sulfinic anhydride 295 was heated to 70 °C in a 1,4-dioxane/D$_2$O mixture for 34 h, unfortunately this failed to result in any desulfonylation. This suggested that the D$_2$O was involved in the loss of SO$_2$ and a primary kinetic isotope effect may have been observed. The temperature was increased to refluxing 1,4-dioxane, this time a product with the same R$_f$ as 2,7-di-tert-butynaphthalene (306) was obtained in good yield (scheme 3.37).

Close examination of the $^1$H- and $^{13}$C-NMR spectra showed that the dideuterated compound was not the sole product obtained from this reaction. The $^1$H-NMR spectrum revealed that 5 aromatic protons were present (figure 3.8), whereas the $^{13}$C-NMR spectrum showed a product with 3 C-H environments. This was indicative that a mixture of two compounds was present.
and this presumption was supported by mass spectrometry. Two peaks were observed corresponding to the mono-deuterated \((309) (M = 241 \text{ g mol}^{-1})\) and the di-deuterated \((310) (M = 242 \text{ g mol}^{-1})\). No peak was observed for \(306 (M = 240 \text{ g mol}^{-1})\). It is not clear how the mono-deuterated compound \(309\) is formed in this reaction.

Figure 3.8 \(^1\text{H}-\text{NMR}\) spectra of \(306\), and a mixture of \(309\) and \(310\)

The desulfonylation of the sulfinic anhydride may occur via hydrolysis to the bissulfinic acid \(305\). The \(pK_a\) of a typical aromatic sulfinic acid is between 1 and 2 which suggests it is highly dissociated and the equilibrium favours its conjugate base, the sulfinate anion \(311\). Entropy favours the loss of \(\text{SO}_2\) resulting in 2,7-di-tert-butynaphthalene \((306)\) (scheme 3.38). This may be aided by the buttressing effect of the ortho tert-butyl groups. Sulfinyl sulfone \(226\) was stable when refluxed in a mixture of water/1,4-dioxane.

Scheme 3.38 Proposed pathway for the loss of \(\text{SO}_2\) from \(295\)
Efforts to synthesise sulfinic esters 312 and 313 were unsuccessful in 1,4-dioxane/alcohol mixtures (scheme 3.39).

\[
\begin{align*}
\text{S} & \quad \text{S} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\end{align*}
\]

1:1 1,4-dioxane/ROH

\[
\begin{align*}
\text{295} & \quad \rightarrow \quad \text{312} \quad \text{R} = \text{Me} \\
\text{313} & \quad \text{R} = \text{Et}
\end{align*}
\]

Scheme 3.39 Attempted synthesis of sulfinic esters

Attempts to further oxidise 226 to bissulfone 314 were unsuccessful. Reaction of sulfinyl sulfone 226 with excess \(m\)CPBA and DMD resulted in recovery of starting material in quantitative yield (scheme 3.40).

\[
\begin{align*}
\text{S} & \quad \text{S} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\end{align*}
\]

\[
\begin{align*}
\text{226} & \quad \rightarrow \quad \text{314}
\end{align*}
\]

Scheme 3.40 Attempted oxidation to bissulfone 314 from sulfinyl sulfone 226

Conditions used for the oxidation of thiosulfonate 224 to bissulfone 294 (scheme 3.14) were also employed; the product obtained from this reaction was sulfinyl sulfone 226 in excellent yield (scheme 3.41).

\[
\begin{align*}
\text{S} & \quad \text{S} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\end{align*}
\]

\[
\begin{align*}
\text{224} & \quad \rightarrow \quad \text{226} \quad 96\%
\end{align*}
\]

Scheme 3.41 Attempted oxidation of thiosulfonate 224 to bissulfone 314

3.7 Synthesis of bis(sulfonyl)hydroxylamines

Preliminary studies towards the synthesis of 284 have been carried out in the group.\(^\text{234}\) It was shown that the equilibrium shown in scheme 3.10 could be exploited favouring the bissulfinfinic acid in aqueous dioxane and reacted in the presence of sodium nitrite and acid, to generate the nitrosonium ion, to form 1,1,3,3-tetraoxo-\(IH,3H\)-1\(\lambda_6,3\lambda_6\)-dithia-2-aza-phenalen-2-ol (284) in
45% yield (scheme 3.42). Optimisation of these conditions afforded hydroxylamine in a 69% yield.

![Scheme 3.42 Preparation of bis(sulfonyl)hydroxylamine, 284](image)

The structure of **284** was confirmed by X-crystallography (figure 3.9).

![Figure 3.9 X-ray crystal structure of bis(sulfonyl)hydroxylamine 284](image)

The bis(sulfonyl)hydroxylamine ring adopts a half-chair like conformation and peri-strain is evident to a small extent. The bond angles at C(1), C(9) and C(8) are 121.6°, 126.7° and 122.5° respectively. The naphthalene moiety shows small twists along the dihedral angles of C(1)-C(9)-C(10)-C(4) and C(5)-C(9)-C(10)-C(8), -0.25° and 1.17° respectively. In addition, the hydroxyl group exhibits hydrogen bonding to an ethyl acetate molecule (the recrystallisation solvent). The hydroxyl group is *pseudo*axial and the nitrogen lone pair is *pseudo*equatorial. This conformation is presumed to be stabilised by stereoelectronics: the nitrogen lone pair can overlap with the C-S(O₂) σ* orbital, as is typical for sulfonamides.²³⁵
Attempted synthesis of bis(sulfonyl)hydroxylamine 315 from sulfinyl sulfone 207, using the same conditions as for the synthesis for 284, resulted in recovery of starting material in 96% yield (scheme 3.43).

![Scheme 3.43 Attempted synthesis of bis(sulfonyl)hydroxylamine 315](image)

Similarly treatment of sulfinyl sulfone 226 under the same conditions was unsuccessful, with unreacted starting material recovered in 98% yield (scheme 3.44).

![Scheme 3.44 Unsuccessful synthesis of bis(sulfonyl)hydroxylamine 313](image)

### 3.8 Reactions of bis(sulfonyl)hydroxylamine 284

Bis(sulfonyl)hydroxylamine 284 was stable for up to a three month period at room temperature in a DMSO solution. With the addition of D$_2$O, exchange of the hydroxyl proton was observed, however both samples remained unchanged over the three month period.

Hydroxylamine 284 was thermally stable in a solution of DMSO up to temperatures of 100 °C and in a range of solvents at higher temperatures (table 3.5).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temperature (°C)</th>
<th>284 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>t-BuOH</td>
<td>82</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>DMSO</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>toluene</td>
<td>108</td>
<td>92</td>
</tr>
<tr>
<td>4</td>
<td>octane</td>
<td>125</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>PhCl</td>
<td>132</td>
<td>96</td>
</tr>
</tbody>
</table>

*Table 3.5 Monitoring the thermal decomposition of hydroxylamine 284*
Efforts to trap a nitrene, if discharged, from hydroxylamine 284 with norbornene (24) in a sealed tube were unsuccessful leading to recovery of the bis(sulfonyl)hydroxylamine 284 in a 94% yield (scheme 3.45).

Scheme 3.45 Attempted trapping of reactive species

As hydroxylamine 284 was found to be thermally stable, the photoreactivity of 284 was explored. Bis(sulfonyl)hydroxylamine 284 was stable to irradiation with both a 125 W medium pressure Hg lamp and a 500 W halogen lamp (table 3.6).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>284 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>125 W medium pressure Hg lamp, pyrex filter, MeCN, 48 h</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>500 W halogen lamp, MeCN, 48 h</td>
<td>97</td>
</tr>
</tbody>
</table>

Table 3.6 Monitoring the photochemical decomposition of hydroxylamine 284

Attention therefore turned to the formation of nitroxide 318 as a compound that could potentially fragment to release NO (figure 3.10).

Figure 3.10 Nitroxide 318

The generation of nitroxides from hydroxylamines has been reported. Glidewell described the oxidation of N,N-bis(arylsulfonyl)hydroxylamines, 319, using PbO2. The product obtained from this reaction was N,N,O-tris(arylsulfonyl)hydroxylamine, 320. The
reaction is proposed to occur via a nitroxide radical, as an EPR signal was observed when 319 was reacted with excess PbO$_2$ (scheme 3.46).

![Scheme 3.46 Oxidation of N,N-bis(arylsulfonyl)hydroxylamine using PbO$_2$](image)

Balakirev investigated the decomposition of $N,N$-bis($p$-tolylsulfonyl)hydroxylamine, 264, in an air-saturated solution of CHCl$_3$. The products obtained from this reaction were tosic acid (321), tosyl chloride (322) and $N,N,O$-trisubstituted hydroxylamine 323 (scheme 3.47), a product in agreement with Glidewell. The tosyl chloride was explained as a result of sulfonyl radicals reacting with the solvent.

![Scheme 3.47 Decomposition of N,N-bis(p-tolysulfonyl)hydroxylamine 264 in an air saturated solution of CHCl$_3$](image)

$N,N$-Bis($p$-tolylsulfonyl)hydroxylamine 264 was treated with ceric ammonium sulfate to form the nitroxide radical. EPR signals of spin trapped sulfonyl radicals were observed, supporting the proposed formation of tosyl chloride and the decomposition pathway proposed by Glidewell.$^{175}$

Hydroxylamine 284 was reacted individually in the presence of MnO$_2$, PbO$_2$ and ceric ammonium sulfate$^{175}$ as a means of generating the nitroxide radical, however only starting material was recovered in each case (scheme 3.48, table 3.7, entries 1-3).

![Scheme 3.48 Attempted formation of nitroxide 318](image)
Oxidation of hydroxylamine 324 with Cu(OAc)₂·H₂O, conditions reported by Catala, gave nitroxide (scheme 3.49).²³⁶,²³⁹

![Scheme 3.49 Synthesis of β-sulfinyl nitroxide](image)

When bis(sulfonyl)hydroxylamine 284 was subjected to these conditions, a colour change from clear to purple was observed but the major compound isolated was starting hydroxylamine 284 (scheme 3.50, entry 4).

![Scheme 3.50 Attempted synthesis of bis(sulfonyl) nitroxide 318](image)

The reaction was reported to be more efficient in the presence of oxygen;²³⁹ however this resulted in recovery of starting material 284 (entry 5).

In a final attempt to generate nitroxy radical 318, di-tert-butoxydiazene (327), a known H-abstractor, was synthesised in low yield (scheme 3.51).²⁴⁰ Hydroxylamine 284 was heated in the presence of diazene 326, however starting material was recovered (entries 6 and 7).

![Scheme 3.51 Preparation of di-tert-butoxydiazene (327)](image)
<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>284 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MnO₂ (4.89 equiv.), CHCl₃, 24 h, rt → reflux</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>PbO₂ (2.00 equiv.), CH₂Cl₂, O₂, 24 h, rt</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>Ce(NH₄)₄(SO₄)₄·H₂O (2.66 equiv.), PhH, 24 h, rt</td>
<td>93</td>
</tr>
<tr>
<td>4</td>
<td>Cu(OAc)₂·H₂O (0.016 equiv.), NH₄OH, MeOH, 12 h, rt</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>Cu(OAc)₂·H₂O (0.016 equiv.), NH₄OH, MeOH, O₂, 12 h, rt</td>
<td>89</td>
</tr>
<tr>
<td>6</td>
<td>327 (1.20 equiv.), PhH, 24 h, 65 °C</td>
<td>96</td>
</tr>
<tr>
<td>7</td>
<td>327 (1.20 equiv.), MeCN, 24 h, 65 °C</td>
<td>93</td>
</tr>
</tbody>
</table>

Table 3.7 Attempted preparation of nitroxide 318

As the generation of the nitroxide radical proved difficult, the chemistry of the hydroxylamine anion 328 was explored. Bis(sulfonyl)hydroxylamine was treated with t-BuOK in t-BuOH and NEt₃ in CH₂Cl₂ (Scheme 3.52).

![Scheme 3.52 Generation of anion 328](image)

In both cases a precipitation was observed, suggesting formation of the anion. No change was observed when the precipitate was heated for 24 h in CH₂Cl₂. The reaction mixture was then quenched with 1 M HCl. After work-up, the ¹H-NMR suggested a new compound had been formed, however the IR and mass spectra were identical to those for hydroxylamine 284. X-ray crystallography revealed the structure of the compound to be hydrated bis(sulfonyl)hydroxylamine (C₁₀H₈NO₅S₂·H₂O) 329 (figure 3.11).
The difference in the NMR spectra was thought to be due to the bis(sulfonyl)hydroxylamine 284 existing in the hydrated form 329. Dilution studies on hydroxylamine 284 were undertaken to see how the concentration influenced the hydrogen bonding of the hydroxyl proton. NMR spectra were analysed at different concentrations (10^{-1} M - 10^{-4} M) and an upfield shift of the hydroxyl proton by 0.14 ppm was observed when diluting a sample from 10^{-1} M to 10^{-2} M (figure 3.12). Further dilution did not affect the splitting or shifts of the NMR.

There is also a difference in the NMR signals between 8.44-8.49 ppm; at 10^{-1} M the splitting of this peak is clearly 2 double doublets, however on dilution to 10^{-2} M, the peak at 8.44 ppm has shifted downfield and is overlapping with the signal at 8.49 ppm.
The concentration dependence of the chemical shift has been studied for aromatic compounds and related to intermolecular interactions. The noticeable change in the NMR spectra shown in figure 3.12 may be related to the molecular packing in the unit cell of the X-ray of 329. At higher concentrations, the system could be more ordered, in this case the naphthalene moiety of the molecule may exhibit intermolecular stacking, in a face to face manner. The packing in the X-ray of the hydrated sample indicates this occurrence (figure 3.13).

![X-ray of a unit cell of stacked bis(sulfonyl)hydroxylamine 329](image)

*Figure 3.13 X-ray of a unit cell of stacked bis(sulfonyl)hydroxylamine 329*

When the sample is less concentrated, stacking could be less apparent and individual molecules are dispersed, as observed in the packing of a unit cell of the X-ray sample crystallised with ethyl acetate (figure 3.14).

![Less ordered X-ray of a unit cell of bis(sulfonyl)hydroxylamine 284](image)

*Figure 3.14 Less ordered X-ray of a unit cell of bis(sulfonyl)hydroxylamine 284*

N-Hydroxy-O-benzenedisulfonylimide (266) has been reported by Fochi as a selective oxidising agent (scheme 3.53). The oxidation reactions of aldehydes to acids, benzyl alcohols to
aldehydes, thiols to disulfides, and sulfides to sulfoxides were investigated using hydroxylamine 266 and resulted in fair to excellent yields, with high selectivity for the oxidation of the sulfide to the sulfoxide. For example, oxidation of thioanisole to the sulfoxide is achieved in 0.5 h at 60 °C using 1.2 equiv. of 266 in a mixture of AcOH/MeCN.

Under analogous conditions, oxidation of thioanisole 330 with bis(sulfonyl)hydroxylamine 284 gave sulfoxide in a poorer 15% yield over a longer reaction time. The other product obtained was bissulfonic anhydride 333; this is assumed to occur via hydrolysis of intermediate bis(sulfonyl)amine 332 (scheme 3.54).
Conclusions

Three sulfinyl sulfones 207, 226 and 228 have been successfully prepared through oxidation. In the process of the investigations, the rare sulfinic anhydride 295 was synthesised in low yield via portionwise addition of mCPBA to disulfide 65 or thiosulfinate 216. Sulfinic anhydride 295 was heated in aqueous dioxane and via a proposed bissulfinic acid provided 2,7-di-tert-butyl naphthalene (306), probably as a result of a desulfonylation reaction. It is clear that water is important in this desulfonylation reaction as deuterium incorporation is observed in the presence of D2O. A remarkable deoxygenation of 295 was also observed upon heating in PhCl.

Hydroxylamine 284 has been successfully synthesised from sulfinyl sulfone 228, yet studies towards the breakdown of 284 have proved to be difficult. Attempts to prepare hydroxylamines 315 and 316 from sulfinyl sulfones 207 and 226 were unsuccessful; this may be due to the unfavourable equilibrium between the sulfinyl sulfone and the bissulfinic acid. Hydroxylamine 284 was found to be stable both thermally and photochemically. Attempted generation of nitroxyl radical 318 with a range of oxidants failed to provide any of the desired compound. Although not isolated, precipitation in the reaction mixture suggests that the anion was formed upon treatment of 284 with base. The anion appeared stable to thermolysis, however analysis of the resulting NMR indicated another compound had formed. X-ray crystallography confirmed the structure as the hydrated hydroxylamine 329. Dilution studies revealed the NMR spectra differed depending on the concentration of the sample being analysed. This could be explained in terms of the stacking of the naphthalene moieties and the extent of intermolecular interaction at varying concentrations.

Hydroxylamine 284 has been investigated as an oxidising agent for the selective oxidation of thioanisole 330 to sulfoxide 331. Although the yield is not comparable to the use of N-hydroxy-O-benzenedisulfonimide (266) as an oxidant, the reaction was selective.
**Future work**

The desulfonylation of sulfinic anhydride 295 has shown deuterium incorporation and this could be further investigated by exploring the reaction in a solution of H₂O and d₈-1,4-dioxane. Sulfinic acids 334 and 335 could also be explored to distinguish whether the desulfonylation is a result of the buttressing of the *ortho tert*-butyl groups (figure 3.15).

![Figure 3.15 Buttressed sulfinic acids proposed for desulfonylation](image)

Efforts to synthesise nitroxide 318 so far have failed. Future work would include synthesis of nitroxide 318 with other reagents, such as AIBN. This could then be explored as a reactive species to generate NO, NOH or HNO either thermally or photochemically. EPR studies could also provide evidence of NO by a change in the spectrum upon reaction with nitronyl nitroxide (scheme 3.55).

![Scheme 3.55 EPR evidence for the generation of NO](image)

Headspace analysis of a sample could provide evidence of the reactive species generated. A mass peak of 30 u would signify the loss of nitric oxide whereas indirect loss of nitroxyl would probably be detected as nitrous oxide and a loss of 44 u.
Chapter Four: Experimental
General experimental

$^1$H and $^{13}$C NMR data were recorded on a Bruker AC300, Bruker AV300, Bruker AMX400 or a Bruker DRX500 spectrometer. Spectra were recorded in D$_2$O referenced to residual H$_2$O ($^1$H, 4.79 ppm; $^{13}$C, SR = 161.3, corresponding to external TSP capillary set at 0 ppm), CD$_2$Cl$_2$ referenced to residual CH$_2$Cl$_2$ ($^1$H, 5.33 ppm; $^{13}$C, 53.8 ppm), C$_6$D$_6$ referenced to residual C$_6$H$_6$ ($^1$H, 7.15 ppm; $^{13}$C, 128.0 ppm), acetone-d$_6$ referenced to residual acetone ($^1$H, 2.05 ppm; $^{13}$C, 30.8 ppm), CD$_3$CN referenced to residual CH$_3$CN ($^1$H, 1.92 ppm; $^{13}$C, 1.2 ppm), DMSO-d$_6$ referenced to residual DMSO ($^1$H, 2.50 ppm; $^{13}$C, 39.4 ppm), $^{31}$P-NMR, referenced to a sample of PPh$_3$ calibrated to H$_3$PO$_4$ in DMSO, -6.0 ppm) and deuterochloroform referenced to residual CHCl$_3$ ($^1$H, 7.26 ppm; $^{13}$C, 77.0 ppm). Chemical shifts ($\delta$) are reported in ppm and coupling constants ($J$) are reported in Hz. The following abbreviations are used to describe multiplicity; s-singlet, d-doublet, t-triplet, q-quartet, m-multiplet, br-broad, ap. apparent. All coupling constants are reported as observed and not averaged. Mass spectra were recorded on a LCT spectrometer utilising electrospray ionisation (recorded in the positive mode) with a methanol mobile phase, or electron impact ionisation, and are reported as ($m/z$ (%)). h MS were recorded on a LCT spectrometer using lock mass incorporated into the mobile phase. IR spectra were recorded neat, from nujol or as KBr disks on a Perkin Elmer 1600 series FT-IR, Perkin Elmer FT-IR Paragon 1000 or a Perkin Elmer 100-series FT-IR spectrometer. HPLC was carried out on a DIONEX summit P580 quaternary low pressure gradient pump with a built-in vacuum degasser using a Summit UVD 170s UV/Vis multi-channel detector with analytical flow cell and Chromeleon software and HPLC grade solvents. Analytical separations used a flow rate of 1 mL/min and semi-preparative used a flow rate of 3 mL/min. UV/Vis spectra were recorded on a UV-3101PC Shimadzu spectrophotometer. Melting points were determined using open glass capillaries on a Gallenkamp melting point apparatus and are uncorrected. Analytical TLC was carried out on Merck 60 F245 aluminium-backed silica gel plates. Short wave UV (245 nm),
KMnO₄ or anisaldehyde were used to visualise components. Compounds were purified by flash column chromatography using Merck silica gel 60, basic alumina (Brockmann I, standard grade, ~150 mesh 58 Å), florisil® (60-100 U.S. mesh) or Bio-Beads (S-X8 beads, 200 - 400 mesh).

Single crystal data were recorded at room temperature by Dr Benson Kariuki and Dr Louise Male at the University of Birmingham, on a Bruker Smart 6000 diffractometer equipped with a CCD detector and a copper tube source or recorded using synchrotron radiation at Station 9.8, Daresbury laboratory, Cheshire, U.K. All structures were solved by Direct methods and refined by least-squares using SHELX97 [Sheldrick, G.M. SHELX97 [Includes SHELXS97, SHELXL97]. Non-hydrogen atoms were refined anisotropically and a riding model was used for C-H hydrogen atoms.

Matrix isolation was carried out using an APD HC-2 liquid helium refrigerator. High vacuum for matrix isolation experiments was provided by a Balzers Pfeiffer TSH 180H turbomolecular pump, and vacuum was monitored with a Varian 860A vacuum gauge (ca. 10⁻⁷ mbar). Matrices were condensed on a CsI. Flanged to the rotatable outer vacuum sleeve of the cryostat cold head was an electrically heated quartz sublimation/flash vacuum thermolysis (FVT) tube (200 mm x 8 mm ID) capable of reaching temperatures up to ca. 900 °C. Samples were sublimed in a stream of ultra high purity Ar for matrix isolation and/or thermolysis–matrix isolation.

Solvents and reagents were purified as follows:

Solvents were degassed by bubbling argon through a needle immersed in the solvent for 15 min. n-BuLi was purchased as either 2.5 M or 1.6 M solutions in hexanes and the solutions were titrated with menthol in the presence of 1-(biphenyl-4-yl)-3-phenyl-2-azapropene (“BLUE”). TMEDA was distilled from calcium hydride. Diethyl ether and hexane were distilled from sodium. Tetrahydrofuran was distilled from sodium and benzophenone. Thionyl
chloride was distilled from quinoline. 1,2-Dihydroacenaphthylene was recrystallised from EtOH. Sulfur was recrystallised from toluene.

$mCPBA$ was purified by washing with a pH 7 phosphate buffer unless otherwise stated:
A buffer solution was prepared from 0.1 M NaOH (154 mL) and 0.2 M KH$_2$PO$_4$ (94 mL) and made up to 376 mL with distilled water. $mCPBA$ (77% w/w, 10 g) was dissolved in diethyl ether (100 mL) and washed four times with the buffer solution. The organic extract was dried over MgSO$_4$ and carefully evaporated under reduced pressure to yield pure $mCPBA$ (7.3 g).

Dimethyl dioxirane (DMD) was prepared using a modified literature procedure:\textsuperscript{143}
A single neck 3 L round bottom flask was equipped with a jacketed air condenser (containing solid CO$_2$) connected to a 2 neck 500 mL round bottom receiving flask cooled to -78 °C. The 2 neck flask was connected to a vacuum pump. The 3 L flask was charged with NaHCO$_3$ (29 g, 345 mmol), H$_2$O (127 mL) and acetone (96 mL) and cooled to -5 °C. Oxone® (60 g, 97.5 mmol) was added in one portion, the suspension was vigorously stirred for 10 min and the ice-cold bath was removed. Vacuum (30 mmHg) was applied and the yellow dimethyl dioxirane solution was distilled under reduced pressure into the receiving flask cooled to -78 °C. After 30 min the vacuum was removed and the DMD was purged with argon.

The dioxirane content of the solution was assayed using phenyl methyl sulfide and analysis of the methyl peaks of phenyl methyl sulfoxide and phenyl methyl sulfide by $^1$H-NMR. Generally concentrations in the range of 0.02–0.05 M are obtained.

All other reagents and solvents were purchased from Aldrich, Alfa Aesar, Fisher Scientific, Merck or TCI Europe and were used as received. The following cooling baths were used; 0 °C (ice/water) and -78 °C (dry ice/acetone). All reactions in non-aqueous solvents were carried out under argon in oven-dried glassware.
Experimental for Chapter One

Naphtho[1,8-cd][1,2]dithiole (50)

Disulfide 50 was prepared according to the literature procedure.26 A 500 mL 2-necked round bottom flask was equipped with a magnetic stirrer, reflux condenser and purged with argon. A solution of n-BuLi in hexanes (1.65 M, 72.7 mL, 120 mmol) was added to the flask and diluted with Et₂O (80.0 mL). The mixture was cooled to -0 °C and 1-bromonaphthalene (13.9 mL, 100 mmol) was added dropwise over a period of 5 min. The temperature was allowed to rise to 10 °C (a strong exotherm results if the temperature rises above this temperature) and stirring was continued for an additional 15 min. The suspension was cooled to -10 °C and stirring was stopped. After standing for 10 min, the supernatant solution was removed via cannula. Hexane (250 mL) was added and the stirring was continued for 10 min at -20 °C. The stirring was interrupted, left to stand for 10 min and the supernatant was removed using a cannula. The procedure was repeated twice, after which a solution of n-BuLi in hexanes (1.65 M, 78.8 mL, 130 mmol) and TMEDA (21.2 mL, 140 mmol) was added to the suspension. The suspension was refluxed for 3 h and allowed to cool to room temperature. The reaction was cooled to -78 °C. Stirring was stopped and the supernatant solution was removed via cannula. The solid was dissolved in THF (80.0 mL) and stirred for 20 min. Sulfur (6.54 g, 202 mmol) was added and the reaction mixture was stirred overnight warming to room temperature. 1 M HCl (30.0 mL) was added, the mixture was filtered through celite and the organic phase was separated. The aqueous layer was acidified (pH < 1) with 1 M HCl and extracted with Et₂O (3 × 30 mL). The combined organic layers were dried over MgSO₄ and the solvent was concentrated under reduced pressure. Purification by column chromatography (60-80 pet ether) and further recrystallisation from EtOH yielded disulfide 50.
(6.97 g, 37%) as a deep red, crystalline solid. R$_f$ 0.48 (60-80 pet ether); mp 110-112 °C (EtOH); found: C, 63.35; H, 3.0. C$_{10}$H$_6$S$_2$ requires C, 63.1; H, 3.2%; $\lambda_{\text{max}}$ (MeCN)/nm 366 (ε/dm$^3$ mol$^{-1}$ cm$^{-1}$ 13 300) and 250 (22 900); $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 1544 (aromatic), 1485, 1349 and 1206; $\delta_H$(300 MHz; CDCl$_3$) 7.15 (2 H, d, J 7.3, SCCH), 7.27 (2 H, t, J 7.7, SCCH); $\delta_H$(300 MHz; C$_6$D$_6$) 6.59 (2 H, d, J 7.5, ArH), 6.80 (2 H, ap. t, J 7.8, ArH) and 6.97 (2 H, d, J 8.2, ArH); $\delta_C$(75 MHz, CDCl$_3$) 115.9 (CH, SCCH), 121.6 (CH, SCCH), 127.8 (CH, SCCH), 134.7 (C, SCC), 135.7 (C, SCC) and 144.0 (C, SC); $\delta_C$(75 MHz, C$_6$D$_6$) 116.0 (CH), 121.7 (CH), 128.0 (CH), 135.1 (C), 136.0 (C) and 144.4 (C); m/z (EI) 189.9907 (M$^+$, C$_{10}$H$_6$S$_2$ requires 189.9911), 158 (5%), 145 (18), 126 (5), 114 (21), 102 (7), 95 (22), 74 (5), 69 (8) and 63 (5).

**Literature data:**$^{26}$ mp 115 °C (ethanol); $\nu_{\text{max}}$ (nujol)/cm$^{-1}$ 1605, 1551 (aromatic); $\delta_H$(360 MHz; CDCl$_3$) 7.15 (2 H, d, J 8.1, ArH), 7.27 (2 H, t, J 7.7, ArH) and 7.35 (2 H, d, J 7.4, ArH); $\delta_C$(90 MHz; CDCl$_3$) 116.0 (CH), 121.7 (CH), 127.9 (CH), 134.8 (C), 135.8 (C) and 144.1 (C); m/z (EI) 190 (M$^+$, 100%), 158 (20), 126 (25), 114 (11) and 95 (13).

**Friedel-Crafts alkylation of disulfide 50**

Using FeCl$_3$ and $t$-BuBr (2 equiv.):

Disulfide 65 was prepared by modification of the literature procedure.$^{47}$ FeCl$_3$ (150 mg, 0.920 mmol) was added to a solution of $t$-BuBr (4.15 mL, 36.8 mmol) and disulfide 50 (3.50 g, 18.4 mmol) in CH$_2$Cl$_2$ (6.60 mL). The mixture was refluxed for 96 h, allowed to cool to room temperature, filtered through a plug of silica (60-80 pet ether) and concentrated under reduced pressure. The resulting dark orange solid was recrystallised from acetone to yield the desired 3,8-di-tert-butynaphtho[1,8-cd][1,2]dithiole (65) (2.45 g, 44%).
HPLC (t = 0 → 30 min, 80:20 MeCN:CH₂Cl₂): Rᵣ 7.98 min; R₂ 0.73 (95:5 hexane:Et₂O); mp 127-130 °C (acetone); νmax (KBr)/cm⁻¹ 2949 (CH), 1501, 1477, 1458, 1432, 1363, 1305 (t-Bu C-H), 1257, 1198, 1123 and 1007; δH(300 MHz; CDCl₃) 1.53 (18 H, s, C(CH₃)₃), 7.38 (2 H, d, J 8.6, ArH) and 7.43 (2 H, d, J 8.5, ArH); δC(75 MHz; CDCl₃) 28.4 (CH₃, C(CH₃)₃), 35.6 (C, C(CH₃)₃), 121.9 (CH), 125.7 (CH), 132.9 (C), 137.0 (C), 138.9 (C) and 139.4 (C); m/z (ESI) 303.1238 ([M + H]⁺, C₁₈H₂₃S₂ requires 303.1241), 303 (100%).

**Literature data.**⁴⁵ mp 129 °C (acetone); found: C, 71.55; H, 7.37. C₁₈H₂₂S₂ requires C, 71.47; H, 7.33%; δH(CDCl₃) 1.50 (18 H, s, C(CH₃)₃), 7.36 (2 H, d, J 8.0, ArH), 7.42 (2 H, d, J 8.0, Ar); m/z 302.5 (M⁺).

Using AlCl₃ and t-BuCl (3 equiv.):

Disulfide 65 was prepared according to the literature procedure.⁴⁵ Disulfide 50 (1.00 g, 5.26 mmol) was dissolved in a mixture of nitromethane (12.5 mL) and t-BuCl (1.73 mL, 15.7 mmol) at 50 °C. Anhydrous AlCl₃ (133 mg, 1.00 mmol) was added and the mixture was heated at 50 °C. After 20 min the reaction mixture was allowed to cool to room temperature. The resulting precipitate was filtered, washed with nitromethane (3 × 5 mL) and recrystallised from acetone to yield disulfide 65 (755 mg, 48%) as orange crystals.

Using FeCl₃ and t-BuBr (3 equiv.):

Disulfide 65 was prepared by modification of the literature procedure.⁴⁷ FeCl₃ (43.0 mg, 0.26 mmol) was added to a solution of t-BuBr (1.78 mL, 15.8 mmol) and disulfide 50 (1.00 g, 5.26 mmol) in CH₂Cl₂ (2.31 mL). The mixture was refluxed for 96 h, allowed to cool to room
temperature, filtered through a plug of silica (60-80 pet ether) and concentrated under reduced pressure. The resulting dark orange solid was recrystallised in acetone to yield disulfide 65 (379 mg, 24%) as a yellow-orange solid. Purification of the remaining crude oil by HPLC yielded additional disulfide 65 (190 mg, 8%) and 2,4,7-tri-tert-butylnaphtho[1,8-cd][1,2]dithiole (68) (313 mg, 18%) as an orange solid. HPLC (t = 0 → 30 min, 80:20 MeCN:CH₂Cl₂): Rₜ 11.03 min; Rᶠ 0.73 (95:5 hexane:Et₂O); mp 149-150 °C; νₘₚₙ (KBr)/cm⁻¹ 2964, 1504, 1477, 1393, 1363 and 1306; δₜ (300 MHz; CDCl₃) 1.51 (9 H, s, C(CH₃)₃), 1.52 (9 H, s, C(CH₃)₃), 1.56 (9 H, s, C(CH₃)₃), 7.43 (1 H, d, J 9.1, ArH), 7.47 (1 H, s, CCHC) and 7.91 (1 H, d, J 9.0, ArH); δₜ (75 MHz; CDCl₃) 28.4 (CH₃, 2 × C(CH₃)₃), 31.1 (CH₃, C(CH₃)₃), 35.5 (C, C(CH₃)₃), 35.9 (C, C(CH₃)₃), 36.0 (C, C(CH₃)₃), 121.7 (CH), 123.3 (CH), 124.3 (CH), 131.2 (C), 137.1 (C), 138.1 (C), 138.3 (C), 138.5 (C), 139.8 (C) and 140.3 (C); m/z (ESI) 358.1792 (M⁺, C₂₂H₃₀S₂ requires 358.1789), 358 (100%).

5,6-Dibromo-1,2-dihydroacenaphthylene (71)

Dibromide 71 was prepared according to the literature procedure.⁵⁰ To a suspension of 1,2-dihydroacenaphthylene (73) (19.3 g, 125 mmol) in DMF (62.5 mL) was added NBS (22.3 g, 125 mmol) in DMF (62.5 mL) over a period of 90 min at 30-40 °C. After the mixture was stirred for 1 h at 30 °C, additional NBS (33.4 g, 187 mmol) was added portionwise over a period of 90 min, whilst maintaining the temperature between 30-40 °C. The mixture was stirred for 2 h at 30 °C and allowed to stand in the refrigerator overnight. The precipitate was filtered and washed sequentially with DMF (2 × 10 mL) and methanol (10 mL) to afford 71 (9.79 g, 25%) as a pale yellow solid. Rᶠ 0.60 (9:1 hexane:Et₂O); mp 167-169 °C (EtOH); δₜ (300 MHz; CDCl₃) 3.29 (4 H, s, CH₂), 7.08 (2 H, d, J 7.4, BrCCHC) and 7.78 (2 H, d,
$J$ 7.4, BrCCH$); \delta_C (75$ MHz; CDCl$_3$) 30.0 (CH$_2$, CH$_2$), 114.3 (C), 120.9 (CH), 127.7 (C), 135.8 (CH), 141.9 (C) and 147.0 (C); $m/z$ (EI) 314 (M$^+$, 32%), 312 (67), 310 (35), 232 (11), 152 (100), 115 (5), 76 (33) and 63 (6).

**Literature data:**$^{50,53,242}$ mp 167-169°C (EtOH); $\nu_{\text{max}}$ (KBr)/$\mu$ 6.33, 7.40, 9.12, 11.6 and 12.9; $\delta_H$ (270 MHz; CDCl$_3$) 3.28 (4 H, s, CH$_2$), 7.06 (2 H, d, $J$ 7.4, BrCCHCH) and 7.76 (2 H, d, $J$ 7.4, BrCCH); $\delta_C (68$ MHz; CDCl$_3$) 29.99, 114.31, 120.87, 131.80, 135.77, 141.75 and 147.00; $m/z$ (EI) 314 (M$^+$, 31%), 312 (64), 310 (32) and 152 (100).

5,6-Dibromoacenaphthylene (72)

![Dibromoacenaphthylene](image)

Dibromide 72 was prepared according to the literature procedure.$^{51}$ DDQ (4.39 g, 19.3 mmol) was added to a stirred solution of 5,6-dibromo-1,2-dihydroacenaphthylene (71) (4.00 g, 12.8 mmol) in benzene (139 mL) and the resulting solution refluxed for 48 h. The mixture was allowed to cool to room temperature and pentane (500 mL) was added to the mixture. The reaction mixture was passed through basic alumina, concentrated under reduced pressure and recrystallised from EtOH (~50 mL) to yield 72 (1.12 g, 28%) as a yellow, crystalline solid. $R_f$ 0.81 (hexane); mp 137-138°C (EtOH); found: C, 46.7; H, 1.8. C$_{12}$H$_6$Br$_2$ requires C, 46.5; H, 1.95%; $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 2924, 2854 and 1458; $\delta_H (300$ MHz; CDCl$_3$) 6.93 (2 H, s, BrCCCCCH), 7.41 (2 H, d, $J$ 7.4, ArH) and 7.87 (2 H, d, $J$ 7.3, ArH); $\delta_C (75$ MHz; CDCl$_3$) 121.0 (C), 125.1 (CH), 125.7 (C), 129.1 (CH), 131.1 (C), 135.4 (CH) and 140.3 (C); $m/z$ (EI) 312 (M$^+$, 51%), 310 (100), 308 (53), 231 (18), 150 (82), 115 (6), 98 (6), 75 (48) and 62 (7).

**Literature data:**$^{51}$ mp 132-133°C (hexane); found: C, 46.87; H, 2.03. C$_{12}$H$_6$Br$_2$ requires C, 46.50; H, 1.95%; $\delta_H (250$ MHz; CDCl$_3$) 6.85 (2 H, s, BrCCCCCH), 7.40 (2 H, d, $J$ 7.4,
BrCCCH) and 7.86 (2 H, d, J 7.4, BrCCCH); δ_c(15 MHz; CDCl₃) 121.0 (C, BrC), 125.1 (CH, BrCCCH), 125.7 (C, BrCCC), 129.1 (CH, BrCCCCCH), 135.4 (CH, BrCCH), 135.8 (C, BrCC) and 140.3 (C, BrCCCC); m/z (CI) 313 (M⁺), 311, 309.

1,2-Dihydroacenaphtho[5,6-cd][1,2]dithiole (69)

Disulfide 69 was prepared according to the literature procedure. A solution of n-BuLi in hexanes (1.12 M, 3.05 mL, 3.42 mmol) was slowly added over 5 min to a stirred solution of 5,6-dibromo-1,2-dihydroacenaphthylene (71) (530 mg, 1.69 mmol) and TMEDA (0.51 mL, 3.38 mmol) in THF (50.7 mL) at -78 °C. The mixture was stirred for 15 min at the same temperature, after which sulfur (110 mg, 3.42 mmol) was added and the reaction mixture stirred for a further 2 h at room temperature. The mixture was quenched with acetic acid (0.50 mL) and exposed to air overnight. The resulting solution was concentrated under reduced pressure and then washed with water (3 × 5 mL). The aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL) and the combined organic phases were dried over MgSO₄. The solvent was removed under reduced pressure and the crude product was subjected to column chromatography using biobeads to afford disulfide 69 (30.0 mg, 9%) as a red solid. R_f 0.43 (hexane); mp 189-191 °C; δ_H(300 MHz; acetone-d₆) 3.30 (4 H, s, CC₃H₂), 7.12 (2 H, d, J 7.1, ArH), 7.18 (2 H, d, J 7.4, ArH); m/z (EI) 216.0059 (M⁺ - C₁₂H₈S₂ requires 216.0067), 152 (13%).

Literature data: mp 190.3 °C; λ_max (THF)/nm 250 (ε/dm³ mol⁻¹ cm⁻¹19 600), 351 (11500), 369 (14000) and 422 (99.1); δ_H(CHCl₃) 3.25 (4 H, s), 6.90 (4 H, s); m/z (M⁺ - 216).
Acenaphthylene (75)

5-Bromo-1,2-dihydroacenaphthylene (74) (500 mg, 2.15 mmol) was added portionwise over a period of 5 min at -20 °C to a solution of n-BuLi in hexanes (1.30 M, 1.98 mL, 2.57 mmol) and Et₂O (1.72 mL). The temperature was allowed to rise to 10 °C and stirring was continued for an additional 15 min. The suspension was cooled to -10 °C and stirring stopped. After standing for 10 min, the supernatant solution was removed via cannula. Hexane (5.36 mL) was added, stirring continued for 10 min, the suspension was cooled to -20 °C and then left to stand for 10 min. The supernatant was removed using a cannula. The procedure was repeated twice, after which a solution of n-BuLi in hexanes (1.30 M, 2.15 mL, 2.79 mmol) and TMEDA (0.45 mL, 3.00 mmol) was added to the suspension. The suspension was refluxed for 3 h and allowed to cool to room temperature. The reaction mixture was cooled to -78 °C and stirring was stopped and the supernatant solution was removed via cannula. The solid was dissolved in THF (1.72 mL) and the resulting solution stirred for 20 min. Sulfur (139 mg, 4.33 mmol) was added and the reaction mixture was stirred overnight, warming to room temperature. 1 M HCl (~ 3 mL) was then added, the mixture filtered through celite and the organic phase was separated. The aqueous phase was acidified with 1 M HCl (pH < 1) and extracted with Et₂O (3 × 3 mL). The combined organic layers were dried over MgSO₄ and solvent was removed under reduced pressure. Purification of the residue by column chromatography (hexane) yielded 75 (108 mg, 28%) as a white solid. Rf 0.64 (60-80 pet ether); 𝜅_max(KBr)/cm⁻¹ 2922, 1597, 1424, 1362 and 1263; δ_H(300 MHz; CDCl₃) 7.08 (2 H, s, ArH), 7.55 (2 H, dd, J 8.1 and 6.8, CHCH), 7.69 (2 H, d, J 6.8, ArH) and 7.81 (2 H, d, J 8.2, ArH); δ_C(75 MHz, CDCl₃) 124.1 (CH), 127.1 (CH), 127.6 (CH), 128.0 (C), 128.1 (C), 129.3 (CH) and 139.5 (C).
5-Bromoacenaphthylene (78)

Bromide 78 was prepared according to the literature procedure.\textsuperscript{51} DDQ (1.47 g, 6.47 mmol) was added to a stirred solution of 5-bromo-1,2-dihydroacenaphthylene (74) (90\%, 1.00 g, 4.30 mmol) in benzene (25.0 mL) and refluxed for 60 h. The mixture was allowed to cool to room temperature and pentane (130 mL) was added. The reaction mixture was passed through basic alumina, concentrated under reduced pressure and recrystallised from EtOH (~50 mL) to yield bromide 78 (254 mg, 26\%) as a yellow, crystalline solid. R\textsubscript{f} 0.53 (hexane); \nu\textsubscript{max} (KBr)/cm\textsuperscript{-1} 2923, 2854, 1473, 1364, 1227, 1207 and 1044; \delta\textsubscript{H}(300 MHz; CDCl\textsubscript{3}) 6.98 (1 H, d, J 5.3, Ar\textit{H}), 7.02 (1 H, d, J 5.3, Ar\textit{H}), 7.44 (1 H, d, J 7.3, Ar\textit{H}), 7.57 (1 H, dd, J 8.1 and 7.0, Ar\textit{H}), 7.66 (1 H, d, J 6.8, Ar\textit{H}), 7.72 (1 H, d, J 7.3, Ar\textit{H}) and 7.96 (1 H, d, J 8.2, Ar\textit{H}); \delta\textsubscript{C}(75 MHz; CDCl\textsubscript{3}) 122.9 (C), 124.7 (CH), 124.9 (CH), 126.4 (CH), 128.2 (C), 128.7 (CH), 129.1 (CH), 129.5 (CH), 129.6 (C), 130.8 (CH), 139.3 (C) and 139.9 (C); m/z (El) 231 (M\textsuperscript{+}, 100\%), 229 (96), 150 (97), 115 (9), 98 (12), 75 (40), 62 (10) and 44 (6).\textsuperscript{1}

\textbf{Literature data.}\textsuperscript{51, 246} mp 53-55 °C; found: C, 62.09; H, 3.22. C\textsubscript{12}H\textsubscript{7}Br requires C, 62.37; H, 3.05\%; \nu\textsubscript{max} (KBr)/cm\textsuperscript{-1} 3100, 3070, 3030, 1480, 1420, 1380, 1360, 1210, 1168, 1082, 1071, 1028, 1019, 881, 720-640 and 520; \delta\textsubscript{H}(60 MHz; CDCl\textsubscript{3}) 6.78 (2 H, s) and 7.0-7.9 (5 H,

\textsuperscript{1} Impurity in starting material: m/z 309.8 (68\%)
m, ArH); δC(15 MHz; CDCl₃) 122.9, 124.7, 124.9, 126.4, 128.3, 128.7, 129.1, 129.5, 130.8, 139.4 and 140.0; m/z (Cl) 231 (M⁺).

5,6-Dichloro-1,2-dihydroacenaphthylene (81)

Dichloride was prepared according to the literature procedure.⁵⁷ To a solution of ice-cold acenaphthene (73) (6.00 g, 38.9 mmol) and AlCl₃ (0.180 g, 1.33 mmol) in CH₂Cl₂ (118 mL) was added SO₂Cl₂ (8.52 mL, 106 mmol) over a period of 5 min. The reaction mixture was stirred for 4 h at 0 °C. The reaction mixture was then allowed to proceed to room temperature for 2 days. The crude precipitate was filtered and recrystallised from EtOH (~30 mL), yielding dichloride 81 (2.19 g, 25%) as an orange solid. Rf 0.37 (hexane); mp 154-156 °C (EtOH); νmax (neat)/cm⁻¹ 2921, 1600, 1569, 1413, 1332, 1230 and 1111; δH(300 MHz; CDCl₃) 3.31 (4 H, s, CH₂), 7.13 (2 H, d, J 7.5, ArH) and 7.47 (2 H, d, J 7.4, ArH); δC(75 MHz; CDCl₃) 120.3 (CH), 125.6 (C), 125.9 (C), 131.3 (CH), 142.0 (C) and 145.8 (C); m/z (EI) 226 (M⁺, 8%), 224 (62), 222 (100), 187 (80), 152 (81), 93 (22), 75 (20) and 69 (9).

**Literature data:**⁵⁷, ²⁴⁷ mp 167-169 °C; found: C, 64.48; H, 3.75; Cl, 32.00. C₁₂H₈Cl₂ requires C, 64.40; H, 3.62; Cl, 31.78%; νmax (KBr)/cm⁻¹ 2920, 1850, 1600, 1570, 1410, 1350, 1330, 1260, 1230, 1110, 1025, 915, 870, 830, 740, 720 and 700; δH(500 MHz; CDCl₃) 3.27 (4 H, s), 7.09 (2 H, d, J 7.5, Ar), 7.44 (2 H, d, J 7.5, Ar); δC(125 MHz; CDCl₃) 30.0, 120.3, 125.7, 126.0, 131.4, 142.1, 145.9; m/z (EI) 226 (M, 10%), 224 (66), 222 (60), 187 (80), 152 (100).
5,6-Dichloroacenaphthylene (82)

Dichloride 82 was prepared according to the literature procedure. A solution containing 5,6-dichloro-1,2-dihydroacenaphthylene (81) (1.00 g, 4.48 mmol) and DDQ (1.54 g, 6.77 mmol) in benzene (10.2 mL) was refluxed for 30 h. The reaction mixture was allowed to cool to room temperature and was diluted with pentane (100 mL). The reaction mixture was passed through basic alumina, concentrated in vacuo and recrystallised from EtOH (~10 mL) to yield dichloride 82 (280 mg, 28%) as an orange, crystalline solid. Rf 0.37 (hexane); mp 153-155 °C (EtOH); \( \nu_{\text{max}} \) (Nujol)/cm\(^{-1}\) 2920, 1693, 1564, 1416, 1113 and 1082; \( \delta_H \) (300 MHz; CDCl\(_3\)) 6.96 (2 H, s, Ar\(H\)), 7.51 (2 H, d, \( J \) 7.4, Ar\(H\)) and 7.58 (2 H, d, \( J \) 7.4, Ar\(H\)); \( \delta_C \) (75 MHz; CDCl\(_3\)) 123.9 (C), 124.9 (CH), 129.1 (CH), 131.0 (CH), 131.6 (C) and 2 × 139.2 (C); \( m/z \) (EI) 224 (M\(^{+}\)%, 11%), 222 (67), 220 (100), 185 (19), 150 (30), 110 (11), 92 (6), 81 (16), 75 (11), 69 (33), 57 (10) and 43 (7).

Literature data: mp 163-164 °C; found: C, 65.42; H, 2.64; Cl 31.92. \( \text{C}_{12}\text{H}_6\text{Cl}_2 \) requires C, 65.18; H, 2.74; Cl, 32.07%; \( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 3080, 1580, 1485, 1470, 1440, 1420, 1240, 1200, 1110, 1085, 1060, 1030, 900, 830, 745, 730 and 640; \( \delta_H \) (CCl\(_4\)) 6.90 (2 H, s), 7.42 (2 H, d, Ar\(H\)) and 7.58 (2 H, d, Ar\(H\)).

2,7-Dimethoxynaphthalene (84)

84 was prepared according to the literature procedure. Dimethylsulfate (3.12 mL, 33.0 mmol) was slowly added over 10 min to a well stirred solution of
2,7-dihydroxynaphthalene (83) (2.50 g, 15.6 mmol) in 10% NaOH (14.1 mL) at 0 ºC. After stirring for 2 h, H₂O (30 mL) was added forming a grey precipitate. The solid was filtered and washed with H₂O until a colourless product was obtained, yielding 84 (2.66 g, 91%). Rf 0.23 (9:1 hexane:Et₂O); mp 137-139 ºC; νmax (Nujol)/cm⁻¹ 1625, 1606, 1511, 1460, 1384, 1228 and 1210; δH (300 MHz; CDCl₃) 3.92 (6 H, s, OCH₃), 7.03 (2 H, dd, J 8.9 and 2.5, ArH), 7.08 (2 H, d, J 2.3, ArH) and 7.68 (2 H, d, J 8.9, ArH); δC (75 MHz; CDCl₃) 55.2 (CH₃, OCH₃), 105.3 (CH), 116.0 (CH), 124.3 (C), 129.1 (CH), 135.9 (C) and 158.2 (C); m/z (EI) 188 (M⁺, 100%), 159 (7), 145 (46), 130 (7), 115 (9) and 102 (15).

Literature data:²⁴⁸ mp 139 ºC; νmax (Nujol)/cm⁻¹ 1627 and 1228; δH (500 MHz; CDCl₃) 3.91 (6 H, s, OCH₃), 6.99 (2 H, d, J 8.8, OCCHCH), 7.06 (2 H, s, CCHC) and 7.65 (2 H, d, J 9.0, OCCHCH); δC (67.8 MHz; CDCl₃) 55.4 (CH₃, OCH₃), 105.4 (CH, CCHC), 116.2 (CH, OCCHCH), 124.5 (C, OCCHCC), 129.3 (CH, CCHCH), 135.6 (C, OCHCC) and 158.4 (C, OCCH); m/z (CI) 189 ([M + H]⁺, 100%).

Bromination of 2,7-dimethoxynaphthalene

Using bromine:

The bromination of 84 was followed according to the literature procedure.⁶⁴ A solution of bromine (0.54 mL, 10.6 mmol) in CHCl₃ (4.00 mL) was added dropwise to a solution of 2,7-dimethoxynaphthalene (84) (2.00 g, 10.6 mmol) in CHCl₃ (10.0 mL) over 2 h at 0 ºC. The resultant solution was stirred for 24 h. The mixture was washed with sodium thiosulfate (3 × 25 mL) and the aqueous layer was extracted with CHCl₃ (3 × 10 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. Purification by column chromatography (99:1 hexane:EtOAc) yielded 1,6-dibromo-2,7-
dimethoxynaphthalene (86) (1.27 g, 35%) as a white, crystalline solid, followed by 1,8-dibromo-2,7-dimethoxynaphthalene (85) (200 mg, 10%). Further elution (9:1 hexane:EtOAc) afforded recovered starting material 84 (290 mg, 8%). 86: Rf 0.56 (95:5 hexane:EtOAc); mp 125-127 °C; νmax (KBr)/cm⁻¹ 1616, 1595, 1497, 1397, 1351, 1297, 1261, 1230, 1184, 1156, 1072, and 1035; δH(300 MHz; CDCl₃) 4.02 (3 H, s, COCH₃), 4.06 (3 H, s, COCH₃), 7.14 (1 H, d, J 9.0, ArH), 7.51 (1 H, s, ArH), 7.66 (2 H, d, J 8.9, ArH) and 7.99 (1 H, s, ArH); δH(300 MHz; d₆-DMSO) 3.98 (3 H, s, COCH₃), 4.00 (3 H, s, COCH₃), 7.41 (1 H, d, J 9.0, ArH), 7.44 (1 H, s, ArH), 7.93 (2 H, d, J 9.0, ArH) and 8.29 (1 H, s, ArH); δC(75 MHz, CDCl₃) 56.2 (CH₃, OCH₃), 56.8 (CH₃, OCH₃), 105.3 (CH), 107.1 (C), 111.5 (CH), 111.6 (C), 125.3 (C), 127.6 (CH), 132.2 (CH), 133.5 (C), 154.5 (C) and 155.1 (C); m/z (EI) 343.9035 (M⁺, C₁₂H₁₀Br₂O₂ requires 343.9048), 348 (M⁺, 48%), 346 (100), 344 (50), 303 (28), 288 (10), 260 (8), and 113 (10).

1,8-Dibromo-2,7-dimethoxynaphthalene (85)

Using NBS/pyridine:

Dibromide 85 was prepared by modification of the literature procedure.⁶² A solution of NBS (1.89 g, 10.6 mmol) in chloroform (26.0 mL) was treated with pyridine (0.910 mL, 10.6 mmol) and the resulting solution was refluxed for 1 h. 2,7-Dimethoxynaphthalene (84) (500 mg, 2.66 mmol) in chloroform (1.90 mL) was added dropwise to the resulting orange solution over 10 min. The mixture was refluxed for 9 h, cooled and evaporated under reduced pressure. Column chromatography (95:5 hexane:EtOAc) yielded the dibromide 85 (0.380 g, 41%) as a light brown solid. Further elution (9:1 hexane:EtOAc) afforded 84 (160 mg, 32%); Rf 0.14 (9:1 hexane:EtOAc); mp 129-130 °C; νmax (KBr)/cm⁻¹ 3008, 2937, 2936, 2838, 1611,
1503, 1459, 1328, 1263, 1163 and 1056; $\delta_H$(300 MHz; CDCl$_3$) 4.02 (6 H, s, COCH$_3$), 7.16 (2 H, d, J 9.0, ArH) and 7.74 (2 H, d, J 9.0, ArH); $\delta_C$(75 MHz, CDCl$_3$) 57.1 (CH$_3$, OCH$_3$), 105.8 (C), 111.5 (CH), 127.3 (C), 130.0 (CH), 131.5 (C) and 156.3 (C); m/z (EI) 343.9039 (M$^+$, C$_{12}$H$_{10}$Br$_2$O$_2$ requires 343.9048), 348 (M$^+$, 51%), 346 (100%), 344 (36), 288 (8), 250 (8), 235 (15), 222 (5), 179 (7), 158 (15), 113 (11), 100 (7) and 74 (6).

3,8-Dimethoxynaphtho[1,8-cd][1,2]dithiole (87)

A solution of n-BuLi in hexanes (1.30 M, 1.78 mL, 2.31 mmol) was added dropwise to a solution of 1,8-dibromo-2,7-dimethoxynaphthalene (85) (400 mg, 1.16 mmol) in Et$_2$O (5.00 mL) over 10 min at room temperature. The mixture was stirred for 45 min. Sulfur (0.075 g, 2.34 mmol) was added and stirred for an additional 2 h. The organic phase was extracted with Et$_2$O (3 × 10 mL). The combined organic layers were dried over MgSO$_4$ and the solvent was removed under reduced pressure. Purification of the residue by column chromatography (9:1 hexane:EtOAc) yielded disulfide 87 (0.120 g, 42%) as a red solid. $R_f$ 0.29 (9:1 hexane: EtOAc); mp 119-120 °C (ethanol); $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 2937, 2834 (OCH$_3$), 1615, 1505, 1427, 1265 and 1061; $\delta_H$(300 MHz; CDCl$_3$) 3.95 (6 H, s, COCH$_3$), 7.00 (2 H, d, J 8.8, ArH) and 7.39 (2 H, d, J 8.8, ArH); $\delta_H$(300 MHz; acetone-d$_6$) 3.97 (6 H, s, COCH$_3$), 7.19 (2 H, d, J 8.9, ArH) and 7.52 (2 H, d, J 8.9, ArH); $\delta_C$(75 MHz, CDCl$_3$) 56.4 (CH$_3$, OCH$_3$), 112.6 (CH), 123.4 (CH), 126.1 (C), 126.2 (C), 137.5 (C) and 150.0 (C); m/z (EI) 250.0127 (M$^+$, C$_{12}$H$_{10}$O$_2$S$_2$ requires 250.0122), 235 (100%), 220 (40), 192 (9), 164 (10), 137 (4), 125 (6), 95 (3), 81 (12), 69 (25), 57 (7) and 43 (7).
Nitration of disulfide 50

Disulfide 50 was nitrated by modification of the literature procedure. To a solution of naphtho[1,8-cd][1,2]dithiole (50) (100 mg, 0.53 mmol) in freshly distilled acetic anhydride (0.10 mL) at -5 ºC was added dropwise a solution of cold conc. HNO₃ (23.4 μL, 0.53 mmol) in acetic anhydride (0.09 mL) over 10 min. The mixture was stirred at -5 ºC for 90 min and then poured into a solution of saturated aqueous NaHCO₃ (1.02 mL). The resulting solution was extracted with CH₂Cl₂ (3 × 10 mL) and washed with H₂O (3 × 5 mL) and brine (3 × 5 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. Column chromatography (9:1 hexane:EtOAc) yielded a mixture of 3-nitronaphtho[1,8-cd][1,2]dithiole (90) and 5-nitronaphtho[1,8-cd][1,2]dithiole (91) (46.0 mg, 37%). Rₜ 0.29 (9:1 hexane:EtOAc); HPLC (t = 0 → 40 min, 1:1 MeCN:H₂O): 90: Rₜ 28.13 min; mp 188-190 ºC; v max (neat)/cm⁻¹ 2921, 2849, 1594, 1543 (NO₂), 1497, 1464, 1422, 1325, 1263, 1201, 1160, 1134 and 1058; δH(300 MHz; CDCl₃) 7.48 (1 H, d, J 9.1, ArH), 7.55-7.68 (3 H, m, ArH) and 8.13 (1 H, d, J 9.1, ArH); m/z (EI) 234.9756 (M⁺ - C₁₀H₅NO₂S₂ requires 234.9762), 205 (14%), 189 (33), 183 (4), 177 (15), 169 (5), 155 (7), 145 (27), 133 (3), 127 (11), 113 (14), 99 (19), 85 (54), 71 (72), 57 (100), 49 (8) and 43 (62). 91: Rₜ 25.86 min; mp 180-182 ºC; v max (neat)/cm⁻¹ 2918, 2849, 1535 (NO₂), 1493, 1472, 1377 (NO₂), 1279, 1241, 1211, 1164, 1133, 1066 and 1039; δH(300 MHz; CDCl₃) 7.17 (1 H, d, J 8.5, ArH), 7.37 (1 H, d, J 7.7, ArH), 7.58 (1 H, dd, J 7.7 and 8.6, SCCHCHCH), 8.34 (1 H, d, J 8.4, ArH) and 8.50 (1 H, d, J 9.0, ArH); m/z (EI) 234.9769 (M⁺ - C₁₀H₅NO₂S₂ requires 234.9762), 205 (6%), 189 (17), 169 (5), 155 (6), 145 (11), 127 (11), 113 (13), 99 (18), 85 (57), 71 (78), 57 (100), 49 (13), 43 (76).
1,2,3-Trithiaphenalene 2-oxide (49)

![Chemical Structure](image)

Trisulfide-2-oxide 49 was prepared according to the literature procedure. A solution of disulfide 50 (1.34 g, 7.05 mmol) in dry THF (1.40 mL) was added to an ice-cold suspension of NaBH₄ (400 mg, 10.6 mmol) in EtOH (2.20 mL) at 5 °C, and stirred for 1 h. The mixture was quenched with 10% HCl (10 mL). The aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL) and the combined organic layers were washed with water (3 × 10 mL), dried over MgSO₄ and concentrated in vacuo to give a white, crystalline solid. The solid was dissolved in Et₂O (235 mL) and transferred to a dropping funnel with pyridine (0.65 mL, 8.04 mmol). The mixture was added dropwise over 30 min to a solution of SOCl₂ (0.75 mL, 10.2 mmol) in Et₂O (93.0 mL) at 0 °C and was stirred for 4 h warming to room temperature. The reaction was quenched with 10% H₂SO₄ (35.0 mL), extracted with Et₂O (3 × 10 mL) and washed with brine (3 × 10 mL). The organic layers were combined, dried over MgSO₄, concentrated in vacuo and purified by column chromatography (60-80 pet ether) to afford disulfide 50 (0.331 g, 25%). Further elution (7:3 60-80 pet ether:Et₂O) afforded the title compound which was recrystallised from EtOH to afford 49 (1.01 g, 60%) as a yellow, crystalline solid.

RF 0.31 (7:3 60-80 pet ether:Et₂O); mp 119-121 °C (EtOH); λ_max (MeCN)/nm 364 (ε/dm³ mol⁻¹ cm⁻¹ 6 620) and 249 (19 800); ν_max (KBr)/cm⁻¹ 2360, 1546 (aromatic), 1491, 1421, 1327, 1204 and 1093 (SO); δ_H (300 MHz; CDCl₃) 7.54 (2 H, t, J 7.6, Ar_H), 7.62 (2 H, dd, J 7.3 and 1.6, Ar_H) and 7.94 (2 H, dd, J 7.9 and 1.6, Ar_H); δ_H (300 MHz; CD₂Cl₂) 7.56-7.65 (4 H, m, Ar_H) and 7.97 (2 H, dd, J 7.7 and 1.8, Ar_H); δ_H (300 MHz; C₆D₆) 6.84 (2 H, t, J 7.8, Ar_H) and 7.08 (2 H, dd, J 7.3 and 1.0, Ar_H) and 7.24 (2 H, dd, J 8.2 and 0.8, Ar_H); δ_C (75 MHz; CDCl₃) 122.3 (C), 124.2 (C), 126.7 (CH), 131.3 (CH), 132.2 (CH) and 134.9 (C); δ_C (75 MHz; CD₂Cl₂) 122.7 (C), 124.5 (C), 127.1 (CH), 131.6 (CH), 132.6 (CH)
and 135.1 (C); m/z (ESI) 260.9475 ([M + Na]+, C₁₀H₆OS₃Na requires 260.9478), 261.0 (100%).

**Literature data:** The maximum (nujol)/cm⁻¹ 1097 (SO); δ_H (360 MHz; CDCl₃) 7.56 (2 H, t, J 7.6, ArH), 7.60 (2 H, dd, J 7.3 and 1.5, ArH) and 7.93 (2 H, dd, J 8.0 and 1.5, ArH); δ_C (90 MHz; CDCl₃) 122.2 (CH), 124.2 (CH), 126.8 (CH), 131.3 (C), 132.3 (C) and 134.9 (C); m/z (EI) 238.3371 (M⁺, C₁₀H₆OS₃ requires 238.3368), 208 (44%), 134 (55), 106 (100), 102 (65), 76 (23) and 51 (10).

4,9-Di-tert-butyl-1,2,3-trithiaphenalene 2-oxide (58)

![Chemical structure](image)

Trisulfide-2-oxide 58 was prepared according to the literature procedure. Disulfide 65 (700 mg, 2.31 mmol) was dissolved in THF (4.05 mL) at room temperature. LiAlH₄ (176 mg, 4.23 mmol) was added and the reaction mixture was refluxed for 1 h. The reaction mixture was allowed to cool to room temperature and then quenched with H₂O (0.080 mL) and 10 M HCl (0.220 mL). The aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL), the combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue (703 mg, 2.31 mmol) was dissolved in Et₂O (77.0 mL) and transferred to a dropping funnel with pyridine (0.220 mL, 2.63 mmol). The mixture was added dropwise over 30 min to a solution of SOCl₂ (0.240 mL, 3.35 mmol) in Et₂O (30.0 mL) at 0 °C and allowed to stir for 4 h warming to room temperature. The reaction was quenched with 10% H₂SO₄ (3.75 mL), extracted with Et₂O (3 × 5 mL) and washed with brine (2 × 5 mL). The organic layers were combined, dried over MgSO₄ and concentrated under reduced pressure. Chromatography on florisil® (98:2 hexane:Et₂O) afforded disulfide 65 (0.607 g, 87%) followed by (95:5 hexane:Et₂O) to afford the *title compound* 58 (0.107 g, 13%) as a yellow, crystalline
solid. \( R_f \) 0.27 (95:5 hexane:Et\(_2\)O); mp 154-156 °C (CH\(_2\)Cl\(_2\)/hexane); \( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 2961 (CH), 1464, 1391, 1360, 1245 and 1106 (SO); \( \delta_H \) (300 MHz; CDCl\(_3\)) 1.62 (18 H, s, C(CH\(_3\))\(_3\)) and 7.75 (4 H, s, SCCC\( \text{H} \) and SCCCC\( \text{H} \)); \( \delta_C \) (75 MHz; CDCl\(_3\)) 31.9 (CH\(_3\)), 37.7 (C, C(CH\(_3\))\(_3\)), 121.6 (C), 125.7 (CH), 129.0 (CH), 131.0 (C), 131.9 (C) and 151.1 (C); \( m/z \) (ESI) 373.0740 ([M + Na]\(^+\), C\(_{18}\)H\(_{22}\)OS\(_3\)Na requires 373.0731), 341 (92%), 319 (15) and 302 (24).

4,9-Dimethoxy-1,2,3-trithiaphenalene 2-oxide (103)

\[ \text{\begin{tikzpicture}[baseline=-0.5ex]
\node (A) at (0,0) {$S$};
\node (B) at (1,0) {$S$};
\node (C) at (2,0) {$O$};
\node (D) at (3,0) {$S$};
\node (E) at (4,0) {$O$};
\node (F) at (5,0) {$S$};
\node (G) at (6,0) {$O$};
\node (H) at (7,0) {$S$};
\node (I) at (8,0) {$O$};
\node (J) at (9,0) {$S$};
\node (K) at (10,0) {$O$};
\node (L) at (11,0) {$S$};
\node (M) at (12,0) {$O$};
\node (N) at (13,0) {$S$};
\node (O) at (14,0) {$O$};
\node (P) at (15,0) {$S$};
\node (Q) at (16,0) {$O$};
\node (R) at (17,0) {$S$};
\node (S) at (18,0) {$O$};
\node (T) at (19,0) {$S$};
\node (U) at (20,0) {$O$};
\node (V) at (21,0) {$S$};
\node (W) at (22,0) {$O$};
\node (X) at (23,0) {$S$};
\node (Y) at (24,0) {$O$};
\end{tikzpicture}} \rightarrow \text{\begin{tikzpicture}[baseline=-0.5ex]
\node (A) at (0,0) {$S$};
\node (B) at (1,0) {$S$};
\node (C) at (2,0) {$O$};
\node (D) at (3,0) {$S$};
\node (E) at (4,0) {$S$};
\node (F) at (5,0) {$O$};
\node (G) at (6,0) {$S$};
\node (H) at (7,0) {$O$};
\node (I) at (8,0) {$S$};
\node (J) at (9,0) {$O$};
\node (K) at (10,0) {$S$};
\node (L) at (11,0) {$O$};
\node (M) at (12,0) {$S$};
\node (N) at (13,0) {$O$};
\node (O) at (14,0) {$S$};
\node (P) at (15,0) {$O$};
\node (Q) at (16,0) {$S$};
\node (R) at (17,0) {$O$};
\node (S) at (18,0) {$S$};
\node (T) at (19,0) {$O$};
\node (U) at (20,0) {$S$};
\node (V) at (21,0) {$O$};
\node (W) at (22,0) {$S$};
\node (X) at (23,0) {$O$};
\node (Y) at (24,0) {$S$};
\node (Z) at (25,0) {$O$};
\end{tikzpicture}} \]

A solution of disulfide 87 (1.00 g, 4.00 mmol) in dry THF (0.80 mL) was added to an ice cold suspension of NaBH\(_4\) (227 mg, 6.00 mmol) in EtOH (1.25 mL) at 5 °C. After stirring for 1 h the mixture was quenched with 10% HCl (10.0 mL). The aqueous phase was extracted with CH\(_2\)Cl\(_2\) (3 \times 10 mL) and the combined organic layers were washed with water (3 \times 10 mL), dried over Na\(_2\)SO\(_4\) and concentrated in vacuo to give a white, crystalline solid. The solid was dissolved in Et\(_2\)O (133 mL) and transferred to a dropping funnel with pyridine (0.37 mL, 4.56 mmol). The mixture was added dropwise over 30 min to a solution of SOCl\(_2\) (0.42 mL, 5.80 mmol) in Et\(_2\)O (52.7 mL) at 0 °C and was stirred for 4 h warming to room temperature. The reaction was quenched with 10% H\(_2\)SO\(_4\) (35.0 mL), extracted with Et\(_2\)O (3 \times 10 mL) and washed with brine (3 \times 10 mL). The organic layers were combined, dried over MgSO\(_4\), concentrated in vacuo and purified by column chromatography (9:1 hexane:Et\(_2\)O) to afford disulfide 87 (256 mg, 26%). Further elution (1:1 hexane:Et\(_2\)O) yielded the title compound which was recrystallised from EtOH to afford 103 (439 mg, 37%) as a yellow, crystalline solid. \( R_f \) 0.11 (1:1 hexane:Et\(_2\)O); mp 146-148 °C (EtOH); \( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 2933, 1601, 1508, 1455, 1325, 1268, 1163, 1084 (SO) and 1050; \( \delta_H \) (300 MHz; CDCl\(_3\)) 4.02 (6 H, s, COCH\(_3\)), 7.26 (2 H, d, J 9.0, Ar\( \text{H} \)) and 7.86 (2 H, d, J 9.1, Ar\( \text{H} \)); \( \delta_C \) (75 MHz, CDCl\(_3\)) 56.0 (CH\(_3\),...
OCH₃), 105.0 (C), 110.2 (CH), 124.8 (C), 125.1 (C), 130.5 (CH) and 155.1 (C); m/z (EI) 297.9786 (M⁺, C₁₂H₁₀O₃S₃ requires 297.9792), 250 (86), 235 (100%), 220 (44), 192 (12), 125 (6), 84 (13), 66 (8), and 48 (6).

2,5-Dihydro-3,4-dimethylthiophene 1-oxide (2)

\[
\begin{align*}
\text{S} & \quad \text{S} \\
\text{S} & \quad \text{O} \\
\text{S} & \quad \text{S}
\end{align*}
\]

Thermally:
Sulfoxide 2 was prepared according to the literature procedure.⁴² A solution of 2,3-dimethyl-1,3-butadiene (16) (0.71 mL, 6.30 mmol) and 1,2,3-trithiaphenalene 2-oxide (49) (150 mg, 0.630 mmol) in chlorobenzene (63.0 mL) was degassed for 15 min. The solution was refluxed for 10 h, until disappearance of compound 49 by TLC. The solvent was concentrated in vacuo and purification by column chromatography (60-80 pet ether) first yielded disulfide 50 (119 mg, 99%). Further elution (95:5 CH₂Cl₂:EtOH) afforded the sulfoxide 2 (80 mg, 98%) as a pale yellow oil. Rf 0.38 (95:5 CH₂Cl₂:EtOH); \( \nu_{\text{max}} \) (neat)/cm⁻¹ 1266 and 1029 (SO); \( \delta_{\text{H}} \) (300 MHz; CDCl₃) 1.77 (6 H, s, CH₃), 3.44 (2 H, d, \( J = 16.5 \), SCH) and 3.81 (2 H, d, \( J = 17.1 \), SCH); \( \delta_{\text{C}} \) (75 MHz; CDCl₃) 14.4 (CH₃, CCH₃), 64.3 (CH₂, OSC) and 126.0 (C, CCH₃); m/z (EI) 130.0454 (M⁺, C₆H₁₀OS requires 130.0452), 114 (11%), 111 (15), 99 (12), 82 (38), 67 (100), 54 (20) and 45 (6).

Literature data:²⁶ \( \nu_{\text{max}} \) (nujol)/cm⁻¹ 1050 (SO); \( \delta_{\text{H}} \) (400 MHz; CDCl₃) 1.71 (6 H, s, CH₃), 3.38 (2 H, d, \( J = 16.6 \), SCH) and 3.81 (2 H, d, \( J = 17.1 \), SCH); \( \delta_{\text{C}} \) (100 MHz; CDCl₃) 14.9 (CH₃, CCH₃), 64.6 (CH₂, OSC) and 126.4 (C, CCH₃); m/z (EI) 130 (M⁺, 83%), 113 (7), 99 (6), 82 (38), 67 (100) and 54 (21).
Photochemically:
A solution of 2,3-dimethyl-1,3-butadiene (16) (0.24 mL, 3.15 mmol) and 1,2,3-trithiaphenalene 2-oxide (49) (75.0 mg, 0.315 mmol) in chlorobenzene (31.5 mL) was degassed for 15 min in a water-cooled flask. The solution was irradiated with a sun lamp at room temperature for 3 h. The solution was concentrated in vacuo and purification of the residue by column chromatography (60-80 pet ether) first yielded disulfide 50 (56.0 mg, 93%). Further elution (95:5 CH₂Cl₂:EtOH) afforded the title compound 2 (23.0 mg, 55%).

2,5-dihydro-3,4-diphenylthiophene 1-oxide (3)

![Chemical Structure](image)

Sulfoxide 3 was prepared according to the literature procedure.²⁶ A solution of 2,3-diphenyl-1,3-butadiene (17) (0.325 mg, 1.58 mmol) and 1,2,3-trithiaphenalene 2-oxide (49) (150 mg, 0.630 mmol) in chlorobenzene (63.0 mL) was degassed for 15 min. The solution was refluxed for 5.75 h, until disappearance of compound 49 by TLC. The solution was concentrated in vacuo and purification of the residue by column chromatography (60-80 pet ether) first yielded disulfide 50 (110 mg, 92%). Further elution (99:1 CH₂Cl₂:EtOH) afforded sulfoxide 3 (104 mg, 65%) as a white solid. Rf 0.16 (99:1 CH₂Cl₂:EtOH); mp 132-133 °C; \( \nu_{max} \) (KBr)/cm⁻¹ 1025 (SO); \( \delta_t \) (300 MHz; CDCl₃) 4.12 (2 H, d, \( J = 16.6 \), SCH₂), 4.42 (2 H, d, \( J = 16.6 \), SCH₂) and 7.21-7.34 (10 H, m, ArH); \( \delta_c \) (75 MHz; CDCl₃) 64.3 (CH₂, SCH₂), 127.8 (CH), 128.3 (2 × CH), 128.5 (2 × CH), 131.8 (C) and 135.4 (C); \( m/z \) (EI) 254.0771 (M⁺, C₁₆H₁₄OS requires 254.0765), 236 (7%), 205 (100), 191 (19), 179 (5), 165 (8), 152 (3), 128 (13), 115 (11), 103 (6), 91 (28), 77 (13) and 51 (7).

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**Literature data:** mp 134-135 °C, \( v_{\text{max}} \) (nujol)/cm\(^{-1} \) 1038 (SO), \( \delta_{\text{H}} \) (360 MHz; CDCl\(_3\)) 4.05 (2 H, d, \( J \) 16.2, SCH\(_2\)), 4.40 (2 H, d, \( J \) 16.2, SCH\(_2\)) and 7.15-7.25 (10 H, m, ArH); \( \delta_{\text{C}} \) (90 MHz; CDC\(_13\)) 64.8 (CH\(_2\), SCH\(_2\)), 128.4-129.0 (10 \( \times \) CH), 132.4 (2 \( \times \) C) and 135.9 (2 \( \times \) C); \( m/z \) (EI) 254.0759 (M\(^+\), C\(_{16}\)H\(_{14}\)OS requires 254.0765), 236 (16%), 205 (68), 190 (100), 178 (14), and 86 (59).

2,5-dihydro-3-methylthiophene 1-oxide (21)

Sulfoxide 21 was prepared according to the literature procedure.\(^{26}\) 1,2,3-Trithiaphenalene 2-oxide (49) (25.0 mg, 0.105 mmol) was degassed in chlorobenzene (10.5 mL). Isoprene (18) (0.263 mL, 2.63 mmol) was added and the resulting solution refluxed for 8 h, until disappearance of 49 by TLC. The solvent was removed under reduced pressure and purification of the residue by column chromatography (60-80 pet ether) first afforded 50 (19.2 mg, 96%). Further elution (99:1 CH\(_2\)Cl\(_2\):EtOH) afforded 21 (11.9 mg, 98%) as an oil. \( R_f \) 0.21 (99:1 CH\(_2\)Cl\(_2\):EtOH); \( v_{\text{max}} \) (neat)/cm\(^{-1} \) 1029 (SO); \( \delta_{\text{H}} \) (300 MHz; CDCl\(_3\)) 1.92 (3 H, s, CCH\(_3\)), 3.38-3.53 (2 H, m), 3.73-3.87 (2 H, m) and 5.60 (1 H, s, CH\(_2\)CH); \( \delta_{\text{C}} \) (75 MHz; CDC\(_13\)) 16.7 (CH\(_3\), CCH\(_3\)), 59.9 (CH\(_2\)), 62.9 (CH\(_2\)), 119.0 (CH, CH\(_2\)CH) and 135.5 (C, CCH\(_3\)); \( m/z \) (EI) 116 (M\(^+\), 87%), 99 (8), 85 (4), 67 (100), 53 (38) and 42 (9).

**Literature data:** \( v_{\text{max}} \) (CH\(_2\)Cl\(_2\))/cm\(^{-1} \) 1087 (SO); \( \delta_{\text{H}} \) (360 MHz; CDCl\(_3\)) 1.85 (3 H, s, CCH\(_3\)), 3.31-3.46 (2 H, m), 3.66-3.80 (2 H, m) and 5.53 (1 H, s); \( \delta_{\text{C}} \) (100 MHz; CDC\(_13\)) 18.9 (CH\(_3\)), 62.2 (CH\(_2\)), 65.2 (CH\(_2\)), 121.4 (CH) and 137.7 (C, CCH\(_3\)); \( m/z \) (EI) 116 (M\(^+\), 100%), 99 (16), 85 (21), 68 (45), 67 (92) and 53 (62).
3-(4’-Methyl-3’-pentenyl)-2,5-dihydrothiophene 1-oxide (22)

Sulfoxide 22 was prepared according to the literature procedure.26 A solution of myrcene (19) (0.090 mL, 0.525 mmol) and 1,2,3-trithiaphenalene 2-oxide (49) (0.050 mg, 0.210 mmol) in chlorobenzene (21.0 mL) was degassed for 15 min. The solution was refluxed for 6 h, until disappearance of compound 49 by TLC. The solution was concentrated in vacuo and purification by column chromatography (60-80 pet ether) first yielded 50 (35.9 mg, 90%). Further elution (99:1 CH₂Cl₂:EtOH) afforded sulfoxide 22 (35.2 mg, 91%) as a pale yellow oil. R_f 0.35 (99:1 CH₂Cl₂:EtOH); ν_max (neat)/cm⁻¹ 1032 (SO); δ_H (300 MHz; CDCl₃) 1.59 (3 H, s, CH₃), 1.66 (3 H, s, CCH₃), 2.17-2.27 (4 H, m, CCH₂CH₂CH), 3.41 (1 H, d, J 17.0, SCH), 3.50 (1 H, d, J 17.1, SCH), 3.74 (1 H, d, J 17.0, SCH), 3.83 (1 H, d, J 17.1, SCH), 5.07 (1 H, br t, J 5.0, CH₃CCH) and 5.59 (1 H, br s, SCH₂CH); δ_C (75 MHz; CDCl₃) 17.7 (CH₃), 25.6 (CH₃), 26.2 (CH₂), 31.2 (CH₂), 59.7 (CH₂), 61.6 (CH₂), 117.9 (CH), 123.0 (CH), 132.6 (C) and 139.9 (C); m/z (EI) 184.0930 (M⁺, C₁₀H₁₆OS requires 184.0922), 166 (14%), 135 (14), 121 (7), 116 (10), 110 (22), 97 (86), 93 (12), 79 (8), 69 (100), 53 (19) and 45 (14).

**Literature data:**26 ν_max (CH₂Cl₂)/cm⁻¹ 1032 (SO); δ_H (300 MHz; CDCl₃) 1.61 (3 H, s, CCH₃), 1.69 (3 H, s, CCH₃), 2.20-2.29 (4 H, m, CCH₂CH₂CH), 3.43 (1 H, d, J 17.0, SCH), 3.52 (1 H, d, J 17.1, SCH), 3.75 (1 H, dd, J 16.9 and 1.2, SCH), 3.84 (1 H, d, J 17.1, SCH), 5.09 (1 H, br s, CH₃CCH) and 5.61 (1 H, br s, SCH₂CH); δ_C (90 MHz; CDCl₃) 18.1 (CH₃), 26.1 (CH₃), 26.7 (CH₂), 31.7 (CH₂), 60.1 (CH₂), 62.1 (CH₂), 118.4 (CH), 123.4 (CH), 133.0 (C) and 140.3 (C); m/z (EI) 184.0921 (M⁺, C₁₀H₁₆OS requires 184.0922), 135 (30%), 121 (17), 116 (24), 93 (33) and 69 (100).
Attempted reaction of trisulfide-2-oxide (49) with cyclooctadiene

\[
\begin{array}{c}
\text{S-S-S} \\
\downarrow \\
49
\end{array} \rightleftharpoons 
\begin{array}{c}
\text{S-S-O} \\
\downarrow \\
50
\end{array} \rightleftharpoons 
\begin{array}{c}
\text{S-S} \\
\downarrow \\
\text{O}
\end{array}
\]

A solution of cyclooctadiene (0.07 mL, 0.525 mmol) and 1,2,3-trithiapentalene 2-oxide (49) (50.0 mg, 0.420 mmol) in chlorobenzene (42.0 mL) was degassed for 15 min. The solution was refluxed for 12 h. The solution was concentrated \textit{in vacuo} and purification of the residue by column chromatography (60-80 pet ether) yielded disulfide 50 (79 mg, 99%).

A solution of cyclooctadiene (0.65 mL, 5.26 mmol) and 1,2,3-trithiapentalene 2-oxide (49) (50.0 mg, 0.260 mmol) in chlorobenzene (26.0 mL) was degassed for 15 min in a water-cooled flask. The solution was irradiated with a sun lamp at room temperature for 2 h. The solution was concentrated \textit{in vacuo} and purification of the residue by column chromatography (60-80 pet ether) yielded disulfide 50 (49.4 mg, 100%).

(9H-fluoren-9-yl)triphenylphosphonium bromide (109)

\[
\begin{array}{c}
\text{Br} \\
\downarrow \\
108
\end{array} \rightleftharpoons 
\begin{array}{c}
\text{Br} \\
\downarrow \\
\text{PPh}_3
\end{array} \rightleftharpoons 
\begin{array}{c}
\text{Br} \\
\downarrow \\
109
\end{array}
\]

Phosphonium salt 109 was prepared according to the literature procedure.\textsuperscript{80} A solution of 9-bromofluorene (108) (2.00 g, 8.16 mmol) and PPh\textsubscript{3} (2.35 g, 8.98 mmol) in acetone (81.6 mL) was stirred overnight at room temperature. The resulting precipitate was filtered to yield (9H-fluoren-9-yl)triphenylphosphonium bromide (109) (1.82 g, 44%) as a white solid.

mp 287-288 °C; \(v_{\text{max}}\) (KBr)/cm\textsuperscript{-1} 2995, 2794, 1585, 1434, 1149 and 1109; \(\delta_H\) (300 MHz; d\textsubscript{6}-DMSO) 7.16 (2 H, d, J 7.8), 7.26 (2 H, t, J 7.5), 7.41-7.42 (1 H, m), 7.46 (2 H, d, J 6.8),
7.63-7.69 (6 H, m) and 7.77-7.86 (11 H, m); δ$_c$(75 MHz; $d_6$-DMSO) 40.8 (CH), 117.1 (d, $J$ 84.8, C), 121.0 (CH), 126.0 (CH), 127.7 (CH), 129.5 (CH), 130.0 (d, $J$ 12.1, CH), 133.3 (d, $J$ 9.1 CH), 134.8 (C), 134.9 (CH) and 141.9 (C); δ$_p$(121 MHz; $d_6$-DMSO) 30.2; m/z (EI) 426.1531 ([M - HBr]$^+$, C$_{31}$H$_{23}$P requires 426.1537), 262 (10%), 241 (21), 213 (5) and 183 (18).

**Literature data:**$^{80}$ mp 289-291 °C.

Fluoren-9-ylidene-triphenyl-$\lambda^5$-phosphane (110)

Ylide 110 was prepared by a general literature procedure.$^{81}$ (9$H$-Fluoren-9-yl)triphenylphosphonium bromide (109) (1.35 g, 2.66 mmol) was dissolved in boiling EtOH (100 mL). The solution was removed from the heat and NH$_4$OH solution (0.37 mL, 2.93 mmol) was added whilst still warm, turning the solution yellow. The mixture was allowed to stir overnight cooling to room temperature. The resulting yellow precipitate was filtered and washed with ice cold EtOH (3 × 5 mL) to afford the ylide 110 (904 mg, 80%). mp 273-275 °C; $v_{\text{max}}$(KBr)/cm$^{-1}$ 3036, 1583, 1464, 1430, 1306, 1277, 1210, 1185, 1151, 1110, 1095, 996, 749, 725 and 692; δ$_h$(300 MHz; $d_6$-DMSO) 6.16 (2 H, d, $J$ 8.0, ArH), 6.72-6.78 (2 H, m, ArH), 6.84 (2 H, t, $J$ 7.2, ArH), 7.63-7.81 (15 H, m, ArH) and 8.04 (2 H, d, $J$ 7.5, ArH); δ$_c$(75 MHz; $d_6$-DMSO) 115.5 (CH), 115.9 (CH), 119.1 (CH), 122.6 (CH), 124.7 (d, $J$ 88.7, C), 129.5 (d, $J$ 11.9, CH), 133.1 (CH), 133.7 (d, $J$ 10.1 CH), 140.6 (C), 141.0 (CH) and 141.2 (C); δ$_p$(121 MHz; $d_6$-DMSO) 7.1; m/z (EI) 426.1547 (M$^+$, C$_{31}$H$_{23}$P requires 426.1537), 262 (10%), 241 (21), 213 (5) and 183 (18).
9-ethyldiene-9H-fluorene (111)

Olefin 111 was prepared by a literature procedure.\textsuperscript{81} A solution of ylide 110 (210 mg, 0.491 mmol) and acetaldehyde (0.072 mL, 0.246 mmol) in CHCl\textsubscript{3} was refluxed for 60 h. The solution was allowed to cool to room temperature and the solvent was removed under reduced pressure. Purification by column chromatography (60-80 pet ether) afforded 9-ethyldiene-9H-fluorene (111) (18.0 mg, 38%). R\textsubscript{f} 0.48 (60-80 pet ether); \nu\textsubscript{max} (KBr)/cm\textsuperscript{-1} 2924, 2854, 1648 (C=C) and 1445; \delta\textsubscript{H}(300 MHz; CDCl\textsubscript{3}) 2.41 (3 H, d, J 7.6, CHCH\textsubscript{3}), 6.88 (1 H, q, J 7.5, CHCH\textsubscript{3}), 7.29-7.44 (4 H, m, ArH), 7.66 (1 H, d, J 6.7, ArH), 7.72 (1 H, d, J 6.7, ArH), 7.77 (1 H, d, J 6.8, ArH) and 7.91 (1 H, d, J 6.9, ArH); \delta\textsubscript{C}(75 MHz, CDCl\textsubscript{3}) 15.3 (CH\textsubscript{3}), 119.4 (CH), 119.6 (CH), 119.8 (CH), 124.8 (CH), 125.0 (CH), 126.8 (2 \times CH), 127.3 (CH), 127.6 (CH), 136.6 (C), 137.7 (C), 138.5 (C), 139.3 (C) and 140.7 (C); m/z (EI) 192.0932 (M\textsuperscript{+}, C\textsubscript{15}H\textsubscript{12} requires 192.0939), 189 (27%), 165 (37), 94 (11) and 82 (7).

**Literature data:**\textsuperscript{82, 249} \nu\textsubscript{max} (CCl\textsubscript{4}/CS\textsubscript{2})/cm\textsuperscript{-1} 3065, 1650, 1447, 1294, 1033, 935, 827, 781, 771, 739, 729 and 621; \delta\textsubscript{H}(400 MHz; CDCl\textsubscript{3}) 2.26 (3 H, d, J 7.6, CHCH\textsubscript{3}), 6.72 (1 H, q, J 7.6, CHCH\textsubscript{3}), 7.20 (1 H, m, ArH), 7.24 (2 H, m, ArH), 7.28 (1 H, m, ArH), 7.54 (1 H, m, ArH), 7.62 (1 H, m, ArH), 7.67 (1 H, m, ArH) and 7.79 (1 H, br d, J 7.1, ArH); \delta\textsubscript{C}(101 MHz, CDCl\textsubscript{3}) 15.2 (CH\textsubscript{3}), 119.4 (CH), 119.58 (CH), 119.74 (CH), 124.8 (CH), 125.0 (CH), 126.79 (CH), 126.81 (CH), 127.3 (CH), 127.5 (CH), 136.5 (C), 137.7 (C), 138.5 (C), 139.3 (C) and 140.7 (C); m/z (EI) 192 (M\textsuperscript{+}, 100%), 191 (64), 190 (11), 189 (27), 187 (9), 166 (4), 165 (35), 164 (4), 163 (4), 95 (13), 83 (12), 82 (6), 45 (4) and 41 (4).
Reaction of trisulfide oxide 49 with ylide 110

A solution of trisulfide-2-oxide 49 (0.180 mL, 0.756 mmol) and ylide 110 (650 mg, 1.51 mmol) in PhCl (75.6 mL) was degassed for 15 min. The solution was refluxed for 2 h, until disappearance of compound 49 by TLC. The solution was concentrated in vacuo and purification of the residue by column chromatography (60-80 pet ether) first yielded disulfide 50 (209 mg, 84%). Further elution (95:5 60-80 pet ether:Et₂O) yielded a mixture of 9-fluorenone (112) and fluorenethione S-oxide (113) (58.0 mg). Further purification by HPLC yielded 112 (27 mg, 20%) followed by a mixture of 113 and an unidentified compound (20 mg). Rₜ 0.25 (95:5 60-80 pet ether:Et₂O). Analysis on crude mixture: νₘₐₓ (KBr)/cm⁻¹ 1718, 1686, 1655, 1599, 1560, 1448, 1299, 1120 (CSO), 1087 and 1018 (CSO); HPLC (t = 0 → 40 min, 0 → 100% H₂O in MeCN): Fluorenone 112: Rₜ 29.56 min; δₜ(300 MHz; CDCl₃) 7.27-7.32 (2 H, m, ArH), 7.46-7.53 (4 H, m, ArH) and 7.66 (2 H, d, J 7.3, ArH); m/z (EI) 180 (M⁺, 100%), 152 (29) and 79 (24). Fluorenethione S-oxide 113 and unidentified compound: Rₜ 32.97 min; peak assignable to 113 δₜ(300 MHz; CDCl₃) 8.65 (1 H, d, J 7.7, ArH) and 7.16-7.66 (11 H, m, assignable to 7 H for 113); m/z (EI) 212.0288 (M⁺, C₁₃H₈OS requires 212.0299), 196 (43), 184 (69), 163 (26), 152 (34) and 139 (11).

**Literature data:** 83, 84, 250-253 9-Fluorenone 112: mp 85 °C (MeOH); νₘₐₓ (KBr)/cm⁻¹ 1720 (CO); δₜ(CDCl₃) 7.25 (2 H, m, ArH), 7.43 (4 H, m, ArH) and 7.63 (2 H, d, J 7.6, ArH); δₚ(CDCl₃) 120.2, 124.1, 128.9, 134.0, 134.6, 144.3 and 193.7; m/z (EI) 180 (M⁺).

Fluorenethione-S-oxide 113: mp 103-108 °C (benzene/hexane); νₘₐₓ (KBr)/cm⁻¹ 1119 (CSO) and 1020 (CSO); δₜ(300 MHz, CDCl₃) 7.17 (1 H, m, ArH), 7.30 (1 H, m, ArH), 7.36 (1 H, m, ArH), 7.43 (1 H, m, ArH), 7.56 (1 H, m, ArH), 7.58 (1 H, m, ArH), 7.66 (1 H, dm, J 7.6, ArH) and 8.64 (1 H, dm, J 7.6, ArH); δₚ(CDCl₃) 179.21 (CO); m/z (EI) 212 (M⁺).
General kinetic experimental

A solution of 2,3-dimethyl-1,3-butadiene (2) and 1,2,3-trithiaphenalene 2-oxide (49) in octane was degassed for 15 min. The solution was refluxed for 10 h with samples (300 µL) removed from the reaction mixture every 30 min. The samples (5 µL) were analysed by HPLC. HPLC (t = 0 → 25 min, 60:40 MeCN:H₂O): 2 Rₜ 5.65 min, 49 Rₜ 9.87 min, 16 Rₜ 12.29 min, 50 Rₜ 20.60 min.

Triphenylphosphine sulfide (126)

A solution of 1,2,3-trithiaphenalene 2-oxide (49) (72.6 mg, 0.340 mmol) in chlorobenzene (34.0 mL) was degassed in a sealed tube for 15 min. The solution was heated at 140 °C for 10 h, until disappearance of compound 49 by TLC and allowed to cool to room temperature. PPh₃ (40.0 mg, 0.152 mmol) was added to the mixture, which was stirred for 2 h at room temperature. The solution was concentrated in vacuo and purification of the residue by column chromatography (60-80 pet ether) first yielded 50 (52.0 mg, 90%). Further elution (95:5 60-80 pet ether:EtOAc) afforded triphenylphosphine sulfide (126) (40.0 mg, 90%). Rₜ 0.23 (95:5 60-80 pet ether:EtOAc); δ̇H(300 MHz; CDCl₃) 7.42-7.50 (9 H, m, ArH) and 7.69-7.76 (6 H, m, ArH); δ̇C(100 MHz; CDCl₃) 128.5 (d, J 12.5, CH), 131.5 (d, J 2.5, CH), 132.3 (d, J 10.6, CH) and 133.0 (d, J 85.3, C); m/z (EI) 294 (M⁺, 100%), 262 (17), 222 (7), 190 (8), 193 (8), 158 (8), 149 (20), 139 (17), 107 (11), 97 (7), 85 (5), 77 (11), 63 (6), 57 (17) and 43 (14).

Literature data:⁵⁵⁴ mp 161-163 °C; found: C, 73.37; H, 5.15. C₁₅H₁₅PS requires C, 73.45; H, 5.14%; ν_max(KBr)/cm⁻¹ 1440, 1105, 710, 690 and 640; δ̇H(300 MHz; CDCl₃) 7.25-7.50 (9 H, m) and 7.50-7.80 (6 H, m); δ̇C(75 MHz, CDCl₃) 128.5 (d, J 13), 131.5 (d, J 3), 132.2
(d, J 11) and 133.0 (d, J 85); \( \delta_p \) (121 MHz, CDCl\(_3\)) 43.4 (m); \( m/z \) (EI) 294.0635 (M\(^+\), C\(_{18}\)H\(_{15}\)PS requires 294.0632), 262 (15), 217 (15) and 183 (100).

Matrix isolation of sulfur monoxide

Trisulfide-2-oxide 49 (20 mg, 0.093 mmol) was heated from 50 °C \( \rightarrow \) 100 °C (5 \times 10\(^{-6}\) mbar) until sublimation occurred through a FVT tube at 700 °C. The product was deposited at 20 K with an Ar flow rate of ca. 2 mbar/min. \( v_{\text{max}} \) (Ar matrix, ca. 20 K, cm\(^{-1}\)) 1137.0 (\(^{32}\)S\(^{16}\)O) and 1125.0 (\(^{34}\)S\(^{16}\)O).

**Literature data:**\(^{89}\) \( v_{\text{max}} \) (Ar matrix, cm\(^{-1}\)) 1136.7 (\(^{32}\)S\(^{16}\)O) and 1125.9 (\(^{34}\)S\(^{16}\)O).

General procedure for the attempted radical trapping of trisulfide-2-oxide 49 thermally:

A solution of spin trap (table 4.1 for equiv.) and trisulfide-2-oxide 49 (50 mg, 0.210 mmol) in PhCl (21.0 mL) was degassed for 15 min. The sample was heated at reflux for 10 h. The solution was concentrated *in vacuo* and purification of the residue by column chromatography (60-80 pet ether) yielded 50 (table 4.1).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Radical trap</th>
<th>mass/mg (equiv.)</th>
<th>Time (h)</th>
<th>50 (%)</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>tert-butylcatechol</td>
<td>34.9 (1.0)</td>
<td>9.8</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>1, 4-benzoquinone</td>
<td>22.7 (1.0)</td>
<td>9.9</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>DPPH</td>
<td>207 (2.5)</td>
<td>10</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>TEMPO</td>
<td>82.0 (2.5)</td>
<td>10</td>
<td>95</td>
</tr>
</tbody>
</table>

**Table 4.1** Attempted radical trapping of trisulfide-2-oxide 49
Reaction of 1,2,3-trithiaphenalene 2-oxide (49) with cyclohepta-1,3,5-triene (7)

![Reaction Diagram]

A solution of cycloheptatriene (7) (0.11 mL, 1.05 mmol) and 1,2,3-trithiaphenalene 2-oxide (49) (100 mg, 0.42 mmol) in chlorobenzene (42.0 mL) was degassed for 15 min. The solution was refluxed for 6 h, until disappearance of compound 49 by TLC. The solution was concentrated in vacuo and purification of the residue by column chromatography (60-80 pet ether) yielded a mixture of dimer 8, disulfide 50 and trisulfide 138 (70.8 mg). The following yields were calculated by NMR analysis: disulfide 50 (55.0 mg, 69%), bicycloheptyl-2,4,6,2',4',6'-hexaene (8) (9.99 mg, 13%) and naphtho[1,8-de][1,2,3]trithiine (138) (5.85 mg, 4%). R_f 0.48 (60-80 pet ether); peaks assignable to bicycloheptyl-2,4,6,2',4',6'-hexaene (8): \( \delta_H(300 \text{ MHz}; \text{CDCl}_3) 1.99 (2 \text{ H, s}), 5.30 (2 \text{ H, d, } J = 3.9), 5.33 (2 \text{ H, d, } J = 3.9), 6.27-6.32 (4 \text{ H, m}) \) and 6.72 (4 \text{ H, t, } J = 3.0); peaks assignable to naphtho[1,8-de][1,2,3]trithiine (138): \( \delta_H(300 \text{ MHz}; \text{CDCl}_3) 7.43 (2 \text{ H, t, } J = 7.7, \text{ ArH}), 7.66 (2 \text{ H, dd, } J = 7.2 \text{ and } 1.1, \text{ ArH}) \) and 7.86 (2 \text{ H, dd, } J = 8.3 \text{ and } 1.0, \text{ ArH}).

**Literature data:**

*ditropyl 8:* mp 60-61 °C; \( \nu_{\text{max}} (\text{CCl}_4)/\text{cm}^{-1} 3016 \text{ and } 2833; \delta_H(400 \text{ MHz; CDCl}_3) 1.98 (2 \text{ H, br s}), 5.30 (2 \text{ H, d, } J = 4.03), 5.33 (2 \text{ H, d, } J = 4.03), 6.29 (2 \text{ H, t, } J = 3.15), 6.30 (2 \text{ H, t, } J = 2.67) \) and 6.72 (4 \text{ H, t, } J = 2.97); \( \delta_C(100 \text{ MHz, CDCl}_3) 42.0, 125.0, 125.7 \text{ and } 131.0; m/z (EI) 182 (M^+, 0.5%), 165 (8), 152 (4), 104 (16), 91 (100), 78 (19), 65 (15) \text{ and } 39 (11). 

*naphtho[1,8-de][1,2,3]trithiine (138):* mp 152-154 °C (hex); \( \nu_{\text{max}} (\text{CH}_2\text{Cl}_2)/\text{cm}^{-1} 1644; \delta_H(360 \text{ MHz; CDCl}_3) 7.42 (2 \text{ H, dd, } J = 8.0 \text{ and } 7.4), 7.64 (2 \text{ H, dd, } J = 7.2 \text{ and } 1.2), 7.85 (2 \text{ H, dd, } J = 8.2 \text{ and } 1.3); \delta_C(100 \text{ MHz; CDCl}_3) 116.4, 122.1, 125.2, 128.3, 129.2, 131.2, 133.3, 134.7, 135.8 \text{ and } 136.1; m/z (EI) 221.96316 (M^+, C_{10}H_6S_3 \text{ requires } 221.96317), 190 (87), 158 (15), 145 (32), 114 (40) \text{ and } 95 (59).
Alkene 140 was prepared according to the literature procedure.\textsuperscript{91} A solution of n-BuLi in hexanes (2.40 M, 7.48 mL, 17.9 mmol) was added to a solution of PPh\textsubscript{3}MeBr (6.42 g, 17.9 mmol) in THF (59.9 mL) at room temperature over 10 min. The resulting orange solution was stirred for 1.5 h at room temperature. Cyclopropyl(phenyl)methanone (139) (2.50 mL, 17.9 mmol) was added to the mixture over a period of 5 min and stirred for 1 h at room temperature. The solution was heated at 65 °C for 5 h and then allowed to cool to room temperature. A mixture of 1:1 hexane:Et\textsubscript{2}O (~30 mL) was added to the mixture and the resulting precipitate was filtered. The filtrate was evaporated under reduced pressure and the resulting crude oil was purified by column chromatography (60-80 pet ether) followed by distillation under reduced pressure (118 °C, 30 mmHg) to afford 140 (1.54 g, 54\%) as a clear oil. R\textsubscript{f} 0.65 (60-80 pet ether); \(\nu\text{max} (\text{neat})/\text{cm}^{-1}\) 3083, 3007, 1624 (C=C), 1495 and 1262; \(\delta\text{H}(300 \text{ MHz}; \text{CDCl}_3) 0.55-0.60 (2 \text{ H}, \text{ m}, \text{ CHCH}_2\text{CH}_2), 0.79-0.85 (2 \text{ H}, \text{ m}, \text{ CHCH}_2\text{CH}_2), 1.59-1.68 (1 \text{ H}, \text{ m}, \text{ CH}_2\text{CHC}), 4.92 (1 \text{ H}, \text{ s}, \text{ C}==\text{CH}_2), 5.26 (1 \text{ H}, \text{ s}, \text{ C}==\text{CH}_2), 7.22-7.35 (3 \text{ H}, \text{ m}, \text{ ArH}) \text{ and } 7.57-7.60 (2 \text{ H}, \text{ m}, \text{ ArH}); \delta\text{C}(75 \text{ MHz}; \text{CDCl}_3) 6.6 (\text{CH}, \text{ CCHCH}_2), 15.6 (\text{CH}, \text{ CCHCH}_2), 108.9 (\text{CH}_2, \text{ C}==\text{CH}_2), 126.0 (\text{CH}), 127.4 (\text{CH}), 128.1 (\text{CH}), 141.6 (\text{C}) \text{ and } 149.3 (\text{C}, \text{ CHC}==\text{CH}_2); m/z (\text{El}) 144.0945 (\text{M}^+, \text{ C}_{11}\text{H}_{12} \text{ requires } 144.0939), 129 (100\%), 115 (28), 103 (42), 91 (17), 77 (30), 71 (6), 66 (12), 63 (14) \text{ and } 51 (26).

\textbf{Literature data:}\textsuperscript{256, 257} \(\nu\text{max} (\text{neat})/\mu\) 12.80, 12.15, 11.98, 11.25, 10.68, 9.81, 9.55, 9.26, 7.96, 7.80, 7.25, 7.03, 6.98, 6.50, and 3.20; \(\delta\text{H}(\text{CDCl}_3) 0.40-0.49 (2 \text{ H}, \text{ m}, \text{ cp-cis-CH}_2), 0.64-0.74 (2 \text{ H}, \text{ m}, \text{ cp-trans-CH}_2), 1.47-1.58 (1 \text{ H}, \text{ m}, \text{ CH}_2\text{CHC}), 4.79 (1 \text{ H}, \text{ t}, J 1.2, \text{ C}==\text{CH}_2), 5.14 (1 \text{ H}, \text{ d}, J 0.84, \text{ C}==\text{CH}_2), 7.12-7.24 (3 \text{ H}, \text{ m}, \text{ ArH}) \text{ and } 7.43-7.48 (2 \text{ H}, \text{ m}, \text{ ArH});
\[ \delta_c(CDCl_3) \] 6.6 (CH\(_2\), CCHCH\(_2\)), 15.6 (CH, CCHCH\(_2\)), 108.9 (CH\(_2\), C=CH\(_2\)), 126.0 (CH), 127.4 (CH), 128.1 (CH), 141.5 (C) and 149.3 (C, CHC=CH\(_2\)); \( m/z \) (EI) 144 (M\(^+\), 68%).

3,4-Diphenyl-thiophene (142)

![Diagram of 3,4-Diphenyl-thiophene](image)

Thiophene 142 was prepared according to the literature procedure.\(^{26}\) Sulfoxide 3 (80.0 mg, 0.310 mmol) was dissolved in acetic anhydride (12.4 mL) and the resulting solution was refluxed for 3 h. The solution was removed in vacuo, the residue was diluted with CH\(_2\)Cl\(_2\) (10 mL), washed with saturated aqueous NaHCO\(_3\) (3 \(\times\) 10 mL) and extracted with CH\(_2\)Cl\(_2\) (3 \(\times\) 5 mL). The organic layers were combined, dried over Na\(_2\)SO\(_4\) and the solvent was removed in vacuo. Purification by column chromatography (60-80 pet ether) yielded thiophene 142 (58.0 mg, 80%) as a white, crystalline solid. R\(_f\) 0.47 (60-80 pet ether); mp 112-113 \(^\circ\)C; \( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 3099 and 1437; \( \delta_\text{H}(300 \text{ MHz}; CDCl}_3 \) 7.12-7.22 (12 H, m, ArH); \( \delta_\text{C}(75 \text{ MHz}; CDCl}_3 \) 124.0 (CH), 126.8 (CH), 128.1 (CH), 129.0 (CH), 136.5 (C) and 141.7 (C); \( m/z \) (EI) 236.0650 (M\(^+\), C\(_{16}\)H\(_{12}\)S requires 236.0660), 221 (18%), 208 (3), 202 (15), 189 (10), 165 (3), 117 (11), 110 (5), 104 (8), 89 (4), 63 (2) and 59 (2).

**Literature data:**\(^{26, 258}\) mp 112-113 \(^\circ\)C; \( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 1460, 850, 795, 770, 750, 730, 720 and 680; \( \delta_\text{H}(500 \text{ MHz}; CDCl}_3 \) 7.10-7.20 (12 H, m, ArH); \( \delta_\text{C}(90 \text{ MHz}; CDCl}_3 \) 124.4 (CH), 127.3 (CH), 128.5 (CH), 129.4 (CH), 136.5 (C) and 141.7 (C); \( m/z \) (EI) 236 (M\(^+\), 100%), 221 (15), 202 (8), 189 (13), 163 (3) and 89 (5).

Thiophene 142 was prepared according to the literature procedure.\(^{26}\) TFAA (0.036 mL, 0.260 mmol) was added dropwise over 1 min to sulfoxide 3 (59.0 mg, 0.230 mmol) in CH\(_2\)Cl\(_2\) (23.0 mL) at 0 \(^\circ\)C. The mixture was stirred for 5 min, washed with saturated aqueous
NaHCO₃ (3 × 10 mL) and extracted with CH₂Cl₂ (3 × 5 mL). The organic layers were combined, dried over Na₂SO₄ and the solvent removed in vacuo. Purification by column chromatography (60-80 pet ether) yielded thiophene 142 (58.0 mg, 80%) as a white, crystalline solid.

3-(4-Methyl-pent-3-enyl)-thiophene (143)

Thiophene 143 was prepared according to the literature procedure.²⁶ TFAA (0.170 mL, 1.20 mmol) was added dropwise over 1 min to a solution of sulfoxide 22 (200 mg, 1.09 mmol) in CH₂Cl₂ (109 mL) at 0 °C. The mixture was stirred for 10 min at 0 °C, washed with NaHCO₃ solution (3 × 5 mL) and extracted with CH₂Cl₂ (3 × 5 mL). The organic layers were combined, dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by column chromatography (pentane) to afford thiophene 143 (63.0 mg, 35%) as a clear oil. Rᵣ 0.57 (hexane); νₑₛₑₑₑ (neat)/cm⁻¹ 2966, 2924, 2854, 1450 and 1265; δ₁₁(300 MHz; CDCl₃) 1.58 (3 H, s, CH₃), 1.69 (3 H, s, CCH₃), 2.30 (2 H, ap. q, J 7.4, CHCH₂), 2.63-2.68 (2 H, m, CHCH₂CH₂), 5.17 (1 H, t with unresolved fine coupling, J 7.1, C(CH₃)₂CHCH₂), 6.94-6.96 (2 H, m, SCHCH and SCHC) and 7.24 (1 H, dd, J 4.8 and 3.0, SCHCH); δ₂(75 MHz; CDCl₃) 17.7 (CH₃), 25.7 (CH₃), 29.1 (CH), 30.4 (CH), 119.9 (CH), 123.7 (CH), 125.0 (CH), 128.3 (CH), 132.2 (C) and 142.8 (C); m/z (EI) 166.0812 (M⁺, C₁₀H₁₄S requires 166.0816), 110 (33%), 97 (100), 69 (69), 53 (10) and 45 (11).

**Literature data:**²⁶,⁹³ νₑₛₑₑₑ (neat)/cm⁻¹ 3110, 2980, 2935, 2860, 1442, 1378, 1240, 1104, 1079, 839 and 775; δ₁¹(360 MHz; CDCl₃) 1.49 (3 H, s, CCH₃), 1.60 (3 H, s, CCH₃), 2.18-2.25 (2 H, m, CHCH₂), 2.57 (2 H, t, J 7.3, CHCH₂CH₂), 5.05-5.15 (1 H, m, C(CH₃)₂CHCH₂), 6.85 (1 H,
d, $J$ 3.0, $SCHC$), 6.86 (1 H, d, $J$ 4.8, $SCHCH$) and 7.14 (1 H, dd, $J$ 4.8 and 3, $SCHCH$); 
$\delta$ (90 MHz; $CDCl_3$) 124.4, 127.3, 128.5, 129.4, 136.9 and 142.1; $m/z$ (EI) 236 (M$^+$, 100%), 221 (15), 202 (8), 189 (13), 163 (3) and 89 (5).

(5-Benzo[1,3]dioxol-5-yl-thiophen-2-yl)piperidin-1-yl-methanone (145)

A solution of piperine (540 mg, 1.89 mmol) and 1,2,3-trithiaphenalene 2-oxide (49) (150 mg, 0.630 mmol) in chlorobenzene (63.0 mL) was degassed for 15 min. The solution was refluxed for 14 h, until disappearance of 49 by TLC. The solvent was removed under reduced pressure and purification of the residue by column chromatography (60-80 pet ether) yielded disulfide 50 (111 mg, 93%). Further elution (60:40 60-80 pet ether:Et$_2$O) afforded thiophene 145 (43.3 mg, 22%) as a white, crystalline solid followed by a mixture of 144, 146 and 147 (120 mg, 23%, BRSM). Attempts to purify 144, 146 and 147 by HPLC proved unsuccessful.

145: $R_f$ 0.20 (50:50 60-80 pet ether:Et$_2$O); $v_{max}$ (KBr)/cm$^{-1}$ 2924, 2854, 1599 (CO) and 1455; 
$\delta$ (300 MHz; $CDCl_3$) 1.64-1.71 (6 H, m, NCH$_2$CH$_2$CH$_2$), 3.68-3.71 (4 H, m NCH$_2$), 6.00 (2 H, s, OCH$_2$O), 6.83 (1 H, d, $J$ 8.0, ArH), 7.07-7.08 (2 H, m, ArH), 7.12 (1 H, d, $J$ 1.6, ArH) and 7.20 (1 H, d, $J$ 3.8, ArH); $\delta$ (75 MHz; $CDCl_3$) 24.6 (2 $\times$ CH$_2$), 26.1 (CH$_2$), 101.3 (CH$_2$, 144)
OCH$_2$O), 106.5 (CH), 108.7 (CH), 120.0 (CH), 121.8 (CH), 127.9 (C), 129.4 (CH), 135.8 (C), 147.1 (C), 147.7 (C), 148.2 (C) and 163.2 (C); m/z (ES) 338.0830 ([M + Na]$^+$, C$_{17}$H$_{17}$NO$_3$SNa requires 338.0827), 338 (100%). (tentatively assigned as isomers of piperine): HPLC (t = 0 → 40 min, 0 → 100% H$_2$O in MeCN): R$_t$ 27.98, 28.33 and 30.20 min. Peaks assignable to piperine 144: 1.55-1.67 (br m), 3.59 (br s), 5.98 (s) and 6.42 (d, J 14.9), 6.98 (d, J 1.6).

Peaks assignable to isopiperine 146: 1.55-1.67 (br m), 3.59 (br s), 5.96 (s), 5.96 (d, J 11.4) and 7.01 (d, J 1.3). m/z (ESI) 308.1 ([M + Na]$^+$, 100%). Peaks assignable to isochavicine 147: 1.55-1.67 (br m), 3.59 (br s), 5.97 (s), 6.27 (dd, J 11.5 and 11.5) and 7.73 (dd, J 14.7 and 11.8).

**Literature data:** $^{26, 95}$ 145: $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 1606 (CO); $\delta_{\text{H}}$ (500 MHz; CDCl$_3$) 1.64-1.72 (6 H, m, NCH$_2$CH$_2$CH$_2$), 3.69-3.72 (4 H, m NCH$_2$), 6.00 (2 H, s, OCH$_2$O), 6.83 (1 H, d, J 8.0, ArH), 7.08-7.09 (2 H, m, ArH), 7.11 (1 H, dd, J 8.1 and 1.8, ArH) and 7.21 (1 H, d, J 3.8, ArH); $\delta_{\text{C}}$ (90 MHz; CDC$_1$$_3$) 25.3 (CH$_2$), 26.5 (CH$_2$), 101.8 (CH$_2$, OCH$_2$O), 107.0 (CH), 109.1 (CH), 120.4 (CH), 122.2 (CH), 128.3 (C), 129.9 (CH), 136.2 (C), 147.5 (C), 148.2 (C), 148.6 (C) and 163.6 (C, CO); m/z (EI) 315.0883 (M$^+$, C$_{17}$H$_{17}$NO$_3$S requires 315.0929), 285 (76%), 201 (91), 173 (60), 143(46), 115 (100) and 100 (14). Piperine (144): $\delta_{\text{H}}$(CDCl$_3$) 1.55-1.70 (6 H, br m), 3.52 (2 H, br s), 3.63 (2 H, br s), 5.98 (2 H, s, OCH$_2$O), 6.44 (1 H, d, J 14.7, OCCH), 6.76 (1 H, dd, J 15.0 and 8.5, OCCHCHCH), 6.77 (1 H, d, J 15.0, ArCH), 6.78 (1 H, d, J 8.0, ArH), 6.89 (1 H, dd, J 8.0 and 1.6, ArH), 6.98 (1 H, d, J 1.6, ArH) and 7.40 (1 H, ddd, J 14.7, 8.5 and 1.8, OCCHCH). Isopiperine (146): $\delta_{\text{H}}$(CDCl$_3$) 1.55-1.70 (6 H, br m), 3.48 (2 H, br s), 3.63 (2 H, br s), 5.96 (2 H, s, OCH$_2$O), 5.99 (1 H, d, J 11.2, OCCH), 6.50 (1 H, dd, J 11.2 and 11.2, OCCHCH), 6.61 (1 H, d, J 15.6, ArCH), 6.75 (1 H, d, J 8.0, ArH), 6.90 (1 H, dd, J 8.0 and 1.6, ArH), 7.03 (1 H, d, J 1.6, ArH) and 7.42 (1 H, ddd, J 11.2, 11.2 and 1.0, OCCHCHCH). Isochavicine (147): $\delta_{\text{H}}$(CDCl$_3$) 1.62 (6 H, br m), 3.52 (2 H, br s), 3.62 (2 H, br s), 5.97 (2 H, s, OCH$_2$O), 6.27 (1 H, dd, J 11.8 and 11.8, OCCHCHCH), 6.48
(1 H, d, J 14.7, OCCH), 6.60 (1 H, d, J 11.8, ArCH), 6.82 (3 H, m, ArH) and 7.75 (1 H, ddd, J 14.7, 11.8 and 1.1, OCCHCH).

Attempted isomerisation of piperine (144)
A solution thiophenol (0.04 mL, 0.350 mmol), dicumyl peroxide (0.095 g, 0.35 mmol) and piperine (1.00 g, 3.50 mmol) in degassed chlorobenzene was refluxed for 12 h. The solution was concentrated in vacuo and purification of the residue by column chromatography (60:40 60-80 pet ether:Et₂O) afforded recovered piperine 144 (0.99 g, 99%).

Methyl 3-(hydroxymethyl)-5,6-dihydropyridine-1(2H)-carboxylate (154)

Alcohol 154 was prepared according to the literature procedure. Benzyl bromide (11.4 mL, 96.2 mmol) was added to a stirred solution of pyridine-3-methanol (153) (8.90 mL, 91.6 mmol) in CH₂Cl₂ (33.5 mL) over a period of 2.5 h. The mixture was allowed to stir overnight at room temperature and then evaporated to afford the crude salt as a cream solid. To an ice cold solution of the salt (25.7 g, 91.6 mmol) in methanol (100 mL) was added portionwise NaBH₄ (6.92 g, 183 mmol) over a period of 6 h with constant cooling. The mixture was allowed to stir overnight warming to room temperature and concentrated under reduced pressure. The resulting viscous oil was treated with 1 M NaOH (83.0 mL) and extracted with Et₂O (3 × 40 mL). The organic layers were combined, dried over MgSO₄ and concentrated under reduced pressure to afford the crude N-benzyl-tetrahydropyridine as a viscous oil, which was used in the next step without purification. To a solution of the crude N-benzylamine (18.4 g, 91.6 mmol) in benzene (133 mL) was added solid NaHCO₃ (3.81 g, 45.3 mmol). Methyl chloroformate (8.40 mL, 109 mmol) was added dropwise to the stirred
mixture at room temperature over 2 h and the resulting mixture was refluxed for 16 h. The mixture was allowed to cool to room temperature and concentrated under reduced pressure to afford an orange oil. The oily residue was dissolved in EtOAc (100 mL) and washed with water (3 × 20 mL), 0.5 M HCl (3 × 20 mL) and brine (3 × 20 mL). The organic layer was dried over MgSO₄, concentrated and purified by column chromatography (Et₂O) to give the allylic alcohol 154 (4.85 g, 31%) as a pale yellow, viscous oil. R_f 0.29 (Et₂O); v_max (neat)/cm⁻¹ 3433 (OH), 2998, 2954, 2916, 2859 (CH) and 1703 (CO). The resonances ¹H- and ¹³C-NMR spectra are broad presumably due to a mixture of rotamers δ_H(300 MHz; CDCl₃) 1.64-1.98 (1 H, br m, OH), 2.15 (2 H, ap. br s, CH₂CH₂CH), 3.50 (2 H, br t, J 5.7, NCH₂CH₂), 3.70 (3 H, s, OCH₃), 3.96 (2 H, ap. br s, NCH₂C), 4.05 (2 H, ap. br s, CH₂OH) and 5.82 (1 H, br s, CH=C); δ_C(75 MHz; CDCl₃) 24.4 (CH₂, CH₂CH₂CH), 40.1 (CH₂, NCH₂CH₂), 43.7 (CH₂, NCH₂C), 52.5 (CH₃, OCH₃), 64.6 (CH₂, CH₂OH), 120.8 and 121.5 (CH, C=CH), 135.0 and 135.3 (C, C=CH) and 156.1 (C, CO); m/z (EI) 171.0900 (M⁺, C₈H₁₃NO₃ requires 171.0895), 153 (37%), 140 (100), 108 (7), 94 (15), 67 (17), 55 (30) and 42 (32).

Methyl 3-formyl-5,6-dihydropyridine-1(2H)-carboxylate (152)

Manganese dioxide (2.99 g, 29.2 mmol) was added to a solution of alcohol 154 (500 mg, 2.92 mmol) in CH₂Cl₂ (12.4 mL) at 0 °C. The mixture was allowed to warm to room temperature over 1 h and then refluxed for 4 h. The mixture was filtered through celite, washed with CH₂Cl₂ (3 × 15 mL) and concentrated under reduced pressure. Purification of the residue by column chromatography (7:3 60-80 pet ether:Et₂O) yielded aldehyde 152 as a white solid (384 mg, 78%) followed by alcohol 154 (100 mg, 20%). R_f 0.52 (Et₂O); mp 81-83 °C; found: C, 57.1; H, 6.7; N, 8.35. C₈H₁₁NO₃ requires C, 56.8; H, 6.55; N, 8.3%;
\( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 2922, 2853, 1703 (CO) and 1687 (CO). The \(^1\)H- and \(^{13}\)C-NMR spectra are broad presumably due to a mixture of rotamers \( \delta_\text{H}(300 \text{ MHz}; \text{CDCl}_3) \) 2.45 (2 H, ap. br s, CH\(_2\)CH\(_2\)CH), 3.58 (2 H, ap. br s, NCH\(_2\)CH\(_2\)), 3.70 (3 H, s, OCH\(_3\)), 4.13 (2 H, br s, NCH\(_2\)C), 6.92 (1 H, ap. br s, CH=CHO) and 9.42 (1 H, s, CHO); \( \delta_\text{C}(75 \text{ MHz}; \text{CDCl}_3) \) 26.0 (CH\(_2\), CH\(_2\)CH), 39.8 (CH\(_2\), NCH\(_2\)CH\(_2\)), 40.9 (CH\(_2\), NCH\(_2\)C), 52.7 (CH\(_3\), OCH\(_3\)), 138.8 (C, C=CH), 147.3 and 147.8 (CH, C=CH), 156.0 (C, CO) and 191.6 (C, CHO); m/z (EI) 169.0740 (M\(^+\), C\(_8\)H\(_{11}\)NO\(_3\) requires 169.0739), 154 (30%), 140 (34), 126 (5), 110 (12), 94 (13), 88 (10), 81 (46), 73 (6), 69 (50), 59 (25), 53 (29) and 42 (32).

5-Vinyl-3,6-dihydro-2\(H\)-pyridine-1-carboxylic acid methyl ester (151)

\[
\begin{align*}
\text{152} & \quad \rightarrow \quad \text{151}
\end{align*}
\]

A solution of \( n \)-BuLi in hexanes (2.48 M, 1.25 mL, 3.11 mmol) was added to a solution of PPh\(_3\)MeBr (1.36 g, 3.82 mmol) in THF (0.70 mL) at -78 °C over 5 min. The resulting yellow solution was allowed to warm to -5 °C. A solution of aldehyde 152 (500 mg, 2.96 mmol) in THF (9.10 mL) was added to the mixture at -5 °C and the resulting mixture was stirred for 2 h warming to room temperature. Water (10 mL) was added to the reaction mixture, which was extracted with Et\(_2\)O (3 \times 5 mL). The combined organic layers were dried over MgSO\(_4\) and concentrated under reduced pressure. Purification by column chromatography (7:3 60-80 pet ether:Et\(_2\)O) yielded diene 151 (378 mg, 76%) as a clear oil. R\(_f\) 0.42 (7:3 60-80 pet ether:Et\(_2\)O); \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\) 2925, 1702, 1452 and 1412. The \(^1\)H- and \(^{13}\)C-NMR spectra are broad presumably due to a mixture of rotamers \( \delta_\text{H}(400 \text{ MHz}; \text{CDCl}_3) \) 2.21 (2 H, ap. br s, CH\(_2\)CH\(_2\)CH), 3.51 (2 H, ap. br s, NCH\(_2\)CH\(_2\)), 3.70 (3 H, s, OCH\(_3\)), 4.06 (2 H, br s, NCH\(_2\)C), 4.95 (1 H, d, J 11.0, CCH=CH\(_2\)), 4.19-5.13 (1 H, br m, CCH=CH\(_2\)), 5.83 (1 H, ap. br s, C=CH) and 6.27 (1 H, dd, J 17.8 and 11.0, CCH=CH\(_2\)); \( \delta_\text{C}(75 \text{ MHz}; \text{CDCl}_3) \)
25.2 (CH₂, CH₂CH₂CH), 40.3 (CH₂, NCH₂CH₂), 42.7 (CH₂, NCH₂C), 52.5 (CH₃, OCH₃), 110.9 and 111.2 (CH₂, C=CH₂), 126.5 and 127.2 (CH, C=CH), 133.1 and 133.5 (C, C=CH), 136.7 (CH, CCH=CH₂) and 156.0 (C, CO); m/z (EI) 167.0954 (M⁺, C₉H₁₃NO₂ requires 167.0946), 152 (64%), 136 (6), 108 (14), 91 (9), 79 (100), 67 (7) and 53 (13).

6,7-Dihydro-4H-thieno[3,2-c]pyridine-5-carboxylic acid methyl ester (149)

A solution of diene 151 (100 mg, 0.599 mmol) and 1,2,3-trithiapentalene 2-oxide (49) (855 mg, 3.59 mmol) in chlorobenzene (359 mL) was degassed for 15 min. The solution was refluxed for 6 h until disappearance of 49 by TLC. The solution was concentrated in vacuo and purification of the residue by column chromatography (60-80 pet ether) first yielded disulfide 50 (659 mg, 97% based on 49 used). Further elution (70:30 60-80 pet ether:Et₂O) afforded diene 151 (25.0 mg, 25%) followed by thiophene 149 (86.0 mg, 73%) as a clear oil. Rf 0.10 (70:30 60-80 pet ether:Et₂O); νmax (neat)/cm⁻¹ 2993, 2953, 2847 and 1701 (CO). The ¹H- and ¹³C-NMR spectra are broad presumably due to a mixture of rotamers δH(300 MHz; CDCl₃) 2.86 (2 H, ap. br s, CH₂CH₂C), 3.66-3.85 (5 H, m, OCH₃ and NCH₂CH₂), 4.55 (2 H, br s, NCH₂C), 6.78 (1 H, ap. br s, SCHCH) and 7.12 (1 H, d, J 5.1, SCHCH); δC(75 MHz; CDCl₃) 24.6 and 24.9 (CH₂, CH₂CH₂CH), 41.5 (CH₂, NCH₂C), 44.0 (CH₂, NCH₂CH₂), 52.5 (CH₃, OCH₃), 123.0 (CH, SCH), 124.5 and 124.7 (CH, SCHCH), 131.6 and 131.9 (C, SCC), 132.7 and 133.2 (C, SCC) and 156.0 (C, CO); m/z (EI) 197.0503 (M⁺, C₉H₁₁NO₂S requires 197.0511), 182 (53%), 166 (6), 138 (15), 110 (100), 84 (6) and 66 (8).
A 2 M NaOH aqueous solution (9.54 mL) was added to a solution of thiophene 149 (188 mg, 0.95 mmol) in methanol (28.9 mL) and heated to reflux for 12 h. The organics were extracted with Et₂O (3 × 5 mL), dried over Na₂SO₄ and then concentrated to ~ 5 mL. 4 M HCl in dioxane was added (pH 1) to the ethereal phase to precipitate the crude compound. The solid was filtered, washed with ice-cold Et₂O (5 mL) and recrystallised with i-PrOH (~ 8 mL) to afford the pyridinium chloride 155 (137 mg, 82%) as a white, crystalline solid. mp 224-226 °C (i-PrOH); νmax (KBr)/cm⁻¹ 2933, 2778, 2706 (R₂NH₂⁺), 2652, 2615, 2092, 2043, 1933 and 1158; δH(300 MHz; D₂O) 3.13 (2 H, t, J 6.0, NCH₂C), 3.53 (2 H, t, J 6.1, NCH₂CH₂), 4.28 (2 H, s, NCH₂C), 6.88 (1 H, d, J 5.2, SCHC) and 7.34 (1 H, d, J 5.2, SCHCH); δC(75 MHz, D₂O) 23.9 (CH₂, NCH₂CH₂), 44.5 (CH₂, NCH₂C), 45.7 (CH₂, NCH₂CH₂), 127.5 (CH, SCHCH), 127.6 (CH, SCHCH), 129.6 (C, SCC) and 134.2 (C, SCC); m/z (EI) 139.0449 ([M - HCl]⁺, C₇H₉NS requires 139.0456), 110 (100%), 81 (7), 69 (13), 66 (7), 57 (5) and 43 (5).
Experimental for Chapter Two

Naphtho[1,8-\textit{cd}][1,2]dithiole 1-oxide (107)

Using \textit{m}CPBA:

Monoxide 107 was prepared according to the literature procedure. A solution of \textit{m}CPBA (77\% w/w, 5.16 g, 23.1 mmol) in CH$_2$Cl$_2$ (120 mL) was added dropwise to a stirred solution of naphtho[1,8-\textit{cd}][1,2]dithiole (50) (2.96 g, 15.4 mmol) in CH$_2$Cl$_2$ (64.0 mL) at 0 °C over 30 min. The solution was allowed to warm to room temperature over 2 h. The mixture was washed with 5\% NaHCO$_3$ solution (10 mL) and extracted with CH$_2$Cl$_2$ (3 \times 10 mL). The combined organic layers were dried over Na$_2$SO$_4$, concentrated under reduced pressure and purified by column chromatography (6:4 hexane:Et$_2$O) to yield monoxide 107 (3.15 g, 99\%) as a yellow solid. R$_f$ 0.29 (6:4 hexane:Et$_2$O); mp 87-89 °C; $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 2361, 1486, 1073 (SO) and 1054; $\delta_H$(300 MHz; CDCl$_3$) 7.60-7.69 (2 H, m, Ar$\text{H}$), 7.80-7.85 (2 H, m, Ar$\text{H}$), 8.16 (1 H, d, J 8.1, Ar$\text{H}$) and 8.21 (1 H, d, J 7.3, Ar$\text{H}$); $\delta_C$(75 MHz, CDCl$_3$) 122.0 (CH), 124.6 (CH), 127.4 (CH), 127.7 (CH), 128.8 (CH), 129.3 (C), 131.8 (CH), 133.5 (C), 137.5 (C) and 148.7 (C); m/z (EI) 205.9869 (M$^+$, C$_{10}$H$_6$OS$_2$ requires 205.986), 190 (14\%), 177 (46), 158 (11), 145 (8), 134 (17), 114 (23), 102 (6), 88 (5) and 68 (7).

\textbf{Literature Data:\textsuperscript{137, 259} mp 87-89 °C; $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 1475, 1390, 1200, 1070 (SO), 800 and 750; $\delta_H$(400 MHz; CDCl$_3$) 7.60 (1 H, dd, J 8 and <1), 7.65 (1 H, t, J 8) 7.80 (1 H, t, J 8), 7.82 (1 H, dd, J 8 and <1), 8.14 (1 H, dd, J 8 and <1) and 8.19 (1 H, dd, J 8 and <1); $\delta_C$(100 MHz, CDCl$_3$)$^\text{ii}$ 95.1, 97.6, 100.4, 101.9, 102.4, 104.8, 106.6, 110.6, 110.7 and 121.8; m/z (EI) 205.979 (M$^+$, C$_{10}$H$_6$OS$_2$ requires 205.986), 190 and 158.

$^\text{ii}$ Not calibrated to 77 ppm
Using DMD:

A solution of DMD in acetone (0.046 M, 12.0 mL, 0.552 mmol) was added to a solution of disulfide 50 (100 mg, 0.526 mmol) in acetone (5.26 mL) at 0 °C over 5 min. The mixture was allowed to warm to room temperature over 2 h, concentrated under reduced pressure and purified by column chromatography (6:4 hexane:Et₂O) to yield monoxide 107 (78.0 mg, 72%) as a yellow solid.

Naphtho[l,8-cd][1,2]dithiole 1,1-dioxide (63)

Using mCPBA:

Thisulfonate 63 was prepared by modification of the literature procedure. A solution of mCPBA (63.0 mg, 0.37 mmol) in CH₂Cl₂ (2.73 mL) was added dropwise to a stirred solution of monoxide 107 (72.0 mg, 0.35 mmol) in CH₂Cl₂ (1.00 mL) at 0 °C over 30 min. The mixture was stirred for 14 h at room temperature, washed with 5% NaHCO₃ solution (10 mL) and extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were dried over Na₂SO₄, concentrated under reduced pressure and purified by column chromatography (8:2 CH₂Cl₂:hexane) to yield dioxide 63 (66.0 mg, 85%) as a white solid. Rf 0.61 (8:2 CH₂Cl₂:hexane); mp 147-149 °C; found: C, 54.1; H, 2.5. C₁₀H₆O₂S₂ requires C, 54.0; H, 2.7%; \nu_{max}(KBr)/cm⁻¹ 1487, 1310 (SO₂), 1203, 1165 and 1129 (SO₂); δH(300 MHz; CDCl₃) 7.51 (1 H, d, J 7.3, ArH), 7.66 (1 H, t, J 7.9, ArH), 7.77-7.82 (2 H, m, ArH), 8.09 (1 H, d, J 7.3, ArH) and 8.17 (1 H, d, J 8.1, ArH); δC(75 MHz; CDCl₃) 120.8 (CH), 122.1 (CH), 122.4 (C), 124.8 (CH), 127.4 (CH), 128.5 (CH), 130.1 (C), 132.2 (C), 132.7 (CH) and 139.6 (C); m/z (El) 221.9810 (M⁺, C₁₀H₆O₂S₂ requires 221.9809),
174 (82%), 158 (100), 145 (5), 114 (61), 102 (13), 93 (10), 87 (17), 79 (7), 74 (16) and 50 (5).

**Literature data:**
mp 148-149 °C (methanol); found: C, 54.1; H, 2.8; S, 28.85; O, 14.6. C_{10}H_{6}S_{2}O_{2} requires C, 54.0; H, 2.7; S, 28.85; O, 14.6%; ν_{max}/cm^{-1} 1310 (SO_{2}) and 1130 (SO_{2}); δ_{H}(300 MHz; CDCl_{3}) 7.49 (1 H, dd, J 8.0 and 1.0), 7.65 (1 H, t, J 8.0), 7.78 (1 H, t, J 8.0), 7.80 (1 H, dd, J 8.0 and 1.0), 8.08 (1 H, dd, J 8.0 and 1.0) and 8.16 (1 H, dd, J 8.0 and 1.0); m/z 222 (M^{+}, 100%), 174 (61), 158 (91), 114 (30) and 113 (24).

Using DMD:
A solution of DMD in acetone (0.046 M, 8.24 mL, 0.379 mmol) was added to a solution of monoxide 107 (78.0 mg, 0.379 mmol) in acetone (3.79 mL) at 0 °C over 5 min. The mixture was allowed to warm to room temperature over 2 h, concentrated under reduced pressure and purified by column chromatography (8:2 CH_{2}Cl_{2}:hexane) to yield dioxide 63 (80.0 mg, 95%) as a white solid.

Using mCPBA:
A solution of mCPBA (2.27 g, 13.2 mmol) in CHCl_{3} (80.7 mL) was added dropwise to a stirred solution of disulfide 50 (1.00 g, 5.26 mmol) in CHCl_{3} (182 mL) at 0 °C over 1 h. The mixture was refluxed for 14 h, washed with 5% NaHCO_{3} solution (10 mL) and extracted with CH_{2}Cl_{2} (3 × 10 mL). The combined organic layers were dried over Na_{2}SO_{4}, concentrated under reduced pressure and purified by column chromatography (8:2 CH_{2}Cl_{2}:hexane) to yield dioxide 63 (938 mg, 80%) as a white solid.
Using DMD:
A solution of DMD in acetone (0.046 M, 24.0 mL, 1.10 mmol) was added to a solution of disulfide 50 (100 mg, 0.526 mmol) in acetone (5.26 mL) at 0 °C over 5 min. The mixture was allowed to warm to room temperature over 2 h, concentrated under reduced pressure and purified by column chromatography (8:2 CH₂Cl₂:hexane) to yield dioxide 63 (72.0 mg, 62%) as a white solid.

Using tetrahydrothiopyran-4-one (203) and Oxone®:
Disulfide 50 (250 mg, 1.31 mmol) and tetrahydrothiopyran-4-one (203) (7.60 mg, 0.066 mmol) were dissolved in MeCN (3.99 mL) and aqueous Na₂.EDTA (0.33 M, 3.99 mL) at room temperature. A mixture of Oxone® (2.10 g, 3.42 mmol) and NaHCO₃ (0.51 g, 6.12 mmol) was added to the reaction portionwise over 3 h. The mixture was stirred for 3 h and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (3 × 5 mL), dried over MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (8:2 CH₂Cl₂:hexane) afforded dioxide 63 (125 mg, 43%).

Electrochemistry:
Preparation of glassware and solutions for electrochemistry
All glassware was cleaned by heating in a 1:1 mixture of concentrated nitric acid and sulfuric acids followed by thorough rinsing with pure water. Glassware was soaked in pure water for several hours and then rinsed and dried overnight in a designated oven. Water used throughout (including solution preparation and rinsing) was purified by a Millipore™ system (resistivity 18.2 MΩ). Electrolytes were made as 0.08 M solutions of Bu₄NCIO₄ (Fluka, electrochemical grade) in dry CH₂Cl₂. Disulfides 50 and 87 were made up in this solution at a concentration of 1 mM.
Cyclic voltammetry

Cyclic voltammetry experiments were conducted in a standard three-electrode cell of 30 mL volume. The counter electrode was a Pt coil (cleaned along with the cell) and the reference electrode was a saturated calomel electrode (SCE) contained within a salt bridge (saturated KCl). The working electrode was a Au disc of diameter 2 mm (Radiometer, Copenhagen). This was prepared by polishing with successively finer grades of alumina powder (1 μm, 0.3 μm and 0.05 μm, Buehler) rinsing and placing in pure water in an ultrasonic bath for several min. The electrode was dried with a stream of argon before placing in the cell. The electrolyte was purged of oxygen by bubbling argon through the cell for at least 15 min prior to measurements.

Cyclic voltammetry measurements were carried out using an Autolab PGStat 10 system with GPES software (EcoChemie, NL).

3,8-Dimethoxy-naphtho[1,8-cd][1,2]dithiole 1,1-dioxide (206)

Using mCPBA:

A solution of mCPBA (314 mg, 1.76 mmol) in Et₂O (3.00 mL) was added dropwise to a solution of 3,8-dimethoxy-naphtho[1,8-cd][1,2]dithiole (87) (200 mg, 0.800 mmol) in Et₂O (2.00 mL) at 0 °C over 30 min, which was stirred overnight at room temperature. The mixture was washed with 5% NaHCO₃ solution (3 × 5 mL). The organic phase was dried over Na₂SO₄ and concentrated under vacuum. Purification by column chromatography (8:2 60-80 pet ether:EtOAc) afforded the title compound 206 (204 mg, 90%) as a yellow solid. Rf 0.66 (EtOAc); mp 151-153 °C; νmax (KBr)/cm⁻¹ 2938, 2936, 1619, 1505, 1344 (SO₂), 1267, 1171 (SO₂) and 1050; δH (300 MHz; CDCl₃) 3.99 (3 H, s, OCH₃), 4.08 (3 H, s, OCH₃), 7.47 (1 H, d,
\[ J \, 8.9, \, ArH \], \, 7.55 \, (1 \, H, \, d, \, J \, 8.9, \, ArH) \], \, 7.96 \, (1 \, H, \, d, \, J \, 8.9, \, ArH) \] and \, 7.98 \, (1 \, H, \, d, \, J \, 8.9, \, ArH); \, \delta_H(300 \, MHz; \, acetone-d_6) \, 4.08 \, (3 \, H, \, s, \, OCH_3), \, 4.17 \, (3 \, H, \, s, \, OCH_3), \, 7.47 \, (1 \, H, \, d, \, J \, 8.9, \, ArH), \, 7.55 \, (1 \, H, \, d, \, J \, 8.9, \, ArH), \, 7.96 \, (1 \, H, \, d, \, J \, 8.9, \, ArH) \] and \, 8.28 \, (1 \, H, \, d, \, J \, 8.9, \, ArH); \, \delta_C(75 \, MHz; \, CDCl_3) \, 56.5 \, (CH_3, \, OCH_3), \, 56.7 \, (CH_3, \, OCH_3), \, 111.6 \, (CH), \, 112.9 \, (CH), \, 118.3 \, (C), \, 123.4 \, (C), \, 127.2 \, (CH), \, 130.6 \, (C), \, 133.3 \, (C), \, 135.0 \, (CH), \, 153.3 \, (C) \, and \, 158.8 \, (C); \, m/z \, (EI) \, 282.0028 \, (M^+, \, C_{12}H_{10}O_4S_2 \, requires \, 282.0021), \, 266 \, (100%), \, 251 \, (59), \, 235 \, (83), \, 220 \, (43), \, 207 \, (70), \, 192 \, (19), \, 177 \, (4), \, 164 \, (18), \, 152 \, (5), \, 145 \, (10), \, 132 \, (7), \, 120 \, (8), \, 114 \, (3), \, 101 \, (4), \, 93 \, (7), \, 69 \, (8) \, and \, 63 \, (4).

Oxidation of disulfide 87 in an NMR tube using DMD:

A solution of DMD in acetone (0.033 M, 0.30 mL, 0.01 mmol) was added to a solution of disulfide 87 (5.00 mg, 0.02 mmol) in acetone-d_6 (0.35 mL) in an NMR tube. The reaction was monitored immediately after the addition and after 15 min. The ratio of disulfide 87 and dioxide 206 remained the same by integration of the peaks.

4-Methoxy-benzenethiosulfonic acid S-(4-methoxy-phenyl) ester (213)

Using \(m\)CPBA:

A solution of \(m\)CPBA (52.0 mg, 0.359 mmol) in \(CH_2Cl_2\) (3.6 mL) was added dropwise to a stirred solution of 1,2-bis(4-methoxyphenyl)disulfane (208) (100 mg, 0.359 mmol) in \(CH_2Cl_2\) (3.60 mL) over 5 min at -78 °C, which was stirred for 1 h. The mixture was washed with 5% \(NaHCO_3\) solution and extracted with \(CH_2Cl_2\) (3 \times 5 mL). The combined organic layers were dried over \(Na_2SO_4\), concentrated under reduced pressure and the crude mixture was purified by column chromatography (9:1 60-80 pet ether:Et_2O) to yield 1,2-bis(4-methoxyphenyl)disulfane (208) (43.0 mg, 43%). Further elution (8:2 60-80 pet ether:EtOAc)
afforded the title compound 213 (45.0 mg, 40%) as a white solid. Rf 0.21 (8:2 60-80 pet ether:EtOAc); mp 84-86 °C; νmax (KBr)/cm⁻¹ 1590, 1494, 1322 (SO₂), 1295, 1261 and 1183 (SO₂); δH(300 MHz; CDCl₃) 3.82 (3 H, s, OCH₃), 3.85 (3 H, s, OCH₃), 6.82-6.88 (4 H, m, ArH), 7.24-7.27 (2 H, m, ArH) and 7.47-7.50 (2 H, m, ArH); δC(100 MHz, CDCl₃) 55.4 (CH₃, OCH₃), 55.7 (CH₃, OCH₃), 113.8 (CH), 114.9 (CH), 118.9 (C), 129.8 (CH), 134.9 (C), 138.3 (CH), 162.2 (C) and 163.5 (C); m/z (EI) 310.0322 (M⁺, C₁₄H₁₂O₄S₂ requires 310.0334), 188 (5%), 171 (17), 155 (56), 139 (100), 123 (10), 95 (13), 84 (32), 77 (15), 69 (20), 57 (8) and 43 (9).

Literature data:²⁶²,²⁶³ mp 89-90 °C; found: C, 54.3; H, 4.5; S, 20.4. C₁₄H₁₄O₄S₂ requires C, 54.2; H, 3.2; S, 20.7%; νmax (KBr)/cm⁻¹ 1330 (SO₂) and 1142 (SO₂); δH(400 MHz; CDCl₃) 3.85 (3 H, s), 3.88 (3 H, s), 6.86 (2 H, d, J 9), 6.89 (2 H, d, J 9), 7.29 (2 H, d, J 9) and 7.52 (2 H, d, J 9); δC(100 MHz, CDCl₃) 55.59, 55.83, 113.95, 115.03, 118.99, 129.99, 134.98, 138.46, 163.32 and 163.65; m/z (EI) 310 (M⁺, 18%), 171 (20), 155 (55) and 139 (100).

1,2-Bis(2-methoxyphenyl)disulfane (209)

A solution of iodine (0.241 g, 0.948 mmol) in EtOH (0.59 mL) was added to a solution of 2-methoxybenzenethiol (214) (0.087 mL, 0.713 mmol) in EtOH (0.20 mL), which was stirred for 30 min. The mixture was washed with water (3 x 5 mL), sodium thiosulfate solution (3 x 5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure to afford disulfide 209 (94 mg, 95%). Rf 0.28 (98:2 60-80 pet ether:EtOAc); mp 118-119 °C; νmax (KBr)/cm⁻¹ 2966, 2939, 2837, 1578, 1473, 1237 and 1021; δH(300 MHz; CDCl₃) 3.90 (6 H, s, OCH₃), 6.84-6.94 (4 H, m, ArH), 7.16-7.22 (2 H, m, ArH) and 7.52 (2 H, dd, J 7.8 and 1.5, ArH); δC(75 MHz, CDCl₃)
55.8 (CH₃, OCH₃), 110.4 (CH), 121.3 (CH), 124.5 (C), 127.5 (CH), 127.7 (CH) and 156.5 (C); m/z (EI) 278 (M⁺, 100%), 246 (3), 214 (3), 140 (29), 125 (14), 111 (7), 93 (8), 77 (6), 65 (12) and 45 (9).

**Literature data:**[264] mp 114-116 °C; v_max (CHCl₃)/cm⁻¹ 1577, 1471, 1270, 1236, 1021 and 729; δ_H(200 MHz; CDCl₃) 3.38 (6 H, s), 6.87 (4 H, m), 7.17 (2 H, dt, J 7.8 and 1.3) and 7.52 (2 H, dd, J 7.8 and 1.6); δ_C(50 MHz, CDCl₃) 56.38, 111.05, 121.83, 128.28 and 157.12.

S-2-Methoxyphenyl 2-methoxybenzenesulphonothioate (215)

![Chemical Structure]

A solution of DMD in acetone (0.033 M, 10.8 mL, 0.36 mmol) was added to a solution of disulfide 209 (100 mg, 0.36 mmol) in acetone (3.60 mL) at -78 °C. The mixture was stirred for 10 min, concentrated under reduced pressure and purified by column chromatography (60-80 pet ether) to firstly yield disulfide 209 (47.0 mg, 47%) . Further elution (6:4 60-80 pet ether:EtOAc) afforded the title compound 215 (53.0 mg, 47%) as a white solid. R_f 0.17 (6:4 60-80 pet ether:EtOAc); mp 110-111 °C; v_max (KBr)/cm⁻¹ 1585, 1478, 1433, 1320 (SO₂), 1279, 1250, 1145 (SO₂) and 1126; δ_H(300 MHz; CDCl₃) 3.45 (3 H, s, OC₃H₃), 4.03 (3 H, s, OCH₃), 6.76 (1 H, d, J 8.3, ArH), 6.85-6.96 (2 H, m, ArH), 7.08 (1 H, d, J 8.3, ArH) and 7.38-7.96 (4 H, m, ArH); δ_C(100 MHz, CDCl₃) 55.3 (CH₃, OCH₃), 56.3 (CH₃, OCH₃), 111.0 (CH), 112.5 (CH), 116.0 (C), 119.2 (CH), 120.9 (CH), 129.9 (CH), 132.1 (C), 133.4 (CH), 135.1 (CH), 139.1 (CH), 157.2 (C) and 160.0 (C); m/z (ESI) 333.0225 ([M + Na]⁺, C₁₄H₁₄O₄S₂Na requires 333.0231), 331.1 (100%).

**Literature data:**[265] mp 110 °C (ethanol).
3,8-Di-tert-butynaphtho[1,8-cd][1,2]dithiole 1-oxide (216)

Using mCPBA:
To an ice-cold solution of 3,8-di-tert-butynaphtho[1,8-cd][1,2]dithiole (65) (100 mg, 0.331 mmol) in CH₂Cl₂ (2.60 mL) was added a solution of mCPBA (63.0 mg, 0.364 mmol) in CH₂Cl₂ (1.00 mL) dropwise over 20 min. The solution was allowed to warm to room temperature and stirred for a further 2 h. The mixture was washed with 5% NaHCO₃ solution (3 × 5 mL) and extracted with CH₂Cl₂ (3 × 3 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in vacuo. Purification by column chromatography (CH₂Cl₂) yielded the title compound 216 (84.0 mg, 80%) as a white solid. Rᵣ 0.50 (CH₂Cl₂); mp 146-148 °C (EtOAc); νₑₑₑ (KBr)/cm⁻¹ 2963, 1365 and 1071 (SO); δₑₑₑ(300 MHz; CDCl₃) 1.58 (9 H, s, C(CH₃)₃), 1.73 (9 H, s, C(CH₃)₃), 7.72 (1 H, d, J 8.6, ArH), 7.76 (1 H, d, J 8.7, ArH), 7.81 (1 H, d, J 8.6, ArH) and 8.01 (1 H, d, J 8.6, ArH); δₑₑₑ(75 MHz; CDCl₃) 30.4 (CH₃), 33.2 (CH₃), 36.3 (C), 38.1 (C), 125.3 (CH), 126.7 (CH), 127.0 (CH), 130.9 (C), 131.2 (C), 131.4 (C), 131.7 (CH), 145.4 (C), 146.1 (C) and 151.6 (C); m/z (EI) 318.1098 (M⁺, C₁₈H₂₂OS₂ requires 318.1112), 303 (19), 286 (21), 271 (10), 262 (45), 249 (41), 238 (18), 229 (34), 212 (17), 198 (17), 184 (11), 83 (47), 69 (20), 57 (32) and 49 (63).

Using DMD:
A solution of DMD in acetone (0.033 M, 7.70 mL, 0.257 mmol) was added to a solution of disulfide 65 (74.0 mg, 0.245 mmol) in acetone (2.45 mL) over 5 min. The mixture was allowed to warm to room temperature over 1 h, concentrated under reduced pressure and
purified by column chromatography (CH$_2$Cl$_2$) to yield the title compound 216 (53.0 mg, 68%) as a white solid.

Reduction of vic-disulfoxide 217 with 4 M HCl in dioxane

![Reduction of vic-disulfoxide 217 with 4 M HCl in dioxane](image)

HCl (4 M in dioxane, 1.33 mL, 5.32 mmol) was added to a solution of vic-disulfoxide 217 (20.0 mg, 0.050 mmol) and the mixture was stirred for 30 min. The mixture was washed with 5% NaHCO$_3$ solution (3 × 3 mL) and extracted with CH$_2$Cl$_2$ (3 × 3 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated in vacuo. Purification by column chromatography (CH$_2$Cl$_2$) yielded thiosulfinate 216 (18.0 mg, 94%) as a white solid.

trans 3,8-Di-tert-butynaphtho[1,8-cd][1,2]dithiole 1,2-dioxide (217)

![trans 3,8-Di-tert-butynaphtho[1,8-cd][1,2]dithiole 1,2-dioxide (217)](image)

Using mCPBA:

To an ice-cold solution of 3,8-di-tert-butynaphtho[1,8-cd][1,2]dithiole (65) (100 mg, 0.331 mmol) in CH$_2$Cl$_2$ (2.59 mL) was added a solution of mCPBA (156 mg, 0.694 mmol) in CH$_2$Cl$_2$ (2.00 mL) dropwise over 20 min. The solution was stirred for a further 2 h, slowly warming to room temperature. The mixture was washed with 5% NaHCO$_3$ solution (3 × 5 mL) and extracted with CH$_2$Cl$_2$ (3 × 3 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated in vacuo. Purification by column chromatography (8:2 hexane:EtOAc) yielded the title compound 217 (102 mg, 92%) as a white solid. R$_f$ 0.31 (8:2 hexane:EtOAc); mp 178-180 °C (EtOAc); $\lambda_{\text{max}}$ (MeCN)/nm 316 (ε/dm$^3$ mol$^{-1}$ cm$^{-1}$)
74 900) and 231 (67 800); $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 2959, 1495, 1367, 1117, 1067 and 1040 (SO); $
abla$H(300 MHz; CDCl$_3$) 1.70 (18 H, s, C(CH$_3$)$_3$), 7.81 (2 H, d, $J$ 8.6, Ar$H$) and 8.05 (2 H, d, $J$ 8.6, Ar$H$); $
abla$c(75 MHz; CDCl$_3$) 33.2 (CH$_3$), 38.0 (C), 127.4 (CH), 132.2 (CH), 132.7 (C), 138.7 (C), 139.5 (C) and 155.1 (C); $m/z$ (EI) 334.1045 (M$^+$, C$_{18}$H$_{22}$O$_2$S$_2$ requires 334.1061), 319 (10%), 286 (100), 271 (89), 255 (47), 239 (21), 229 (9), 215 (24), 198 (19), 184 (18), 165 (17), 152 (10), 139 (6), 57 (24) and 43 (9).

Using DMD:

A solution of DMD (0.033 M, 59.0 mL, 1.96 mmol) in acetone was added to a solution of disulfide 65 (282 mg, 0.930 mmol) in acetone (9.30 mL) at room temperature and the mixture was stirred for 30 min. The solvent was evaporated under reduced pressure and the crude product was recrystallised from EtOAc to yield the title compound 217 (250 mg, 80%) as a white solid.

![Structural diagram]

Using $m$CPBA:

To an ice-cold solution of monoxide 216 (53.0 mg, 0.167 mmol) in CH$_2$Cl$_2$ (1.30 mL) was added a solution of $m$CPBA (30.0 mg, 0.175 mmol) in CH$_2$Cl$_2$ (0.48 mL) dropwise over 20 min. The solution was stirred for a further 2 h, slowly warming to room temperature. The mixture was washed with 5% NaHCO$_3$ solution (3 × 5 mL) and extracted with CH$_2$Cl$_2$ (3 × 3 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated in vacuo. Purification by column chromatography (8:2 hexane:EtOAc) yielded the title compound 217 (48.0 mg, 86%) as a white solid.
Using DMD:

A solution of DMD in acetone (0.046 M, 0.93 mL, 0.043 mmol) was added to a solution of monoxide 216 (13.0 mg, 0.041 mmol) in acetone (0.40 mL) at room temperature and the mixture was stirred for 30 min. The solvent was evaporated under reduced pressure and the crude product was recrystallised from EtOAc to yield the title compound 217 (11.0 mg, 81%) as a white solid.

3,8-Di-tert-butynaphtho[1,8-cd][1,2]dithiole 1,1-dioxide (224)

A solution of trans vic-disulfoxide 217 (60.0 mg, 0.180 mmol) in mesitylene (18.0 mL) was degassed for 15 min. The mixture was refluxed for 38 h. The solvent was evaporated under reduced pressure and purification by column chromatography (9:1 60-80 pet ether:EtOAc) afforded the title compound 224 (55.0 mg, 92%) as a white solid. Rf 0.25 (8:2 60-80 pet ether:CH2Cl2); mp 139-140 °C; \( \lambda_{\text{max}} \) (MeCN)/nm 249 (ε/dm³ mol⁻¹ cm⁻¹ 28 200) and 217 (21 700); \( \nu_{\text{max}} \) (KBr)/cm⁻¹ 2964, 1313 (SO₂) and 1138 (SO₂); \( \delta_{\text{H}} \) (300 MHz; CDCl₃) 1.48 (9 H, s, C(CH₃)₃), 1.69 (9 H, s, C(CH₃)₃), 7.68 (1 H, d, \( J = 8.9 \), ArH), 7.72 (1 H, d, \( J = 8.9 \), ArH), 7.84 (1 H, d, \( J = 8.6 \), ArH) and 8.00 (1 H, d, \( J = 8.6 \), ArH); \( \delta_{\text{C}} \) (75 MHz; CDCl₃) 29.8 (CH₃, C(CH₃)₃), 31.9 (CH₃, C(CH₃)₃), 36.3 (C, C(CH₃)₃), 37.5 (C, C(CH₃)₃), 124.9 (C), 125.2 (CH), 126.2 (C), 126.5 (CH), 126.9 (CH), 129.8 (C), 132.5 (CH), 135.5 (C), 143.2 (C) and 150.1 (C); m/z (ESI) 357.0953 ([M + Na]⁺, C₁₈H₂₂O₂S₂Na requires 357.0959), 357 (100%).
A solution of *cis* vic-disulfoxide 225 (20.0 mg, 0.060 mmol) in mesitylene (6.00 mL) was degassed for 15 min. The mixture was refluxed for 34 h. The solvent was evaporated under reduced pressure and purification by column chromatography (9:1 60-80 pet ether:EtOAc) afforded the *title compound* 224 (19.0 mg, 95%) as a white solid.

Representative thermal rearrangement of *trans* vic-disulfoxide 217

A solution of *trans* vic-disulfoxide 217 (100 mg, 0.299 mmol) in chlorobenzene (30.0 mL) was degassed for 15 min. The mixture was heated at 108 °C for 38 h. The solvent was evaporated under reduced pressure and purification by column chromatography (95:5 60-80 pet ether:EtOAc) afforded sulfinyl sulfone 226 (4.00 mg, 4%), thiosulfonate 224 (5.00 mg, 5%), followed by *trans* vic-disulfoxide 217 (55.0 mg, 55%). Further elution (8:2 60-80 pet ether:EtOAc) afforded *cis* 3,8-di-tert-butynaphtho[1,8-*cd*][1,2]dithiole 1,2-dioxide (225) (10.0 mg, 10%) as a white solid. 225: R<sub>f</sub> 0.15 (8:2 60-80 pet ether:EtOAc); mp 172-174 °C; λ<sub>max</sub> (MeCN)/nm 301 (ε/dm<sup>3</sup> mol<sup>-1</sup> cm<sup>-1</sup> 1 200) and 228 (32 400); ν<sub>max</sub> (KBr)/cm<sup>-1</sup> 2961, 2925, 1116, 1099, 1068 and 1042 (SO); δ<sub>H</sub> (300 MHz; CDCl<sub>3</sub>) 1.76 (18 H, s, C(CH<sub>3</sub>)), 7.81 (2 H, d, J 8.7, ArH) and 7.98 (2 H, d, J 8.7, ArH); δ<sub>C</sub> (75 MHz; CDCl<sub>3</sub>) 33.0 (CH<sub>3</sub>), 38.3 (C), 127.3 (CH), 131.7 (CH), 131.8 (C), 135.9 (C), 137.2 (C), 141.4 (C), 146.2 (C), 153.7 (C), 159.0 (C), 162.0 (C), 162.5 (C), 167.7 (C), 171.4 (C), 172.1 (C).
137.4 (C) and 154.9 (C); m/z (EI) 334.1066 (M+, C₁₈H₂₂O₂S₂ requires 334.1061), 319 (75%), 281 (12), 269 (6), 255 (16), 239 (43), 225 (7), 207 (30), 199 (15), 184 (10), 152 (9), 142 (7), 115 (5), 106 (7), 91 (5), 73 (7), 64 (10), 57 (27) and 44 (43). 226: Rf 0.48 (7:3 60-80 pet ether:EtOAc); mp 199-201 °C (EtOAc); v_max (KBr)/cm⁻¹ 2964, 1319 (SO₂), 1141, 1131 and 1074 (SO); δ_H (300 MHz; CDCl₃) 1.71 (9 H, s, C(CH₃)₃), 1.73 (9 H, s, C(CH₃)₃), 7.86 (1 H, d, J 8.9, ArH), 7.90 (1 H, d, J 8.7, ArH), 8.07 (1 H, d, J 8.9, ArH) and 8.08 (1 H, d, J 8.7, ArH); δ_C (100 MHz; CDCl₃) 31.6 (CH₃), 33.4 (CH₃), 37.6 (C), 38.6 (C), 127.6 (CH), 127.9 (CH), 130.5 (C), 130.8 (C), 131.4 (C), 132.4 (CH), 132.9 (CH), 133.7 (C), 152.5 (C) and 154.7 (C); m/z (ESI) 373.0910 ([M+Na]+, C₁₈H₂₂O₃S₂Na requires 373.0908), 373 (100).

Monitoring the stability of vic-disulfoxide

TFA (29.7 μL, 5 mol%) was added to a solution of pure vic-disulfoxide 217 or 225 (2.50 mg, 0.008 mmol) in CDCl₃ (0.750 mL) in a NMR tube. A spectrum was recorded every 3/4 days for 6 months. No change was observed by NMR spectroscopy.

2,2-Dimethylpropane-1,3-diyl bis(4-methylbenzenesulfonate) (230)

Ditosylate 230 was prepared according to the literature procedure. A solution of 2,2-dimethylpropane-1,3-diol (229) (6.24 g, 60.0 mmol) in pyridine (30.0 mL) was added to an ice-cold solution of p-TsCl (25.2 g, 132 mmol) in pyridine (100 mL) over 45 min. The solution was stirred for 1 h warming to room temperature and stored in the freezer (-20 °C) overnight. The mixture was extracted with CHCl₃ (3 × 100 mL), washed with ice/c.HCl (100 g/50 mL), ice/1 M HCl (100 g/50 mL), water (200 mL), ice/1 M NaOH (100 g/100 mL) and water (200 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure to yield ditosylate 230 (21.8 g, 88%) as a white solid. Rf 0.23
(60-80 pet ether); $v_{\text{max}}$ (KBr)/cm$^{-1}$ 2982, 1598, 1359 (OSO$_2$), 1177 (OSO$_2$) and 1096;
$\delta_\mathrm{H}(300$ MHz; CDCl$_3$) 0.86 (6 H, s, CH$_2$CCH$_3$), 2.44 (6 H, s, ArCH$_3$), 3.70 (4 H, s, CH$_2$),
7.33 (4 H, d, J 8.2, Ar$H$) and 7.71 (4 H, d, J 8.3, Ar$H$); $\delta_\mathrm{C}(75$ MHz; CDCl$_3$) 20.9 (CH$_3$),
21.6 (CH$_3$), 35.3 (C), 73.6 (CH$_2$), 127.8 (CH), 129.9 (CH), 132.4 (C) and 145.0 (C).

**Literature data:**$^{163, 266}$ mp 120-122 °C, $\delta_\mathrm{H}(200$ MHz; CDCl$_3$) 0.88 (6 H, s, CH$_2$CCH$_3$),
2.46 (6 H, s, ArCH$_3$), 3.71 (4 H, s, CH$_2$), 7.35 (4 H, d, J 8.2, Ar$H$) and 7.74 (4 H, d, J 8.3, Ar$H$); m/z (EI) 412.1019 (M$^+$, C$_{19}$H$_{24}$O$_6$S$_2$ requires 412.1014).

4,4-Dimethyl[1,2]dithiolane (231) and 5,5-dimethyl[1,2,3]trithiane (232)

![Diagram]

4,4-Dimethyl[1,2]dithiolane (231) was prepared according to the literature procedure.$^{164}$ A mixture of disulfonate ester (230) (10.0 g, 24.3 mmol), sulfur (778 mg, 24.3 mmol) and sodium sulfide hydrate (60%, 3.16 g, 24.3 mmol) in DMF (48.5 mL) was heated at 80 °C for 67 h. The mixture was allowed to cool to room temperature and poured on to a mixture of ice/water (50 g/50 mL). The organic layer was extracted with hexane (3 × 10 mL) and the aqueous layer was acidified (pH < 1) and re-extracted with hexane (3 × 10 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. Purification by column chromatography (60-80 pet ether) yielded trithiane 232 (533 mg, 13%) followed by dithiolane 231 (1.05 g, 32%). **231:** R$_f$ 0.37 (60-80 pet ether); $v_{\text{max}}$(neat)/cm$^{-1}$ 2959, 2924, 2867, 1463, 1382 and 1364; $\delta_\mathrm{H}(300$ MHz; CDCl$_3$) 1.25 (6 H, s, C(CH$_3$)$_2$) and 2.88 (4 H, s, SCH$_2$C); $\delta_\mathrm{C}(75$ MHz, CDCl$_3$) 27.0 (CH$_3$, C(CH$_3$)$_2$), 47.3 (C, C(CH$_3$)$_2$) and 51.3 (CH$_2$, SCH$_2$C); m/z (EI) 134.0230 (M$^+$, C$_{5}$H$_{10}$S$_2$ requires 134.0224), 88 (12%), 78 (8), 69 (100), 60 (5), 55 (40) and 45 (14). **232:** R$_f$ 0.50 (60-80 pet ether); $v_{\text{max}}$(neat)/cm$^{-1}$ 2954, 2933, 2892, 2864, 1466, 1380 and 1364; $\delta_\mathrm{H}(300$ MHz; CDCl$_3$) 1.04 (3 H, br s, C(CH$_3$)), 1.25 (3 H,
br s, C(CH₃), 2.55 (2 H, br s, SCH₂C) and 3.19 (2 H, br s, SCH₂C); δc(75 MHz, CDCl₃) 26.5 (CH₃), 46.2 (CH₂) and 56.2 (C); m/z (EI) 165.9951 (M⁺, C₅H₁₀S₃ requires 165.9945), 133 (6%), 110 (22), 101 (24), 87 (10), 74 (6), 69 (100), 55 (83) and 45 (57).

**Literature data:**²⁶⁷ 231: νmax (neat)/cm⁻¹ 2950, 2870, 1385, 1365, 970 and 895; δH(CDCl₃) 1.18 (6 H, s) and 2.88 (4 H, s); m/z (EI) 134 (M⁺), 119 and 70.

4,4-Dimethyl[1,2]dithiolane 1,1-dioxide (233)

Using hv/O₂:

1,1-Dioxide 233 was prepared by a literature procedure.¹⁶¹ O₂ was bubbled into a solution of disulfide 231 (126 mg, 0.940 mmol) and methylene blue (2.40 mg, 0.006 mmol) in acetone (9.40 mL). The solution was irradiated at room temperature for 2 h. The solvent was removed under reduced pressure. Purification by column chromatography (60-80 pet ether) yielded disulfide 231 (30.0 mg, 24%). Further elution (8:2 60-80 pet ether:EtOAc) afforded the **title compound** 233 (39.0 mg, 25%) as a white solid. Rf 0.35 (8:2 60-80 pet ether:EtOAc); mp 45-47 °C; νmax (KBr)/cm⁻¹ 2972, 2936, 1467, 1307 (SO₂), 1229, 1166 and 1123 (SO₂); δH(300 MHz; CDCl₃) 1.40 (6 H, s, C(CH₃)), 3.29 (2 H, s, SCH₂C) and 3.45 (2 H, s, O₂SCH₂C); δc(75 MHz, CDCl₃) 27.5 (CH₃, 2 × C(CH₃)₂), 40.2 (C, C(CH₃)₂), 49.4 (CH₂, SCH₂C) and 70.0 (CH₂, O₂SCH₂C); m/z (ESI) 166.0128 (M⁺, C₅H₁₀O₂S₂ requires 166.0122), 69 (15) and 56 (100).

**Literature data:**²⁶⁸ mp 49 °C.

Using mCPBA:

A solution of mCPBA (540 mg, 3.13 mmol) in CH₂Cl₂ (31.3 mL) was added dropwise to a stirred solution of disulfide 231 (200 mg, 1.49 mmol) in CH₂Cl₂ (14.9 mL) at room
temperature over 20 min. The mixture was stirred for 14 h at room temperature, washed with 5% NaHCO₃ solution (10 mL) and extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were dried over Na₂SO₄, concentrated under reduced pressure and purified by column chromatography (8:2 60-80 pet ether:EtOAc) to afford the title compound 231 (196 mg, 79%) as a white solid.

Photomediated epimerisation of vic-disulfoxides 217 and 225

General procedure:
A solution of pure vic-disulfoxide 217 or 225 (2.50 mg, 0.008 mmol) in solvent (0.750 mL) was degassed for 15 min in a water-cooled NMR tube. The sample was irradiated with a 500 W halogen lamp for 7 h, with constant cooling. The solvent was removed under reduced pressure. The ratio of products was determined by integration of the aromatic protons in the ¹H NMR spectrum in CDCl₃.

Typical procedure for the attempted spin trapping of vic-disulfoxide photochemically:
A solution of spin trap (0.149 mmol) and vic-disulfoxide 217 or 225 (20.0 mg, 0.059 mmol) in solvent (6.00 mL) was degassed for 15 min in a water-cooled flask. The sample was irradiated with a 500 W halogen lamp for 7 h, with constant cooling. The solvent was evaporated under reduced pressure and purification by column chromatography (95:5 60-80 pet ether:EtOAc) afforded, thiosulfonate 224 followed by trans vic-disulfoxide 217. Further elution (8:2 60-80 pet ether:EtOAc) yielded cis 3,8-di-tert-butynaphtho[1,8-cd][1,2]dithiole 1,2-dioxide (225) as a white solid.
Typical procedure for the attempted spin trapping of vic-disulfoxide thermally:

A solution of spin trap (0.149 mmol) and vic-disulfoxide 217 or 225 (20.0 mg, 0.059 mmol) in solvent (6.00 mL) was degassed for 15 min. The sample was heated at reflux for 32 h. The solvent was evaporated under reduced pressure and purification by column chromatography (95:5 60-80 pet ether:EtOAc) afforded sulfinyl sulfone 226, thiosulfonate 224, followed by trans vic-disulfoxide 217. Further elution (8:2 60-80 pet ether:EtOAc) afforded cis vic-disulfoxide 225 (10.0 mg, 10%) as a white solid.

Benzenesulfinic chloride (245)

\[
\begin{align*}
\text{244} & \quad \text{245} \\
\text{SH} & \quad \text{S-Cl}
\end{align*}
\]

Sulfinyl chloride was prepared by a literature procedure.\textsuperscript{153} Sulfuryl chloride (1.66 mL, 20.5 mmol) was added dropwise over 30 min to a solution of thiophenol (1.00 mL, 9.78 mmol) in acetic acid (590 mg, 9.78 mmol) at -40 °C. The solution was stirred for a further 30 min at -40 °C and then 2 h at room temperature. The mixture was warmed to 30 °C over 4 h and the solvent was removed under reduced pressure to afford the crude sulfinyl chloride 245 (1.56 g, 99%) as an unstable yellow solid which was characterised via the preparation of 1-(phenylsulfinyl)piperidine (247).

1-(Phenylsulfinyl)piperidine (247)

\[
\begin{align*}
\text{245} & \quad \text{247} \\
\text{S-Cl} & \quad \text{S-N}
\end{align*}
\]

Compound 247 was prepared according to the literature procedure.\textsuperscript{152} The crude sulfinyl chloride 245 (200 mg, 1.25 mmol) was dissolved in Et\textsubscript{2}O (0.65 mL) and added to a solution of
piperidine (0.25 mL, 2.5 mmol) in Et₂O (0.68 mL) at 5 °C. The solution was stirred for 1 h at room temperature forming a milky white solution. The mixture was filtered, washed with Et₂O (3 × 5 mL) and the filtrate was concentrated under reduced pressure. Purification by column chromatography afforded the title compound 247 (53.0 mg, 20%) as a white solid.

Rf 0.33 (1:1 hexane:Et₂O); δH (300 MHz; CDCl₃) 1.52-1.62 (6 H, m, 2 × NCH₂CH₂ and NCH₂CH₂CH₂), 2.91-2.98 (2 H, m, NCH₂), 3.08-3.13 (2 H, m, NCH₂), 7.46-7.53 (3 H, m, ArH) and 7.65-7.67 (2 H, m, ArH); δC (75 MHz; CDCl₃) 23.8 (CH₂), 26.1 (CH₂), 46.9 (CH₂, NCH₂), 126.1 (CH), 128.7 (CH), 130.6 (CH) and 143.3 (C); m/z (EI) 209 (M⁺, 18%), 161 (96), 132 (92), 125 (20), 109 (4), 97 (8), 84 (100), 77 (19), 69 (21), 65 (4), 55 (37), 49 (50) and 42 (46).

Literature data.⁵¹,²⁶⁹ mp 84-85 °C, ʋmax (KBr)/cm⁻¹ 2950, 2870, 1435, 1086, 1050, 905, 952 and 868; δH (400 MHz; CDCl₃) 1.41-1.53 (6 H, m, 2 × NCH₂CH₂ and NCH₂CH₂CH₂), 2.83-2.87 (2 H, m, NCH₂), 2.89-3.04 (2 H, m, NCH₂), 7.37-7.42 (3 H, m, ArH) and 7.56-7.59 (2 H, m, ArH); δC (100 MHz; CDCl₃) 23.8 (CH₂), 26.1 (CH₂), 46.9 (CH₂, NCH₂), 126.1 (CH), 128.7 (CH), 130.6 (CH) and 143.3 (C); m/z (EI) 210 ([M + H]⁺, 18%).

Attempted imination of trans-217

Sulfuric acid (0.018 mL, 0.338 mmol) was added to a solution of sodium azide (10.7 mg, 0.165 mmol) and trans-217 (50.0 mg, 0.150 mmol) in CHCl₃ (0.15 mL) at 0 °C. A colour change from clear to red/brown was observed. The mixture was stirred for 15 min at the same temperature. Ice/water (0.5 mL) was added and the organic layer was separated. The aqueous layer was extracted with CHCl₃ (3 × 5 mL). The combined organic layers were dried over
Na₂SO₄ and concentrated *in vacuo*. Purification by column chromatography (8:2 hexane:EtOAc) afforded sulfinyl sulfone 226 (30.0 mg, 57%) as a white solid.

**Experimental for Chapter Three**

Naphtho[1,8-cd][1,2]dithiole 1,1,2-trioxide (228)

A solution of *m*CPBA (3.18 g, 18.4 mmol) in CH₂Cl₂ (51.0 mL) was added dropwise to a solution of disulfide 50 (1.00 g, 5.26 mmol) in CH₂Cl₂ (41.1 mL) over 30 min. The mixture was stirred for 24 h and then washed with 5% NaHCO₃ solution (3 × 5 mL). The organic layer was concentrated to half the volume and hexane (~10 mL) was added to precipitate the crude trioxide. The resulting product was filtered and recrystallised from CH₂Cl₂:hexane to give the pure sulfinyl sulfone 228 (560 mg, 45%) as a white solid. Rₙ 0.61 (8:2 CH₂Cl₂:hexane); mp 148-150 °C (CH₂Cl₂:hexane); ν<sub>max</sub> (KBr)/cm<sup>-1</sup> 3077, 1489, 1404, 1345, 1313 (SO₂), 1182, 1152 (SO₂), 1134 (SO₂) and 1083 (SO); δ<sub>H</sub>(300 MHz; CDCl₃) 7.85-7.92 (2 H, m, ArH), 8.25-8.28 (3 H, m, ArH); δ<sub>C</sub>(75 MHz; CDCl₃) 123.9 (CH), 125.8 (C), 2 × 128.6 (CH), 129.8 (CH), 132.4 (C), 132.9 (CH), 133.1 (CH), 135.5 (C) and 137.4 (C); m/z (ESI) 260.9651 ([M + Na]<sup>+</sup>, C₁₀H₆NO₃S₂Na requires 260.9656), 260.9 (100%).

**Literature data:**<sup>138</sup> mp 168-169 °C; ν<sub>max</sub> (KBr)/cm<sup>-1</sup> 1330, 1166, 1136 and 1081.

Sulfinyl sulfone was prepared according to the literature procedure.<sup>138</sup> Thiolsulfonate 63 (160 mg, 0.721 mmol) was dissolved in dioxane (4.34 mL) and a solution of H₂O₂ (30%, 0.097 mL, 0.721 mmol) and NaOH (58.0 mg, 1.44 mmol) in water (2.88 mL) was added. The
A mixture was stirred for 15 min and evaporated to dryness. The resulting disodium salt was dissolved in H$_2$O (2.17 mL) and acidified slowly with c.HCl (pH<1). The white solid was filtered to yield the crude trioxide and recrystallised from CH$_2$Cl$_2$:hexane to give sulfinyl sulfone 228 (78.0 mg, 45%).

Naphtho[l,8-cd][1,2]dithiole 1,1,2,2-tetraoxide (294)

Bissulfone 294 was prepared according to the literature procedure. A solution of $m$CPBA (219 mg, 1.27 mmol) in CHCl$_3$ (3.50 mL) was added dropwise to a solution of dioxide 63 (100 mg, 0.450 mmol) in CHCl$_3$ (3.50 mL) over 10 min. The mixture was stirred for 24 h then washed with 5% NaHCO$_3$ solution (3 × 3 mL) and water (3 × 3 mL). The organic layer was concentrated and hexane (~5 mL) was added to precipitate the crude tetraoxide. The resulting product was purified using column chromatography (6:4 CH$_2$Cl$_2$:pet ether) to afford bissulfone 294 (58.0 mg, 51%) as a white solid. $R_f$ 0.70 (CH$_2$Cl$_2$), $\nu_{\text{max}}$(KBr)/cm$^{-1}$ 2924, 2854, 1460, 1350 (SO$_2$), 1181 (SO$_2$), 1153 and 1120 (SO$_2$); $\delta_H$(300 MHz; CDCl$_3$) 7.93 (2 H, t, $J$ 7.9, ArH), 8.20 (2 H, d, $J$ 7.3, ArH) and 8.31 (2 H, d, $J$ 8.4, ArH); $\delta_C$(75 MHz; CDCl$_3$) 121.2 (C), 123.6 (CH), 128.0 (C), 128.4 (CH), 131.0 (C) and 133.6 (CH); $m/\epsilon$ (ES) 276.9598 ([M + Na]$^+$, C$_{10}$H$_6$O$_4$S$_2$Na requires 276.9605), 277 (100%).

**Literature data:** mp >200 °C; found: C, 46.91; H, 2.65. C$_{10}$H$_6$O$_4$S$_2$ requires C, 47.23; H, 2.38%; $\nu_{\text{max}}$(KBr)/cm$^{-1}$ 1350 (SO$_2$), 1180 (SO$_2$) and 1120 (SO$_2$).
3,8-Dimethoxynaphtho[1,8-cd][1,2]dithiole 1,2,2-trioxide (207)

A solution of mCPBA (214 mg, 1.24 mmol) in CH₂Cl₂ (3.43 mL) was added dropwise to a solution of 3,8-dimethoxynaphtho[1,8-cd][1,2]dithiole (87) (100 mg, 0.400 mmol) in CH₂Cl₂ (3.12 mL) over 10 min at 0 °C and stirred for 16 h at room temperature. The mixture was washed with 5% NaHCO₃ solution (3 × 5 mL). The organic phase was dried over Na₂SO₄ and concentrated in vacuo. Purification by column chromatography (EtOAc) afforded the title compound 207 (49.0 mg, 41%) as a yellow solid. Rₛ 0.37 (EtOAc); mp 156-158 °C; νₑₛₑₐₑ(KBr)/cm⁻¹ 2946, 1616, 1551, 1506, 1350 (SO₂), 1270, 1159, 1132 (SO₂), 1077 (SO) and 1045; δ₁H(300 MHz; CDCl₃) 4.14 (3 H, s, OCH₃), 4.15 (3 H, s, OCH₃), 7.27 (1 H, d, J 9.2, ArH), 7.30 (1 H, d, J 9.4, ArH), 8.06 (1 H, d, J 9.0, ArH) and 8.08 (1 H, d, J 9.2, ArH); δ₁C(75 MHz; CDCl₃) 57.0 (CH₃, OCH₃), 57.1 (CH₃, OCH₃), 111.2 (C), 112.1 (CH), 112.3 (CH), 118.3 (C), 122.0 (C), 130.4 (C), 135.4 (CH), 135.5 (CH), 157.4 (C) and 160.3 (C); m/z (ESI) 320.9860 ([M + Na]⁺, C₁₂H₁₀O₅S₂Na requires 320.9867), 321.0 (100%).

3,8-Di-tert-butyl-naphtho[1,8-cd][1,2]dithiole 1,1,2-trioxide (226)

Using DMD:

A solution of DMD in acetone (0.042 M, 28.5 mL, 1.20 mmol) was added to a solution of trans vic-disulfoxide 217 (100 mg, 0.299 mmol) in acetone (3.00 mL) at room temperature. The mixture was stirred for 1 h and then the solvent was concentrated under reduced pressure. The crude product was recrystallised from EtOAc to yield the title compound 226 (104 mg,
99%) as a white solid. Rf 0.48 (7:3 60-80 pet ether:EtOAc); mp 199-201 °C (EtOAc); νmax (KBr)/cm⁻¹ 2964, 1319 (SO₂), 1141 (SO₂), 1131 and 1074 (SO); δH(300 MHz; CDCl₃) 1.71 (9 H, s, C(CH₃)₃), 1.73 (9 H, s, C(CH₃)₃), 7.86 (1 H, d, J 8.9, ArH), 7.90 (1 H, d, J 8.7, ArH), 8.07 (1 H, d, J 8.9, ArH) and 8.08 (1 H, d, J 8.7, ArH); δC(100 MHz; CDCl₃) 31.6 (CH₃, C(CH₃)₃), 33.4 (CH₃, C(CH₃)₃), 37.6 (C, C(CH₃)₃), 38.6 (C, C(CH₃)₃), 127.6 (CH), 127.9 (CH), 130.5 (C), 130.8 (C), 131.4 (C), 132.4 (CH), 132.9 (CH), 133.7 (C), 152.5 (C) and 154.7 (C); m/z (ESI) 373.0910 ([M + Na]⁺, C₁₈H₂₂O₃S₂Na requires 373.0908), 373 (100%).

Using mCPBA:

A solution of mCPBA (28.0 mg, 0.158 mmol) in CH₂Cl₂ (0.44 mL) was added to a solution of trans vic-disulfoxide 217 (52.0 mg, 0.150 mmol) in CH₂Cl₂ (1.17 mL) over 10 min. The solution was stirred for 2 h, washed with 5% NaHCO₃ solution (3 × 3 mL) and extracted with CH₂Cl₂ (3 × 3 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in vacuo. Purification by column chromatography (8:2 hexane:EtOAc) yielded the title compound 226 (51.0 mg, 97%) as a white solid.

Using DMD:

A solution of DMD in acetone (0.047 M, 3.45 mL, 0.162 mmol) was added to a solution of cis vic-disulfoxide 225 (18.0 mg, 0.054 mmol) in acetone (0.54 mL) at room temperature. The mixture was stirred for 1 h and then the solvent was concentrated under reduced pressure. The crude product was recrystallised from EtOAc to yield the title compound 226 (18.0 mg, 95%) as a white solid.
Using \textit{mCPBA}:

A solution of \textit{mCPBA} (19.0 mg, 0.110 mmol) in CH$_2$Cl$_2$ (0.30 mL) was added to a solution of \textit{cis vic}-disulfoxide 225 (35.0 mg, 0.105 mmol) in CH$_2$Cl$_2$ (0.82 mL) over 10 min. The solution was stirred for 2 h, washed with 5\% NaHCO$_3$ solution (3 × 3 mL) and extracted with CH$_2$Cl$_2$ (3 × 3 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated \textit{in vacuo}. Purification by column chromatography (8:2 hexane:EtOAc) yielded the \textit{title compound} 226 (28.0 mg, 76\%) as a white solid.

Using DMD:

A solution of DMD in acetone (0.036 M, 4.23 mL, 0.150 mmol) was added to a solution of thiosulfonate 224 (50.0 mg, 0.150 mmol) in acetone (1.50 mL) at room temperature. The mixture was stirred for 1 h and then the solvent was concentrated under reduced pressure. Purification by column chromatography (8:2 hexane:EtOAc) yielded the \textit{title compound} 226 (48.0 mg, 91\%) as a white solid.

Using \textit{mCPBA}:

A solution of \textit{mCPBA} (28.0 mg, 0.165 mmol) in CH$_2$Cl$_2$ (0.46 mL) was added to a solution of thiosulfonate 224 (50.0 mg, 0.150 mmol) in CH$_2$Cl$_2$ (1.17 mL) over 10 min. The solution was stirred for 4 h, washed with 5\% NaHCO$_3$ solution (3 × 3 mL) and extracted with CH$_2$Cl$_2$ (3 × 3 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated \textit{in vacuo}. Purification by column chromatography (8:2 hexane:EtOAc) yielded the \textit{title compound} 226 (51.0 mg, 97\%) as a white solid.
Using DMD:

A solution of DMD in acetone (0.065 M, 8.19 mL, 0.579 mmol) was added to a solution of disulfide 65 (50.0 mg, 0.166 mmol) in acetone (1.66 mL) at room temperature. The mixture was stirred for 10 h and then the solvent was concentrated under reduced pressure. Purification by column chromatography (8:2 hexane:EtOAc) yielded the title compound 226 (53.0 mg, 91%) as a white solid.

Using mCPBA:

A solution of mCPBA (40.0 mg, 0.231 mmol) in CH$_2$Cl$_2$ (0.64 mL) was added dropwise to a solution of disulfide 65 (20.0 mg, 0.066 mmol) in CH$_2$Cl$_2$ (0.51 mL) over 10 min. The solution was stirred for 14 h, washed with 5% NaHCO$_3$ solution (3 × 3 mL) and extracted with CH$_2$Cl$_2$ (3 × 3 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated in vacuo. Purification by column chromatography (8:2 hexane:EtOAc) yielded the title compound 226 (22.2 mg, 96%) as a white solid.

\[ \text{trans } 4,9\text{-Di-tert-butyl-2-oxa-1,3-dithiaphenalene 1,3-dioxide (295)} \]

mCPBA (5.27 g, 30.6 mmol) was added portionwise over 2 h to disulfide 65 (3.089 g, 10.2 mmol) in CH$_2$Cl$_2$ (79.7 mL). The solution was stirred for 16 h at room temperature. The mixture was washed with 5% NaHCO$_3$ solution (3 × 20 mL). The organic phase was dried over Na$_2$SO$_4$ and concentrated in vacuo. Purification by column chromatography
(9:1 60-80 pet ether:EtOAc) yielded the title compound **295** (500 mg, 14%) as a white solid followed by *trans*-**217** (2.61 g, 73%). **295**: R$_f$ 0.26 (8:2 60-80 pet ether:EtOAc); mp 154-156 °C; $\nu_{\text{max}}$(KBr)/cm$^{-1}$ 2966, 1367 and 1138 (SO); $\delta$H(300 MHz; CDCl$_3$) 1.68 (18 H, s, C(CH$_3$)$_3$), 7.68 (2 H, d, $J$ 8.8, ArH) and 7.92 (2 H, d, $J$ 8.8, ArH); $\delta$C(75 MHz; CDCl$_3$) 33.1 (CH$_3$, CCH$_3$), 36.8 (C, CCH$_3$), 120.4 (C), 125.4 (CH), 132.0 (CH), 132.2 (C), 138.7 (C) and 149.7 (C); m/z (ESI) 373.0924 ([M + Na]$^+$, C$_{18}$H$_{22}$O$_2$NaS$_3$ requires 373.0908), 373.1 (100%).

Attempted oxidation of *trans* vic-disulfoxide

The procedure for the *m*CPBA oxidation of *trans*-**217** was used in the presence of an additive.

Additives used: *m*CBA (1 equiv.) for 10 h resulted in **217** (96%)
tosic acid (1 equiv.) for 18 h resulted in **217** (98%)
BF$_3$ (1 equiv.) for 3 h resulted in **226** (95%)
Meerwein’s reagent (1 equiv.) for 6 h resulted in **226** (92%) and **295** (6%).

Thermolysis of sulfinic anhydride (**295**)

![Thermolysis of sulfinic anhydride](image)

Using PhCl:

A solution of sulfinic anhydride **295** (50.0 mg, 0.142 mmol) in PhCl (4.29 mL) was heated at reflux for 14 h. The solvent was removed under reduced pressure and purified by column chromatography (60-80 pet ether) to afford disulfide **65** (31.0 mg, 72%).
2,7-di-tert-butynaphthalene (306)

Using 1,4-dioxane/H$_2$O:

A solution of sulfinic anhydride 295 (13.0 mg, 0.037 mmol) in a 1:1 mixture of 1,4-dioxane:H$_2$O (0.56 mL:0.56 mL) was heated at 70 °C for 20 h. The mixture was extracted with Et$_2$O (3 × 5 mL). The combined organic layers were dried over MgSO$_4$, concentrated under reduced pressure and purified by column chromatography (60-80 pet ether) to afford 2,7-di-tert-butynaphthalene 306 (7.00 mg, 79%) as a white solid. R$_f$ 0.50 (60-80 pet ether); mp 103-105 °C; $\delta$H(300 MHz; CDCl$_3$) 1.42 (18 H, s, C(CH$_3$)$_3$), 7.52 (2 H, dd, $J$ 8.9 and 1.7, ArH) and 7.73-7.76 (4 H, m, ArH); $\delta$C(100 MHz; CDCl$_3$) 31.3 (CH$_3$, C(CH$_3$)$_3$), 34.8 (CH$_3$, C(CH$_3$)$_3$), 122.8 (CH), 124.1 (CH), 127.0 (CH), 129.8 (C), 133.2 (C) and 148.4 (C); m/z (EI) 240 (M$^+$, 22%), 225 (100), 141 (5) and 57 (31).

**Literature data:**$^{232}$ mp 103 °C; $\nu$$_{max}$ (KBr)/cm$^{-1}$ 3064, 2990-2840, 1632, 1512, 1472, 1368, 1280, 1210, 904, 840, 632 and 480; $\delta$H(300 MHz; CDCl$_3$) 1.41 (18 H, s, C(CH$_3$)$_3$), 7.52 (2 H, dd, $J$ 8 and 2, ArH), 7.73 (2 H, d, $J$ 8, ArH) and 7.75 (2 H, br s, ArH); $\delta$C(75 MHz; CDCl$_3$) 28.85 (CH$_3$, C(CH$_3$)$_3$), 32.34 (CH$_3$, C(CH$_3$)$_3$), 120.49, 121.62, 124.62, 127.47, 130.92 and 146.00; m/z (EI) 240 (M$^+$, 43%), 225 (100) and 57 (42).

Using 1,4-dioxane/D$_2$O:

A solution of sulfinic anhydride 295 (39.0 mg, 0.10 mmol) in a 1:1 mixture of dioxane:D$_2$O (0.56 mL:0.56 mL) was refluxed for 16 h. The mixture was extracted with Et$_2$O (3 × 5 mL). The combined organic layers were dried over MgSO$_4$, concentrated under reduced pressure
and purified by column chromatography (60-80 pet ether) to afford a mixture of the mono and di deuterated compound 304 and 305 (18.0 mg, 74%) as a white solid. The analytical data suggests that the product obtained is a mixture of the monodeuterated (67%) and dideuterated (33%) product; Rf 0.50 (60-80 pet ether); mp 104-106 °C; νmax (neat)/cm⁻¹ 2959, 2965, 1466, 1361 and 847; δH(300 MHz; CDCl3) 1.42 (18 H, s, C(CH3)3), 7.52 (2 H, dd, J 8.8 and 1.1, ArH) and 7.73-7.76 (3 H, m, ArH); δC(100 MHz; CDCl3) 31.3 (CH3, C(CH3)3), 34.8 (CH3, C(CH3)3), 122.9 (CH), 124.1 (CH), 127.0 (CH), 129.8 (C), 133.2 (C) and 148.4 (C); m/z (EI) 242 ([M + 1]+, 27%), 241 (M +, 43), 228 (12), 227 (60) and 226 (100).

1,1,3,3-Tetraoxo-1H,3H-1λ₆,3λ₆-dithia-2-azaphenalen-2-ol (284)

Naphtho[1,8-cd][1,2]dithiole 1,1,2-trioxide (226) (258 mg, 1.08 mmol) and NaNO2 (75.0 mg, 1.08 mmol) were dissolved in H₂O (4.82 mL) and 1,4-dioxane (4.82 mL). Conc. HCl (386 μL) was added dropwise at room temperature and the solution was stirred overnight. The resulting precipitate was filtered and recrystallised from EtOAc (~3 mL) yielding bis(sulfonyl)hydroxylamine 284 (0.212 g, 69%) as a white, crystalline solid. mp 167-169 °C (EtOAc); Rf 0.33 (7:3 Et₂O:hexane); λmax (MeCN)/nm 298 (ε/dm³ mol⁻¹ cm⁻¹ 17 700); νmax (KBr)/cm⁻¹ 3535 (OH), 3092 (CH), 2862, 1497, 1380, 1361 (SO₂N), 1220, 1191, 1174 (SO₂N), 1156, 902, 846 (SO₂) and 829; δH(300 MHz; CD₂CN, 10⁻¹ M) 7.91 (2 H, dd, J 8.3 and 7.5, ArH), 8.44 (2 H, dd, J 8.5 and 1.0, ArH), 8.49 (2 H, dd, J 7.4 and 1.1, ArH) and 9.99 (1 H, s, NOH); δH(300 MHz; CD₂CN, 10⁻² M) 7.93 (2 H, dd, J 8.3 and 7.4, ArH), 8.47 (2 H, dd, J 8.0 and 1.0, ArH), 8.50 (2 H, dd, J 7.4 and 1.1, ArH) and 9.85 (1 H, s, NOH); δH(300 MHz; CD₂Cl₂) 7.90 (2 H, t, J 7.8, ArH), 8.37 (2 H, d, J 8.4, ArH), 8.49 (2 H, d, J 7.4, ArH) and 8.60 (1 H, s, NOH); δC(100 MHz; CD₂CN) 120.8 (C), 128.1 (CH), 129.7 (C),...
130.9 (CH), 134.1 (C) and 136.9 (CH); m/z (ESI) 307.9669 ([M + Na]+, C_{10}H_{7}NO_{5}S_{2}Na requires 307.9663), 308 (100%).

Attempted generation of the nitroxide radical 318

Following a modified literature procedure,\textsuperscript{239} NH\textsubscript{4}OH (0.053 mL, 0.175 mmol) was added to a stirred solution of hydroxylamine 284 (50.0 mg, 0.175 mmol) and Cu(OAc)\textsubscript{2}.H\textsubscript{2}O (0.546 mg, 0.0027 mmol) in MeOH (3.00 mL). The resulting purple mixture was allowed to stir for 12 h. The reaction mixture was washed with water (3 × 3 mL) and extracted with EtOAc (3 × 3 mL) to afford hydroxylamine 284 (45.0 mg, 90%).

Following a modified literature procedure,\textsuperscript{237} MnO\textsubscript{2} (149 mg, 1.71 mmol) was added to a stirred solution of hydroxylamine 284 (100 mg, 0.350 mmol) in CHCl\textsubscript{3} (1.49 mL). The reaction was stirred for 4 h at room temperature and then refluxed for a further 8 h. The mixture was allowed to cool to room temperature and then filtered through celite; column chromatography (7:3 Et\textsubscript{2}O:hexane) yielded hydroxylamine 284 (92.0 mg, 92%).

Following a modified literature procedure,\textsuperscript{238} PbO\textsubscript{2} (47.6 mg, 0.200 mmol) and hydroxylamine 284 (100 mg, 0.350 mmol) was stirred for 4 h in CHCl\textsubscript{3} (1.49 mL) at room temperature under an O\textsubscript{2} atmosphere. The reaction mixture was stirred for 4 h at room temperature and then refluxed for a further 8 h. The mixture was allowed to cool and then filtered through celite; column chromatography (7:3 Et\textsubscript{2}O:hexane) yielded hydroxylamine 284 (98.0 mg, 98%).
Following a modified literature procedure,\textsuperscript{175} Ce(NH\textsubscript{4})\textsubscript{4}(SO\textsubscript{4})\textsubscript{4}.xH\textsubscript{2}O (167 mg, 0.280 mmol) and hydroxylamine 284 (30.0 mg, 0.105 mmol) was stirred for 24 h in benzene (1.49 mL) at room temperature. The reaction mixture was filtered and the filter cake was washed with benzene (3 × 3 mL) and MeCN (3 × 3 mL). The filtrate was concentrated under reduced pressure. Column chromatography (7:3 Et\textsubscript{2}O:hexane) yielded hydroxylamine 284 (28.0 mg, 93%).

Following a modified literature procedure,\textsuperscript{240} a solution of di-\textit{tert}-butoxydiazene 327 (11.0 mg, 0.063 mmol) and hydroxylamine 284 (30.0 mg, 0.105 mmol) in MeCN (10.5 mL) was heated at 65 °C for 24 h. The mixture was allowed to cool to room temperature, washed with water (3 × 3 mL) and extracted with EtOAc (3 × 3 mL). Column chromatography (7:3 Et\textsubscript{2}O:hexane) yielded hydroxylamine 284 (28.0 mg, 93%).

\((E)\text{-}1,2\text{-di-}\text{\textit{tert}-butoxydiazene (327)}\)

327 was prepared according to the literature procedure.\textsuperscript{240} NaN\textsubscript{2}O\textsubscript{2} (805 mg, 7.60 mmol) was added over a 5 min period to a mixture of FeCl\textsubscript{3} (1.20 g, 7.40 mmol) and \textit{t}-BuBr (8.00 ml, 80.0 mmol) in Et\textsubscript{2}O (8.00 mL). The temperature was maintained below 45 °C and allowed to stand for 75 min and then at 5 °C overnight in the refrigerator. The inorganic precipitate was removed by suction filtration and washed with ice cold Et\textsubscript{2}O (3 × 3 mL). The filtrate was washed with water (3 × 3 mL) and extracted with Et\textsubscript{2}O (3 × 5 mL). The combined organic layers were dried over MgSO\textsubscript{4} and the solvent was removed under reduced pressure. Recrystallisation from pentane (7 mL) afforded the \textit{title compound} 327 (201 mg, 16%) as
clear crystals. mp 82-83 °C (pentane); $\delta_H$(300 MHz; CDCl$_3$) 1.39 (18 H, s, C(CH$_3$)$_3$); $\delta_C$(75 MHz, CDCl$_3$) 27.8 (CH$_3$, C(CH$_3$)$_3$) and 81.2 (C, C(CH$_3$)$_3$).

**Literature data:**\textsuperscript{270-272} mp 82-83 °C (pentane); $\nu_{max}$ (KBr)/cm$^{-1}$ 2959, 1368, 1183 and 995 (NO); $\delta_H$(500 MHz; CDCl$_3$) 1.39 (18 H, s); $\delta_C$(125 MHz; CDCl$_3$) 27.8 and 81.2.

Attempted formation of hydroxylamine anion 328

A solution hydroxylamine 284 (50.0 mg, 0.175 mmol) and triethylamine (24.0 μL, 0.175 mmol) was refluxed in CH$_2$Cl$_2$ (17.5 mL) for 24 h. The reaction mixture was allowed to cool to room temperature and 1 M HCl (10 mL) was added and the organic layer was separated. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 5 mL), dried over Na$_2$SO$_4$ and concentrated under reduced pressure. Column chromatography (7:3 Et$_2$O:hexane) afforded 329 (42 mg, 84%).

Potassium tert-butoxide was added to a solution of hydroxylamine 284 (50.0 mg, 0.175 mmol) in tert-butanol (17.5 mL) and the mixture was stirred for 6 h. The mixture was refluxed for 24 h and then allowed to cool to room temperature. 1 M HCl (10 mL) was added and the organic layer was separated. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 5 mL), dried over Na$_2$SO$_4$ and concentrated under reduced pressure. Column chromatography (7:3 Et$_2$O:hexane) afforded 329 (49 mg, 98%).
Oxidation of thioanisole using bis(sulfonyl)hydroxylamine 284:

331 was prepared by a literature procedure.216 Thioanisole (330) (0.10 mL, 0.852 mmol) was heated in acetic acid (1.70 mL) at 60 °C. A solution of hydroxylamine 284 (233 mg, 0.82 mmol) in MeCN (1.70 mL) was added dropwise over a period of 30 min. The solution was heated at 60 °C for a further 2 h. Hydroxylamine 284 (58.0 mg, 0.20 mmol) was added as a solid to the mixture and heated for 4.5 h at 60 °C. The mixture was washed with water (3 × 3 mL), 5% NaOH solution (3 × 3 mL) and extracted with EtOAc (3 × 5 mL). The combined organic phases were dried over MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (7:3 Et₂O:hexane) yielded 3-oxa-1,3-dithiaphenalene 1,1,3,3-tetroxide (333) (35.0 mg, 15%) as a white solid. Further elution (Et₂O) afforded sulfoxide 331 (18.0 mg, 15%). 331: Rf 0.10 (7:3 Et₂O:hexane); mp 29-31 °C; δH(300 MHz; CDCl₃) 2.75 (3 H, s, CH₃) and 7.54-7.70 (5 H, m); δC(75 MHz; CDCl₃) 45.9 (CH₃), 127.4 (2 ×CH), 128.9 (2 × CH), 132.7 (CH) and 143.2 (C). 333: Rf 0.58 (7:3 Et₂O:hexane); mp 211-213 °C; νmax (KBr)/cm⁻¹ 1400, 1384, 1370, 1344, 1180 and 1147; δH(300 MHz; CDCl₃) 7.89 (2 H, dd, J 8.3 and 7.5, ArH) and 8.35 (2 H, dd, J 8.5 and 1.0, ArH) and 8.43 (2 H, dd, J 7.4 and 1.1); δC(100 MHz; CDCl₃) 119.9 (C), 127.0 (CH), 128.5 (CH), 130.5 (C), 133.1 (C), and 135.4 (CH); m/z (ESI) 292.9551 ([M + Na]+, C₁₀H₆O₅S₂Na requires 292.9554), 292.8 (100%).

**Literature data.**273-275 mp 29.5-30 °C, νmax (CHCl₃)/cm⁻¹ 749, 1041 and 3013; δH(300 MHz; CDCl₃) 2.73 (3 H, s, CH₃) and 7.45-7.75 (5 H, m); δC(100 MHz; CDCl₃) 43.83, 123.36, 139.24, 130.92 and 145.51.
Chapter Five: References


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Table 1. Crystal data and structure refinement for BP83.

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X-ray for data for 58

**(bp1m)**: C$_{18}$H$_{22}$OS$_{3}$: Orthorhombic, P-1, FW = 350.54, T = 296, $a = 9.1363(4)$, $b = 9.4337(5)$, $c = 10.8331(5)$ Å, $\alpha = 99.464(3)$, $\beta = 108.734(2)$, $\gamma = 92.962(3)$, $V = 866.72(7)$, $Z = 2$, Final residual wR2 (2σF) = 0.122, R1 = 0.049, with goodness of fit 1.209 on $F^2$. Crystal data for 2: C$_{12}$H$_{10}$O$_3$S$_3$: Monoclinic, P2$_1$/n, FW = 298.38, T = 273, $a = 10.1383(18)$, $b = 6.9855(13)$, $c = 17.520(3)$ Å, $\beta = 95.936(9)$, $V = 1234.1(4)$, $Z = 1$, Final residuals (2σF), wR2 = 0.387, R1 = 0.157, with goodness of fit 1.421 on $F^2$. 
Table 1. Crystal data and structure refinement for s101f2m.

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Table 1. Crystal data and structure refinement for s101f1m.

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<tr>
<td>Completeness to theta = 65.70°</td>
<td>95.2 %</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.7840 and 0.1841</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>1501 / 0 / 136</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.064</td>
</tr>
<tr>
<td>Final R indices [I&gt;2sigma(I)]</td>
<td>R1 = 0.0325, wR2 = 0.0850</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0422, wR2 = 0.0913</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.293 and -0.181 e.Å⁻³</td>
</tr>
</tbody>
</table>
X-ray for data for 103

![Chemical Structure Image]

Table 1. Crystal data and structure refinement for dmto.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>dmto</td>
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<tr>
<td>Empirical formula</td>
<td>C12 H10 O3 S3</td>
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<tr>
<td>Formula weight</td>
<td>298.38</td>
</tr>
<tr>
<td>Temperature</td>
<td>273(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>1.54178 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P21/n</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 10.1383(18) Å, b = 6.9855(13) Å, c = 17.520(3) Å, α = 90°, β = 95.936(9)°, γ = 90°.</td>
</tr>
<tr>
<td>Volume</td>
<td>1234.1(4) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.606 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>5.480 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>616</td>
</tr>
<tr>
<td>Crystal size</td>
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<tr>
<td>Theta range for data collection</td>
<td>4.83 to 65.96°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-11&lt;=h&lt;=10, -6&lt;=k&lt;=7, -17&lt;=l&lt;=20</td>
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<td>Reflections collected</td>
<td>5842</td>
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<tr>
<td>Independent reflections</td>
<td>1869 [R(int) = 0.0842]</td>
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<tr>
<td>Completeness to theta = 65.96°</td>
<td>86.8 %</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Empirical</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.6683 and 0.2902</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>1869 / 0 / 165</td>
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<td>Goodness-of-fit on F²</td>
<td>1.421</td>
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<tr>
<td>Final R indices [I&gt;2sigma(I)]</td>
<td>R1 = 0.1570, wR2 = 0.3872</td>
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<tr>
<td>R indices (all data)</td>
<td>R1 = 0.1807, wR2 = 0.3997</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>1.870 and -0.658 e Å⁻³</td>
</tr>
</tbody>
</table>
X-ray for data for 107

(bp1): C$_{10}$H$_6$O$_2$, $M_r = 206.27$, T = 296(2) K, $\lambda = 1.54178$ Å, Triclinic, P-1, a = 7.629(15) Å, b = 8.665(14) Å, c = 14.72(2) Å, $\alpha = 91.55(9)^\circ$, $\beta = 99.73(10)^\circ$, $\gamma = 110.05(10)^\circ$, V = 897(3) Å$^3$, Z = 4, $\sigma_{cal} = 1.527$ Mg/m$^3$, $\mu = 4.970$ mm$^{-1}$, Crystal size = 0.50 x 0.15 x 0.15 mm$^3$, $\theta_{max} = 64.84^\circ$, Reflections collected = 5035, Independent reflections = 2574, R(int) = 0.0496, Final R1 $[I > 2\sigma(I)] = 0.0534$, Final wR2 $[I > 2\sigma(I)] = 0.1359$, R1 (all data) = 0.0827, wR2 (all data) = 0.1512, Residual electron density = 0.383 e.Å$^{-3}$. The structure contains two molecules in the asymmetric unit. The oxygen atom is disordered between the two S atoms in one of the molecules with 36/64% occupancy for O(2) / O(3).

X-ray for data for 216

(bp365): C$_{18}$H$_{22}$O$_2$, $M_r = 318.48$, T = 293(2) K, $\lambda = 1.54178$ Å, Monoclinic, P2$_1$/c, a = 8.1614(2) Å, b = 20.1864(7) Å, c = 10.1344(3) Å, $\beta = 94.359(2)^\circ$, V = 1664.81(9) Å$^3$, Z = 4, $\sigma_{cal} = 1.271$ Mg/m$^3$, $\mu = 2.854$ mm$^{-1}$, Crystal size = 0.25 x 0.20 x 0.10 mm$^3$, $\theta_{max} = 66.50^\circ$, Reflections collected = 11086, Independent reflections = 2830, R(int) = 0.0378, Final R1 $[I > 2\sigma(I)] = 0.0436$, Final wR2 $[I > 2\sigma(I)] = 0.1179$, R1 (all data) = 0.0512, wR2 (all data) = 0.1237, Residual electron density = 0.631 e.Å$^{-3}$. One $t$-butyl group is rotationally disordered over two sites with 31/69% occupancy.
X-ray for data for 217

(bp395): C\textsubscript{18}H\textsubscript{22}O\textsubscript{2}S\textsubscript{2}, \( M_r = 334.48 \), T = 200(2) K, \( \lambda = 0.67030 \) Å, Triclinic, P-1, a = 8.7247(16) Å, b = 9.4724(18) Å, c = 10.642(2) Å, \( \alpha = 97.649(3)^\circ \), \( \beta = 107.070(2)^\circ \), \( \gamma = 92.469(3)^\circ \), \( V = 830.1(3) \) Å\textsuperscript{3}, \( Z = 2 \), \( \sigma_{\text{cal}} = 1.338 \) Mg/m\textsuperscript{3}, \( \mu = 0.325 \) mm\textsuperscript{-1}, Crystal size = 0.10 x 0.10 x 0.05 mm\textsuperscript{3}, \( \theta_{\text{max}} = 30.06^\circ \), Reflections collected = 10683, Independent reflections = 5577, R(int) = 0.0680, Final R1 [I>2\( \sigma(I) \)] = 0.0711, Final wR2 [I>2\( \sigma(I) \)] = 0.1793, R1 (all data) = 0.0964, wR2 (all data) = 0.2017, Residual electron density = 0.595 e.Å\textsuperscript{-3}. The S\textsubscript{2}O\textsubscript{2} site shows disorder with 87/13% occupancy for O(1)-S(1)-S(2)-O(2) / O(1a)-S(1a)-S(2a)-O(2a).

X-ray for data for 224

(bp376f1): C\textsubscript{18}H\textsubscript{22}O\textsubscript{2}S\textsubscript{2}, \( M_r = 334.48 \), T = 296(2) K, \( \lambda = 1.54178 \) Å, Monoclinic, P2\textsubscript{1}/n, a = 12.1098(5) Å, b = 12.1134(5) Å, c = 12.6884(5) Å, \( \beta = 114.400(2)^\circ \), \( V = 1695.03(12) \) Å\textsuperscript{3}, \( Z = 4 \), \( \sigma_{\text{cal}} = 1.311 \) Mg/m\textsuperscript{3}, \( \mu = 2.874 \) mm\textsuperscript{-1}, Crystal size = 0.23 x 0.20 x 0.10 mm\textsuperscript{3}, \( \theta_{\text{max}} = 66.50^\circ \), Reflections collected = 11118, Independent reflections = 2865, R(int) = 0.0532, Final R1 [I>2\( \sigma(I) \)] = 0.0484, Final wR2 [I>2\( \sigma(I) \)] = 0.1238, R1 (all data) = 0.0585, wR2 (all data) = 0.1290, Residual electron density = 0.318 e.Å\textsuperscript{-3}. The S\textsubscript{2}O\textsubscript{2} site shows disorder with 87/13% occupancy for O(1)-S(1)-S(2)-O(2) / O(1a)-S(1a)-S(2a)-O(2a).
X-ray for data for 225

(bp510): \( \text{C}_{18}\text{H}_{22}\text{O}_2\text{S}_2, M_r = 334.48, T = 296(2) \, \text{K}, \lambda = 1.54178 \, \text{Å}, \text{Triclinic, P-1, } a = 8.6970(4) \, \text{Å}, b = 9.5037(4) \, \text{Å}, c = 10.6581(4) \, \text{Å}, \alpha = 97.635(3)^\circ, \beta = 107.551(2)^\circ, \gamma = 91.727(3)^\circ. \) \( V = 830.18(6) \, \text{Å}^3, Z = 2, \sigma_{\text{cal}} = 1.338 \, \text{Mg/m}^3, \mu = 2.934 \, \text{mm}^{-1}, \) Crystal size = 0.30 x 0.20 x 0.20 mm\(^3\), \( \theta_{\text{max}} 65.74^\circ, \) Reflections collected = 5460, Independent reflections = 2557, R(int) = 0.0267, Final R1 [I>2\( \sigma(I) \)] = 0.0429, Final wR2 [I>2\( \sigma(I) \)] = 0.1148, R1 (all data) = 0.0469, wR2 (all data) = 0.1183, Residual electron density = 0.752 e.Å\(^{-3}\).

X-ray for data for 226

(bp350): \( \text{C}_{18}\text{H}_{22}\text{O}_3\text{S}_2, M_r = 350.48, T = 296(2) \, \text{K}, \lambda = 1.54178 \, \text{Å}, \text{Monoclinic, P2}_1/\text{n, } a = 8.396(4) \, \text{Å}, b = 20.943(11) \, \text{Å}, c = 9.891(5) \, \text{Å}, \beta = 94.459(16)^\circ, V = 1734.0(15) \, \text{Å}^3, Z = 4, \sigma_{\text{cal}} = 1.343 \, \text{Mg/m}^3, \mu = 2.880 \, \text{mm}^{-1}, \) Crystal size = 0.15 x 0.13 x 0.10 mm\(^3\), \( \theta_{\text{max}} 65.74^\circ, \) Reflections collected = 6613, Independent reflections = 2128, R(int) = 0.0710, Final R1 [I>2\( \sigma(I) \)] = 0.0591, Final wR2 [I>2\( \sigma(I) \)] = 0.1007, R1 (all data) = 0.1128, wR2 (all data) = 0.1181, Residual electron density = 0.158 e.Å\(^{-3}\). The S\(_2\)O\(_3\) site shows disorder with 86/14% occupancy for O(1)-O(2)-S(1)-S(2)-O(3) / O(1a)-O(2a)-S(1a)-S(2a)-O(3a).
Table 1. Crystal data and structure refinement for bp516.

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<td>Empirical formula</td>
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<td>Formula weight</td>
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<td>Temperature</td>
<td>293(2) K</td>
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<td>Wavelength</td>
<td>1.54178 Å</td>
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<tr>
<td>Crystal system</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P-1</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
<tr>
<td>a = 9.0991(6) Å</td>
<td>α = 107.604(4)°</td>
</tr>
<tr>
<td>b = 11.3796(7) Å</td>
<td>β = 108.300(4)°</td>
</tr>
<tr>
<td>c = 12.7428(8) Å</td>
<td>γ = 102.799(4)°</td>
</tr>
<tr>
<td>Volume</td>
<td>1118.64(12) Å³</td>
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<tr>
<td>Z</td>
<td>2</td>
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<td>Density (calculated)</td>
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<td>5.595 mm⁻¹</td>
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<tr>
<td>F(000)</td>
<td>488</td>
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<td>Crystal size</td>
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<tr>
<td>Theta range for data collection</td>
<td>3.99 to 65.94°</td>
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<tr>
<td>Index ranges</td>
<td>-10≤h≤9, -13≤k≤12, -14≤l≤14</td>
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<tr>
<td>Reflections collected</td>
<td>7293</td>
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<td>Independent reflections</td>
<td>3418 [R(int) = 0.0399]</td>
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<tr>
<td>Completeness to theta = 65.94°</td>
<td>87.6 %</td>
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<td>Absorption correction</td>
<td>Empirical</td>
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<tr>
<td>Max. and min. transmission</td>
<td>0.4008 and 0.3352</td>
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<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
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<tr>
<td>Data / restraints / parameters</td>
<td>3418 / 0 / 250</td>
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<td>Goodness-of-fit on F²</td>
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<tr>
<td>Final R indices [I&gt;2sigma(I)]</td>
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<td>Largest diff. peak and hole</td>
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Table 1. Crystal data and structure refinement for bp2.

<table>
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<td>Formula weight</td>
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<td>Temperature</td>
<td>296(2) K</td>
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<tr>
<td>Wavelength</td>
<td>1.54178 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P21/n</td>
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<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
<tr>
<td>a</td>
<td>14.1894(3) Å</td>
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<tr>
<td>b</td>
<td>7.1236(2) Å</td>
</tr>
<tr>
<td>c</td>
<td>18.0588(4) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>1684.87(7) Å</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
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<tr>
<td>Density (calculated)</td>
<td>1.472 Mg/m³</td>
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<td>Absorption coefficient</td>
<td>3.207 mm⁻¹</td>
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<td>F(000)</td>
<td>776</td>
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<td>Crystal size</td>
<td>0.30 x 0.20 x 0.20 mm³</td>
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<tr>
<td>Theta range for data collection</td>
<td>3.40 to 70.87°.</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-15&lt;=h&lt;=17, -7&lt;=k&lt;=8, -19&lt;=l&lt;=22</td>
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<tr>
<td>Reflections collected</td>
<td>10441</td>
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<tr>
<td>Independent reflections</td>
<td>3067 [R(int) = 0.0385]</td>
</tr>
<tr>
<td>Completeness to theta = 70.87°</td>
<td>94.3 %</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Empirical</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.5664 and 0.4462</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
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<tr>
<td>Data / restraints / parameters</td>
<td>3067 / 0 / 221</td>
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<tr>
<td>Goodness-of-fit on F²</td>
<td>1.040</td>
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<tr>
<td>Final R indices [I&gt;2sigma(I)]</td>
<td>R1 = 0.0388, wR2 = 0.0992</td>
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<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0515, wR2 = 0.1083</td>
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<td>Extinction coefficient</td>
<td>0.0105(5)</td>
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<tr>
<td>Largest diff. peak and hole</td>
<td>0.257 and -0.271 e.Å⁻³</td>
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Table 1. Crystal data and structure refinement for BP886.

<table>
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<th>Property</th>
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<td>Identification code</td>
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<tr>
<td>Empirical formula</td>
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<tr>
<td>Formula weight</td>
<td>303.30</td>
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<tr>
<td>Temperature</td>
<td>120(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
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<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P 2(1)/n</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
<tr>
<td>$a$ = 6.9698(2) Å</td>
<td>$\alpha = 90^\circ$.</td>
</tr>
<tr>
<td>$b$ = 9.4671(3) Å</td>
<td>$\beta = 94.399(2)^\circ$.</td>
</tr>
<tr>
<td>$c$ = 17.7500(4) Å</td>
<td>$\gamma = 90^\circ$.</td>
</tr>
<tr>
<td>Volume</td>
<td>1167.76(6) Å$^3$</td>
</tr>
<tr>
<td>$Z$</td>
<td>4</td>
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<tr>
<td>Density (calculated)</td>
<td>1.725 Mg/m$^3$</td>
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<td>Absorption coefficient</td>
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<td>$F(000)$</td>
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<td>Crystal size</td>
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<tr>
<td>Theta range for data collection</td>
<td>3.07 to 27.48°</td>
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<tr>
<td>Index ranges</td>
<td>-8&lt;=$h$&lt;=$9$, -12&lt;=$k$&lt;=$12$, -22&lt;=$l$&lt;=$23$</td>
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<tr>
<td>Reflections collected</td>
<td>16422</td>
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<tr>
<td>Independent reflections</td>
<td>2668 [R(int) = 0.0898]</td>
</tr>
<tr>
<td>Completeness to theta = 27.48°</td>
<td>99.9 %</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Semi-empirical from equivalents</td>
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<tr>
<td>Max. and min. transmission</td>
<td>0.9403 and 0.7819</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on $F^2$</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
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<td>Goodness-of-fit on $F^2$</td>
<td>1.082</td>
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<tr>
<td>Final R indices [I&gt;2sigma(I)]</td>
<td>R1 = 0.0552, wR2 = 0.1506</td>
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<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0645, wR2 = 0.1599</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.773 and -0.973 e.Å$^{-3}$</td>
</tr>
</tbody>
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