UNIVERSITY OF
BIRMINGHAM

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

by

Bhaven Patel

A thesis submitted to

The University of Birmingham

For a degree of

DOCTOR OF PHILOSOPHY

School of Chemistry

University of Birmingham

July 2009

Acknowledgments

Firstly, I would like to thank Richard S. Grainger for his inspiration, guidance and support throughout this project.

There are many people I would like to thank for helping me throughout my PhD, but the list is too long. There are a few people that I would to thank though.

A big thank you to all of the Grainger group past and present. I have been in this group for a long time now. A special thanks to Paolo and Emma for helping start in the group 5 years ago and for their continued advice throughout. I would also like to thank Luke, Katia, Shamim, Bene, Tyrone, Claire and Pete for the fun in and out of the lab. Without you guys this would have been very difficult. Thanks to Professor Curt Wentrup, David, Nathan and Ben for my time at UQ.

Many thanks go to the analytical services for their support and assistance; Dr Neil Spencer for NMR, Pete Ashton, Nick May and Lianne Hill for mass spec. Drs Benson Kariuki and Louise Male for X-ray crystallography and Dr Ruth Edge from the EPSRC EPR service in Manchester. Very special thanks to Graham Burns for HPLC, always being there when needed and as a friend.

Thanks for the financial support from the EPSRC.

Cynthia, Tyrone and Richard for having to proof read my work in the final stages, I know this was painful for you all but it is very much appreciated.

All of my friends in Birmingham and London for their support especially Emma, Bene, Carlos, Lucia and Cynthia.

Special thanks must go to my family; thanks to my parents and brother for their support over the years. Thank you all from the bottom of my heart, for always guiding me and being there for me. I would not have got through this without you.

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 dithiols 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*-butylnaphtho[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 H_2O/1,4-dioxane. Deuterium incorporation occurred on running the reaction in D_2O/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(1*H*)-pyrimidinone
DMSO	dimethylsulfoxide
DPPH	2,2-diphenyl-1-picrylhydrazyl
EDG	electron-donating group
EDRF	endothelium-derived relaxing factor
EDTA	ethylenediamine tetraacetate

EI	electron impact
EPR	electron paramagnetic resonance
equiv.	equivalent
ESI	electrospray ionisation
Et	ethyl
EWG	electron-withdrawing group
FT-IR	fourier transform infrared
FVT	flash vacuum thermolysis
g	gramme(s)
GST	glutathione S-transferase
h	hour(s)
[H]	reduction
HMBC	heteronuclear multiple bond correlation
HPLC	high performance liquid chromatography
HMPA	hexamethylphosphoramide
HRMS	high resolution mass spectrometry
HSAB	hard and soft acids and bases
HSQC	heteronuclear single quantum coherence
Hz	hertz
i	*iso*
IR	infrared
ISC	inter system crossing
J	coupling constant (in NMR)
L	litre
m	multiplet

M	molar
*m*CBA	*meta*-chlorobenzoic acid
*m*CPBA	*meta*-chloroperbenzoic acid
Me	methyl
min	minute(s)
mol	moles
mp	melting point
MSH	*O*-mesitylsulfonylhydroxylamine
MTO	methyltrioxorhenium
m/z	mass/charge
n	normal
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance
[O]	oxidation
o/n	overnight
p	*para*
pet ether	60-80 °C petroleum ether
Ph	phenyl
ppm	part(s) per million
Pr	propyl
q	quartet
quant.	quantitative
rt	room temperature
r.d.s.	rate-determining step
s	singlet

t	*tert*
t	triplet
TBAB	tetrabutylammonium bromide
TBAF	tetrabutylammonium fluoride
TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
TGA	thermal gravimetric analysis
THF	tetrahydrofuran
TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine
Ts	*p*-toluenesulfonyl
u	atomic mass unit
UHP	urea-hydrogen peroxide
UV	ultraviolet
vic	*vicinal*
vs.	versus
v	frequency

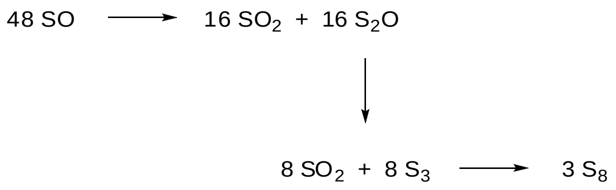
Contents

Chapter One: Sulfur monoxide transfer from 1,8-dithianaphthalene trisulfide-2-oxides

Background and significance

1.1 Sulfur monoxide

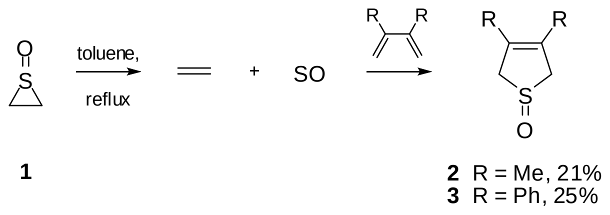
Sulfur monoxide (SO) is a reactive diatomic molecule that is isoelectronic with molecular oxygen. The physical properties and thermal decomposition of sulfur monoxide have been reported.[1] SO is an extremely unstable gas and has a half life of 20 ms, undergoing rapid disproportionation in less than 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.



Scheme 1.1 Sulfur monoxide breakdown in the gas phase

1.2 Previous sulfur monoxide transfer reagents

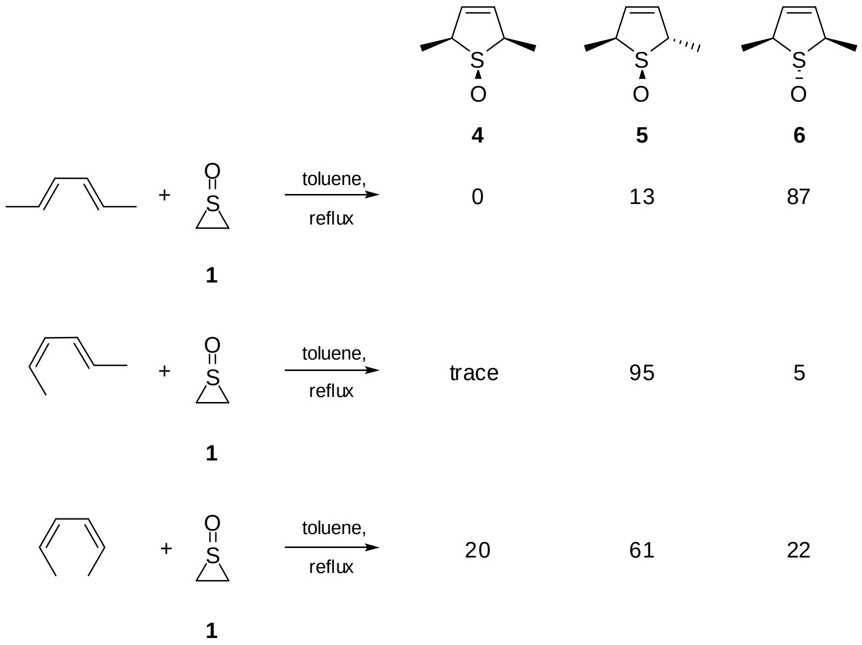
There has been substantial interest in uncovering simple chemical processes to produce SO and trap it *in situ*. Dodson and Sauer reported the first SO transfer reagent; they used strained episulfoxide **1** to transfer sulfur monoxide to 1,3-dienes to furnish dihydrothiophene *S*-oxides in moderate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



Scheme 1.2 SO transfer from ethylene episulfoxide

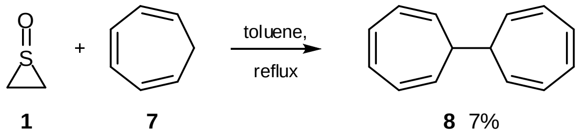
Saito extended this study by analysing the products from the pyrolysis of episulfoxide **1**.[6] It was deduced that the reaction proceeded by collapse of the three-membered ring in **1** to form ethylene and free SO (scheme 1.2).[5] Characteristic signals of ethylene sulfide and ethylene oxide were absent, and peaks attributed to sulfur monoxide in its triplet ground state were observed.[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.[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).[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.[9]



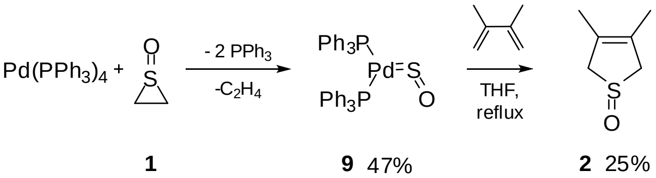
Scheme **1.3** SO transfer to hexa-2,4-dienes

Ethylene episulfoxide **1** has been reported to react with trienes by Dodson.[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.[10] This reaction is presumed to occur *via* H-abstraction from **7** by triplet SO followed by dimerisation of the resulting cycloheptatrienyl radical (scheme 1.4).



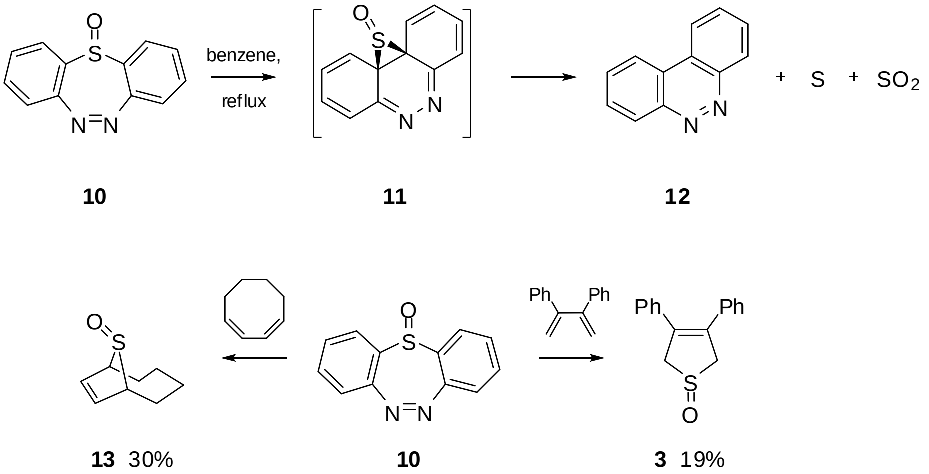
Scheme 1.4 Dimerisation of cycloheptatriene

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.[11] Heyke[12] and Schenk[13] introduced transition metal-coordinated SO transfer reagents. Trapping experiments in the presence of dienes resulted in comparable yields of sulfoxides (scheme 1.5).



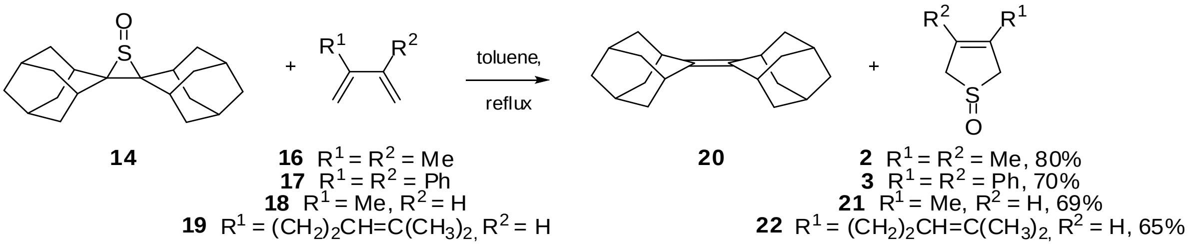
Scheme 1.5 Pd coordinated SO transfer reagent

In 1970, Chow and co-workers reported a different source of SO.[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_2.[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).



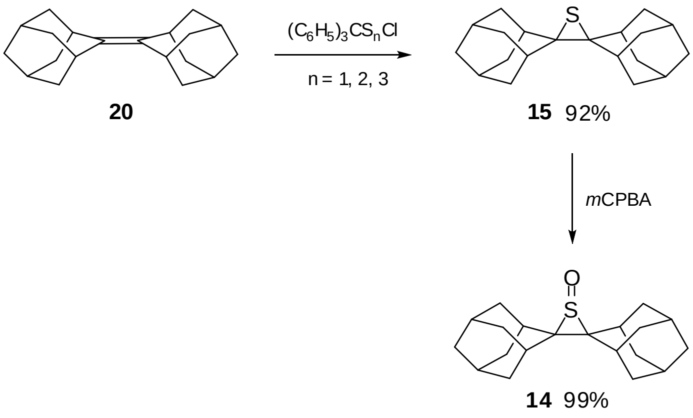
Scheme 1.6 Thermal decomposition of dibenzo{*b*,*f*} [1,4,6]thiadiazepin-1-oxide

Harpp and Abu-Yousef introduced an improved source of SO in 1997.[11, 15] 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).



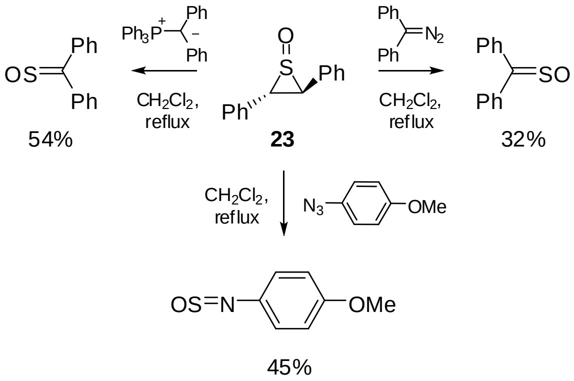
Scheme 1.7 SO transfer from adamantyl-derived episulfoxide

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).



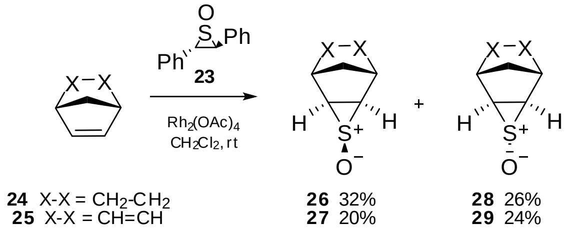
Scheme 1.8 Synthesis of episulfoxide **14**

SO transfer from the *trans* stilbene-derived thiirane oxide **23** to diazoalkanes,[16] azides[17] and ylides has been reported (scheme 1.9).[18]



Scheme 1.9 Reactions of *trans* stilbene-derived episulfoxide **23**

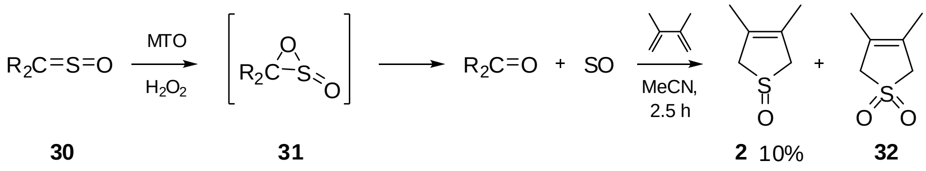
Simpkins furthered the study of this SO transfer reagent by employing **23** in a $Rh_2(OAc)_4$ catalysed reaction.[19, 20] In the absence of the rhodium catalyst no reaction was observed with norbornene **24** or norbornadiene **25**. The addition of the $Rh_2(OAc)_4$ resulted in the reaction occurring at room temperature and isolation of the desired episulfoxides in moderate yields (scheme 1.10).



Scheme 1.10 Rhodium-catalysed SO transfer to strained alkenes

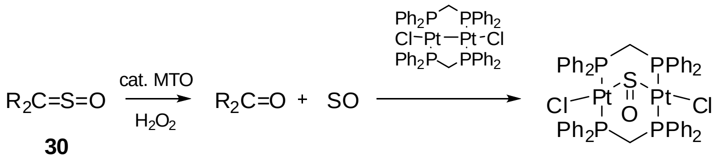
It is assumed that rhodium inserts into the C-S bond and that the resulting Rh(SO) complex is the reacting species. The limitation with this method of SO transfer is that it only occurs with strained alkenes **24** and **25**.

The thermal breakdown of other strained small ring systems **31**[21] and **33**[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_2O_2 oxidation of sulfine **30**, catalysed by CH_3ReO_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**.[21]



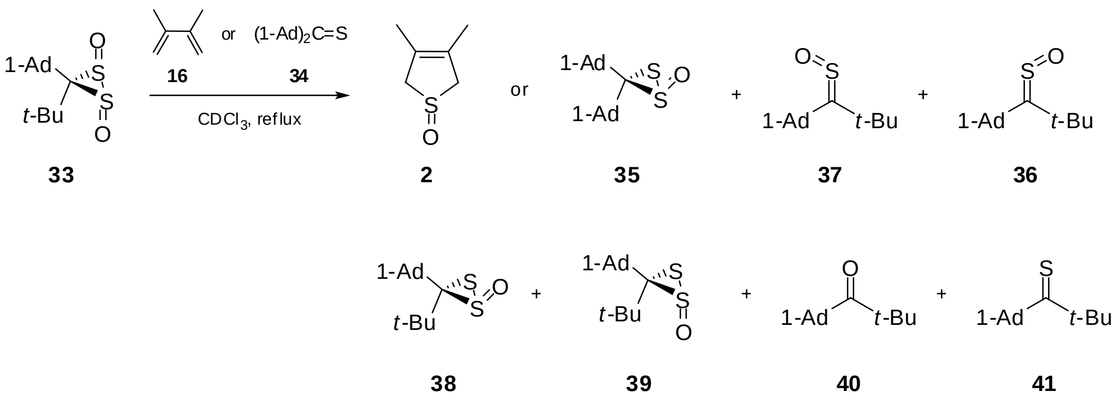
Scheme 1.11 Methyltrioxorhenium-catalysed sulfoxidation

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).[23]



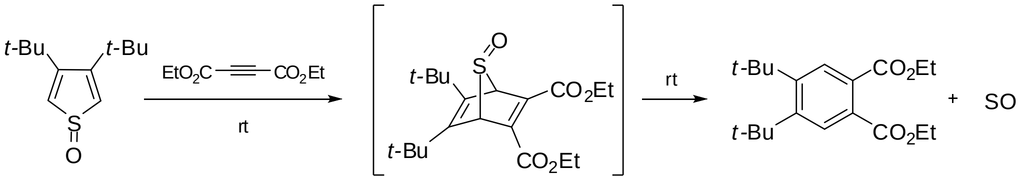
Scheme 1.12 SO insertion into a Pt-Pt bond

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



Scheme 1.13 Thermal breakdown of *vic*-disulfoxide **33**

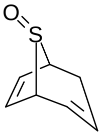
A recent report by Nakayama's group described the cycloaddition of SO to alkenes and alkynes at room temperature.[24] The reaction of 3,4-di-*tert*-butylthiophene 1-oxide (**42**) with dimethyl acetylenedicarboxylate produces bridged bicyclic sulfoxide intermediate **43** which probably decomposes through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



42 **43** **44**

Scheme 1.14 Room temperature SO release from thiophene 1-oxide **42**

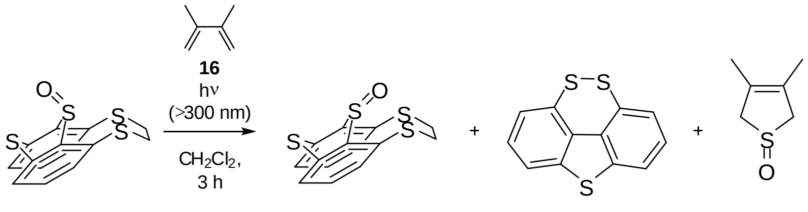
The SO generated *in situ* from **42** has successfully been trapped with dienes and some strained alkenes and alkynes to provide sulfoxides in poor to modest yields. More interestingly in the presence of cycloheptatriene the product observed was not 7,7'-bicycloheptatriene (**8**) but sulfoxide **45**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



45

Figure 1.1 ^{1}SO transfer to cycloheptatriene

Photolysis of structurally fascinating **46** was reported by Morita in 2009 to generate SO.[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-dithiabenzothiophene **48**. The reaction was monitored by ^{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).

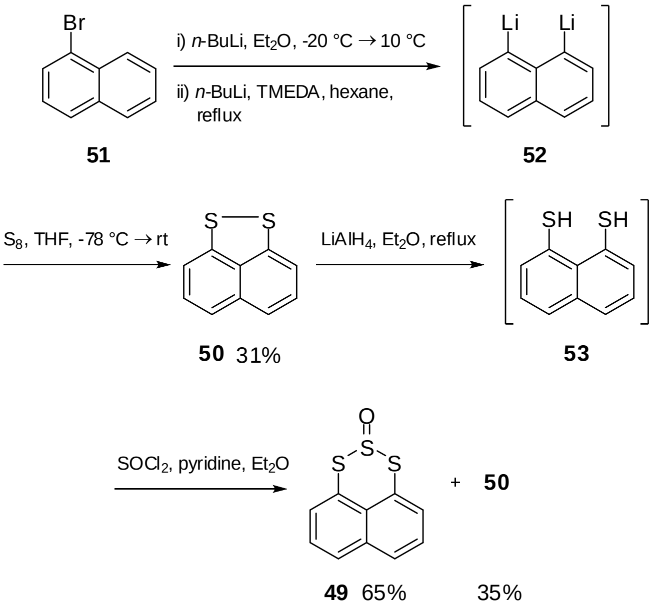


46 **47** 27% **48** 47% **2** 73%

Scheme 1.15 Photolysis of SO transfer reagent **46**

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.[26, 27] 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**)

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 sp^2 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.

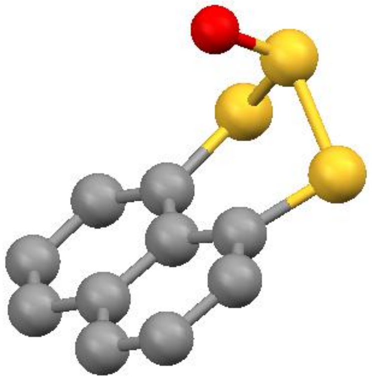
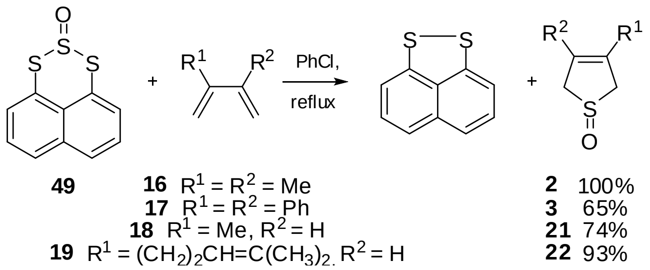


Figure 1.2 X-ray of trisulfide-2-oxide **49**

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]



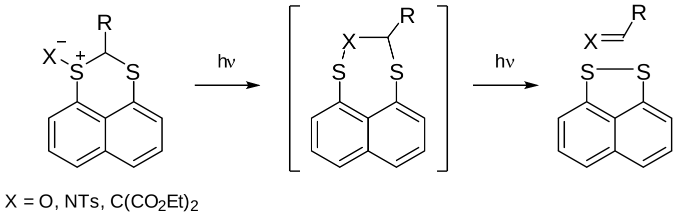
Scheme 1.17 SO transfer from trisulfide-2-oxide to 1,3 dienes

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.[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).



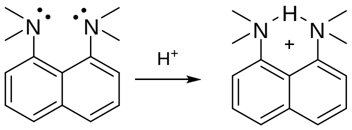
54

50

Scheme 1.18 Photomediated extrusion from 1,8-dithianaphthalene **54**

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.[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.[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).[37]



55

Scheme 1.19 1,8-bisdimethylaminonaphthalene as a proton sponge

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).[38, 39]

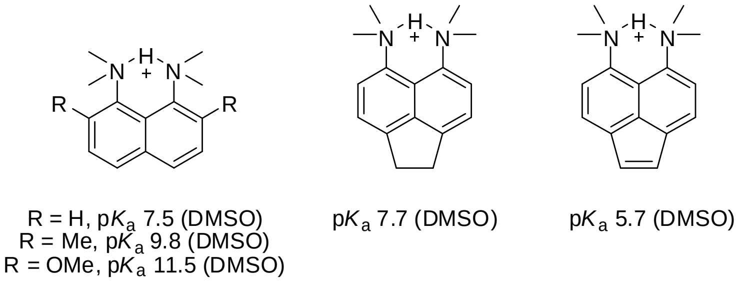
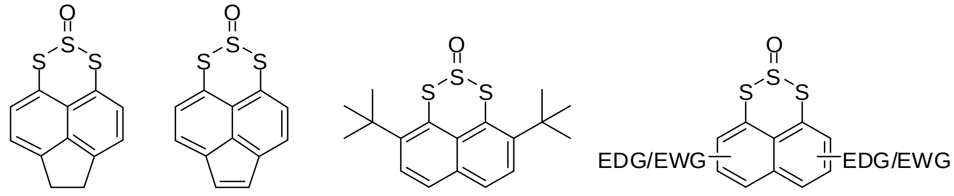


Figure 1.3 pK_a's of substituted proton sponges

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.



56 **57** **58** **59**

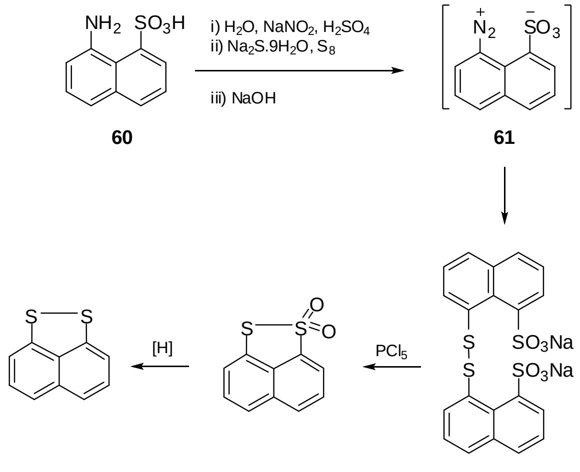
Figure 1.4 Proposed strained trisulfide-2-oxides

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.[26, 27] 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).[40]



Scheme 1.20 Synthesis of disulfide **50** reported by Zweig and Hofmann

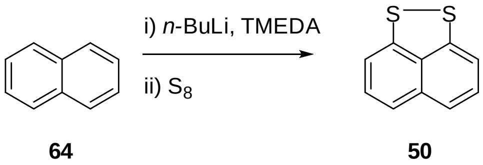
This method uses the inexpensive 8-aminonaphthalene-1-sulfonic acid (**61**) with sodium disulfide to afford the bissulfonate **62**. Treatment of **62** in the presence of PCl_5 produced naphtho[l,8-*cd*][l,2]dithiole 1,l-dioxide (**63**), which in turn is reduced with zinc to disulfide **50**, *via* air oxidation of dithiol **53**. This route yielded only traces of dioxide **63** with either PCl_5 or $SOCl_2$ (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).[26, 27] Two equiv. of *n*-butyllithium were used to form the thermodynamic dilithio species **52**,[41] 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.[42] Komatsu reported activation of S_8 in a solution of toluene by irradiation with a 500 W halogen lamp.[43] 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).

Entry	Sulfur quench of dilithio **52**	**50** (%)
1	Elemental sulfur	13
2	Activated sulfur	25
3	Recrystallised sulfur	37
4	S_2Cl_2	3

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).[44] 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

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.

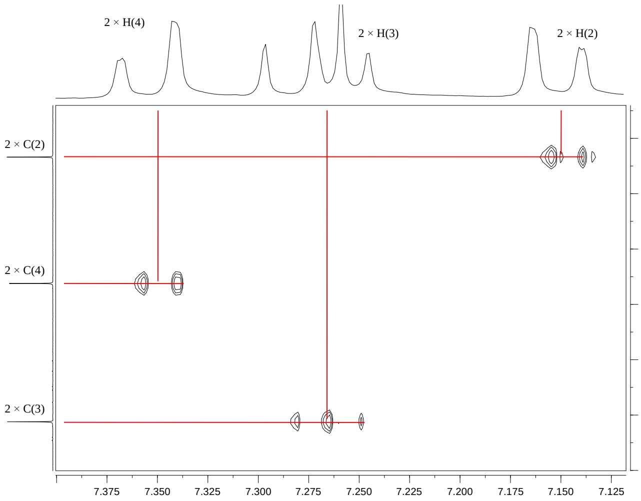


Figure 1.5 HSQC of **50**

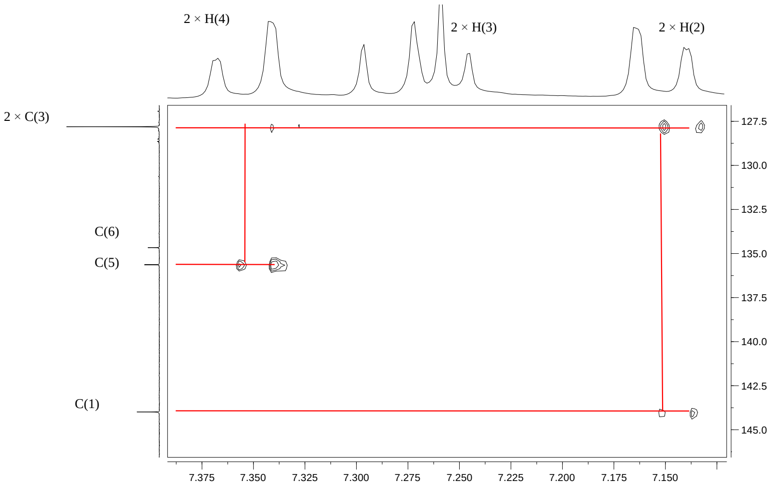
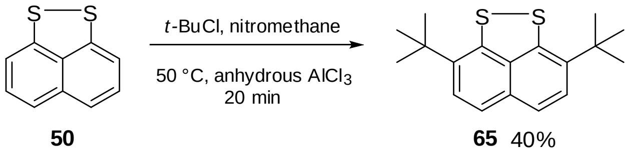


Figure 1.6 HSQC-^{1}J(CC)-ADEQUATE of **50**

To explore the steric buttressing effect, 3,8-di-*tert*-butylnaphtho[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).[45] 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.



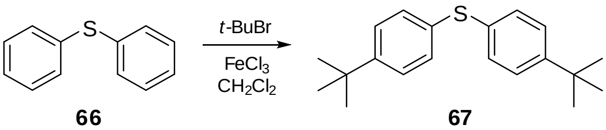
Scheme 1.22 Synthesis of disulfide **65**

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]

Entry	Reaction time (min)	Molar equiv. of $AlCl_3$	**65** (%)
1	20	0.19	48
2	20	0.50	0
3	20	1.00	0
4	40	0.19	0
5	20	0.19	0

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

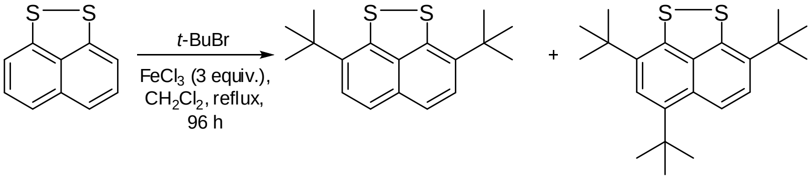
Attention was switched to an alternative set of conditions described by Carpino, who reported the Friedel-Crafts *tert*-butylation of sulfide **66** (scheme 1.23).[47] These conditions were used to find a more reliable method for generating disulfide **65**.



66 **67**

Scheme 1.21 Friedel-Crafts *tert*-butylation of phenyl sulfide **66**

Refluxing disulfide **50** with 3 equiv. of *tert*-butylbromide in CH_2Cl_2 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).



50 **65** 34% **68** 27%

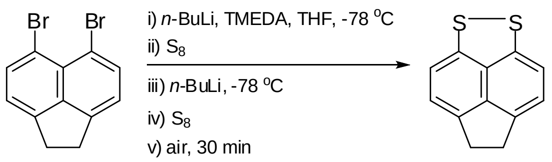
Scheme 1.24 Improved synthesis of disulfide

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).

Entry	Molar equiv. of $FeCl_3$	**65** (%)	**68** (%)
1	2	44	0
2	3	34	27

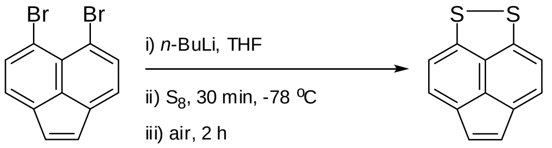
Table 1.3 Friedel-Crafts alkylation of **50** using $FeCl_3$

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 Aso[48] and Meinwald[49] respectively (scheme 1.25 and 1.26).



71 **69**

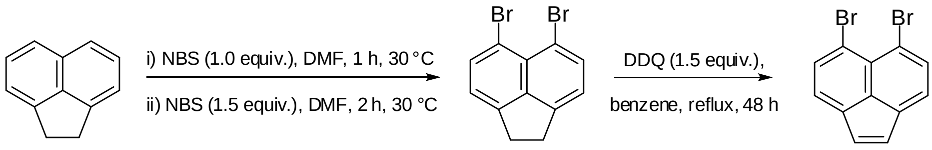
Scheme 1.25 Synthesis of bridged disulfide **69**



72 **70**

Scheme 1.26 Synthesis of bridged disulfide **70**

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).[50] The double bond was introduced *via* DDQ oxidation, as reported by Mitchell, to yield 5,6-dibromoacenaphthylene (**72**).[51] Although reported to give a 75% yield, only a 28% yield of **72** was achieved after purification (scheme 1.27).



73 **71** 25% **72** 28%

Scheme 1.27 Bromination and oxidation of 1,2-dihydroacenaphthylene

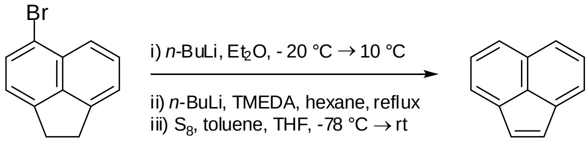
With both dibromo compounds **71** and **72** in hand, attempts to convert them to 1,2-dihydroacenaphtho[5,6-*cd*][1,2]dithiole (**69**) and acenaphtho[5,6-*cd*][1,2]dithiole (**70**) were carried out. Woollins' group has recently synthesised **69** employing conditions reported by Aso using biobeads as a means of purification. [46, 52] The conditions reported by Aso afforded the desired disulfide **69** after separation using biobeads in a 9% yield (table 1.4, entry 1),[48] 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 Et_2O resulted in a mixture of compounds (entry 5).

Entry	Starting dibromide	Conditions	Result
1	**71**	i) *n*-BuLi (1 equiv.), TMEDA, THF ii) S_8 iii) *n*-BuLi (1 equiv.), TMEDA, THF iv) S_8	**69** 9%
2	**72**	i) *n*-BuLi (2 equiv.), THF ii) S_8	mixture of unidentifiable products
3	**71**	i) *n*-BuLi (2 equiv.), TMEDA, THF ii) S_8	mixture of unidentifiable products
4	**72**	i) *n*-BuLi (1 equiv.), TMEDA, THF ii) S_8 iii) *n*-BuLi (1 equiv.), TMEDA, THF iv) S_8	mixture of unidentifiable products
5	**72**	i) *n*-BuLi (2 equiv.), Et_2O ii) S_8	mixture of unidentifiable products

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**).[53] The lithiated species was quenched with D_2O and NMR analysis confirmed that a mixture of both the mono and di-deuterated species were present.

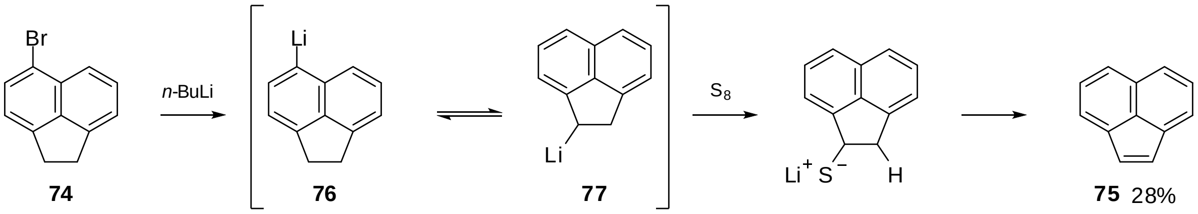
Commercially available 5-bromoacenaphthene (**74**) was then considered in an attempt to use the conditions exploited for 1-bromonaphthalene (**51**) to synthesise **69**.[26] Remarkably, the product of this reaction was acenaphthylene (**75**) (scheme 1.28).



74 **75**

Scheme 1.28 Attempted synthesis of **68**

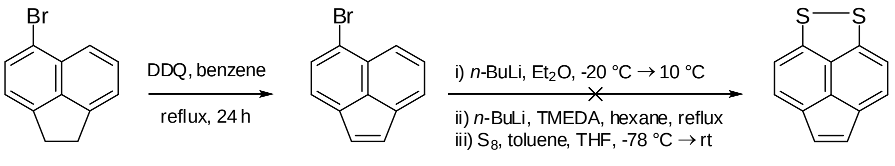
The reaction may proceed through a lithium-halogen exchange to form **76**, with the lithium in the *peri*-position. **76** is thought to be in equilibrium with **77**, where the benzyl position is lithiated. Sulfur quench of **77** followed by aromatisation produces **75** (scheme 1.29). Sulfur and 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.[54, 55] Alternatively **75** may arise from the reaction of sulfur with 1,2-dihydroacenaphthylene (**73**), although this transformation generally requires high temperatures.[55]



74 **76** **77** **75**

Scheme 1.29 Proposed formation of acenaphthylene from 5-bromoacenaphthene

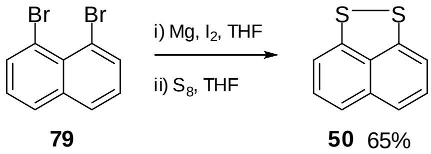
Attention turned to 5-bromoacenaphthylene (**78**) as there are no acidic benzylic protons present. DDQ oxidation of **74** proceeded in moderate yield in refluxing benzene. The product however contained inseparable dibromide **72**, as a result of an impurity in the starting material. Conditions analogous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



74 **78** **70**

Scheme 1.30 Unsuccessful synthesis of **70**

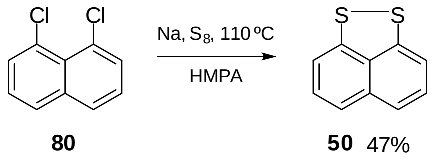
Disulfide **50** has previously been prepared in the group in 35% yield, starting from 1,8-dibromonaphthalene (**79**) *via* the 1,8-diGrignard (scheme 1.31).[26] Attempts to furnish the bridged disulfides **69** and **70** *via* the bisGrignard, starting from **71** and **72**, respectively, resulted 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

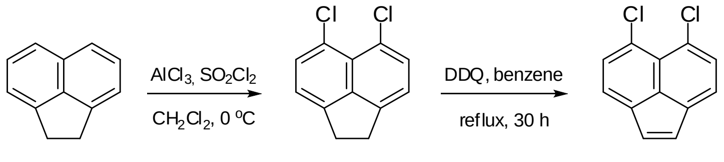
Disulfides are also synthesised from the reaction of both alkyl and aryl dibromo compounds with sodium disulfide (Na_2S_2).[45] Attempted synthesis of disulfides **69** or **70** using Na_2S_2 as the reagent in DMF resulted in a complex mixture of compounds which could not be purified by column chromatography (entries 3 and 4).

Gamage reported the synthesis of disulfide **50** from 1,8-dichloronaphthalene (**80**) using sodium disulfide (scheme 1.32).[56] 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

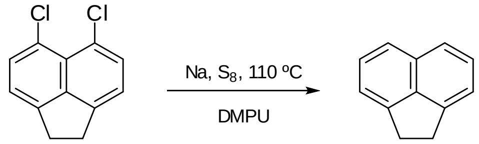
5,6-Dichloro-1,2-dihydroacenaphthylene (**81**) and 5,6-dichloroacenaphthylene (**82**) were successfully synthesised.[57] Chlorination of **73** with sulfuryl chloride in the presence of catalytic aluminium chloride furnished 5,6-dichloroacenaphthene **81**. Oxidation utilising DDQ of **81** resulted in 5,6-dichloroacenaphthylene **82** (scheme 1.33).



73 **81** 25% **82** 28%

Scheme 1.33 Chlorination and oxidation of **73**

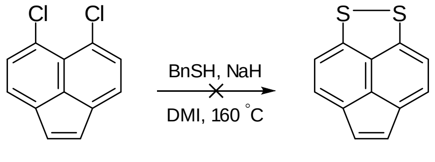
The conditions of Gamage were adopted with dipolar aprotic DMPU used as a replacement for the carcinogenic HMPA.[58] Remarkably, the product obtained from this reaction was 1,2-dihydroacenaphthylene (**73**) in near quantitative yield (scheme 1.34, entry 5) with none of the desired disulfide **69** observed.



81 **73** 99%

Scheme 1.34 Attempted chloride displacement using sodium disulfide

Starting material was recovered when attempting to add sodium thiocyanate[59] to dichloro compounds **81** and **82** (entries 6-9). When reacting dichloride **81** with sodium benzyl thiolate[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).



82 **70**

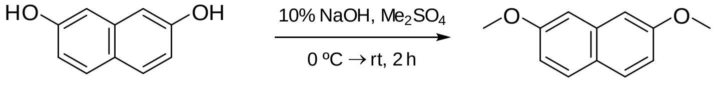
Scheme 1.35 Attempted synthesis of disulfide **70**

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.

Entry	Starting material	Conditions	Results
1	**71**	i) Mg (10.0 equiv.), THF, 65 °C, 3 h ii) S_8 (2.1 equiv.), THF, rt, o/n	**71** 67%
2	**72**	i) Mg (10.0 equiv.), THF, 65 °C, 3 h ii) S_8 (2.1 equiv.), THF, rt, o/n	**72** 87%
3	**71**	Na (6.8 equiv.), S_8 (6.8 equiv.), DMF, 140 °C, 30 min	mixture
4	**712**	Na (6.8 equiv.), S_8 (6.8 equiv.), DMF, 140 °C, 30 min	mixture
5	**81**	Na (2.5 equiv.), S_8 (2.5 equiv.), DMPU, 150 °C, 24 h	**73** 99%
6	**81**	NaSCN (2.1 equiv.), DMF, reflux, 16 h	**81** 93%
7	**82**	NaSCN (2.1 equiv.), DMF, reflux, 16 h	**82** 92%
8	**81**	NaSCN (2.1 equiv.), DMI, reflux, 16 h	**81** 83%
9	**82**	NaSCN (2.1 equiv.), DMI, reflux, 16 h	**82** 88%
10	**81**	BnSH (6.0 equiv.), NaH (6.70 equiv.), DMI, 160 °C	mixture of compounds with **69** as the major product
11	**82**	BnSH (6.0 equiv.), NaH (6.70 equiv.), DMI, 160 °C	**82** 79%

Table 1.5 Conditions utilised for the formation of disulfides **69** and **70**

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.[62] Thus the first step was methylation of diol **83** with dimethyl sulfate to furnish 2,7-dimethoxynaphthalene (**84**) in excellent yields (scheme 1.36).[63]

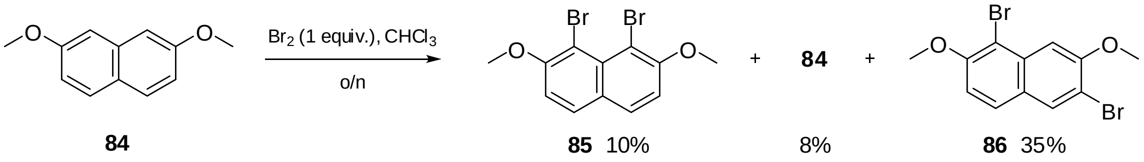


83

84 91%

Scheme 1.36 Methylation of dihydroxynaphthalene

Adams *et al*. reported that mono-bromination of **84** with bromine occurred in the *peri* position.[64] 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 *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).



Scheme 1.37 Bromination of 2,7-dimethoxynaphthalene

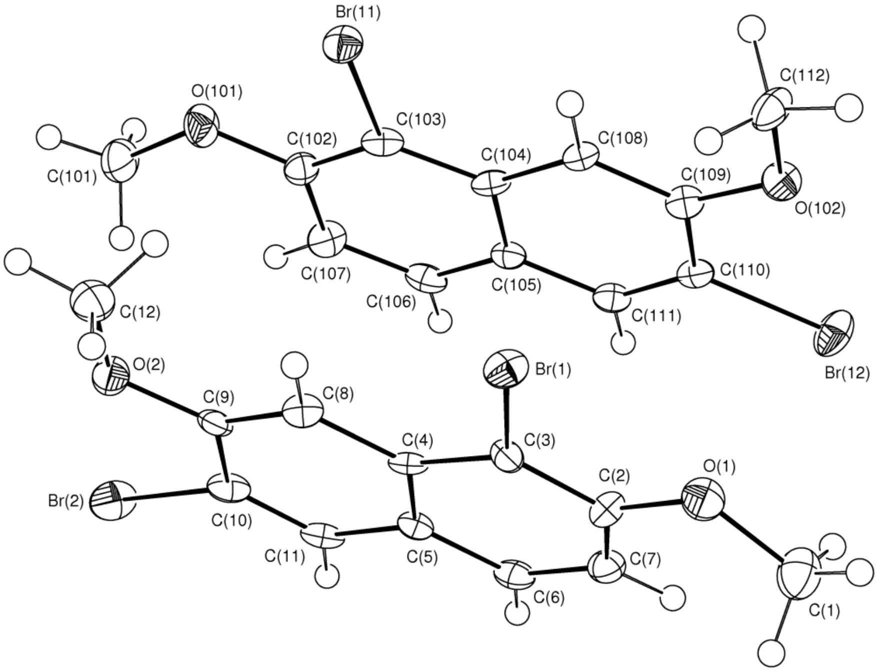
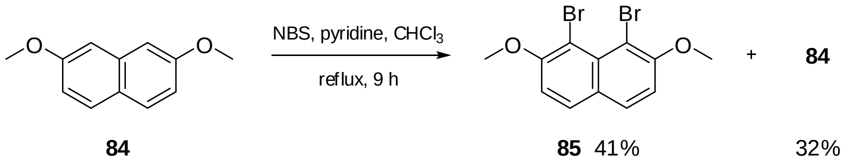


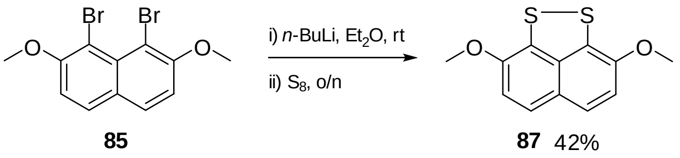
Figure 1.7 Ortep view of **86** with ellipsoids drawn at the 50% probability level

Whiting *et al*. reported regioselective dibromination at the *peri*-positions with the use of NBS and pyridine with both diol **83** and 2,7-diisopropoxynaphthalene.[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.



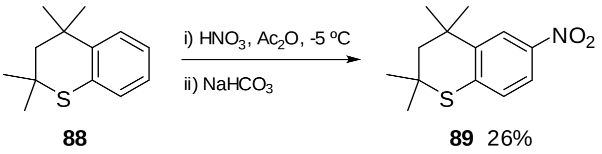
Scheme 1.38 Synthesis of 1,8 dibromo-2,7-dimethoxynaphthalene (**85**)

In order to obtain 3,8-dimethoxynaphtho[1,8-*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.[53] Reaction of 2 equiv. of *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%).



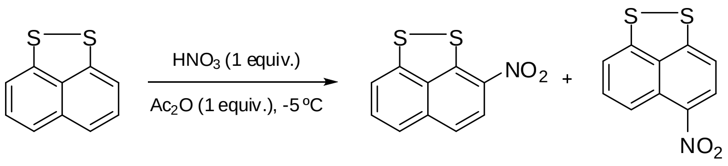
Scheme 1.39 Synthesis of disulfide **87**

Along with **87**, an electron-rich disulfide, electron-deficient disulfides were also explored. The nitration of disulfide **50** with the dinitrogen tetroxide (N_2O_4) has been reported by Oae to quantitatively yield a mixture of *ortho* and *para* regioisomers.[65] Due to the expense of N_2O_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).[66]



Scheme 1.40 Aromatic nitration using HNO_3 and Ac_2O

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-*cd*][1,2]dithiole (**90**) and 5-nitronaphtho[1,8-*cd*][1,2]dithiole (**91**), in a combined 37% yield. The regioisomers were separated by HPLC (scheme 1.41).[66]



50

90
15

91
85

37% mixture

Scheme 1.41 Nitration of disulfide **50**

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

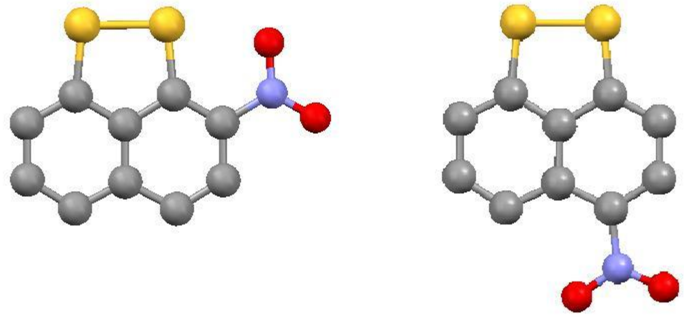
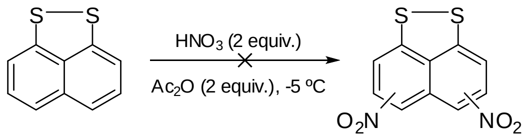


Figure 1.8 X-ray crystal structures of *ortho* **90** and *para* **91**

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 sp^2 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).

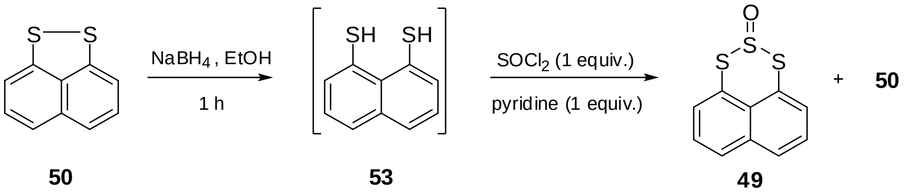


50

Scheme 1.42 Attempted dinitration of disulfide **50**

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.[67, 68] Disulfide **50** was reduced in the presence of $NaBH_4$ to afford the dithiol **53** in quantitative yields. Due to the *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[69] and Bartlett[67] were employed, however yields of 1,2,3-trithiaphenalene 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**)

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.).[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).

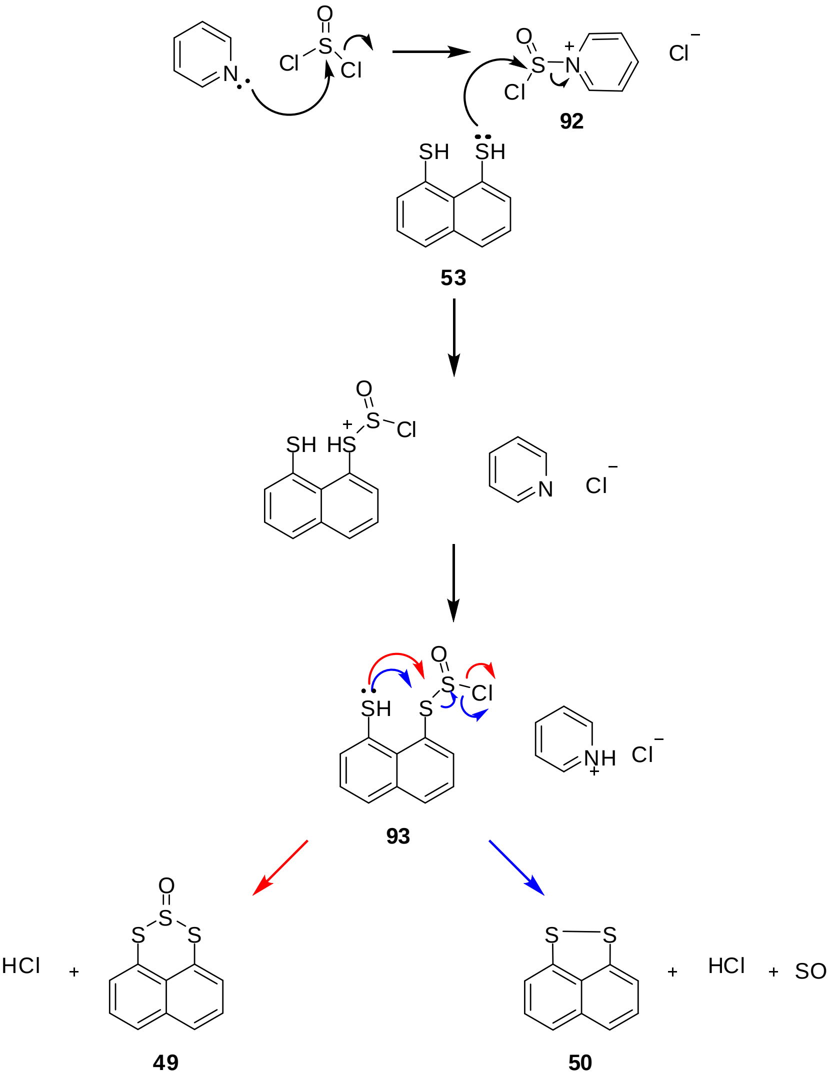
Entry	Conditions[a]	**49** (%)	**50** (%)
1	$SOCl_2$ (1.00 equiv.), pyridine (1.00 equiv.), Et_2O	29	53
2	$SOCl_2$ (1.45 equiv.), pyridine (1.15 equiv.), Et_2O	60	25
3	$SOCl_2$ (1.00 equiv.), Et_2O	23	58
4	$SOCl_2$ (1.00 equiv.), pyridine (2.00 equiv.), Et_2O	20	58
5[b]	$SOCl_2$ (1.45 equiv.), pyridine (1.15 equiv.), Et_2O	18	55

[a] pyridine and dithiol added to $SOCl_2$

[b] $SOCl_2$ added to pyridine and dithiol

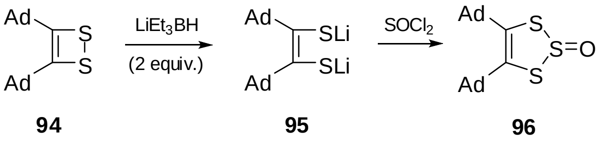
Table 1.6 Conditions employed for the synthesis of trisulfide-2-oxide **49** from dithiol **53**

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**.[26] 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**.



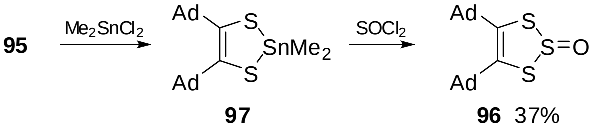
Scheme 1.44 Competition between trisulfide-2-oxide and disulfide formation

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 $SOCl_2$ to give **96** in low yields (scheme 1.45).[70] Unfortunately Super-Hydride® failed to reduce the S-S bond in disulfide **50** resulting in recovery of starting material.



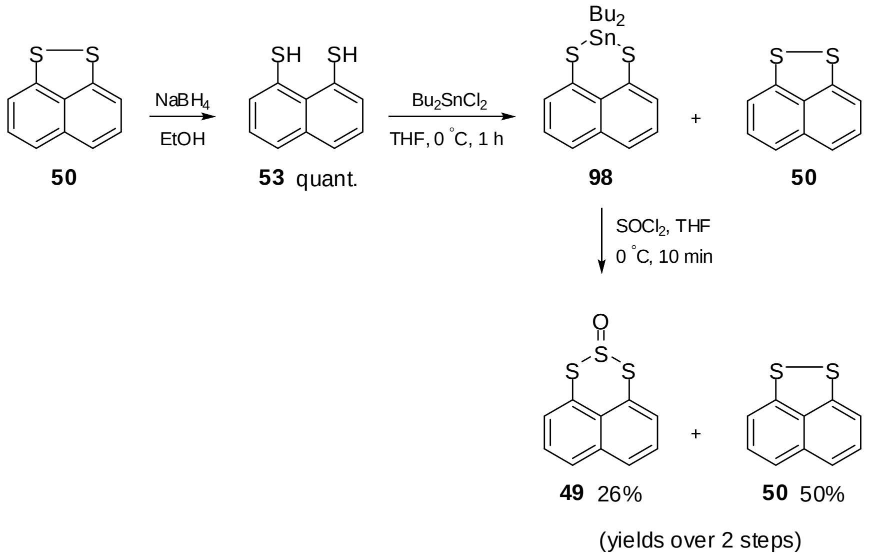
Scheme 1.45 Reduction of **94** using Super-Hydride®

The same authors,[70] and later Ogawa,[71] revealed that dithiolates can be protected with dialkyl tin dichlorides to fashion stannoles and subsequent reaction with $SOCl_2$ formed the trisulfide-2-oxides in improved yields (scheme 1.46).



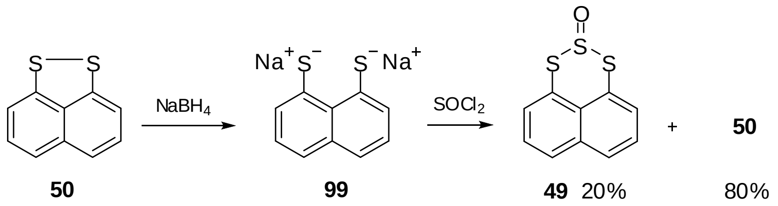
Scheme 1.46 Synthesis of trisulfide-2-oxide **96** *via* 1,2-dithiastannole **97**

Reduction of disulfide **50** with $NaBH_4$ followed by reaction with Bu_2SnCl_2 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 $SOCl_2$ to obtain trisulfide-2-oxide **49** in a 26% yield along with disulfide **50** in a 50% yield (scheme 1.47).



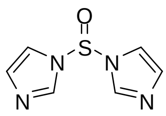
Scheme 1.47 Treatment of dithiol **53** with Bu_2SnCl_2

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 $SOCl_2$ to generate 20% of trisulfide-2-oxide **49**, with recovery of 80% of disulfide **50** (scheme 1.48).



Scheme 1.48 One-pot synthesis of **49**

Altering 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 Grainger[27] (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**.



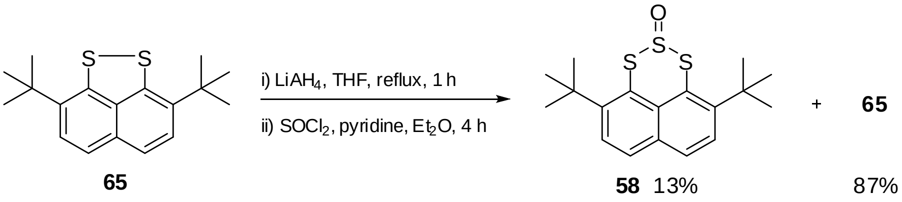
100

Figure 1.9 Thionyl diimidazole

A literature procedure reported the reaction of thiophenol with **100** in the absence of additional base.[69] 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-butylnaphthalene-1,8-dithiol (**101**) in near quantitative yield, as reported by Tesmer (>99%).[45]

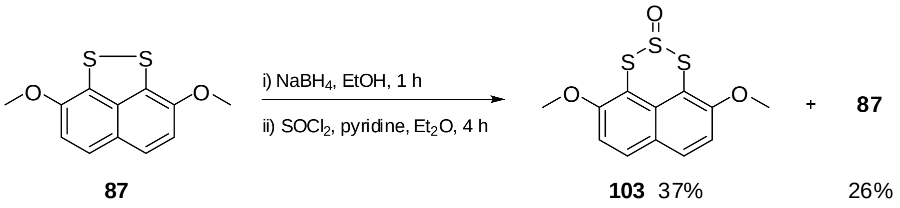
Condensation of dithiol **101** with $SOCl_2$ resulted in 4,9-di-*tert*-butyl-1,2,3-trithiaphenalene 2-oxide (**58**).[42] Purification of **58** proved to be difficult using silica, however the use of Florisil® provided pure trisulfide-2-oxide **58** in a 13% yield, along with 87% of recovered starting material **65** (scheme 1.49).



Scheme 1.49 Synthesis of trisulfide-2-oxide **58**

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.

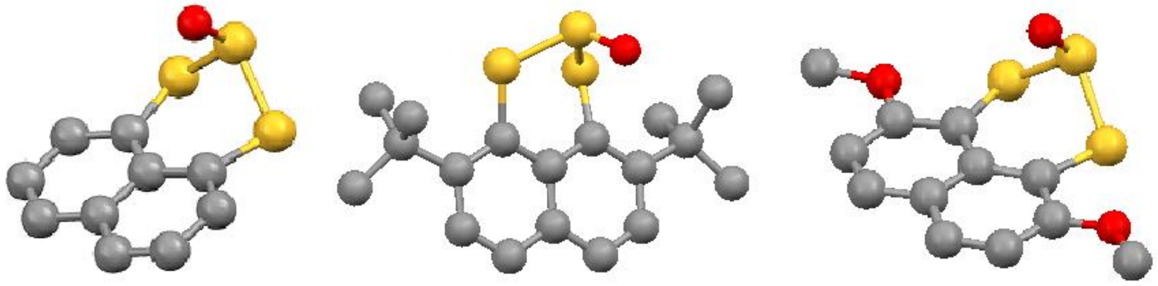
Reduction of disulfide **87** with $NaBH_4$ afforded 2,7-dimethoxynaphthalene-1,8-dithiol (**102**) in quantitative yield as an unstable, white, crystalline solid. The unstable dithiol **102** oxidised back to disulfide **87** in the solid state in 2 h. Treatment of the crude dithiol **102** with $SOCl_2$ in the presence of pyridine gratifyingly afforded 4,9-dimethoxy-1,2,3-trithiaphenalene 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.



Scheme 1.50 Synthesis of trisulfide-2-oxide **103**

1.7 X-ray analyses of trisulfide-2-oxides

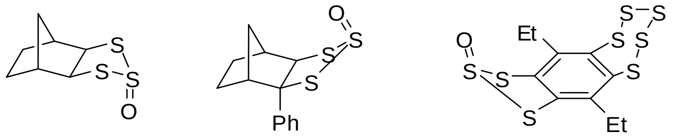
The crystal structures of the two novel trisulfide-2-oxides **58** and **103** were obtained to acquire structural information. The X-rays of trisulfide-2-oxides **49**,[27] **58** and **103** are shown in figure 1.10 respectively.



49 **58** **103**

Figure 1.10 X-ray of trisulfide-2-oxides **49**, **58** and **103**

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 sufur 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.[74-76] 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).[67, 77, 78]



104 **105** **106**

Figure 1.11 Five-membered trisulfide-2-oxides with *pseudo*axial oxygen

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.

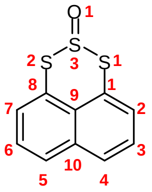
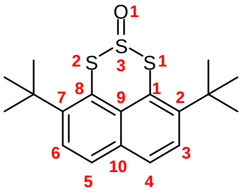
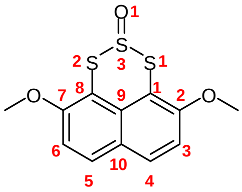
Trisulfide-2-oxide	 **49**	 **58**	 **103**
Torsion angles (°)			
C(10)-C(9)-C(1)-S(1)	172.53	159.59	178.54
C(10)-C(9)-C(8)-S(2)	179.97	163.76	178.56
C(1)-C(9)-C(10)-C(4)	1.27	6.33	-3.14
C(8)-C(9)-C(10)-C(5)	2.53	6.52	3.3
Bond angles (°)			
C(9)-C(1)-S(1)	124.72	122.72	124.8
C(1)-C(9)-C(8)	126.63	126.05	125.64
C(9)-C(8)-S(2)	125.73	119.22	127.36
Non-bonding S-S length (Å)			
S(1)-S(2)	3.096	3.038	3.100

Table 1.7 Selected bond lengths, bond and torsion angles of trisulfide-2-oxides **49**, **58** and **103**

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.[79] 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.

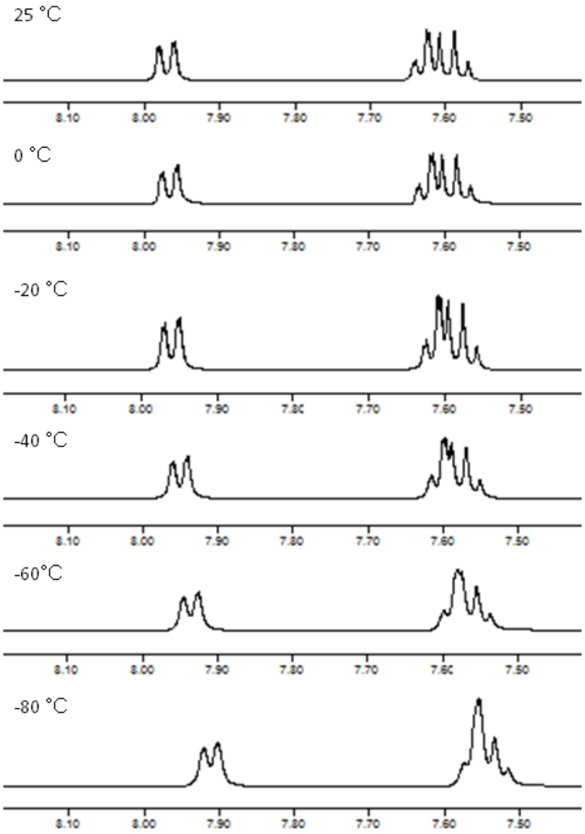
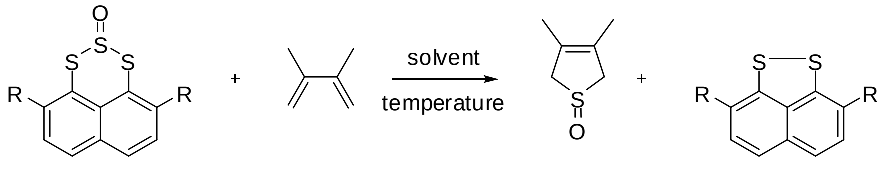


Figure 1.12 Variable temperature NMR of trisulfide-2-oxide **49**

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*][l,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).



49 R = H
58 R = *t*-Bu
103 R = OMe

16
(10 equiv.)

2

50 R = H
65 R = *t*-Bu
87 R = OMe

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

[a] Reactions run at 0.01 M.

[b] Reaction run at 0.1 M.

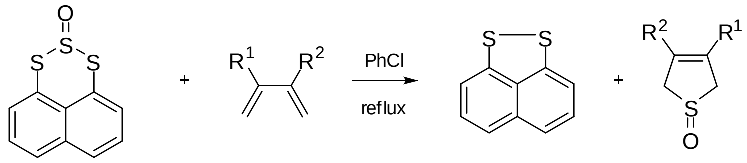
[c] 8% yield of trisulfide-2-oxide **49** was recovered.

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).



49 **17** $R^1 = R^2 = Ph$ **50** **3** 66%

18 $R^1 = Me$, $R^2 = H$ **21** 65%

19 $R^1 = (CH_2)_2CH{=}C(CH_3)_2$, $R^2 = H$ **22** 87%

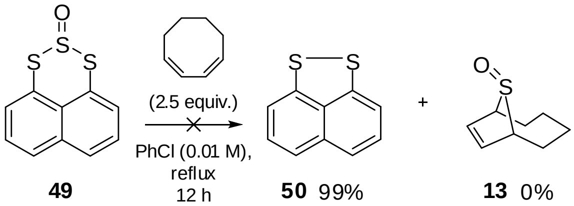
Scheme 1.51 Thermal decomposition of **49** in the presence of 1,3 dienes.

It was noticed that excess diene was necessary for effective SO transfer to occur.[26] 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).

Entry	Diene	**49**: Diene ratio	Time (h)	Sulfoxide (%)	**49** (%)
1	**18**	1:10	6	**21** 66	94
2	**19**	1:2.5	6	**21** 87	98
3	**19**	1:1	6	**22** 39	96
4	**19**	2.5:1	6	**22** 85	97
5	**17**	1:2.5	5.75	**3** 65	92

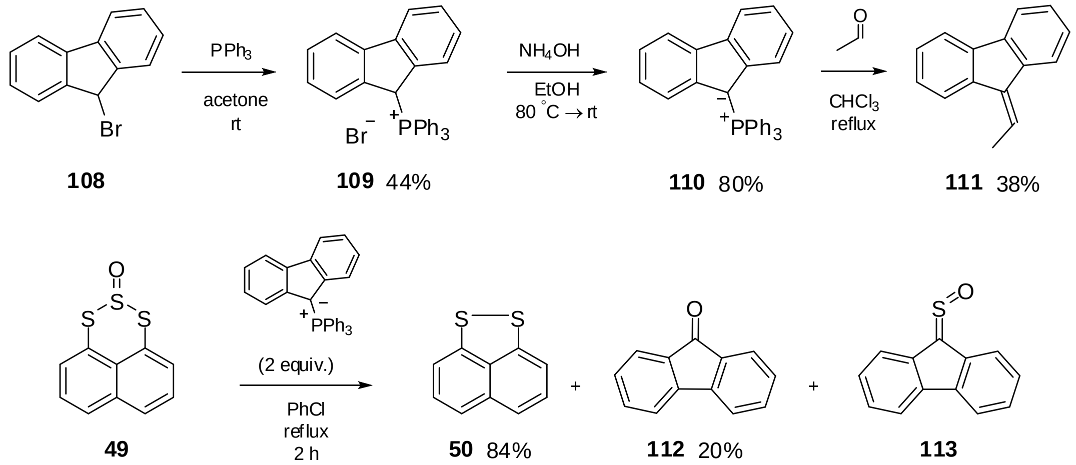
Table 1.9 Thermal decomposition of **49** in the presence of 1,3 dienes.

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



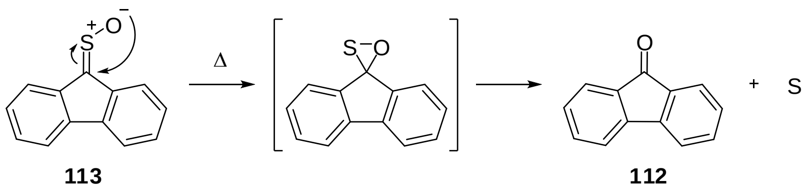
Scheme 1.52 Unsuccessful SO transfer to 1,3 cyclooctadiene

SO transfer from episulfoxide **23** to a variety of ylides has been reported.[18] The reaction of trisulfide-2-oxide **49** with ylide **110** was therefore investigated. Reaction of 9-bromofluorene **108** with PPh_3 gave (9*H*-fluoren-9-yl)triphenylphosphonium bromide (**109**), which upon treatment with aqueous ammonium hydroxide afforded the stable fluoren-9-ylidene-triphenyl-λ^5-phosphane (**110**).[80, 81] The formation of **110** was confirmed by the synthesis of 9-ethylidene-9*H*-fluorene (**111**).[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).



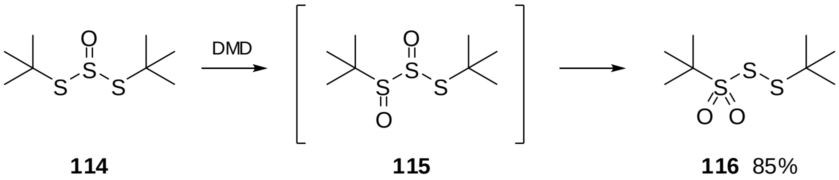
Scheme 1.53 SO transfer to ylide **110**

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},[83] 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**,[84] thought to form *via* a three-membered oxathiirane with loss of sulfur producing ketone **112** (scheme 1.54).



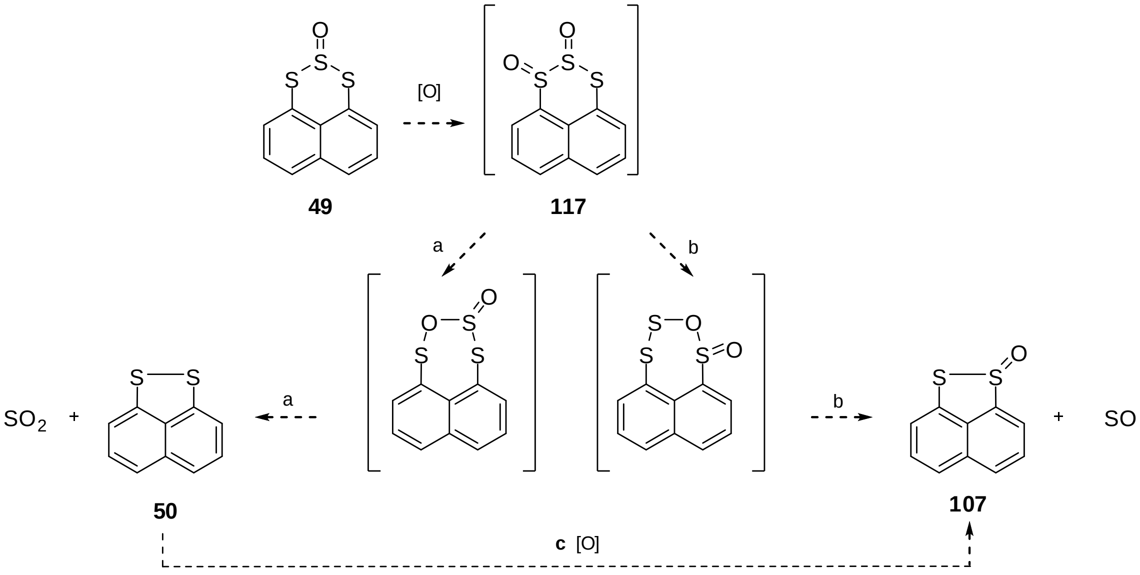
Scheme 1.54 Decomposition of fluorenylidenesulfine **113**

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).[85, 86] 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 thioanhydride (**116**) (see Chapter 2 for a discussion of *vic*-disulfoxides and their rearrangement).



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 *m*CPBA 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**.

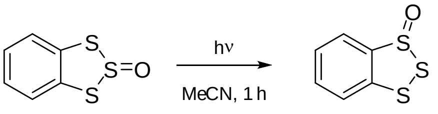


Scheme 1.56 Oxidation of **49** to release SO

Entry	Oxidant (equiv.)	Conditions	**49** (%)	**50** (%)	**107** (%)
1	*m*CPBA (1)	**16** (10 equiv.), CH_2Cl_2, -78 °C → rt, o/n	30	30	40
2	DMD (1)	**16** (10 equiv), CH_2Cl_2, -78 °C → rt, o/n	22	40	37

Table 1.10 Oxidation of trisulfide-2-oxide

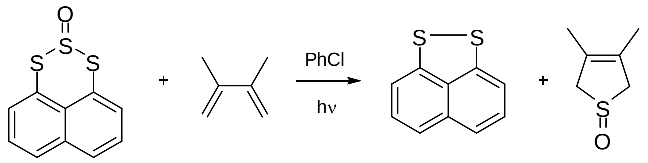
The isomerisation of trisulfide-2-oxide **118** to 1-oxide **119** under photolytic conditions has been reported by Sato (scheme 1.57).[68]



118 **119** 84%

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).



49 **16** **50** **2**

λ_{max} (MeCN)/nm
364 (ε/dm^3 mol^{-1} cm^{-1} 6 620)
249 (19 800)

λ_{max} (MeCN)/nm
366 (ε/dm^3 mol^{-1} cm^{-1} 13 300)
250 (22 900)

Scheme 1.58 Photoinduced SO transfer at room temperature

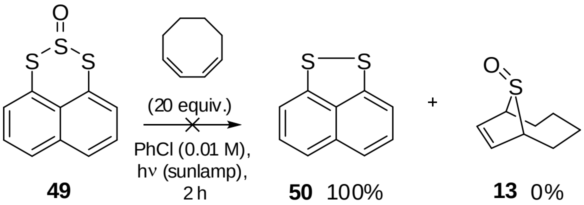
Three separate light sources were employed to transfer SO to diene **16** and although reaction times for the breakdown of trisulfide-2-oxide **49** were improved, yields of the resultant sulfoxide **2** were somewhat lower compared to thermolysis of **49** (table 1.11). Sulfoxide **2** was found to be photostable under these conditions.

Entry	Conditions[a]	**2** (%)	**50** (%)
1	125 W medium pressure Hg lamp, pyrex filter, 1 h	36	99
2	500 W halogen lamp, 1 h	48	95
3	300 W UV sunlamp, 2 h	55	93

[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

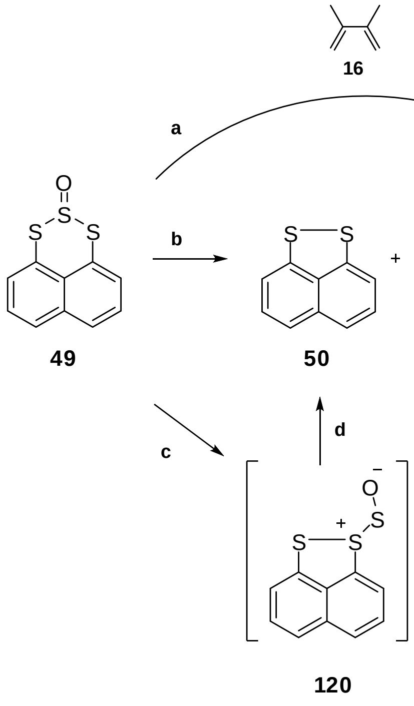
Under photolytic conditions cyclooctadiene again failed to produce any of the expected sulfoxide adduct **13** (scheme 1.59).



Scheme 1.59 Attempted photomediated SO transfer to cyclooctadiene

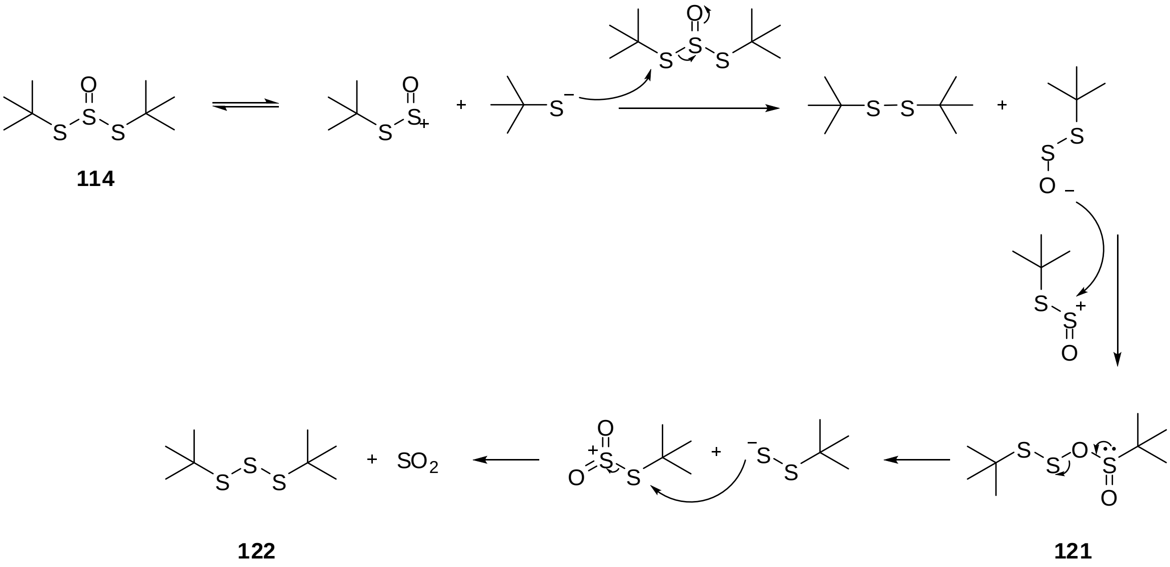
1.9 Mechanistic studies of SO transfer

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**

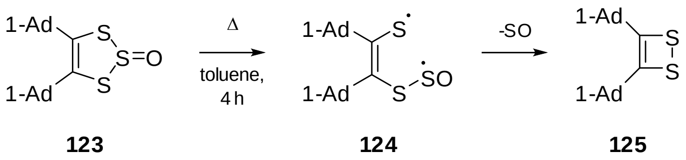
The thermal decomposition of acyclic trisulfide-2-oxides has been examined in detail by Field[69] and Harpp[85] (scheme 1.61).



Scheme 1.61 Thermal decomposition of acyclic trisulfide-2-oxides

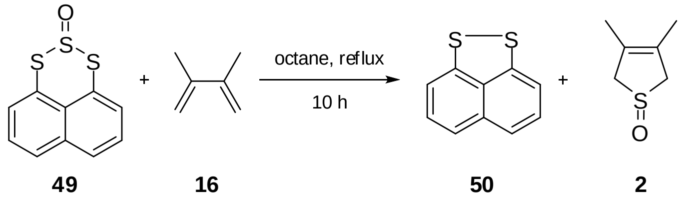
The proposed mechanism suggests initial heterolytic bond fission of **114**. An oxygen transfer affords 1,2-di-*tert*-butyldisulfane and compound **121** following reaction with another molecule of **114**. 1-*tert*-Butyl-2-(tert-butylsulfinyloxy)disulfane (**121**) is then believed to decompose immediately to an equimolar mixture of trisulfide **122** and SO_2.[85]

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

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**

The rate equation for the reaction under consideration is

$$\text{Rate} = -\,k\,[\mathbf{49}]^{\alpha}\,[\mathbf{16}]^{\beta} \qquad \textbf{Equation 1.1}$$

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:

$$\frac{d[\mathbf{49}]}{dt} = \text{Rate} = -k' [\mathbf{49}]^{\alpha}, \qquad \text{where } k' = k\,[\mathbf{16}]_o^{\beta}$$ **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).

$$[\mathbf{49}] = [\mathbf{49}]_o\, e^{-k't}$$ **Equation 1.3**

$$\ln\,[\mathbf{49}] = \ln\,[\mathbf{49}]_o - k't$$ **Equation 1.4**

where k = rate constant, k′ = observed rate constant, t = time, [ ] = concentration, $[\ ]_o$ = initial concentration, α and β 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 0th order reaction with respect to substrate. A straight line is observed for a reactant that is 1st order by plotting ln concentration vs. time and a 2nd order by a plot of 1/concentration vs. time (figure 1.13).

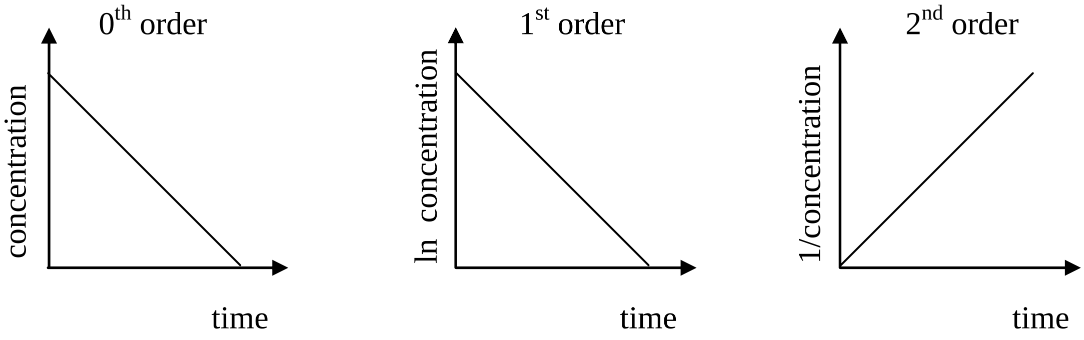


Figure 1.13 Profiles for the order of reactions

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 concentration vs. time, consistent with that of a 1st 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 1st order breakdown for trisulfide-2-oxide.

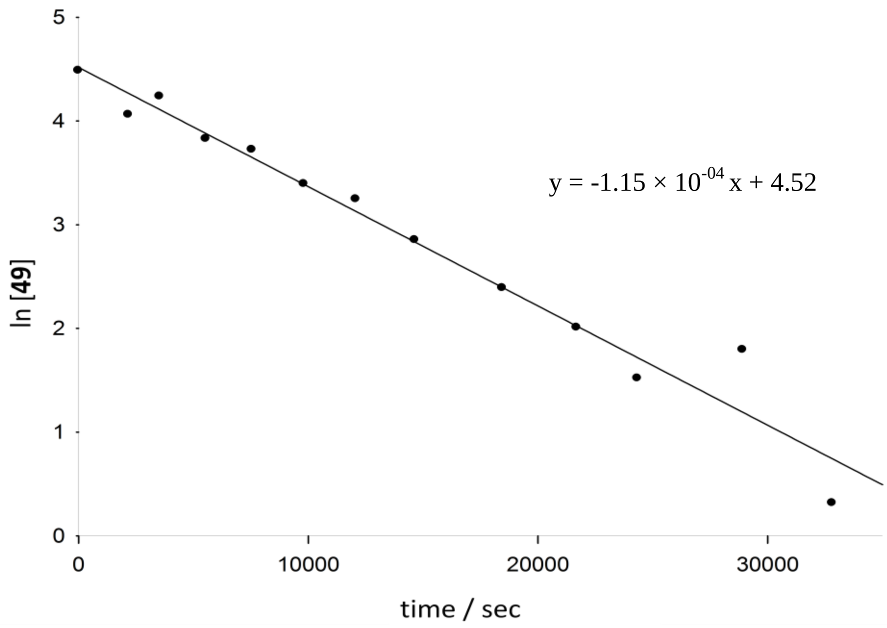


Figure 1.14 First order decomposition of trisulfide-2-oxide **49**

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 1st 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**: $[1.19] = -\ k\ [0.005]^1\ [0.1]^\beta$ **Equation 1.5**

Entry **7**: $[1.17] = -\ k\ [0.005]^1\ [0.3]^\beta$ **Equation 1.6**

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

$$\ln [1.19] = -\ln k + \ln [0.005] + \beta \ln [0.1]$$ **Equation 1.7**

$$\ln [1.17] = -\ln k + \ln [0.005] + \beta \ln [0.3]$$ **Equation 1.8**

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

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

Entry	[**49**] / M	[**16**] / M	$k' / 10^{-4}$ s Run 1	 Run 2	 Average
1	0.0080	0.2	1.15 ± 0.25	1.24 ± 0.12	1.20 ± 0.27
2	0.0075	0.2	1.24 ± 0.17	1.01 ± 0.26	1.13 ± 0.31
3	0.0060	0.2	1.23 ± 0.42	0.98 ± 0.11	1.11 ± 0.44
4	0.0050	0.2	1.11 ± 0.10	1.19 ± 0.44	1.15 ±0.46
5	0.0040	0.2	0.99 ± 0.12	1.40 ± 0.33	1.20 ± 0.35
6	0.0050	0.1	1.19 ± 0.22	1.18 ± 0.16	1.19 ± 0.27
7	0.0050	0.3	1.12 ±0.11	1.21 ± 0.19	1.17 ± 0.22
8	0.0050	0.4	0.93 ± 0.12	1.32 ± 0.32	1.13 ± 0.34
9	0.0050	0.5	1.05 ± 0.42	1.36 ± 0.23	1.21 ± 0.47
10	0.0060	0	0.98 ± 0.14	1.42 ± 0.27	1.20 ± 0.30

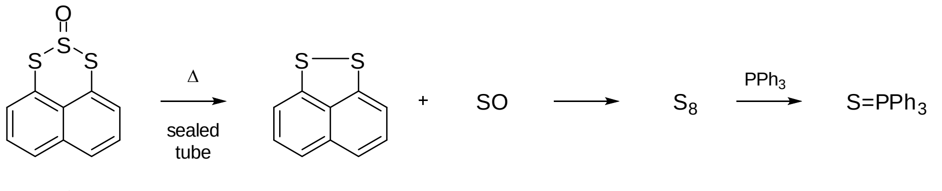
Table 1.12 Observed rate constants for the thermal decomposition of trisulfide-2-oxide **49** in the presence of diene **16**

The averaged observed rate constant for the disappearance of **49** is $1.16 \pm 0.74 \times 10^{-4}$ s^{-1}. The rate constant for the formation of the sulfoxide **2** was calculated to be $1.01 \pm 0.62 \times 10^{-4}$ 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.

Entry	[**49**] / M	[**16**] / M	k′ / 10^{-4} s Run 1	 Run 2	 Average
1	0.0080	0.2	0.82 ± 0.15	0.99 ± 0.12	0.91 ± 0.20
2	0.0075	0.2	1.24 ± 0.31	0.83 ± 0.26	1.04 ± 0.40
3	0.0060	0.2	0.86 ± 0.40	0.88 ± 0.10	0.87 ± 0.42
4	0.0050	0.2	0.90 ± 0.40	1.13 ± 0.16	1.02 ± 0.43
5	0.0040	0.2	0.82 ± 0.21	1.24 ± 0.37	1.03 ±0.43
6	0.0050	0.1	1.07 ± 0.21	0.88 ± 0.25	0.98 ± 0.32
7	0.0050	0.3	1.15 ± 0.08	1.10 ± 0.27	1.13 ± 0.28
8	0.0050	0.4	0.96 ± 0.10	1.14 ± 0.40	1.05 ± 0.41
9	0.0050	0.5	1.17 ± 0.31	0.97 ± 0.27	1.07 ± 0.41

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 SO_2. 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 $Ph_3P{=}S$ was achieved, suggesting efficient production of SO (scheme 1.64).



Scheme 1.64 Evidence for the formation of SO through the formation of $S{=}PPh_3$

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]

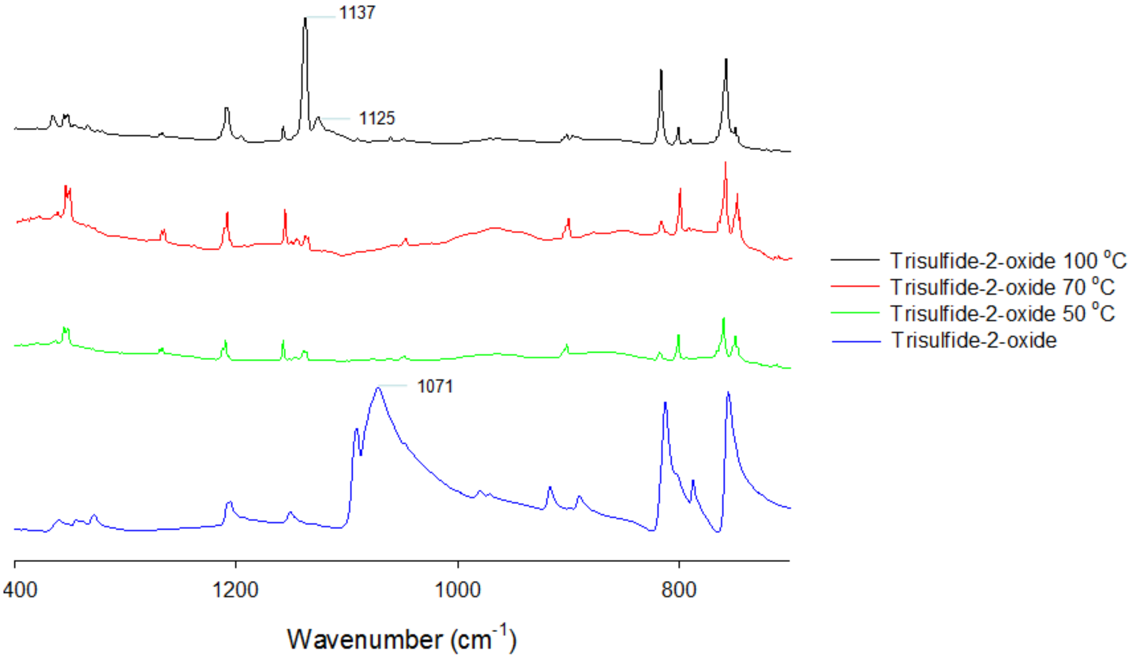


Figure 1.15 FVT of trisulfide-2-oxide **49** monitored by infra red spectroscopy to show the developing free SO

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).

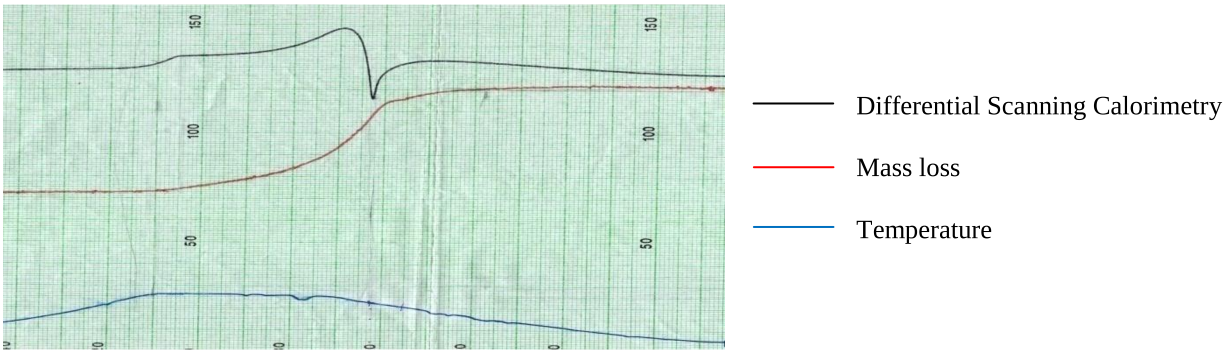


Figure 1.16 TGA plot of the thermolysis of trisulfide-2-oxide **49**

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 SO_2 formed will be half of the number of moles of SO developed (61.97 µmol/2 = 30.99 µmol). The theoretical mass loss of SO_2 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).

Entry	Solvent	Time (h)	**2** (%)	**50** (%)
1	PhCl	10	91	98
2	Pentanol	10	86	37
3	DMF	9.25	95	62

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

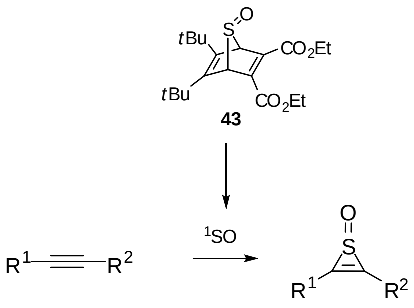
A comparable rate was observed qualitatively in the presence of radical traps (table 1.15), with formation of the disulfide **50** in good yields.

Entry	Radical trap (equiv.)	Time (h)	**50** (%)
1	*tert*-butylcatechol (1.0)	9.8	86
2	1, 4 benzoquinone (1.0)	9.9	86
3	DPPH (2.5)	10	95
4	TEMPO (2.5)	10	95

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.

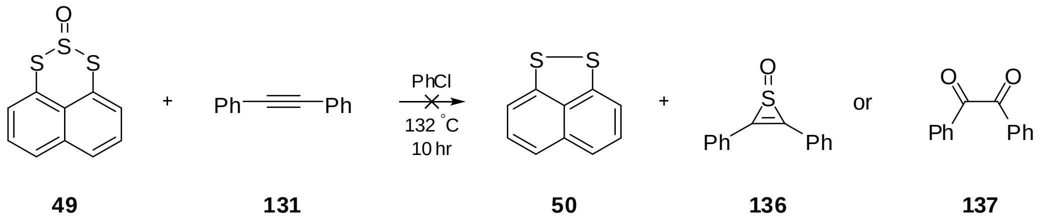
The nature of the SO transferred was also of interest. Nakayama has reported successfully reacting **43** at room temperature with alkenes and alkynes in poor to modest yields (scheme 1.65).[24] This room temperature extrusion is proposed to be concerted and therefore the first example of singlet SO.



127	R^1 = Ph, R^2 = H	**132**	20%
128	R^1 = *t*-Bu, R^2 = H	**133**	10%
129	R^1 = R^2 = Me	**134**	17%
130	R^1 = R^2 = 1-Ad	**135**	7%
131	R^1 = R^2 = Ph	**136**	5%

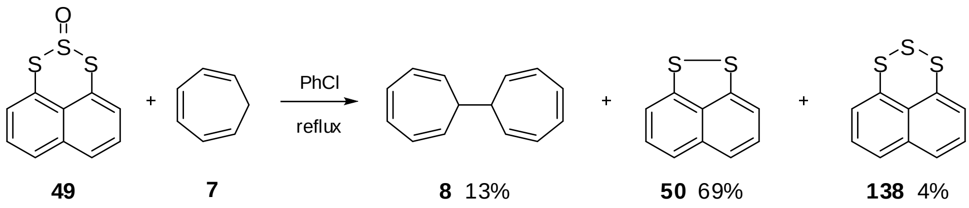
Scheme 1.65 Reaction of SO with alkynes

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).[90]



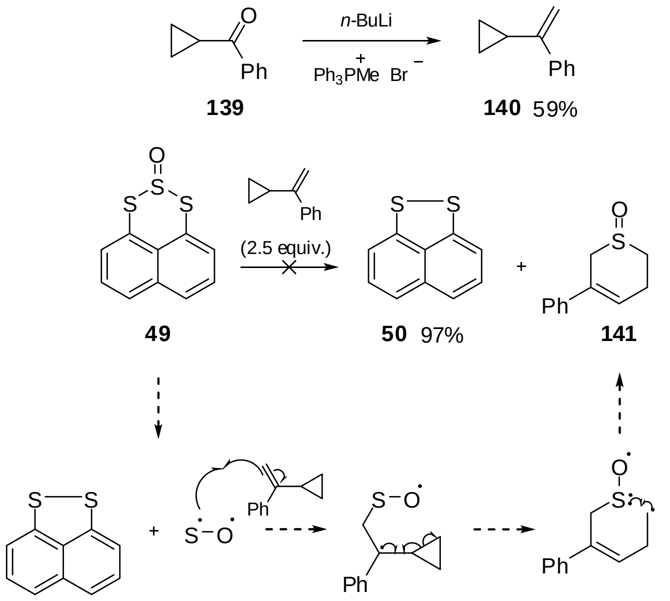
Scheme 1.66 Reaction of **49** with diphenylacetylene

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 ^{1}H-NMR analysis (scheme 1.67).[26] As a result it can be concluded that ground state triplet SO is being formed in this process.



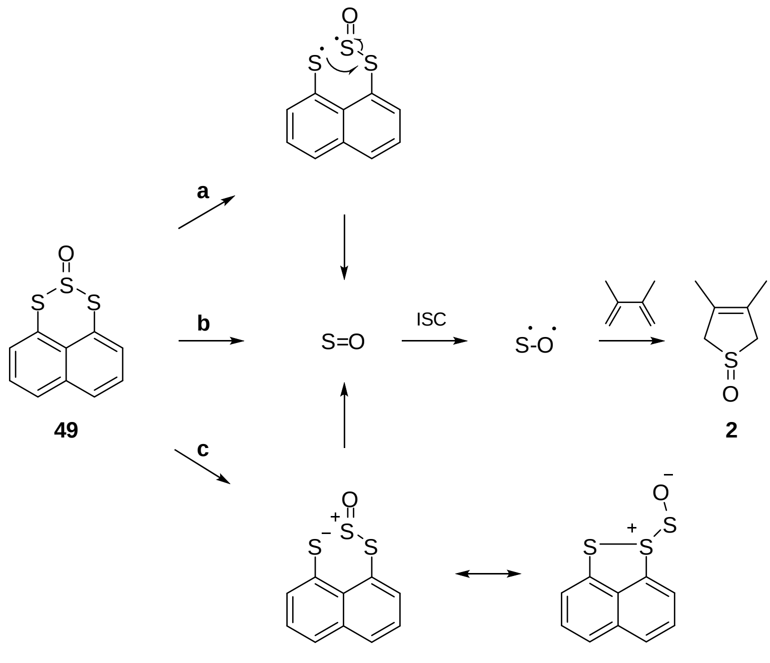
Scheme 1.67 Dimerisation of cycloheptatriene when reacted with trisulfide-2-oxide **49**

Efforts to transfer ^{3}SO 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).



Scheme 1.68 Attempted cyclisation of **140** with trisulfide-2-oxide **49**

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).

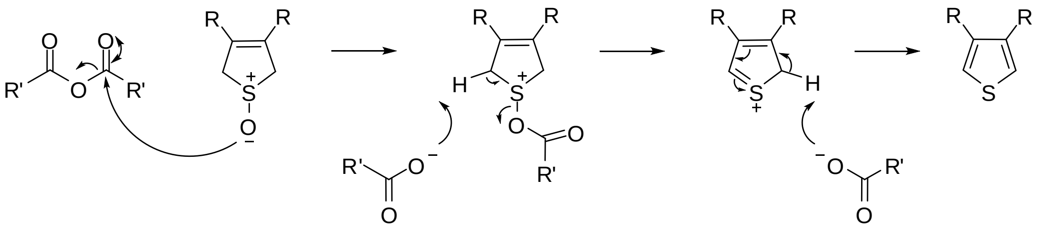


a) homolytic fission b) concerted elimination c) heterolytic fission

Scheme 1.69 Proposed mechanism of SO transfer

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.[92] The Pummerer reaction for the formation of thiophenes from 2,3-dihydrothiophene 1-oxides has been reported in the Grainger group.[26] The Pummerer reaction is considered to occur by activation of sulfoxide, followed by dehydration and aromatisation to form the thiophene (scheme 1.70).

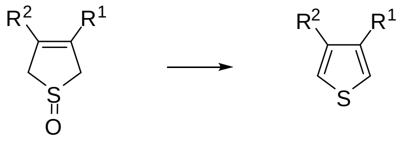


Scheme 1.70 Mechanism of the Pummerer reaction

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.[93] Isolation of **143** was difficult and the low yield of the reaction is a result of the volatility of **143**.



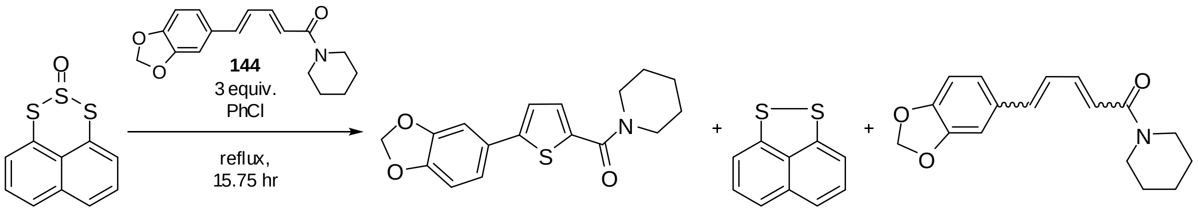
2 $R^1 = R^2 = Me$ — decomposition
3 $R^1 = R^2 = Ph$ — **142** 80%
21 $R^1 = Me, R^2 = H$ — decomposition
22 $R^1 = (CH_2)_2CH{=}C(CH_3)_2, R^2 = H$ — **143** 35%

Scheme 1.71 Thiophene formation from the Pummerer reaction

Entry	Sulfoxide	Conditions	Yield (%)
1	**3**	Ac_2O, 3 h, reflux	**142** 80
2	**22**	Ac_2O, 2.5 h, reflux	decomposition
3	**2**	Ac_2O, 2.5 h, reflux	decomposition
4	**21**	Ac_2O, 2.5 h, reflux	decomposition
5	**3**	TFAA, CH_2Cl_2, 5 min, 0 °C	**142** 74
6	**22**	TFAA, CH_2Cl_2, 10 min, 0 °C	**143** 35

Table 1.16 Formation of thiophenes from dehydration of sulfoxides

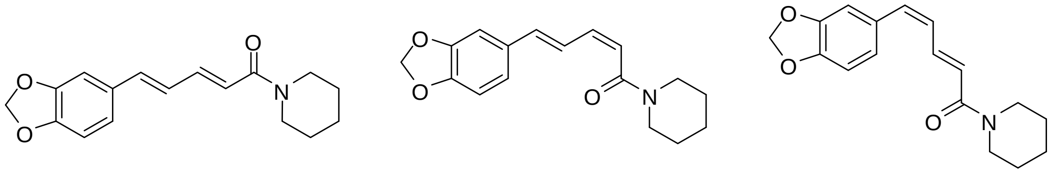
Commercially available 1,3-diene, piperine (**144**), is an extract from black pepper (*Piper nigrum*).[94] Reaction of trisulfide-2-oxide **49** in refluxing chlorobenzene with piperine directly resulted in thiophene **145** (scheme 1.72).



49 **145** 22% **50** 93% 23% (mixture of isomers)

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.[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.

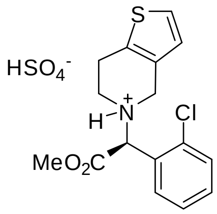


144 **146** **147**

Figure 1.17 Piperine (**144**) and its isomers isopiperine (**146**) and isochavicine (**147**)

Direct formation of the thiophene **145** could be explained from an *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.[96-98]

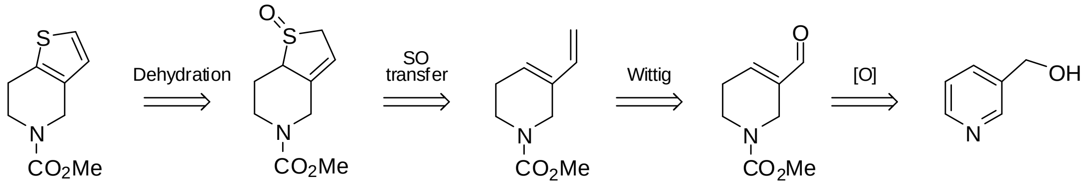
A second example of direct thiophene formation occurred in the formal synthesis of Plavix® (clopidogrel disulfate, **148**) (figure 1.18), an oral anti-platelet agent used to inhibit blood clots in coronary artery disease, peripheral vascular disease and cerebrovascular disease.[99]



142

Figure 1.18 Plavix®

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]

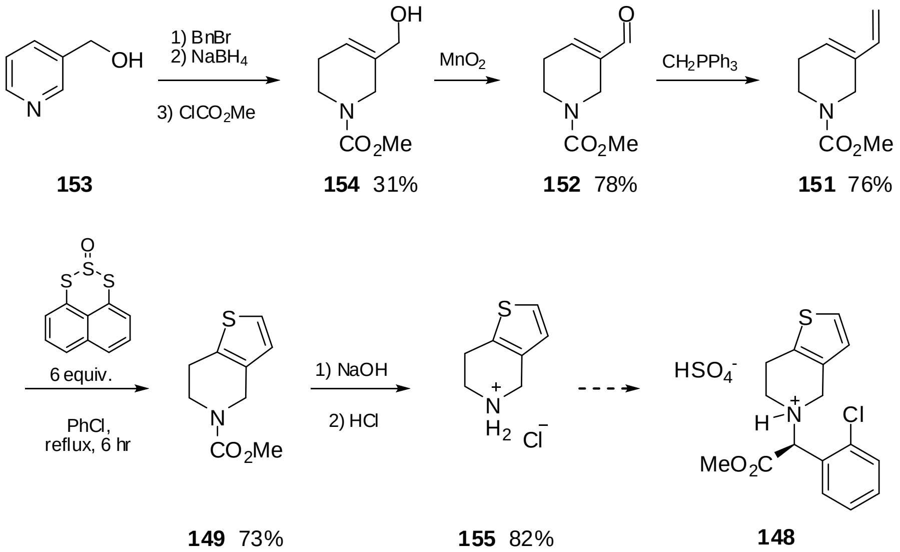


149 **150** **151** **152** **153**

Scheme 1.73 Retrosynthesis of thiophene **149**

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 MnO_2 at room temperature resulted in methyl 3-formyl-5,6-dihydropyridine-1(2*H*)-carboxylate (**152**) (60%) and recovered starting material (30%).[102] Conditions were optimised by refluxing in dichloromethane for 4 h using activated MnO_2 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-4*H*-

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).[104]



Scheme 1.66 Formal synthesis of Plavix®

Entry	**49** (equiv.)	**151** (equiv.)	**50** (%)	**149** (%)	**151** (%)
1	1.0	10	94	0	60
2	2.5	1	100	Trace	31
3	3.0	1	100	35	19
4	6.0	1	97	73	25

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, N_2O_4, reported in the literature; however separation of the isomers was shown to be difficult.

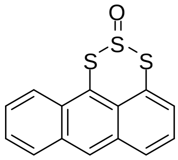
The synthesis of trisulfide-2-oxides **49**, **58** and **103** has been achieved. These compounds are a source of sulfur monoxide and transfer SO in the presence of dienes to produce 2,3-dihydrothiophene 1-oxides thermally. Irradiation of **49** has shown that SO can be transferred at room temperature 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).



156

Figure 1.19 Extending the conjugation of the aromatic system

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 *vic*-disulfoxides

Background and significance

2.1 v*ic*-Disulfoxides

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

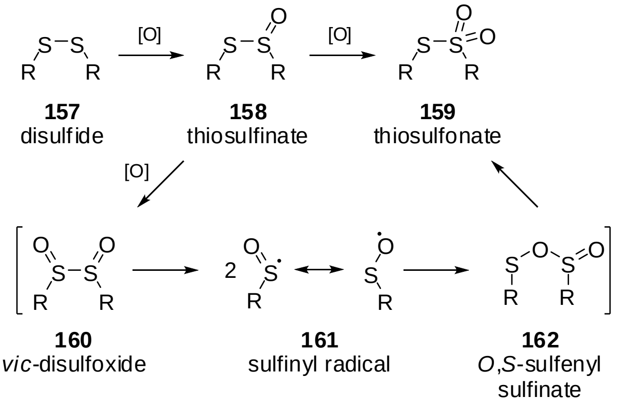
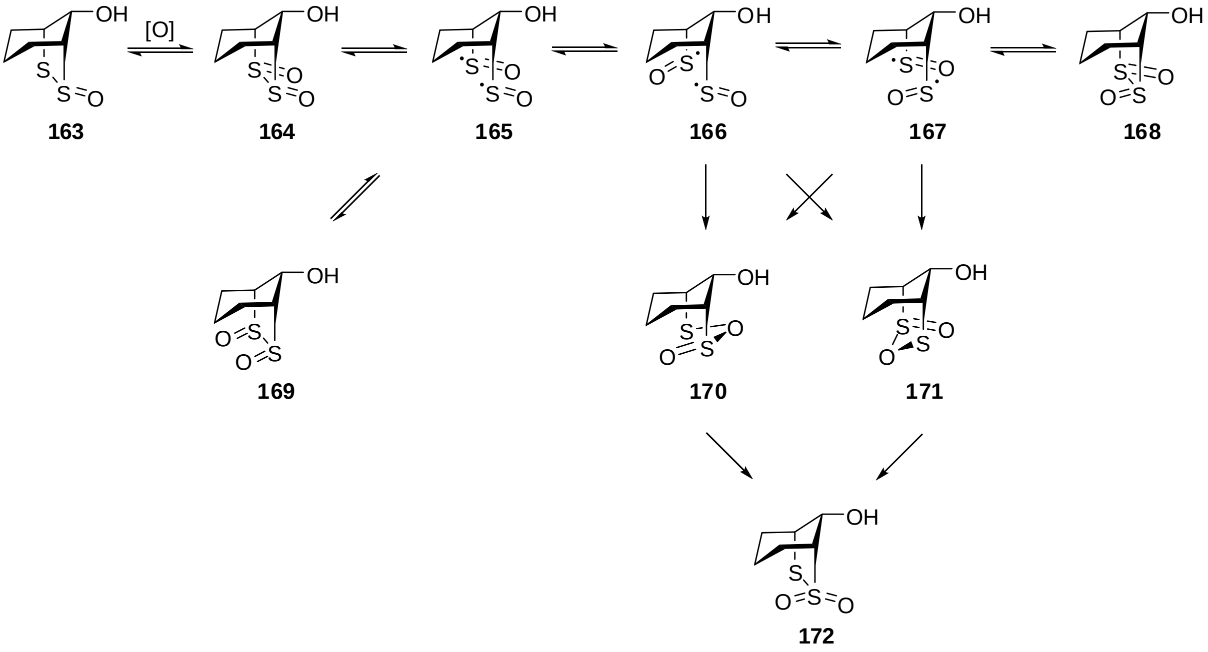


Figure 2.1 Oxidation of disulfides with electrophilic oxidants

vic-Disulfoxides are known to have low thermal stabilities, which is usually attributed to the weakness of the S-S bond.[118] Homolytic fission of **160** forms stabilised sulfinyl radicals which can rapidly recombine in a head-to-tail fashion to form *O*,*S*-sulfenyl sulfinates **162**, which are normally not observed. These rearrange to the more thermally stable thiosulfonate **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 α-disulfoxides by low temperature ^{1}H-NMR studies of the oxidation of alkyl disulfides.[119]

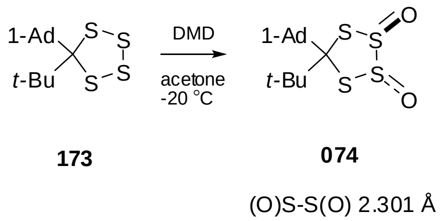
Using low temperature NMR spectroscopy, Harpp later identified *vic*-disulfoxide intermediates in the oxidation of bridged bicyclic thiosulfinate **163** (scheme 2.2).[105, 106] Electrophilic oxidation of thiosulfinate **163** on the *exo*-face is proposed to form symmetrical *vic*-disulfoxide **164**. An unsymmetrical *vic*-disulfoxide was also observed in the ^{1}H-NMR spectrum, which is envisaged to occur *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 *O*,*S*-sulfenyl sulfinates **170** and **171**.



Scheme 2.2 Low-temperature intermediates identified by Harpp

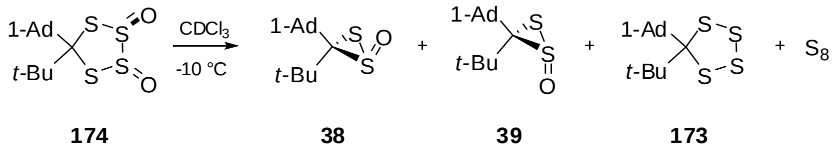
Cyclic *vic*-disulfoxides **164**, **168** and **169** were observed by ^{1}H-NMR spectroscopy at 30 °C suggesting that they were more stable than acyclic *vic*-disulfoxides. These intermediates rearranged to thiosulfonate **172** over time.

In 1999, Nakayama reported the first isolated *vic*-disulfoxide **174** from the oxidation of tetrathiolane **173** at room temperature (scheme 2.3).[119]



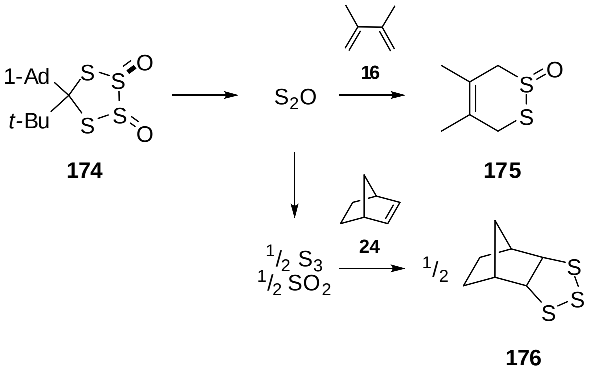
Scheme 2.3 First isolated *vic*-disulfoxide **174**

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**.[119] However, in solution, α-disulfoxide **174** decomposed cleanly to diastereomeric dithiirane 1-oxides **38** and **39**, tetrathiolane **173** and elemental sulfur (scheme 2.4).



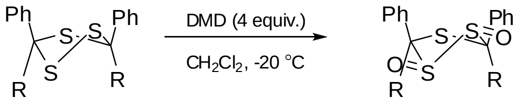
Scheme 2.4 Decomposition of **174** at -10 °C

Trapping experiments using butadiene **16** and norbornene **24** gave **175** and **176** respectively following S_2O extrusion and subsequent disproportionation products (scheme 2.5).[119, 120]



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

In 2002 Nakayama reported the isolation of *vic*-disulfoxides **179** and **180**.[121] Oxidation of trithiolanes **177** and **178** with DMD afforded α-disulfoxides **179** and **180** respectively in good yields (scheme 2.6).



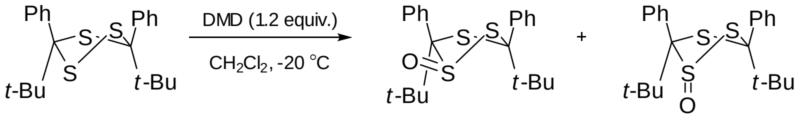
177 R = *t*-Bu
178 R = 1-Ad

179 42%
180 60% (O)S-S(O) 2.249 Å

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 σ^*-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 (≈ 2.05 Å).[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).[121]



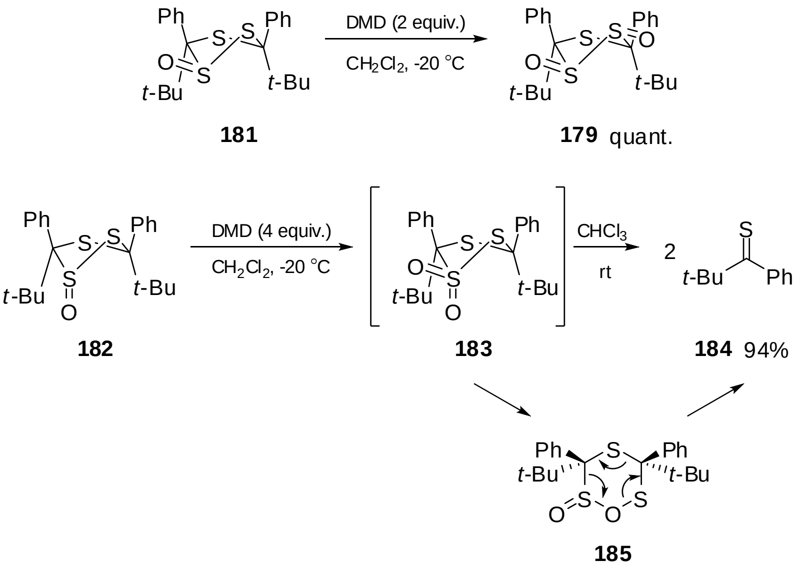
177

181 54%

182 39%

Scheme 2.7 Formation of thiosulfinates **181** and **182** with DMD (1.2 equiv.)

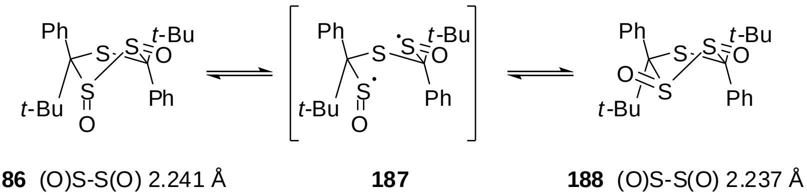
Subsequent oxidation of each individual isomer resulted in two different products. Treatment of **181** with 2 equiv. of DMD yielded *vic*-disulfoxide **179** as a result of oxidation of the sulfenyl sulfur. However **182** required 4 molar equiv. of oxidant to afford 1,1-dioxide **183** which was unstable at room temperature and decomposed rapidly to thioketone **184** (scheme 2.8).[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 thioketone **184** can be explained in terms of extrusion of SO_2 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.[123] 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.

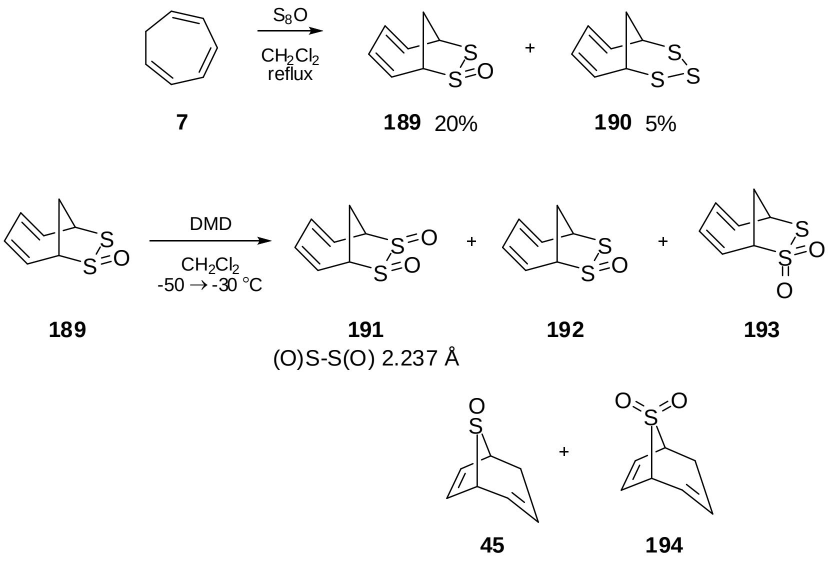


Scheme 2.9 Isomerisation of *vic*-disulfoxides in solution

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.[118]

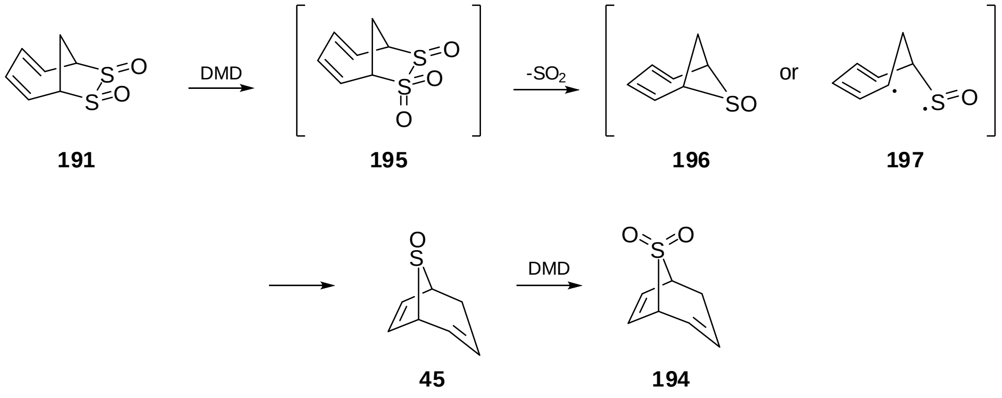
In 2004, Ishii obtained the first example of an eclipsed *vic*-disulfoxide **191**.[124] Cycloheptatriene was heated in the presence of S_8O to afford *exo* monoxide **189** and trisulfide

190. 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 $CDCl_3$ resulted in the 1,1-dioxide **193**.



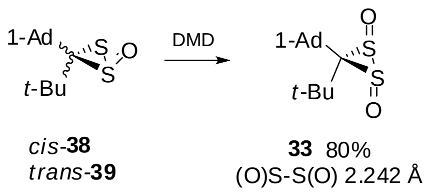
Scheme 2.10 Synthesis and oxidation of thiosulfinate **189**

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



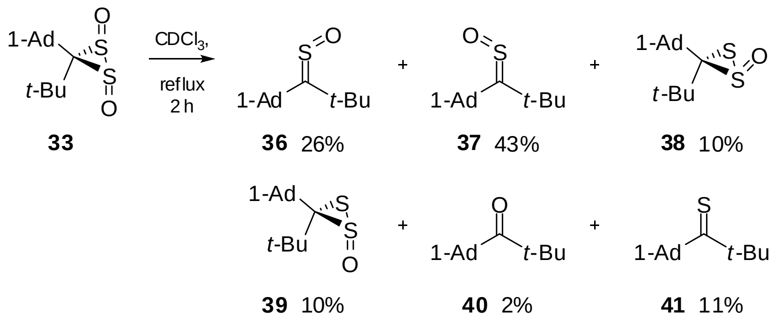
Scheme 2.11 Oxidation of eclipsed *vic*-disulfoxide **191**

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]



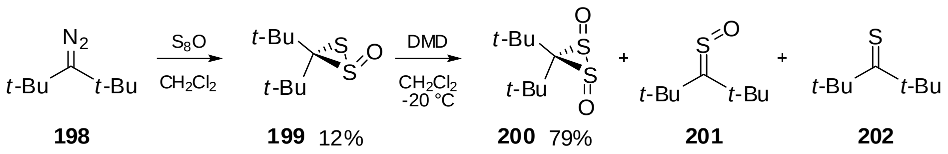
Scheme 2.12 Synthesis of dithiirane *trans*-1,2-dioxide

α-Disulfoxide **33** slowly decomposed in a solution of $CDCl_3$ 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).



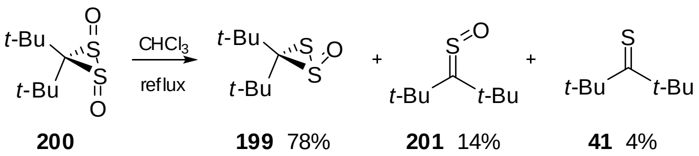
Scheme 2.13 Thermal decomposition of **33**

Ishii reported the synthesis of v*ic*-disulfoxide **200** by the reaction of di-*tert*-butyldiazomethane (**198**) with S_8O to achieve thiosulfinate **199** followed by oxidation using DMD (scheme 2.14).[125]



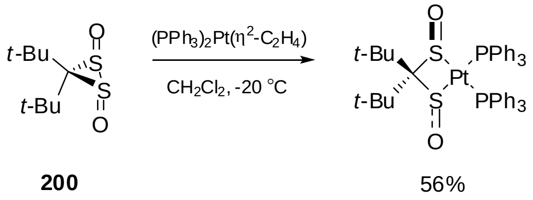
Scheme 2.14 Synthesis of *vic*-disulfoxide **200**

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]



Scheme 2.15 Thermal decomposition of *vic*-disulfoxide **200**

Platinum insertion into S-S bonds has been studied.[126-134] The first example of platinum insertion into the (O)S-S(O) bond of *vic*-disulfoxide **200** was recently reported (scheme 2.16).[125]

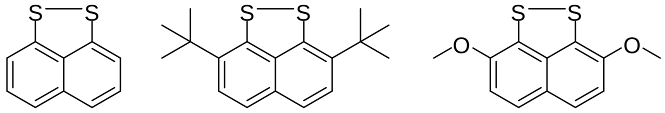


Scheme 2.16 Platinum insertion into a *vic*-disulfoxide

2.2 Aims and objectives

In general, the low thermal stability of *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 *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 **50** and *ortho*-substituted disulfides **65** and **87** will be explored (figure 2.1).



50 **65** **87**

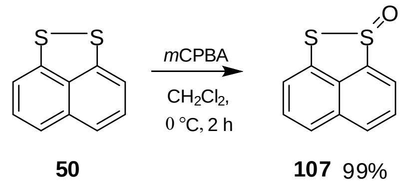
Figure 2.1 Proposed disulfides to investigate the oxidation

Naphthalene disulfide **50** can be easily obtained from oxidation of the corresponding dithiol due to the *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.[135] The S-S bond length for disulfide **50**, obtained from X-ray crystallography, is 2.0879 Å,[136] close to the average value for acyclic aromatic disulfides (≈ 2.03 Å).[122] 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.[136] 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.

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 *m*CPBA.[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 *vic*-disulfoxide was to form it may not be stable in solution with the *m*CBA 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).[140]



Scheme 2.17 Oxidation of disulfide **50** using *m*CPBA

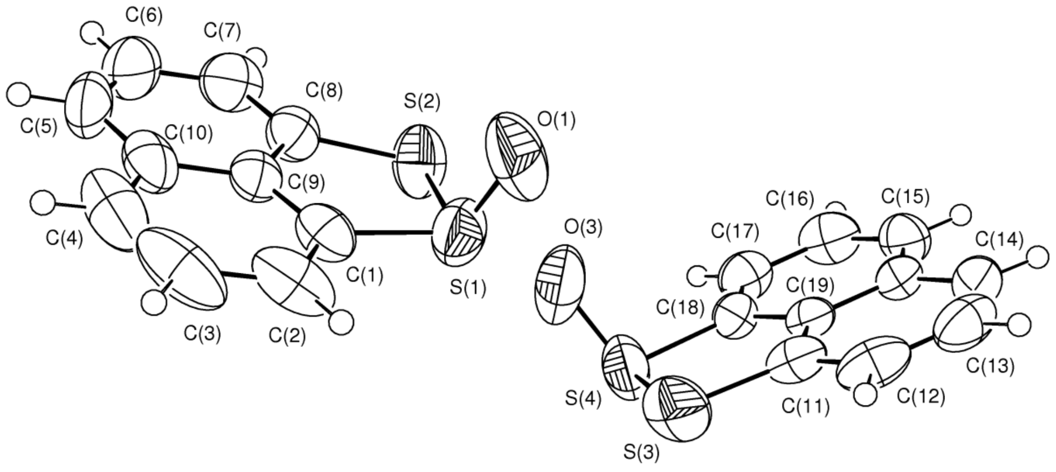
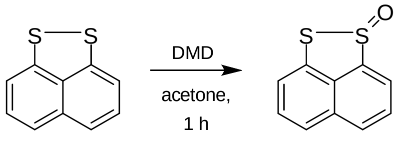


Figure 2.2 X-ray crystal structure of **107**. Thermal ellipsoids are drawn at the 50% probability level

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).[141] A solution of DMD was prepared using a modified literature procedure.[142, 143] Reaction of **50** with one equiv. of DMD resulted in **107** in a lower yield (entry 3).



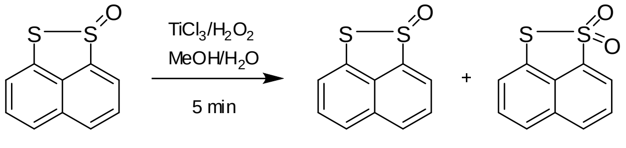
50 **107** 72%

Scheme 2.18 Oxidation of disulfide **50** using DMD

Entry	Oxidation conditions	**107** (%)
1	*m*CPBA (1.50 equiv.), CH_2Cl_2, 0 °C, 2 h	99
2	*m*CPBA (1.50 equiv.), Et_2O, 0 °C, 4 h	83
3	DMD (1.05 equiv.), Acetone, 0 °C, 1 h	72

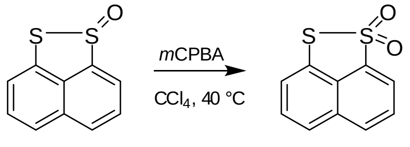
Table 2.1 Preparation of monoxide **107**

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



107 **107** 46% **63** 8%

Scheme 2.19 Oae's conditions for the oxidation of **107**



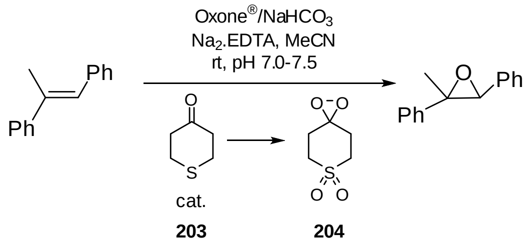
107 **63** 91%

Scheme 2.20 Vivarelli's conditions for the preparation of **63**

Thiosulfonate **63** was prepared using *m*CPBA with CH_2Cl_2 in place of CCl_4, 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 $M^{-1}sec^{-1}$) compared to the first sulfur oxidation (580 $M^{-1}sec^{-1}$);[144] therefore the reaction time was extended to 14 h and yields increased correspondingly (entry 2). Starting from disulfide **50** with 2.5 equiv. of *m*CPBA gave a comparable yield of the desired product (entry 3).

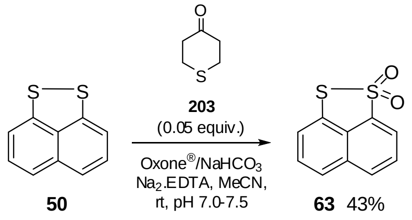
A 95% yield of thiosulfonate **63** was obtained on treating thiosulfinate **107** with 1 equiv. of DMD (entry 4). Reaction of the disulfide **50** with 2.1 equiv. of DMD resulted in only 62% of the desired compound **63** (entry 5), although this may possibly be due to the DMD not having been freshly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

The use of tetrahydrothiopyran-4-one (**203**) and Oxone® has been exploited for epoxidation of alkenes (scheme 2.21).[145] Oxone® is used to oxidise **203** to epoxide **204**.



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

Oxidation of sulfur using tetrahydrothiopyran-4-one (**203**) and Oxone® has not been reported, although Oxone® has been employed in sulfur oxidations.[146] The oxidation of disulfide **50** with catalytic **203** and Oxone® yielded 43% of dioxide **63** (scheme 2.22, entry 6).



Scheme 2.22 Oxidation of disulfide **50** using **203** and Oxone®

Entry	Starting material	Conditions	**63** (%)
1	**107**	*m*CPBA (1.10 equiv.), $CHCl_3$, 2 h, 0 °C	63
2	**107**	*m*CPBA (1.05 equiv.), CH_2Cl_2, 14 h, 0 °C	85
3	**50**	*m*CPBA (2.50 equiv.), $CHCl_3$, 14 h, 0 °C	80
4	**107**	DMD (1.00 equiv.), acetone, 2 h, 0 °C	95
5	**50**	DMD (2.10 equiv.), acetone, 2 h, 0 °C	62
6	**50**	Oxone®, **203** (0.05 equiv.), $NaHCO_3$, Na_2.EDTA, MeCN, 3 h, rt, pH 7.0-7.5	43

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:

- $I_p^{Ox} = I_p^{Red}$
- $E_p^{Ox} - E_p^{Red} = 59\ mV/n$
- $E_p - E_{p/2} = 59\ mV/n$
- $E_p^{Ox} - E_p^{Red}$ does not change the scan rate
- I_p^{Ox} α 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 $n\mathrm{Bu_4NBF_4}$ 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]

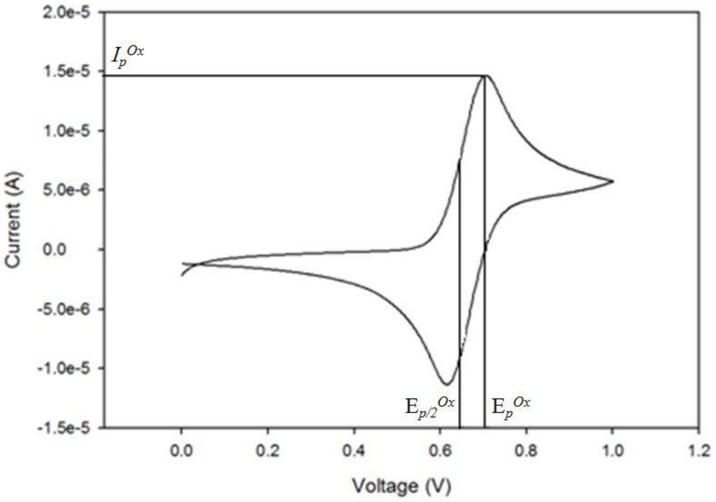


Figure 2.3 Cyclic voltammogram for the single electron oxidation of disulfide **87** (scan rate = 5 mVs)

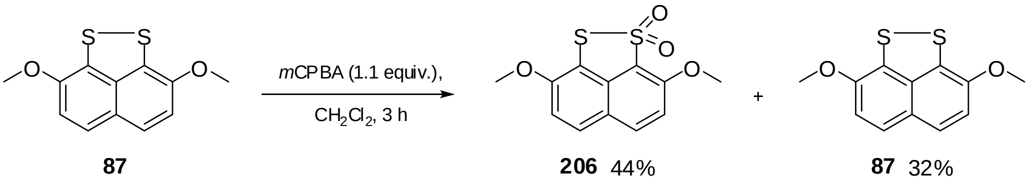
Similar conditions were applied for the single electron oxidation of disulfide **87** and again electrochemical reversibility was observed. The half-wave oxidation potential occurred at 0.66 V (vs. SCE) in dichloromethane, lower than **50** (table 2.3, entry 5).

Entry	Disulfide	Half wave potential (V)
1	**50**	0.88 (vs. SCE)
2[40]	**50**	0.95 (vs. SCE)
3[147]	**50**	0.84 (vs. SCE)
4[48]	**50**	0.68 (vs. Ag/AgCl)
5	**87**	0.66 (vs. SCE)

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

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.

With this information in hand, disulfide **87** was oxidised with 1 equiv. of *m*CPBA at -78 °C in dichloromethane. A new product was observed by TLC and was assumed to be the thiosulfinate 3,8-dimethoxy-naphtho[1,8-*cd*][1,2]dithiole 1-dioxide (**205**); however the product obtained was 3,8-dimethoxy-naphtho[1,8-*cd*][1,2]dithiole 1,1-dioxide (**206**) in a 44% yield, along with starting disulfide in a 32% yield (scheme 2.23, table 2.4, entry 1).



Scheme 2.23 Oxidation of disulfide **87** with *m*CPBA

Disulfide **87** was also oxidised with *m*CPBA 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 *m*CPBA. 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 *m*CPBA were thiosulfonate **206** with recovered starting material. The reaction was repeated with sub-stoichiometeric DMD as the oxidant and identical findings were observed (entries 5 and 6).

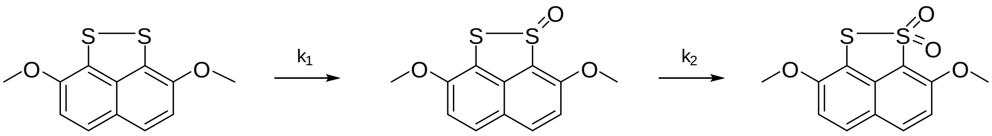
$NaIO_4$[148] and H_2O_2[146] were also employed in the oxidation of disulfide **87** with thiosulfonate **206** again the product obtained together with disulfide **87** (entries 7 and 8).

Entry	Conditions	**87** (%)	**206** (%)	**207** (%)
1	*m*CPBA (1.10 equiv.), CH_2Cl_2, 3 h, 0 °C	32	44	-
2	*m*CPBA (1.10 equiv.), Et_2O, 3 h, 0 °C	42	43	-
3[a]	*m*CPBA (1.10 equiv.), CH_2Cl_2, 3 h, 0 °C	36	37	5
4[a]	*m*CPBA (1.10 equiv.), Et_2O, 3 h, 0 °C	35	38	3
5	*m*CPBA (0.50 equiv.), CH_2Cl_2, 1 h, -78 °C	71	23	-
6	DMD (0.50 equiv.), acetone, 0.5 h, -78 °C	68	23	-
7	$NaIO_4$ (1.05 equiv.), H_2O/ 1,4-dioxane,1 h, 0 °C	39	48	-
8	H_2O_2 (1.00 equiv.), AcOH, 1 h, rt	37	47	-

[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.[144]



87 **205** **206**

Scheme 2.24 Rates of oxidation of disulfide **87** vs. thiosulfinate **205**

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).[107, 149]

$$2\ RS(O)SR \longrightarrow RS(O)_2SR + RSSR$$ **Equation 2.1**

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).[150]

$$RSOSR \longrightarrow RS(O)^{\bullet} + RS^{\bullet}$$ **Equation 2.2**

$$2\ RS(O)^{\bullet} \longrightarrow RS(O)\text{-}O\text{-}SR$$ **Equation 2.3**

$$RS(O)\text{-}O\text{-}SR \longrightarrow RS(O)_2^{\bullet} + RS^{\bullet} \longrightarrow RS(O)_2SR$$ **Equation 2.4**

$$2\ RS^{\bullet} \longrightarrow RSSR$$ **Equation 2.5**

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

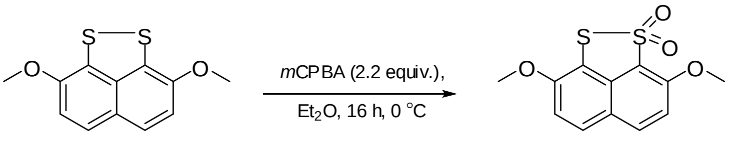
$$RS(O)SR \xrightarrow{H^+} RSOH + RSH \xrightarrow{RS(O)SR} RS(O)_2SR + RSSR$$

Scheme 2.25 Disproportionation of thiosulfinate

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 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 *m*CPBA (scheme 2.26).

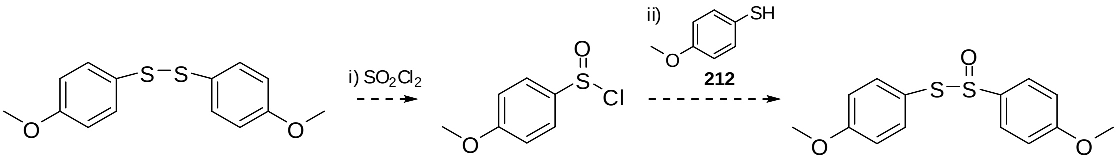


87 **206** 90%

Scheme 2.26 Preparation of dioxide **87**

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 phenomenum.

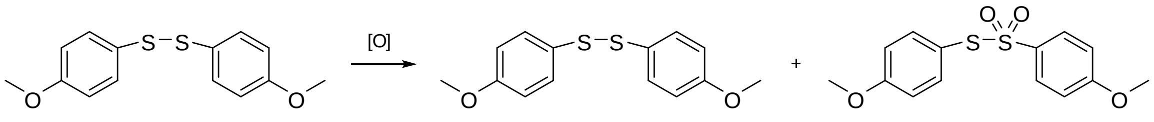
Although the oxidation of acyclic disulfide **208** has not been reported in the literature, thiosulfinate **210** has previously been synthesised by preparation of unstable sulfinyl chloride **211** from 1,2-bis(4-methoxyphenyl)disulfane (**208**) and SO_2Cl_2 and subsequent reaction with thiol **212** (scheme 2.27).[152, 153] Attempted synthesis of **210** using these conditions was unsuccessful, with only disulfide **208** and thiol **212** recovered.



208 **211** **210**

Scheme 2.27 Preparation of thiosulfinate **210**

Oxidation of disulfide **208** with stoichiometric *m*CPBA 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).



208 **208** **213**

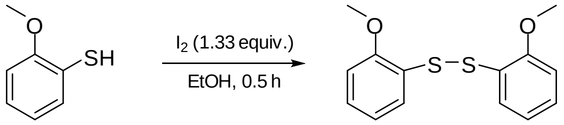
Scheme 2.28 Oxidation of disulfide **208**

Entry	Conditions	**208** (%)	**213** (%)
1	*m*CPBA (1.05 equiv.), CH_2Cl_2, 1 h, -78 °C	43	40
2	DMD (1.00 equiv.), acetone, 0.5 h, -78 °C	45	47

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**.

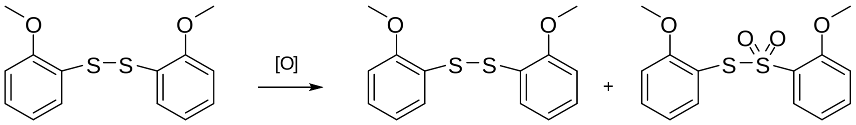
ortho-Substituted 1,2-bis(2-methoxyphenyl)disulfane (**209**) was prepared in 95% yield by oxidation of 2-methoxybenzenethiol (**214**) with iodine (scheme 2.29).^{154}



214 **209**

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).



209 **209** **215**

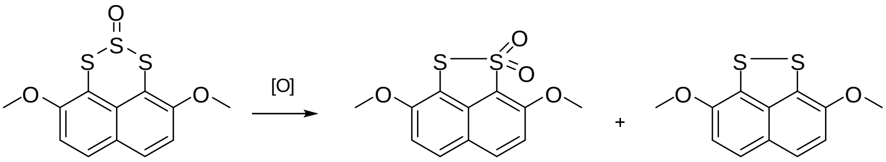
Scheme 2.30 Oxidation of disulfide **209**

Entry	Conditions	**209** (%)	**215** (%)
1	*m*CPBA (1.05 equiv.), CH_2Cl_2, 2 h, -78 °C	48	45
2	DMD (1.00 equiv.), acetone, 10 min, -78 °C	47	47

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 *m*CPBA 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).



103 **206** **87**

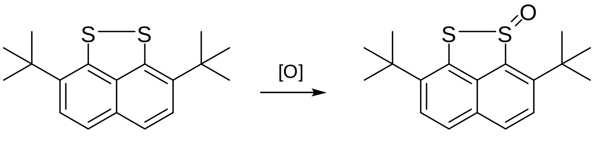
Entry	Conditions	**206** (%)	**87** (%)
1	*m*CPBA (1 equiv.), CH_2Cl_2, -78 °C → rt, o/n	67	31
2	DMD (1 equiv.), acetone, -78 °C → rt, o/n	63	35

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 **c**), 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 *m*CPBA 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).



65 **216**

Scheme 2.30 Preparation of thiosulfinate **216**

Entry	Conditions	**216** (%)
1	*m*CPBA (1.10 equiv.), CH_2Cl_2, 0 °C, 2 h	80
2	DMD (1.05 equiv.), acetone, 0 °C, 2 h	68

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.

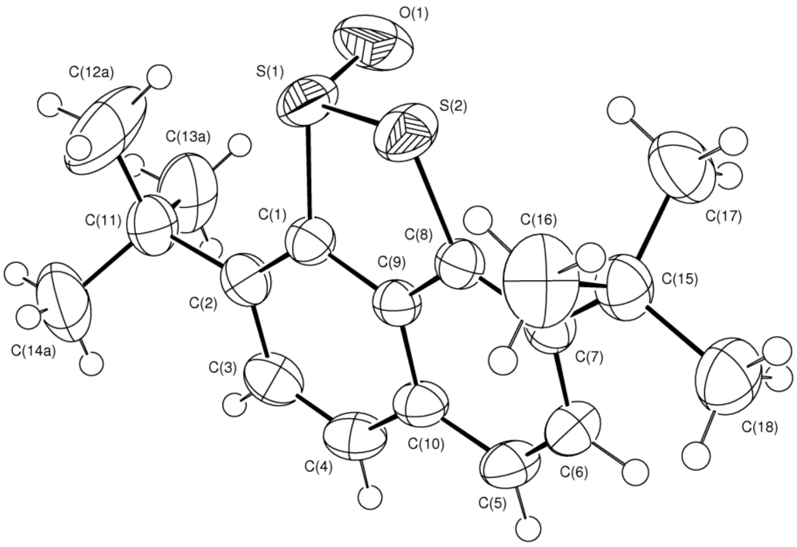
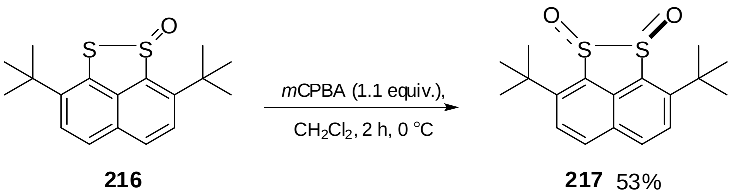


Figure 2.4 X-ray crystal structure of thiosulfinate **216**. Thermal ellipsoids are drawn at the 50% probability level

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.[22, 119-121, 123-125] To begin with, thiosulfinate **216** was oxidised with *m*CPBA in diethyl ether to try to avoid exposure of any *vic*-disulfoxide to the acid byproduct (*m*CBA) from the oxidant. A product precipitated out of solution and analysis of the solid by ^{1}H-NMR spectroscopy suggested formation of a *vic*-disulfoxide (scheme 2.32).



Scheme 2.32 Synthesis of *vic*-disulfoxide **217**

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).

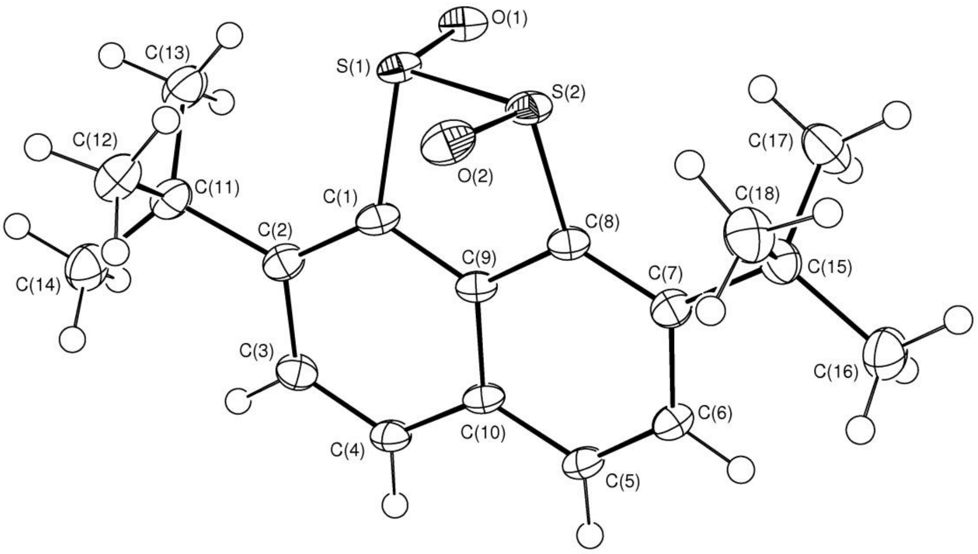


Figure 2.5 X-ray crystal structure of **217**. Thermal ellipsoids are drawn at the 50% probability level

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°.

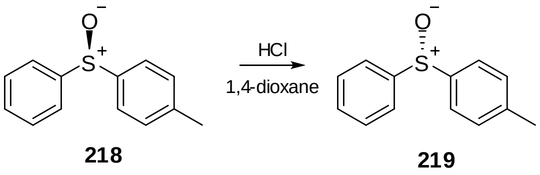
It has been reported that *vic*-disulfoxides are unstable and decompose at room temperature over a short period of time.[124] An NMR sample of *trans vic*-disulfoxide **217** in $CDCl_3$ was monitored over a six-month period and no breakdown was observed. A solution of **217** in CH_2Cl_2 was stirred in the presence of both *m*CBA 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.[120] *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 *m*CPBA in CH_2Cl_2 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).

Entry	Starting material	Conditions	**217** (%)
1	**216**	*m*CPBA (1.10 equiv.), Et_2O, 0 °C, 2 h	53
2	**216**	*m*CPBA (1.05 equiv.), CH_2Cl_2, 0 °C, 2 h	86
3	**216**	DMD (1.05 equiv.), acetone, 0 °C, 30 min	81
4	**65**	*m*CPBA (2.10 equiv.), Et_2O, 0 °C, 2 h	76
5	**65**	*m*CPBA (2.10 equiv.), CH_2Cl_2, 0 °C, 2 h	80
6	**65**	DMD (2.10 equiv.), acetone, 0 °C, 30 min	92

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

The isomerisation of sulfoxides has been reported in the literature using HCl.[155, 156] An attempt to isomerise **217** to the *cis* stereoisomer by the addition of TFA to an NMR sample in $CDCl_3$ 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).[155]

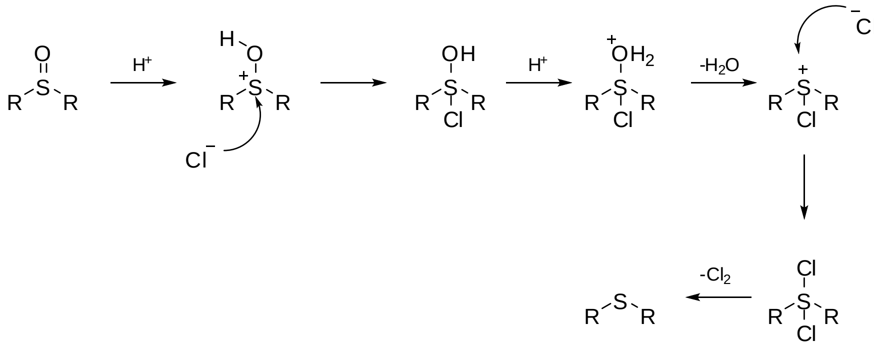


Scheme 2.33 Isomerisation of phenyl *p*-tolyl sulfoxide **218**

Treatment of **217** with 4 M HCl in dioxane resulted in clean reduction to the thiosulfinate **216** rather than epimerisation (scheme 2.34).[155, 156]

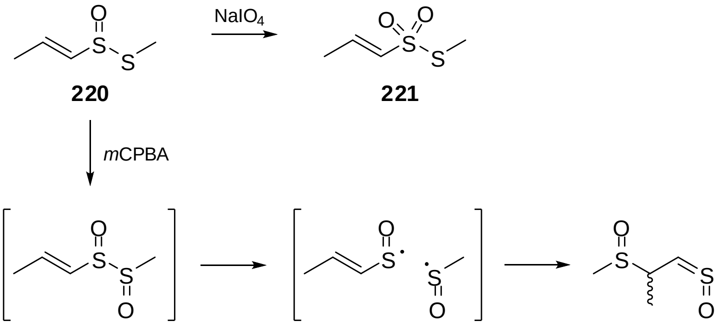
Scheme 2.34 Reduction of *trans vic*-disulfoxide **217** to thiosulfinate **216**

The reduction of sulfoxides by HCl has been reported in the literature and is described in scheme 2.35.[157] 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

Block has reported the oxidation of thiosulfinate **220** using both nucleophilic and electrophilic oxidants (scheme 2.36).[158]



Scheme 2.36 Oxidation of alk(en)yl 1-propenyl disulfide

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 sulfinyl sulfur.[107] 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 sulfinyl sulfur, to produce thiosulfonate **221**.[158]

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).[148, 159] No reaction occurred when sodium periodate was reacted with thiosulfinate **216**, with starting material retrieved in quantitative yield.

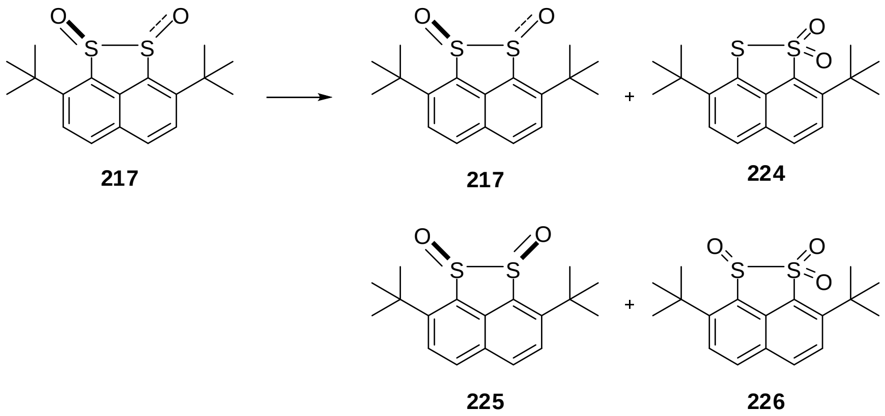
$KMnO_4$ is a stronger oxidant in comparison to the periodate oxidants used. Treatment of disulfide **65** with $KMnO_4$ resulted in a mixture of products including thiosulfonate **224** and *trans vic*-disulfoxide **217**, depending on the conditions used (entrie**s** 3 and 4).[31, 160]

Entry	Conditions	**65** (%)	**216** (%)	**224** (%)	**217** (%)
1	$NaIO_4$ (2.10 equiv.), water/ 1,4-dioxane, 3 days, rt	22	29	-	20
2	Bu_4NIO_4 (2.10 equiv.), $CHCl_3$, 3 days, reflux	50	49	-	-
3	$KMnO_4$ (2.00 equiv.), $MgSO_4$ (2.77 equiv.), water/1,4-dioxane, 3 days, rt	40	-	-	44
4	$KMnO_4$ (2.00 equiv.), TBAB (0.16 equiv.), CH_2Cl_2/H_2O, 3 days, rt	20	32	9	5

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.[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).



Scheme 2.35 Thermal rearrangement of *trans vic*-disulfoxide

Entry	Conditions[a]	**217** (%)[b]	**225** (%) [b]	**224** (%) [b]	**226** (%) [b]
1	PhCl, 80 °C, 38 h	70	10	4	-
2	PhCl, 108 °C, 27.5 h	63	8	3	-
3	PhCl, 108 °C, 38 h	55	10	5	4
4	mesitylene, 108 °C, 38 h	55	10	5	3
5	PhCl, 132 °C, 38 h	49	18	4	2
6	mesitylene, 167 °C, 38 h	-	-	92	-

[a] All reactions run as 0.01 M solutions of **217** in degassed solvent.

[b] Isolated yield after column chromatography.

Table 2.11 Thermal rearrangement of *trans vic*-disulfoxide

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*-butylnaphtho[1,8-*cd*][1,2]dithiole 1,2-dioxide (**225**) is shown in figure 2.6.

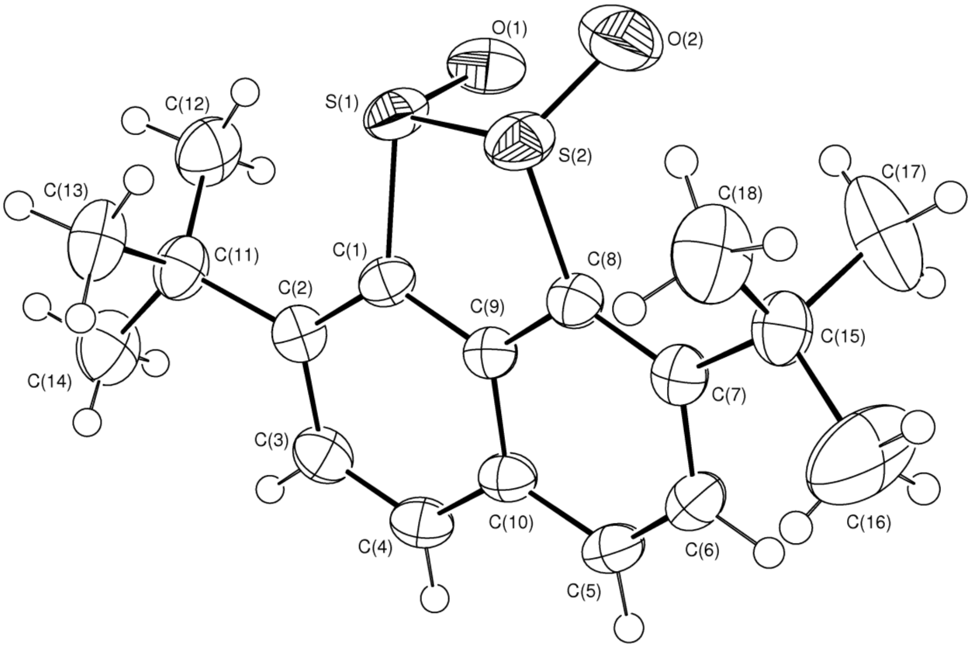


Figure 2.6 X-ray crystal structure of **225**. Thermal ellipsoids are drawn at the 50% probability level

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).

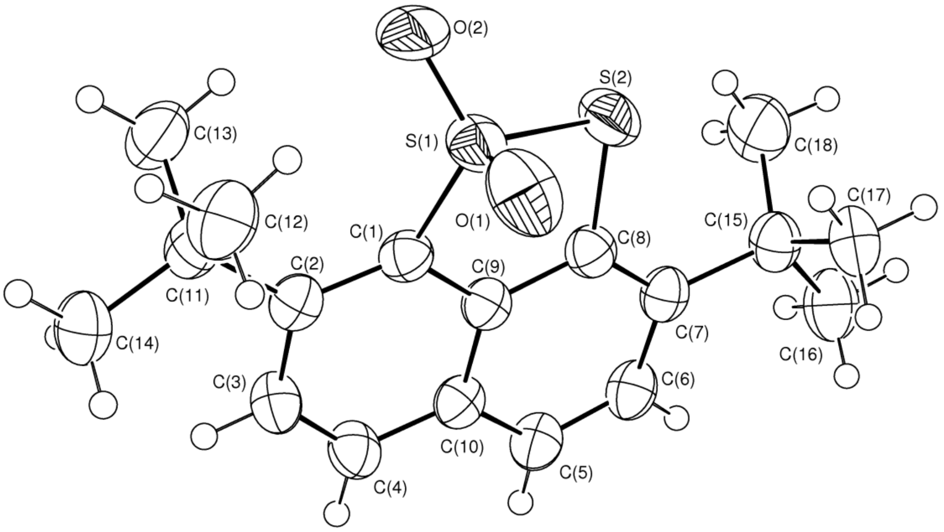


Figure 2.7 X-ray crystal structure of **224**. Thermal ellipsoids are drawn at the 50% probability level

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).

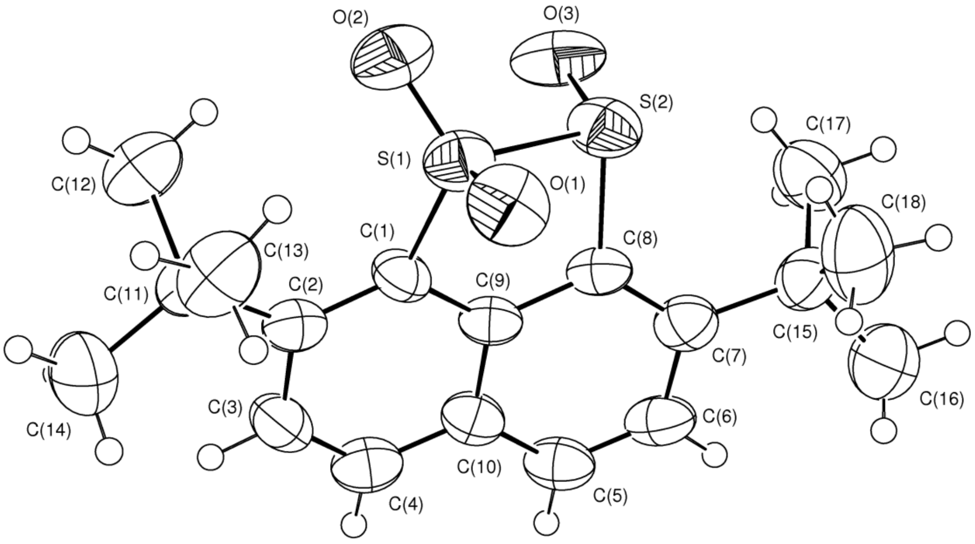
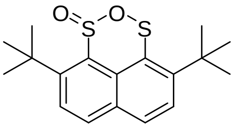


Figure 2.8 X-ray crystal structure of **226**. Thermal ellipsoids are drawn at the 50% probability level

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).



227

Figure 2.9 Proposed intermediate: *O*,*S*-sulfenylsulfinate **227**

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.[107] The longest bonds are accounted for by *vic*-disulfoxides **217** and **225**.

Compound	disulfide		thiosulfinate		*vic*-disulfoxide	
	50[136]	**65**[136]	**107**	**216**	*trans*-**217**[a]	*cis*-**225**
Bond distance						
S-S(Å)	2.0879 [2.096]	2.0580	2.138 [2.141]	2.0890	2.1983	2.2356
Bond angle						
S(1)-C(1)-C(9)	115.03 [114.01]	113.36	117.11 [116.87]	113.42	112.92	113.79
S(2)-C(8)-C(9)	115.11 [117.84]	113.36	113.73 [114.84]	111.91	112.31	112.37
C(1)-C(9)-C(8)	118.65 [117.98]	119.80	118.98 [119.14]	120.03	119.98	121.42
Torsion angle						
C(1)-C(9)-C(10)-C(4)	0.70 [0.30]	0.31	-1.20	-1.48	-0.94	-1.90
C(8)-C(9)-C(10)-C(5)	-179.40 [-179.00]	-179.69	0.50	-3.23	-2.42	-3.40
Out-of-plane displacement						
S(1)	-0.0240 [-0.0377]	0.0841	0.1930 [0.0120]	0.4070	0.5000	0.5020
S(2)	-0.0245 [0.0230]	-0.0841	0.0640 [0.0070]	0.1390	0.3720	0.2300

[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).

Compound	thiosulfonate		sulfinyl sulfone	
	63[136]	**224**[a]	**228**[136]	**226**[a]
Bond distance (Å)				
S-S	2.1143	2.0764	2.2520	2.1790
Bond angle (°)				
S(1)-C(1)-C(9)	116.20	108.97	112.60	108.68
S(2)-C(8)-C(9)	113.00	113.79	118.70	113.81
C(1)-C(9)-C(8)	119.40	121.22	121.50	121.79
Torsion angle (°)				
C(1)-C(9)-C(10)-C(4)	-1.30	1.10	1.60	4.18
C(8)-C(9)-C(10)-C(5)	179.20	0.54	-178.90	2.04
Out-of-plane displacement (Å)				
S(1)	-0.1180	0.3050	-0.0637	0.3030
S(2)	0.1692	0.1720	0.0694	0.5210

[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.

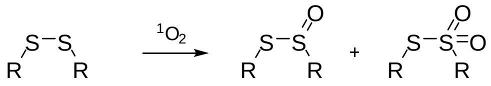
Entry	Conditions[a]	**217** (%) [b]	**225** (%) [b]	**224** (%) [b]	**226** (%) [b]
1	PhCl, 80 °C, 38 h	10	75	5	-
2	PhCl, 108 °C, 38 h	15	50	5	5
3	PhCl, 132 °C, 38 h	20	45	10	5
4	mesitylene, 167 °C, 34 h	-	-	93	-

[a] All reactions run as 0.01 M solutions of **226** in degassed solvent.

[b] Isolated yield after column chromatography.

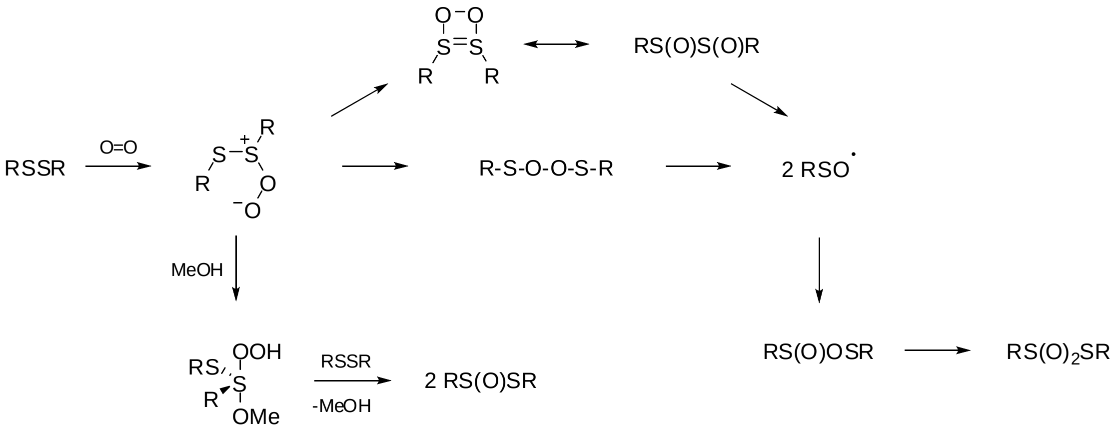
Table 2.14 Thermal rearrangement of *cis vic*-disulfoxide **225**

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



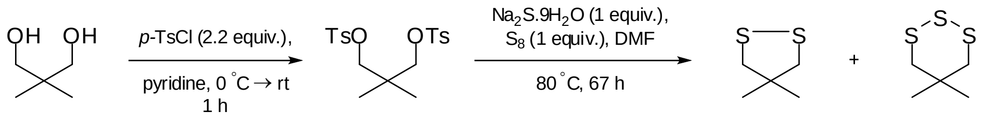
Scheme 2.38 Oxidation of disulfide with singlet oxygen

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).[162]



Scheme 2.39 Photooxidation of disulfides

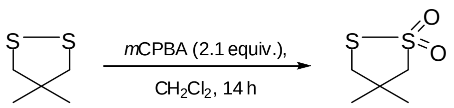
Attempts to synthesise the *cis vic*-disulfoxide using this approach were explored as attack of the singlet oxygen occurs in a *syn* fashion. Initially, oxidations were performed on known disulfide **231**, which was prepared from 2,2-dimethylpropane-1,3-diol (**229**) in two steps (scheme 2.40).[163, 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.



229 **230** 88% **231** 32% **232** 13%

Scheme 2.40 Preparation of dithiolane **231**

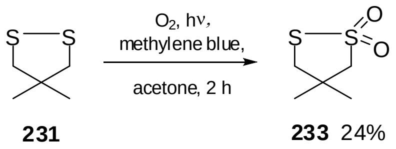
A sample of 4,4-dimethyl-[1,2]dithiolane 1,1-dioxide (**233**) was prepared by *m*CPBA oxidation of disulfide **231** in very good yield so the photooxidation reaction could be monitored (scheme 2.41).



231 **233** 79%

Scheme 2.41 Oxidation of disulfide **231**

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).[161]



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.

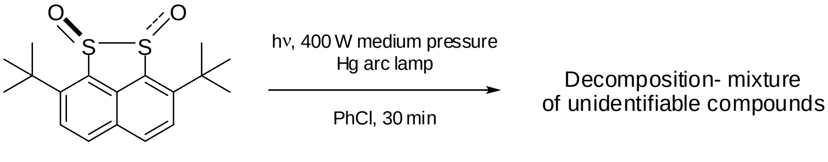
Entry	Conditions	**65** (%)
1	O_2, h*v*, acetone, methylene blue, 500 W halogen lamp, 8 h	100
2	O_2, h*v*, MeOH, methylene blue, 500 W halogen lamp, 8 h	100
3	O_2, h*v*, PhH, methylene blue, 500 W halogen lamp, 8 h	97
4	O_2, h*v*, PhH, methylene blue, 400 W medium pressure Hg arc lamp , pyrex filter, 8 h	100

Table 2.15 Attempted oxidation using $^1O_2$

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

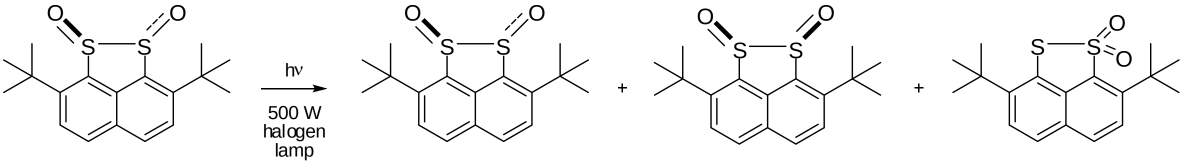
There is a large thermal barrier for the rearrangement of *vic*-disulfoxides **217** and **225**. Little precedent for the irradiation of *vic*-disulfoxides exists in the literature; therefore the photochemical stability of the *vic*-disulfoxides was investigated at room temperature. *vic*-Disulfoxide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



217

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).



217 **217** **225** **224**

Scheme 2.44 Photoepimerisation of *trans vic*-disulfoxide with a 500 W halogen lamp

Entry[a]	Solvent	Time (h)	**217** (%)[b]	**225** (%)[b]	**224** (%)[b]
1	$CDCl_3$	0.25	84	6	0
2	$CDCl_3$	1	73	18	0
3	$CDCl_3$	2	62	32	0
4	$CDCl_3$	4	49	46	3
5	$CDCl_3$	17	43	42	10
6	$CDCl_3$	44	40	39	12
7	PhCl	3	48	45	4
8	PhCl	7	46	46	4
9	PhCl	14	42	43	9

[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 ^{1}H-NMR spectroscopy using a water-cooled NMR tube (table 2.17, figure 2.10).

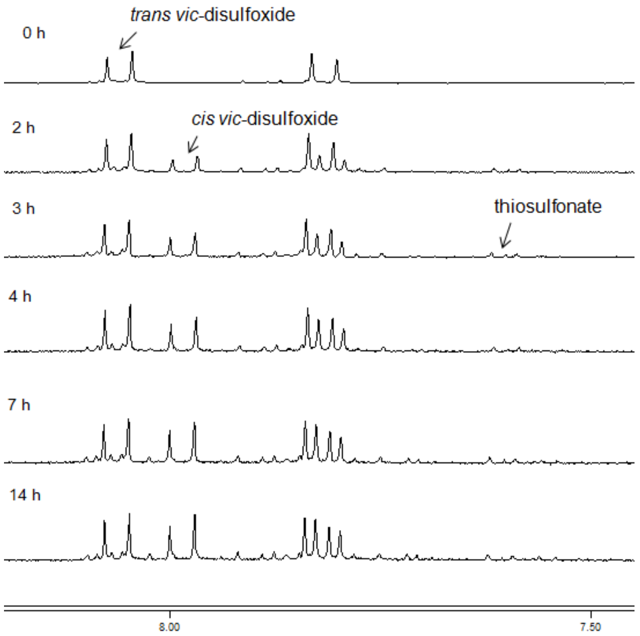
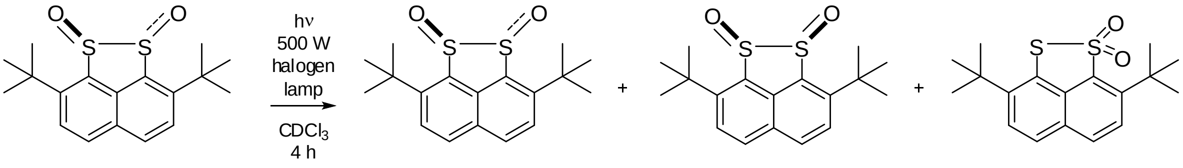


Figure 2.10 Photoepimerisation of *trans vic*-disulfoxide in $CDCl_3$ monitored by ^{1}H-NMR spectroscopy

The ratios of the isolated yields were comparable to the ratio of compounds obtained from ^{1}H-NMR analysis (scheme 2.45).



217 **217** **225** **224**

Isolated yield (%)	49	46	3
NMR yield (%)	51	44	5

Scheme 2.45 Comparison of isolated yields with NMR yields after irradiation of *trans*-**217** for 4 h

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).

Entry[a]	Disulfoxide	Solvent	Time (h)	**217** (%)[b]	**225** (%)[b]	**224** (%)[b]
1	**217**	$CDCl_3$	2	60	40	0
2	**217**	$CDCl_3$	3	53	43	4
3	**217**	$CDCl_3$	4	51	44	5
4	**217**	$CDCl_3$	6	49	46	5
5	**217**	$CDCl_3$	7	49	46	5
6	**217**	$CDCl_3$	14	45	46	9
7	**217**	$CDCl_3$	28	45	45	10
8	**225**	$CDCl_3$	3	41	55	4
9	**225**	$CDCl_3$	7	45	50	5
10	**225**	$CDCl_3$	14	45	46	9
11	**217**	1,2-DCE	3	56	40	4
12	**217**	1,2-DCE	7	51	43	6
13	**217**	1,2-DCE	14	46	44	10
14	**225**	1,2-DCE	3	42	55	3
15	**225**	1,2-DCE	7	44	51	5
16	**225**	1,2-DCE	14	46	45	9
17	**217**	MeCN	3	55	40	5
18	**217**	MeCN	7	51	44	5
19	**217**	MeCN	14	46	45	9
20	**225**	MeCN	3	40	57	3
21	**225**	MeCN	7	46	48	6
22	**225**	MeCN	14	47	43	10
23	**217**	PhH	3	54	41	5
24	**217**	PhH	7	50	44	6
25	**217**	PhH	14	47	46	7
26	**225**	PhH	3	42	54	4
27	**225**	PhH	7	45	50	5
28	**225**	PhH	14	48	45	7
29	**217**	MeOH	3	54	42	4
30	**217**	MeOH	7	51	44	5
31	**217**	MeOH	14	48	45	7
32	**225**	MeOH	3	40	57	3
33	**225**	MeOH	7	47	49	4
34	**225**	MeOH	14	47	45	8

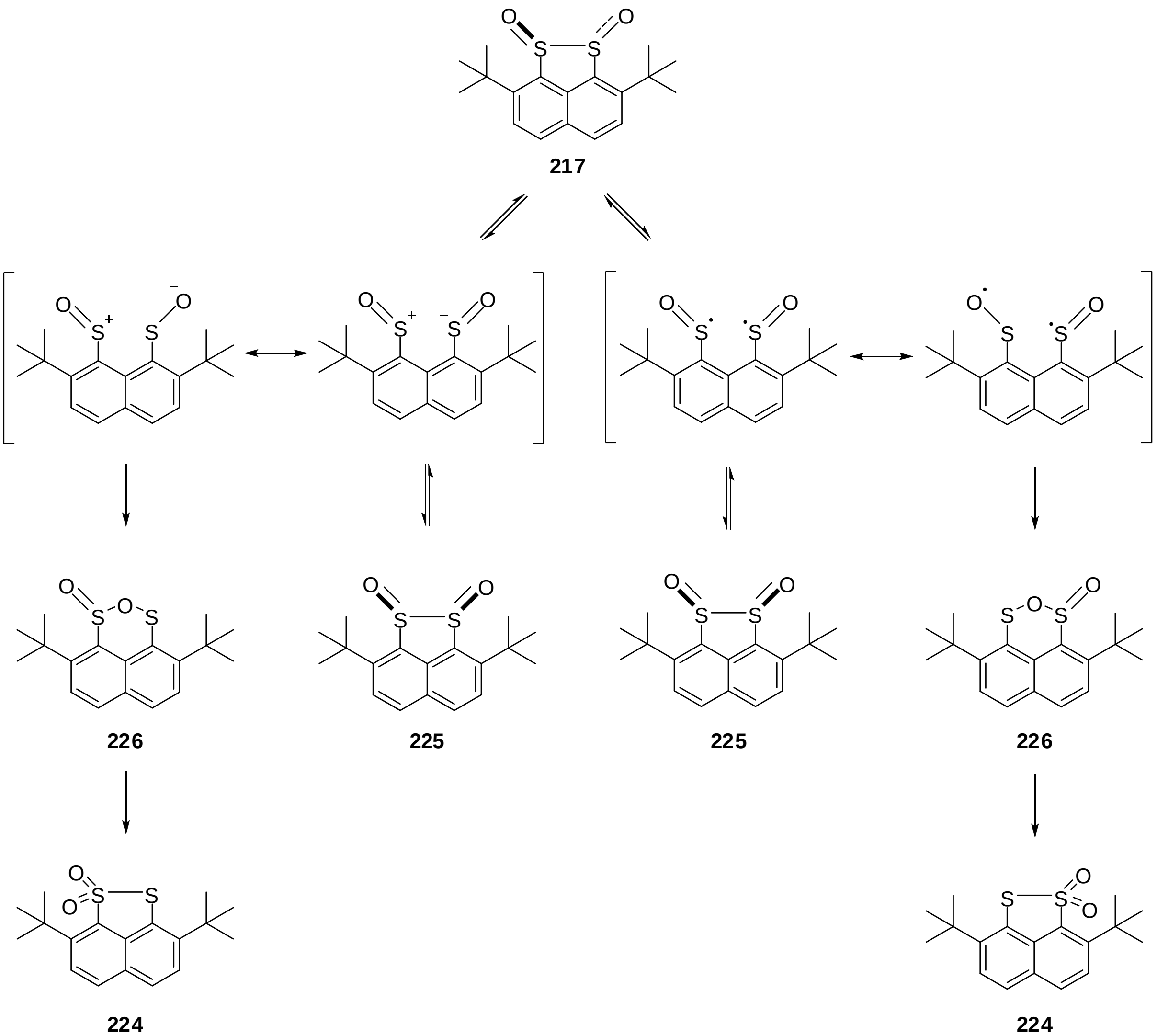
[a] All reactions run by irradiation of a 0.01 M solution of **217** or **225** in degassed solvent in a water cooled NMR tube with a 500 W lamp.

[b] Ratio determined by integration in ^{1}H-NMR in $CDCl_3$ after evaporation of reaction solvent.

Table 2.17 Photomediated epimerisation of *vic*-disulfoxides **217** and **225**

2.8 Radical traps and EPR studies

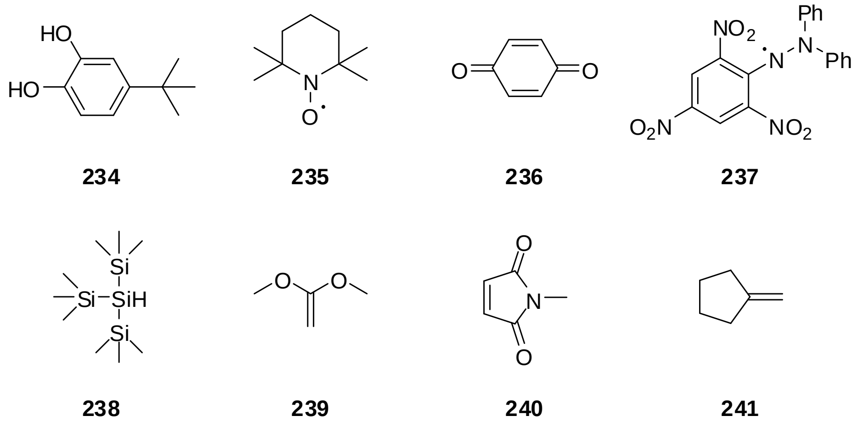
The isomerisation or rearrangement of **217** or **225** is considered to occur either *via* homolytic or heterolytic fission of the S-S bond (scheme 2.46). The direct formation of *cis vic*-disulfoxide, *via* a concerted type rearrangement, is unlikely as the sulfinyl oxygen is unable to access an empty 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.[105] Rotation about the C-S bond and head-to-head recombination would provide the *cis*-**225**.



Scheme 2.46 Proposed rearrangement of *vic*-disulfoxides

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.[165, 166] Both thiyl and sulfonyl radicals have been successfully reacted with radical traps, [167, 168] 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).



234 **235** **236** **237**

238 **239** **240** **241**

Figure 2.11 Radical traps

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**. S_{Hi}[171] at O could possibly occur with the labile C-O bond to form **227**, which could then rearrange to **224**.

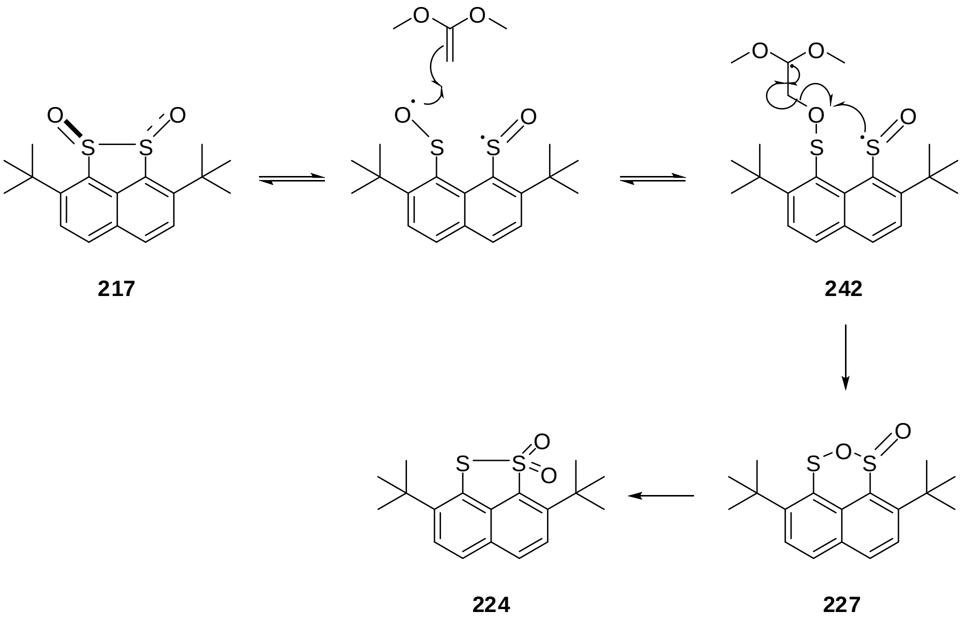
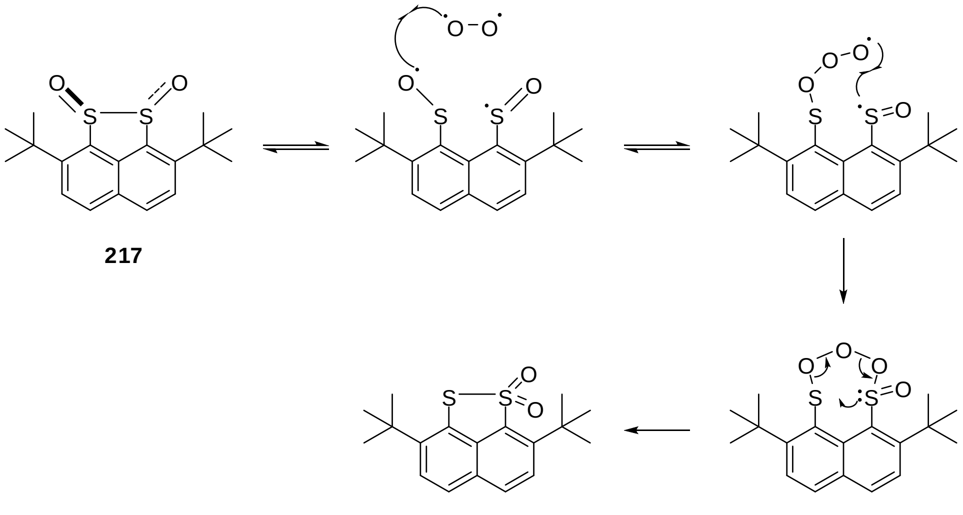


Figure 2.47 Proposed mechanism for the reaction of *trans*-**217** with **239**

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 *vic*-disulfoxide **217** in the presence of O_2 resulted in the rearranged thiosulfonate **224** exclusively (entry 17).

A possible mechanism for the photoinduced rearrangement to thiosulfonate **224** from *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**.



217

224

Scheme 2.48 Rearrangement of *trans vic*-disulfoxide with O_2

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 sensitiser to promote molecular oxygen to the singlet state.

Entry	Radical trap	Conditions	**206** (%)	**214** (%)	**213** (%)	**215** (%)
1	**234**	500 W halogen lamp, MeCN, 7 h, rt	44	43	5	-
2	**234**	PhCl, 24 h, 132 °C	46	13	7	3
3	**235**	500 W halogen lamp, MeCN, 7 h, rt	40	40	6	-
4	**235**	PhCl, 24 h, 132 °C	43	12	6	2
5	**236**	500 W halogen lamp, MeCN, 7 h, rt	46	44	4	-
6	**236**	PhCl, 24 h, 132 °C	44	12	6	4
7	**237**	500 W halogen lamp, MeCN, 7 h, rt	100	-	-	-
8	**237**	PhCl, 24 h, 132 °C	42	14	7	2
9	**238**	500 W halogen lamp, MeCN, 7 h, rt	42	40	5	-
10	**238**	PhCl, 24 h, 132 °C	40	13	8	5
11	**238** and bromoadamantane	500 W halogen lamp, MeCN, 7 h, rt	45	43	4	-
12	**238** and bromoadamantane	PhCl, 24 h, 132 °C	40	15	20	5
13	**239**	500 W halogen lamp, MeCN, 7 h, rt	-	-	95	-
14	**239**	PhCl, 24 h, 132 °C	-	-	76	-
15	**240**	500 W halogen lamp, MeCN, 7 h, rt	44	42	6	-
16[a]	**241**	500 W halogen lamp, MeCN, 7 h, rt	49	47	4	-
17	O_2	500 W halogen lamp, MeCN, 7 h, rt	-	-	90	-
18	O_2	PhCl, 24 h, 132 °C	46	44	6	2

[a] Ratio determined by integration in ^{1}H-NMR in $CDCl_3$ after evaporation of reaction solvent.

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

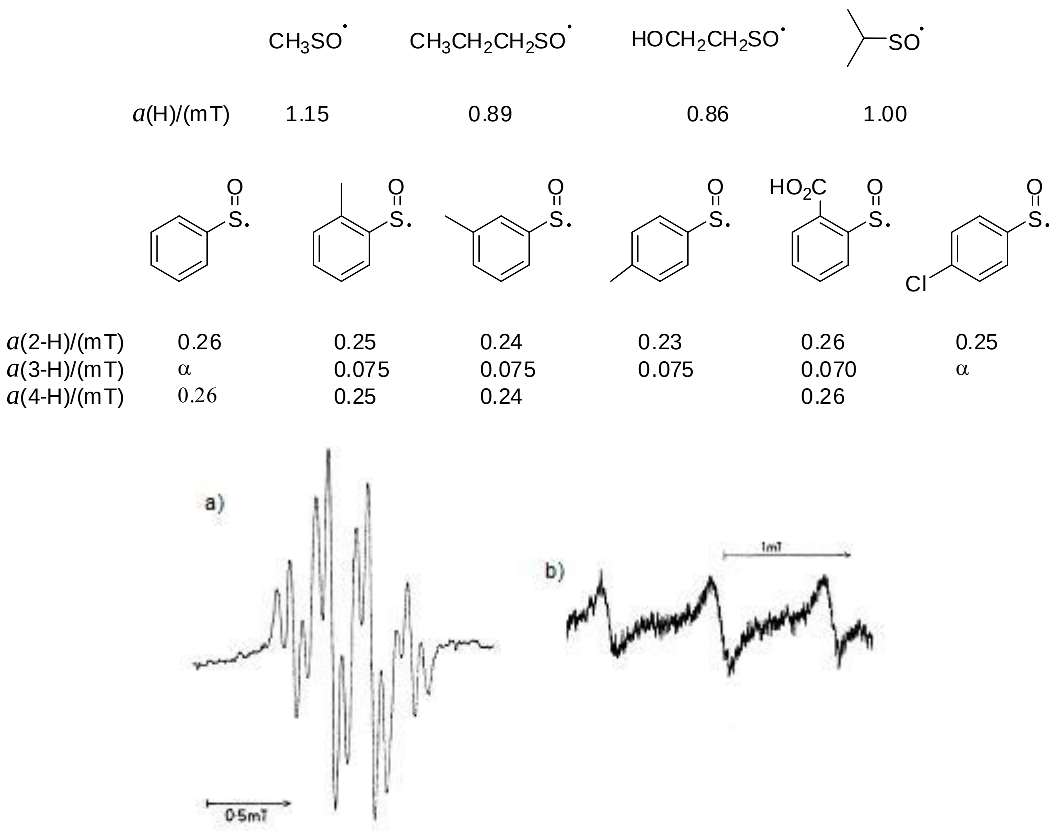
Entry	Solvent	Conditions	**217** (%)	**225** (%)	**224** (%)	**226** (%)
1	propan-2-ol/PhCl[a]	500 W halogen lamp, MeCN, 7 h, rt	45	44	7	-
2	propan-2-ol/PhCl[a]	24 h, 132 °C	45	15	8	5
3	1,4-cyclohexadiene	500 W halogen lamp, MeCN, 7 h, rt	45	43	5	-
4	1,4-cyclohexadiene	24 h, 132 °C	40	13	8	6
5	1,3-dioxolane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

[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]



	$CH_3SO^\bullet$	$CH_3CH_2CH_2SO^\bullet$	$HOCH_2CH_2SO^\bullet$	$(CH_3)_2CHSO^\bullet$
a(H)/(mT)	1.15	0.89	0.86	1.00

	$C_6H_5SO^\bullet$	2-$CH_3C_6H_4SO^\bullet$	3-$CH_3C_6H_4SO^\bullet$	4-$CH_3C_6H_4SO^\bullet$	2-$HO_2CC_6H_4SO^\bullet$	4-$ClC_6H_4SO^\bullet$
a(2-H)/(mT)	0.26	0.25	0.24	0.23	0.26	0.25
a(3-H)/(mT)	α	0.075	0.075	0.075	0.070	α
a(4-H)/(mT)	0.26	0.25	0.24		0.26	

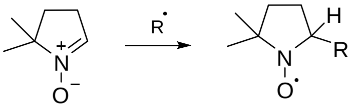
a) EPR spectrum of $C_6H_5SO^\cdot$ at -75 °C b) EPR spectrum of $CH_3CH_2CH_2SO^\cdot$ at -79 °C

Figure 2.12 Sulfinyl radicals detected by EPR[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).[169, 174-176] In these situations the radical is not detected on the sulfur atom but on the resulting nitroxide oxygen radical **232** which is stable and long lived at room temperature. Originally, a three-line spectrum is produced, with coupling of the oxygen-centred radical to the nitrogen (I = 1, 2nI + 1 = 3).

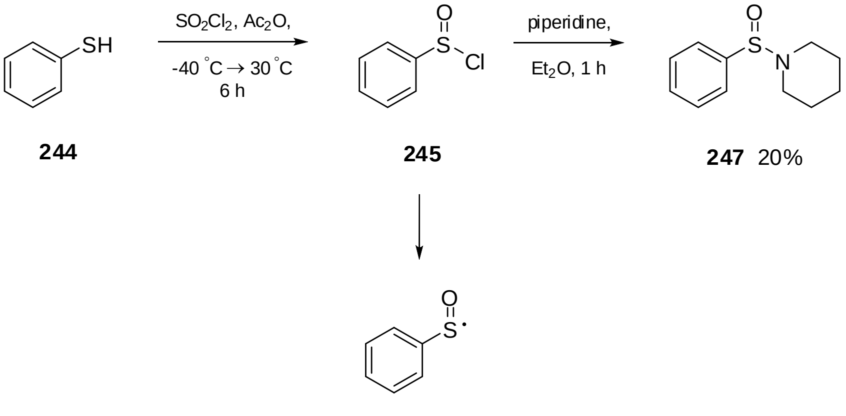


243

R	a(N)/(mT)	a(H)/(mT)
R = $PhCH_2S$	1.36	1.17
R = $(CH_3)_3CS$	1.35	1.12
R = $HOCH_2CH_2SO_2$	1.288	1.303
R = 4-$MeC_6H_4SO_2$	1.45	2.22

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]

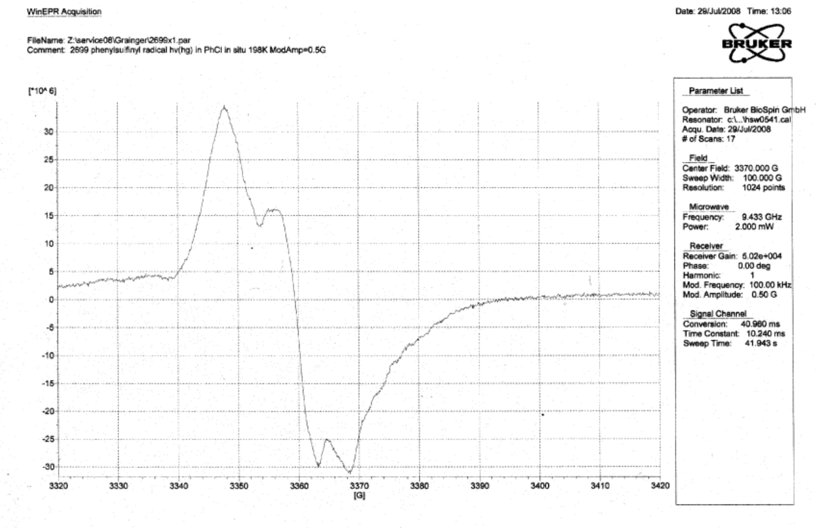


244 **245** **247** 20%

246

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.



WinEPR Acquisition

Date: 29/Jul/2008 Time: 13:06

FileName: Z:\service08\Grainger\2699x1.par
Comment: 2699 phenylsulfinyl radical hv(hg) in PhCl in situ 198K ModAmp=0.5G

Parameter List

Operator: Bruker BioSpin GmbH
Resonator: c:\...\hsw0541.cal
Acqu. Date: 29/Jul/2008
# of Scans: 17

Field
Center Field: 3370.000 G
Sweep Width: 100.000 G
Resolution: 1024 points

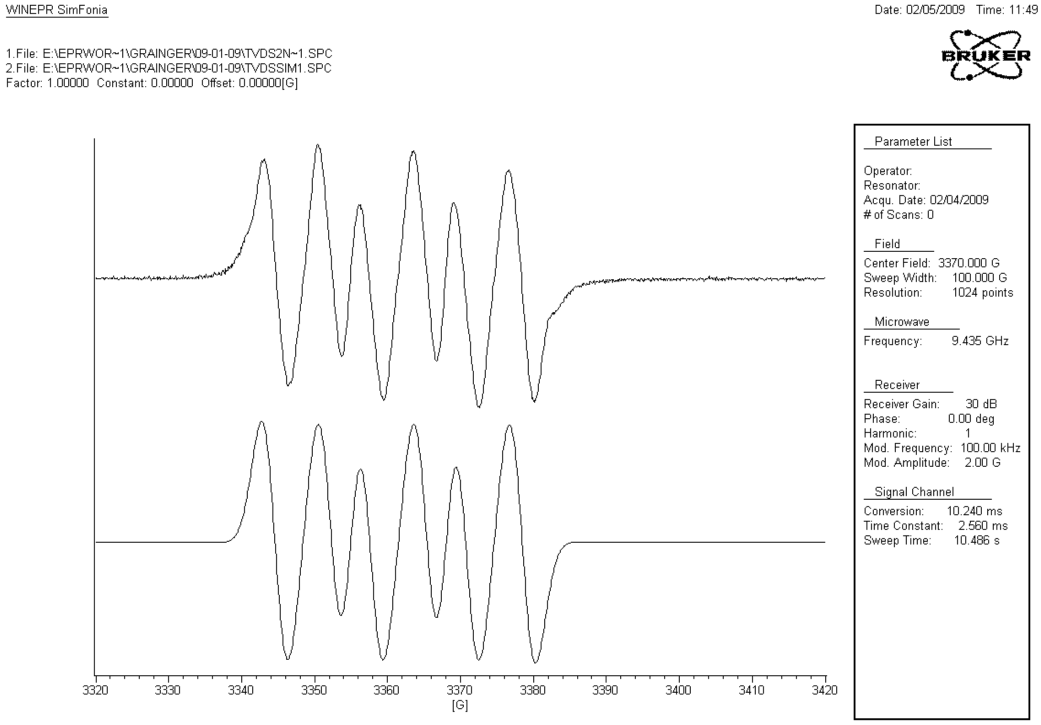
Microwave
Frequency: 9.433 GHz
Power: 2.000 mW

Receiver
Receiver Gain: 5.02e+004
Phase: 0.00 deg
Harmonic: 1
Mod. Frequency: 100.00 kHz
Mod. Amplitude: 0.50 G

Signal Channel
Conversion: 40.960 ms
Time Constant: 10.240 ms
Sweep Time: 41.943 s

Figure 2.13 EPR spectrum of phenyl sulfinyl radical

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).[169]



WINEPR SimFonia

Date: 02/05/2009 Time: 11:49

1.File: E:\EPRWOR~1\GRAINGER\09-01-09\TVDS2N~1.SPC
2.File: E:\EPRWOR~1\GRAINGER\09-01-09\TVDSSIM1.SPC
Factor: 1.00000 Constant: 0.00000 Offset: 0.00000[G]

Parameter List

Operator:
Resonator:
Acqu. Date: 02/04/2009
# of Scans: 0

Field
Center Field: 3370.000 G
Sweep Width: 100.000 G
Resolution: 1024 points

Microwave
Frequency: 9.435 GHz

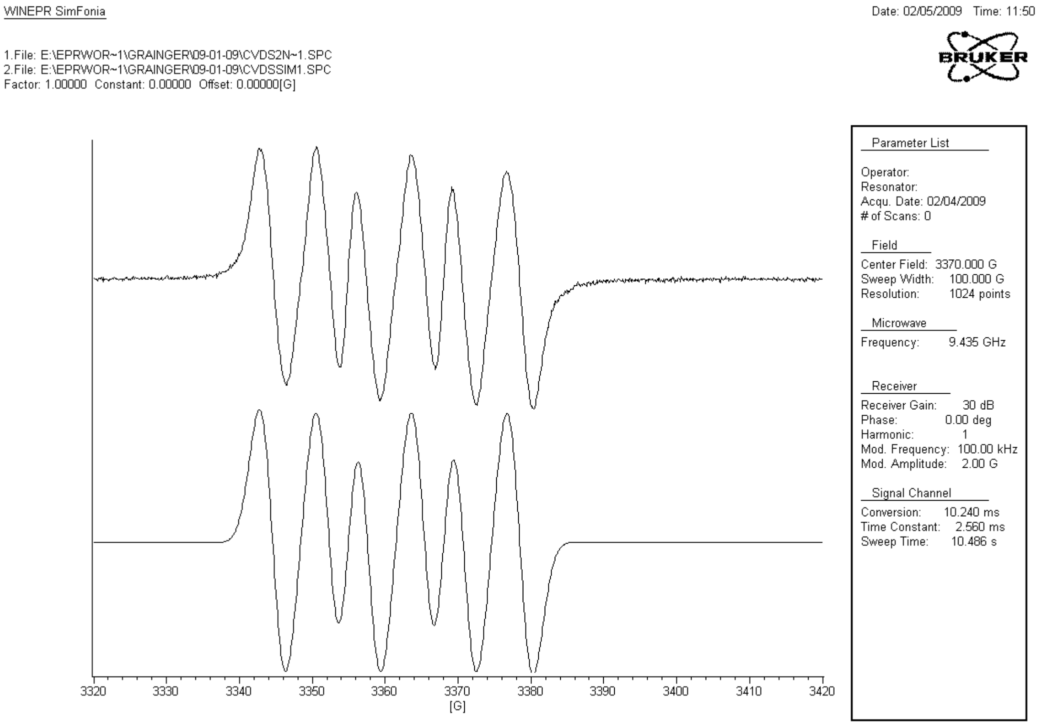
Receiver
Receiver Gain: 30 dB
Phase: 0.00 deg
Harmonic: 1
Mod. Frequency: 100.00 kHz
Mod. Amplitude: 2.00 G

Signal Channel
Conversion: 10.240 ms
Time Constant: 2.560 ms
Sweep Time: 10.486 s

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).



WINEPR SimFonia

Date: 02/05/2009 Time: 11:50

1.File: E:\EPRWOR~1\GRAINGER\09-01-09\CVDS2N~1.SPC
2.File: E:\EPRWOR~1\GRAINGER\09-01-09\CVDSSIM1.SPC
Factor: 1.00000 Constant: 0.00000 Offset: 0.00000[G]

Parameter List

Operator:
Resonator:
Acqu. Date: 02/04/2009
# of Scans: 0

Field
Center Field: 3370.000 G
Sweep Width: 100.000 G
Resolution: 1024 points

Microwave
Frequency: 9.435 GHz

Receiver
Receiver Gain: 30 dB
Phase: 0.00 deg
Harmonic: 1
Mod. Frequency: 100.00 kHz
Mod. Amplitude: 2.00 G

Signal Channel
Conversion: 10.240 ms
Time Constant: 2.560 ms
Sweep Time: 10.486 s

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).

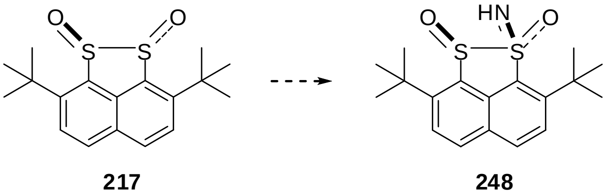
With these observations in hand, the variables of the experiment were considered to make sure the nitroxide radical was formed directly from the *vic*-disulfoxide. Control reactions (irradiation of PhCl, DMPO in PhCl and thiosulfonate **224** in the presence of DMPO in PhCl) failed to produce a spectrum 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 thiyl 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

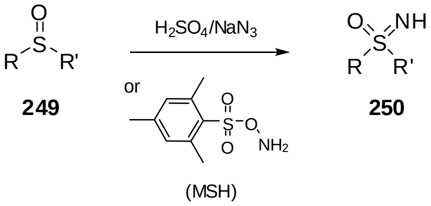
The sulfoximine functionality is highly versatile and is used in building blocks for bioactive molecules and pseudopeptides, chiral auxiliaries for asymmetric synthesis and ligands for enantioselective metal catalysis.[178, 179] v*ic*-Disulfoxides can be envisaged as precursors to a novel functional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



217 **248**

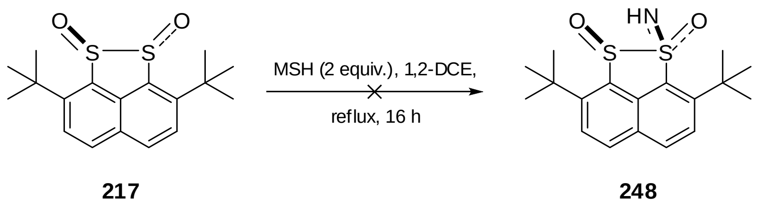
Scheme 2.51 Proposed amination of *trans*-**217**

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).[180, 181]



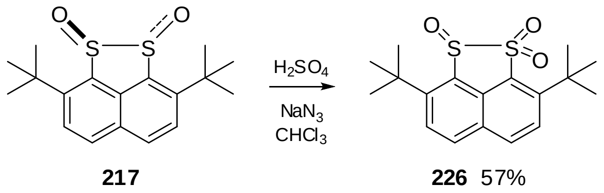
Scheme 2.52 Two possible synthetic routes to sulfoximines

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, *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).



Scheme 2.53 Attempted amination of *trans*-**217** with MSH

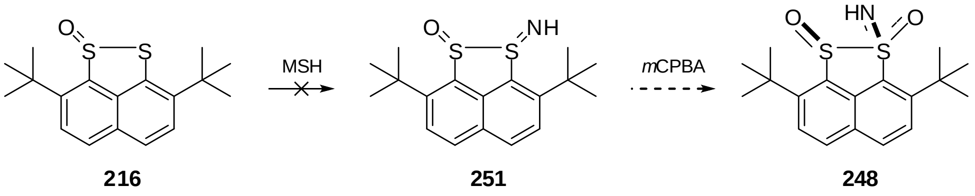
Efforts to synthesise the sulfoximine functional group from *vic*-disulfoxide **217** with hydrazoic acid did lead to the oxidation of **217**, although the product obtained was the sulfinyl sulfone **226** (scheme 2.54, entry 3). Trioxide **226** was also produced through oxidation of **224** with *m*CPBA as described in Chapter 3.



Scheme 2.54 Oxidation to sulfinyl sulfone **226** using hydrazoic acid

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).



Scheme 2.55 Proposed route to sulfoximine **248**

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.

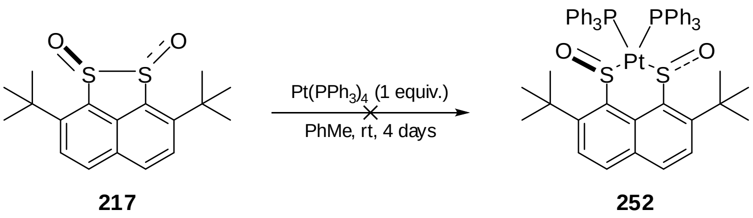
Entry	Starting oxide	Conditions	**217** (%)	**226** (%)
1	**217**	MSH (2.0 equiv.), CH_2Cl_2, rt, 16 h	100	-
2	**217**	MSH (2.0 equiv.), 1,2-DCE, reflux, 16 h	96	-
3	**217**	NaN_3, H_2SO_4, $CHCl_3$, 0 °C, 15 min	-	57
4	**216**	MSH (1.5 equiv.), 1,2-DCE, reflux, 16 h	96	-
5	**216**	NaN_3, H_2SO_4, $CHCl_3$, 0 °C, 15 min	decomposition	

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 $Pt(PPh_3)_4$ resulted in a mixture of unidentifiable compounds (scheme 2.56).



Scheme 2.56 Attempted platinum insertion into *trans*-**217**

Conclusion

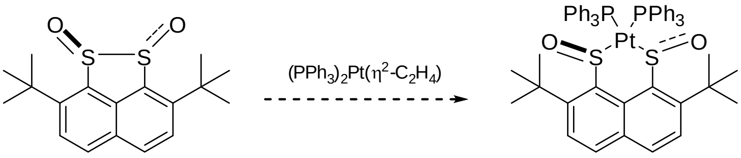
The oxidation of disulfides **50**, **65** and **87** has been explored. The synthesis of the oxides of naphtho[1,8-*cd*][1,2]dithiole (**50**) has been reported in the literature and repeated with optimisation of conditions to improve the yield.

Oxides 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).



217 **252**

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.[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).

$$4\,NH_3 + 5\,O_2 \xrightarrow{Pt} 4\,NO + 6\,H_2O$$

Equation 3.1

$$2\,NO + O_2 \longrightarrow 2\,NO_2$$

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.[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.[184]

3.2 Nitroxyl

Nitroxyl (HNO or NO^-) is a reduced form of nitric oxide; the potential pharmacological activity of HNO in relation to NO has recently received much attention.[185] HNO is a weak acid in solution ($pK_a = 11.4$)[186] and although closely structurally related to NO, HNO (and its deprotonated form, NO^-) possesses very distinct chemical properties. HNO is very reactive and quickly dimerises to hyponitrous acid, $H_2N_2O_2$, which then dehydrates to nitrous oxide N_2O (equation 3.3).

$$HNO \longrightarrow H_2N_2O_2 \xrightarrow{-H_2O} N_2O$$ **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]

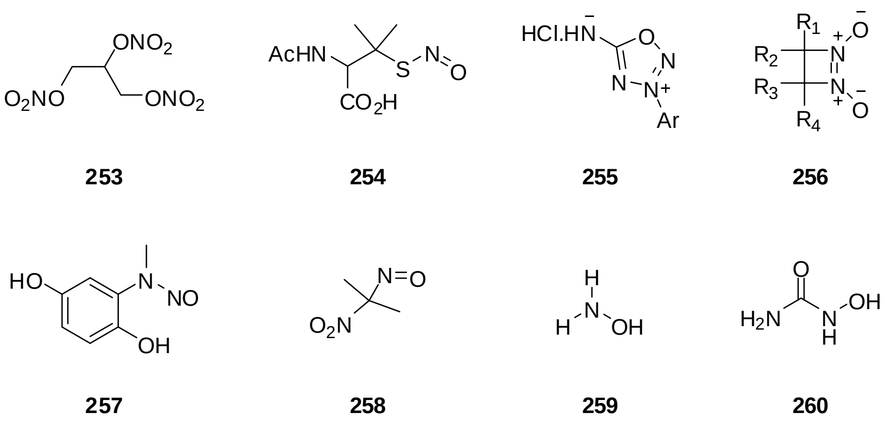
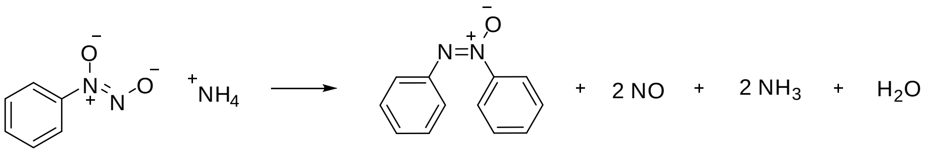


Figure 3.1 Major classes of nitric oxide donors

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]

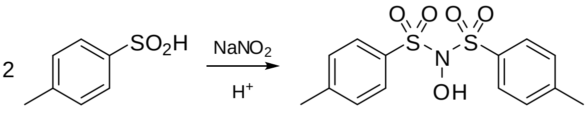


261 **262**

Scheme 3.1 Breakdown of Cupferron to form NO

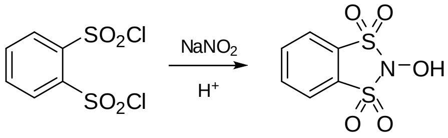
Nitric oxide has also been generated by a photochemical process and photoinduced delivery has been reported as a new controlled method for its release.[204-207] Recent advances in this area include the photomediated release of NO from nanoparticles.[208-210] Irradiation of small, physiologically stable 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]



263 **264**

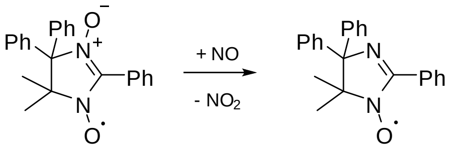
Scheme 3.2 Preparation of *N*,*N*-bis(arylsulfonyl)hydroxylamine



265 **266**

Scheme 3.3 Fochi's synthesis of hydroxylamine from sulfinic chloride

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).



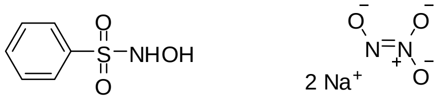
267 **268**

5-line EPR spectrum observed

9-line EPR spectrum observed

Scheme 3.4 EPR evidence for the formation of NO

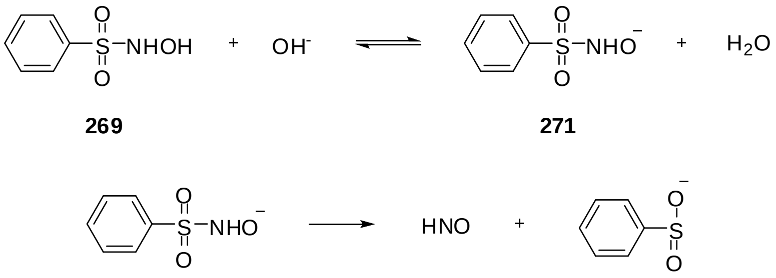
Nitroxyl is very unstable and dimerises almost immediately, therefore it cannot be stored and must be produced *in situ* with reactive agents.[185] Two of the most studied methods known for the generation of HNO are the photochemical or thermal decomposition of Piloty's acid (**269**) or Angeli's salt (**270**) (figure 3.2).[190, 217]



269 Piloty's acid **270** Angeli's salt

Figure 3.2 Sources of HNO

Piloty's acid (**269**) only releases nitroxyl under basic conditions (scheme 3.5), decomposition under physiological conditions may release NO.[188]

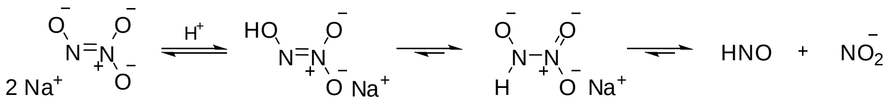


269 **271**

271 **272**

Scheme 3.5 Decomposition of Piloty's acid under basic conditions

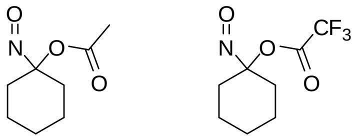
At physiological pH, decomposition of Angeli's salt (**270**) is initiated by protonation of the dianion to produce nitroxyl (HNO) and nitrite, which possesses its own biological properties (scheme 3.6).[217, 218]



270 **273** **274**

Scheme 3.6 Formation of nitroxyl under acidic conditions

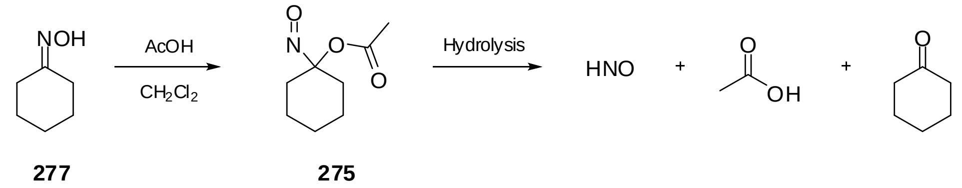
Acyloxy nitroso compounds **275** and **276** release nitroxyl upon hydrolysis (figure 3.3).[219]



275 **276**

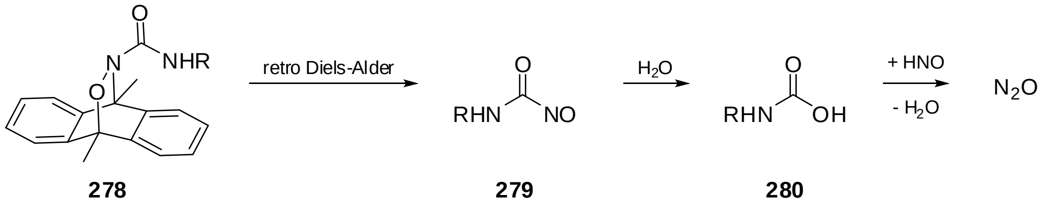
Figure 3.3 HNO donors: acyloxy nitroso compounds

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).



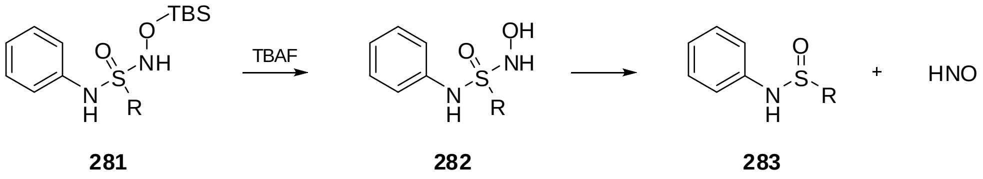
Scheme 3.7 Generation of HNO from acyloxy nitroso **275**

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.[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).



Scheme 3.8 Retro Diels-Alder reaction for the liberation of HNO

The same author later reported *N*-hydroxy sulfonimidamide **281** as a nitroxyl donor.[222] Reaction of protected *N*-hydroxy sulfonimidamide **281** with TBAF furnished unstable hydroxylamine **282** which decomposed to sulfinamide **283** and HNO, detected as N_2O (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.

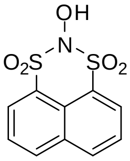


Scheme 3.9 *N*-Hydroxy sulfonimidamide as a source of HNO

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.

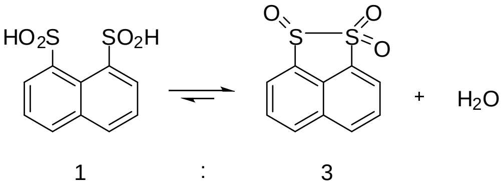
In Chapter 1, it was shown that trisulfide-2-oxides extrude sulfur monoxide as a result of relief of *peri*-strain. Based on the same design principle, *N*-hydroxylamine **284** is proposed as a source of either nitric oxide (NO), nitroxyl (HNO) or hydroxy nitrene (HON) under appropriate conditions (figure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



284

Figure 3.4 Target molecule

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**.



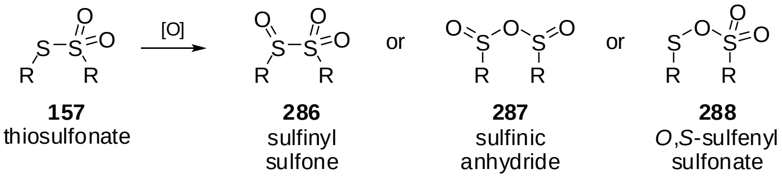
285 **228**

Scheme 3.10 Equilibrium between bissulfinic acid **285** and sulfinyl sulfone **228**

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.

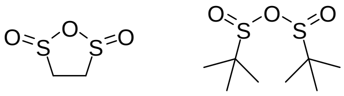
3.5 Synthesis of trioxides

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 thiosulfinates (scheme 3.11).[107]



Scheme 3.11 The RS_2O_3R isomers

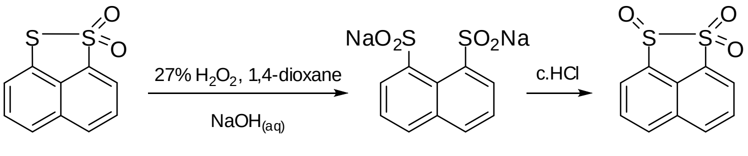
There are many examples of sulfinyl sulfones in the literature,[107] including **226** described previously in Chapter 2. The general method for the preparation of sulfinyl sulfones is the treatment of a sulfinyl chloride with a sulfinate salt, or oxidation of thiosulfonates.[115, 225] Few examples of 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]



290 **291**

Figure 3.5 Examples of sulfinic anhydrides **290** and **291**

The oxidation of thiosulfonate **63** to sulfinyl sulfone **228** using hydrogen peroxide has been reported by Kice (scheme 3.12).[138]



63 **292** **228**

Scheme 3.12 Nucleophilic oxidation of thiosulfonate **63**

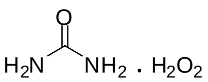
Hydrogen peroxide was reacted with dioxide **63** to give the crude disodium salt **292**. Work by Kice has shown that the equilibrium between sulfinyl sulfone **228** and bissulfinic acid **285** in a 60% aqueous solution of dioxane favours the trioxide **228** in a three to one ratio (scheme 3.10).[223] Thus, acidification of **292** yielded trioxide **228**.

Initially, oxidation using H_2O_2 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 H_2O_2 was thought to have decomposed and for this reason the hydrogen peroxide was titrated using a known procedure.[228] Titration of H_2O_2 with $KMnO_4$ was problematic as the endpoint was difficult to determine; for this reason other oxidants to effect the formation of **228** were screened.

Entry	Starting material	Conditions	Yield (%)
1	**63**	i) H_2O_2 (1.00 equiv.), NaOH (2.05 equiv.), 5 min ii) c.HCl	**228** 45
2	**63**	i) H_2O_2 (1.00 equiv.), NaOH (2.05 equiv.), 5 min ii) c.HCl	**63** 14, **228** 19
3	**63**	*m*CPBA (1.30 equiv.), CH_2Cl_2, 2 h, 0 °C	**63** 98
4	**63**	*m*CPBA (1.30 equiv.), CH_2Cl_2, 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.), $NaHCO_3$, MeCN/H_2O, 3 h, rt, pH 7-7.5	**63** 96
7	**63**	DMD (1.05 equiv.), acetone, 2 h, 0 °C	**63** 99
8	**63**	$NaIO_4$ (1.05 equiv.), H_2O/1,4-dioxane, 4 days, rt	mixture
9	**63**	*m*CPBA (1.50 equiv.), $CHCl_3$, 1 day, precipitation with hexane	**228** 40
10	**50**	*m*CPBA (3.50 equiv.), $CHCl_3$, 1 day, precipitation with hexane	**228** 45

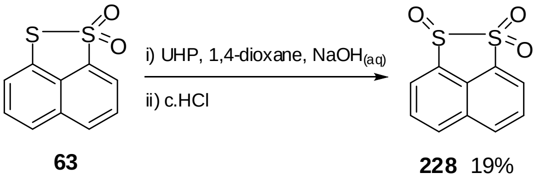
Table 3.1 Conditions for the preparation of sulfinyl sulfone **217**

In the first instance, oxidation was attempted with *m*CPBA 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 *m*CPBA 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 sulfides.[229] The reaction was carried out in a similar manner to that using H_2O_2, but unfortunately only a 19% yield was achieved (scheme 3.13, entry 5).



293 UHP

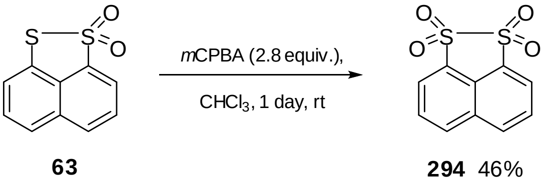
Figure **3.6** Urea-hydrogen peroxide (UHP)



Scheme 3.13 Oxidation of thiosulfonate using UHP

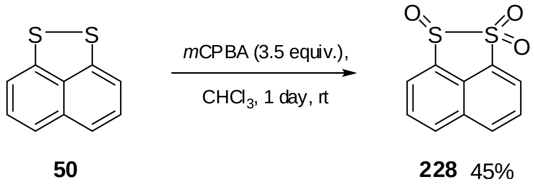
Tetrahydrothiopyran-4-one (**203**) and Oxone® were employed, however dioxide **63** was recovered in almost quantitative yield (entry 6).[145] Gratifyingly, oxidation of **63** using DMD (1.05 equiv.) generated trioxide **228** in 36% yield (entry 7). The final oxidant screened was sodium periodate, which is known to oxidise sulfur at a slower rate than *m*CPBA. $NaIO_4$ 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-*cd*]-1,2-dithiole 1,1,2,2-tetraoxide (**294**) from dioxide **63** with *m*CPBA (scheme 3.14).[230]



Scheme 3.14 Synthesis of tetroxide reported by Kice[45]

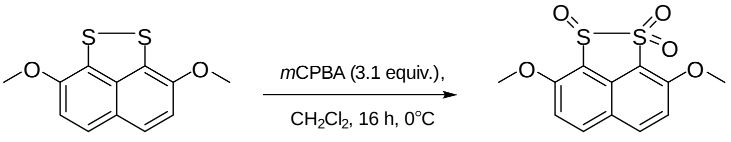
Following the same procedure but using just 1 equiv. of *m*CPBA successfully produced the trioxide **228** from **63** in a 40% yield (entry 9). Treatment of disulfide **50** with 3.5 equiv. of *m*CPBA yielded trioxide **228** in a 45% yield (scheme 3.15, entry 10).



Scheme 3.15 *m*CPBA oxidation of disulfide **50**

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 *m*CPBA resulted in 3,8-dimethoxy-naphtho[1,8-*cd*][1,2]dithiole 1,2,2-trioxide (**207**) in reasonable yield (scheme 3.16).



87

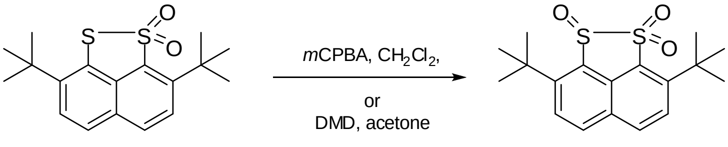
207 41%

Scheme 3.15 Synthesis of trioxide **197**

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 SO_2 followed by oxidation of thiosulfinate **45** (scheme 2.11).[124]

The oxidation of thiosulfonate **224** was explored with electrophilic oxidants. Reaction with 1.1 equiv. of *m*CPBA 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).

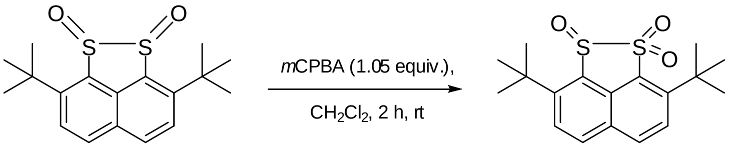


224

226

Scheme 3.17 Oxidation of thiosulfonate **224**

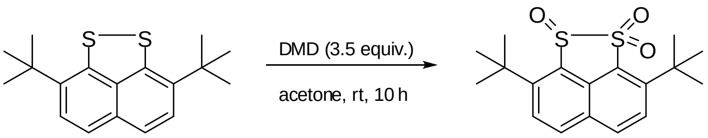
Both *cis*-**225** and *trans*-**217** *vic*-disulfoxides were individually reacted with 1.05 equiv. of *m*CPBA resulting in sulfinyl sulfone **226** in very good yields (scheme 3.18, entries 4 and 6). When subjected to DMD, *cis vic*-disulfoxide **225** required 3 equiv. of oxidant to form sulfinyl sulfone **226**, whereas *trans*-**217** required 4 equiv. to form **226** (entries 3 and 5).



trans-**217** **226** 97%
cis-**225** **226** 76%

Scheme 3.18 Oxidation of *vic*-disulfoxides **217** and **225**

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*CPBA was added dropwise as a solution in dichloromethane to disulfide **65** (entry 8).



65 **226** 91%

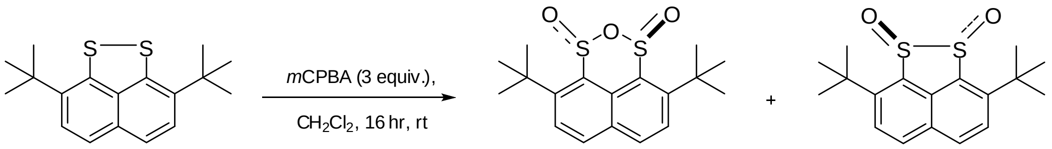
Scheme 3.19 Preparation of sulfinyl sulfone **226** from disulfide **65**

Entry	Starting material	Conditions	**226** (%)
1	**224**	DMD (1.0 equiv.), acetone, rt, 1 h	91
2	**224**	*m*CPBA (1.1 equiv.), CH_2Cl_2, rt, 4 h	97
3	**217**	DMD (4.0 equiv.), acetone, rt, 1 h	99
4	**217**	*m*CPBA (1.0 equiv.), CH_2Cl_2, rt, 2 h	97
5	**215**	DMD (3.0 equiv.), acetone, rt, 1 h	95
6	**215**	*m*CPBA (1.0 equiv.), CH_2Cl_2, rt, 2 h	76
7	**65**	DMD (3.5 equiv.), acetone, rt, 10 h	91
8[a]	**65**	*m*CPBA (3.5 equiv.), CH_2Cl_2, rt, 14 h	96

[a] dropwise addition of *m*CPBA as a solution in CH_2Cl_2

Table 3.2 Oxidation to obtain sulfinyl sulfone **226**

When *m*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.



65 **295** 14% **217** 73%

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**.

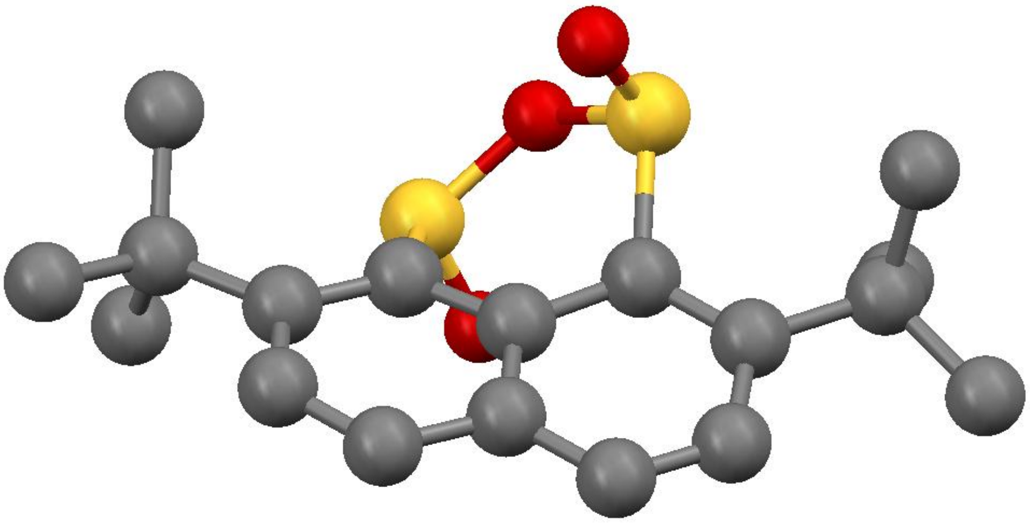
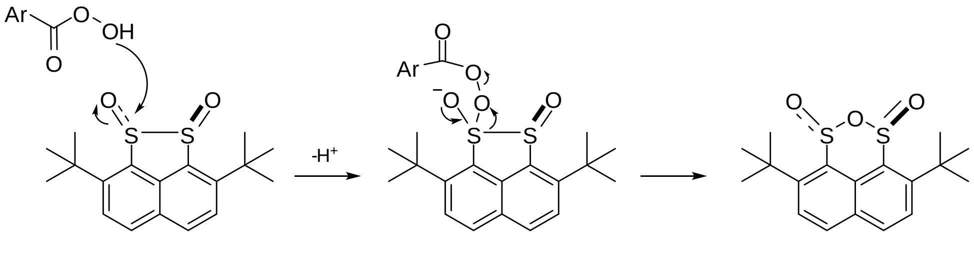


Figure 3.7 X-ray crystal structure of sulfinic anhydride **295**

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 sp^2 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).

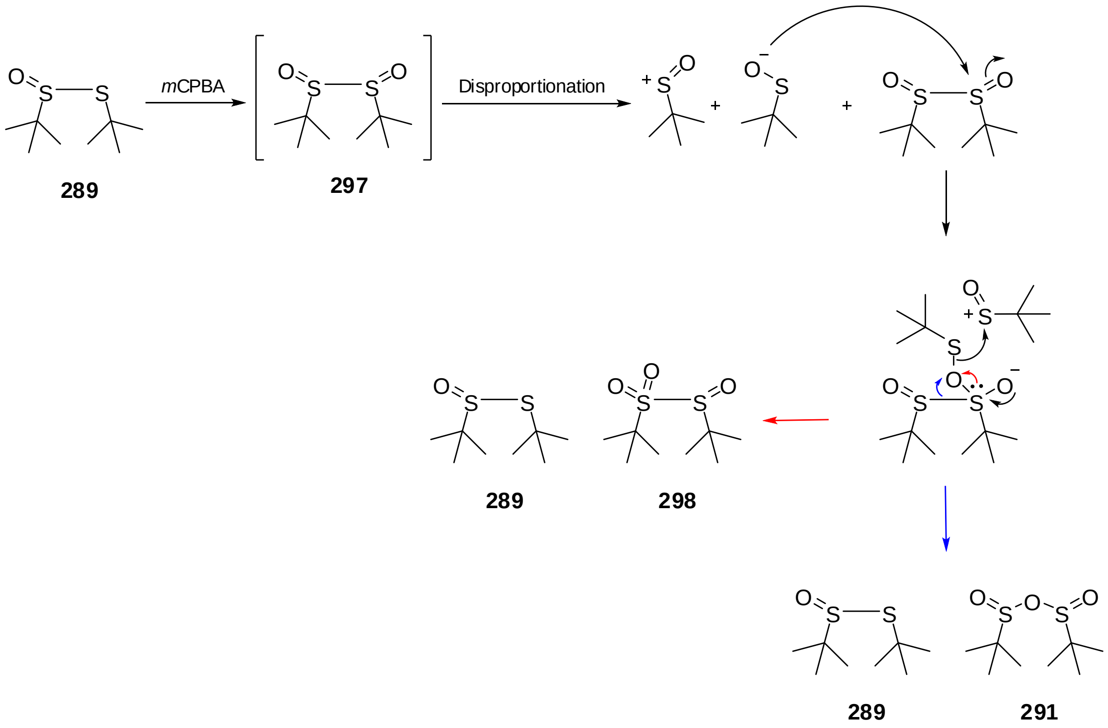
Attempts to optimise the conditions to improve the yield of the sulfinic anhydride **295** proved futile. *vic*-Disulfoxide **217** was initially believed to be an intermediate in the oxidation to form sulfinic anhydride **295** as this was the other product from the reaction. The formation of sulfinic 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**.



217 **296** **295**

Scheme 3.21 Baeyer-Villiger type oxidation to form sulfinic anhydride **295**

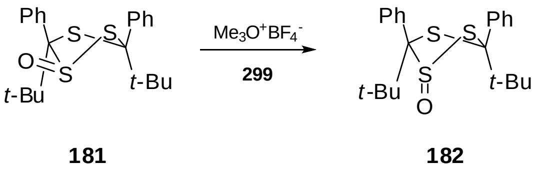
Harpp reported the formation of *tert*-butyl sulfinic anhydride **291** from the oxidation of thiosulfinate **289** with *m*CPBA. It was suggested that *vic*-disulfoxide **297** was formed, followed by disproportionation of the S-S bond and an oxygen transfer mechanism (scheme 3.22).[227]



Scheme 3.22 Oxidation of thiosulfinate **289**, followed by disproportionation of *vic*-disulfoxide **297**

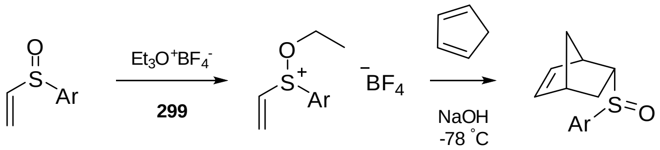
Attempts to effect the reaction of *trans*-**217** with *m*CBA in the presence of *m*CPBA were ineffective with only starting material recovered (table 3.3, entry 1). *vic*-Disulfoxide **217** was also recovered when oxidised with *m*CPBA in the presence tosic acid (entry 2). However, reaction of **217** in the presence of BF_3, a Lewis acid, and *m*CPBA yielded sulfinyl sulfone **226** (entry 3).

Nakayama has reported the isomerisation of thiosulfinate **181** to **182** using Meerwein's reagent (**299**) (scheme 3.23).[123]



Scheme 3.23 Isomerisation of thiosulfinate **181** using Meerwein's reagent

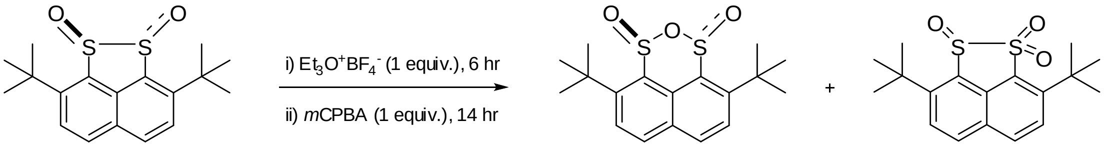
Alternatively, Kagan has described the Diels-Alder reaction of cyclopentadiene at low temperatures with activated sulfoxides using Meerwein's reagent (scheme 3.24).[231]



300 **301** **302**

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 *m*CPBA generated very small amounts of anhydride **295**, along with sulfinyl sulfone **226** as the major product (scheme 3.25, entry 4).



217 **295** 6% **226** 92%

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

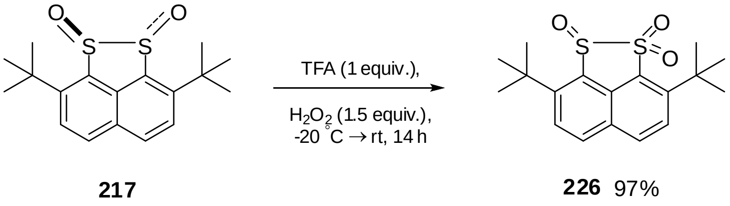
The use of excess salt to form the activated sulfoxide, followed by the addition of *m*CPBA produced the same result within experimental error, suggesting that the amount of Meerwein's reagent used was inconsequential (entry 5). Activated *vic*-disulfoxide was destroyed upon attempted isolation.

Entry	Conditions	**217** (%)	**295** (%)	**226** (%)
1	*m*CPBA (1 equiv.), *m*CBA (1 equiv.), CH_2Cl_2, 10 h	96	-	-
2	mCPBA (1 equiv.), tosic acid (1 equiv.), CH_2Cl_2, 18 h	98	-	-
3	mCPBA (1 equiv.), BF_3 (1 equiv.), CH_2Cl_2, 3 h	-	-	95
4	mCPBA (1 equiv.), Meerwein's reagent (1 equiv.) , CH_2Cl_2, 6 h	-	6	92
5	mCPBA (1 equiv.), Meerwein's reagent (10 equiv.), CH_2Cl_2, 6 h	-	8	92

Table 3.3 Coordinating agents used to promote the formation of sulfinic anhydride **295** from *vic*-disulfoxide

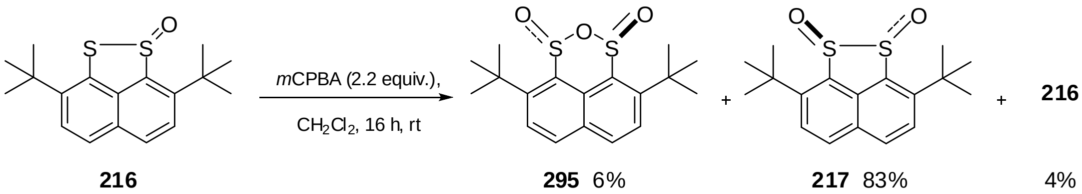
The results obtained from the oxidation of *trans*-**217** suggest that only activation using Meerwein's reagent can produce the sulfinic anhydride **295** and that it possibly may not be an intermediate in the synthesis of anhydride **295**. In addition the yield starting from disulfide **65** is a little bit higher suggesting there may be an alternative pathway involved in the generation of anhydride **295**.

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



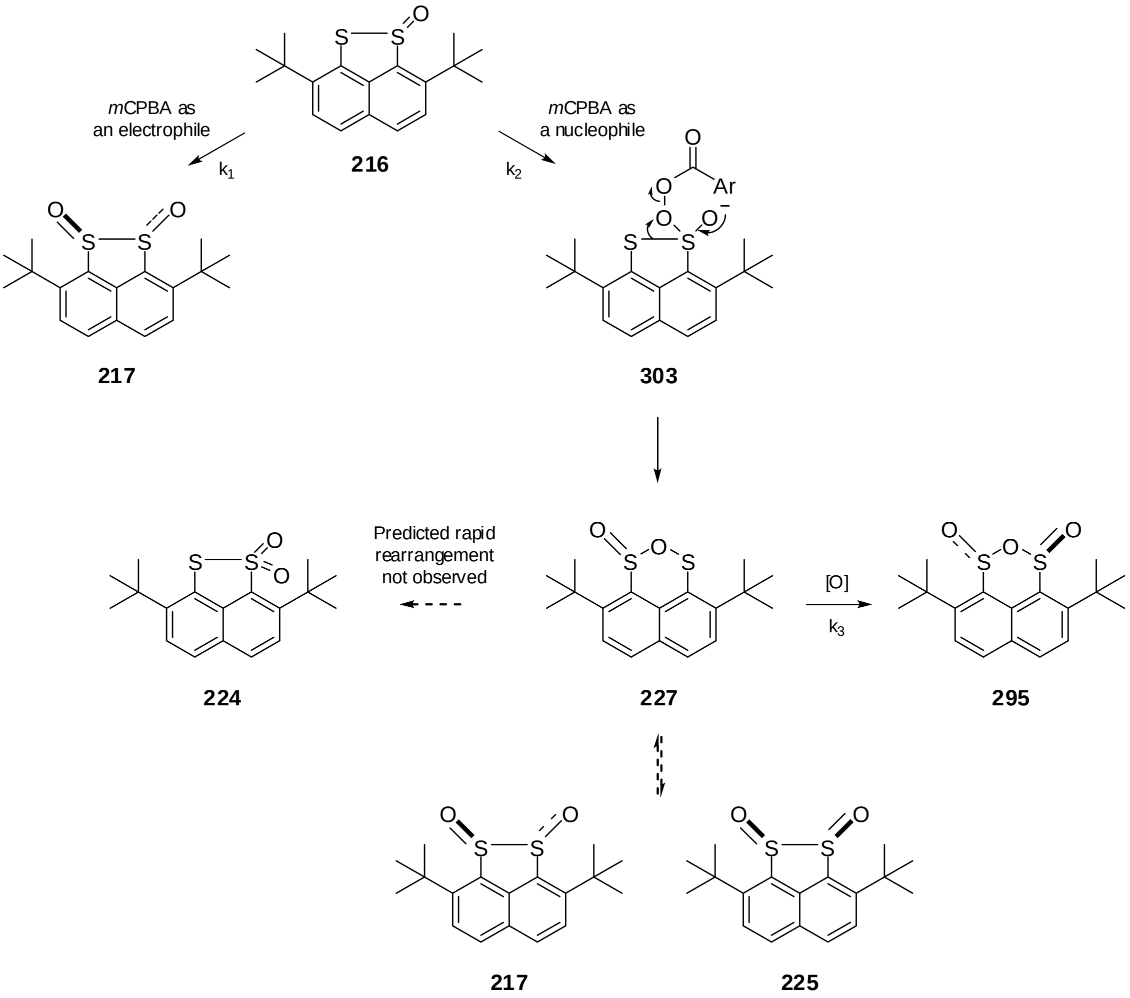
Scheme 3.26 Oxidation of *trans*-**217** using 2,2,2-trifluoroperacetic acid

Reaction of 2.2 equiv. of *m*CPBA added portionwise to thiosulfinate **216** produced the desired anhydride again as the minor product along with the major product *trans*-**217** (scheme 3.27).



Scheme 3.27 Oxidation of thiosulfinate **216** to prepare sulfinic anhydride **295**

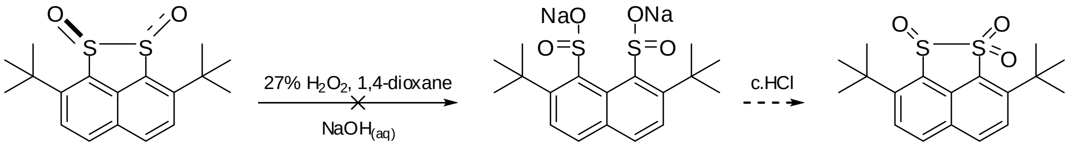
Both *cis* and *trans vic*-disulfoxides are known to be stable at room temperature thus it is not clear if the disproportionation mechanism proposed by Harpp is followed (scheme 3.22), although it cannot be ruled out. An alternative rationalisation is a competing pathway between formation of anhydride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



Scheme 3.28 Competing oxidation pathways between formation of anhydride **295** and *trans vic*-disulfoxide **217**

*m*CPBA 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.

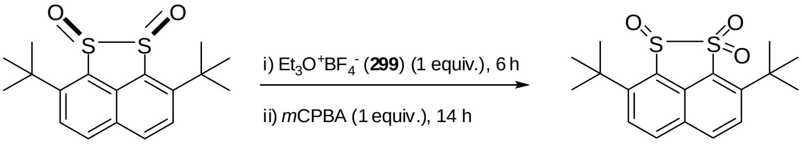
The oxidation of *trans vic*-disulfoxide **217** with H_2O_2 and NaOH, forming HOO^-, a method reported by Kice for thiosulfonate **63**, was also investigated.[138] The solvent ratio for equilibrium between the bissulfinic acid **285** and the sulfinyl sulfone **228** was crucial for favouring the formation 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).



217 **304** **226**

Scheme 3.28 Attempted oxidation of *trans*-**217** with nucleophilic H_2O_2

Use of Meerwein's reagent **299** in the *m*CPBA-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).



225 **226** 98%

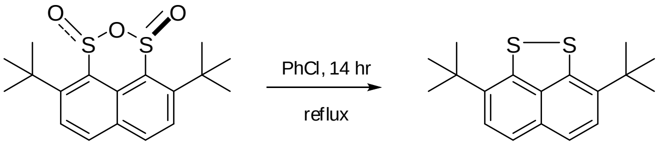
Scheme 3.30 Oxidation of *cis*-**225** assisted by Meerwein's reagent **299**

In summary, sulfinyl sulfones **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 *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.



295

65 72%

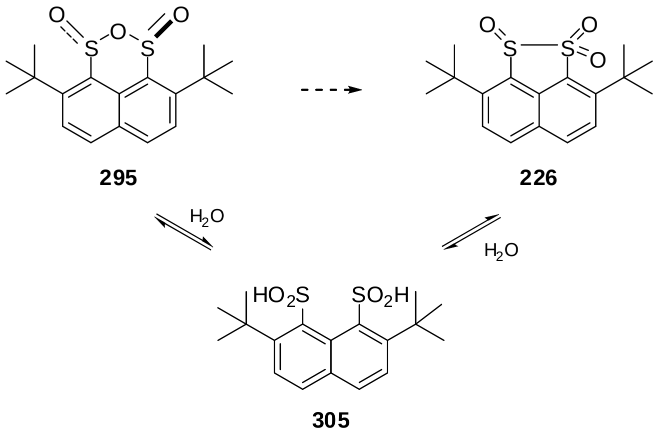
Scheme **3.31** Deoxygenation of sulfinic anhydride **295**

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

Entry	Conditions	**65** (%)	**295** (%)
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	-

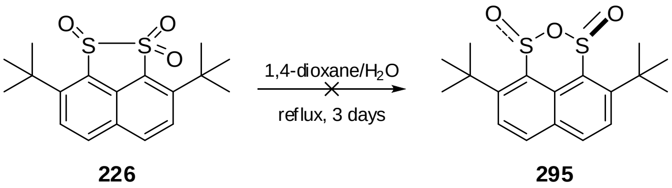
Table 3.4 Thermolysis of sulfinic anhydride **295**

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).



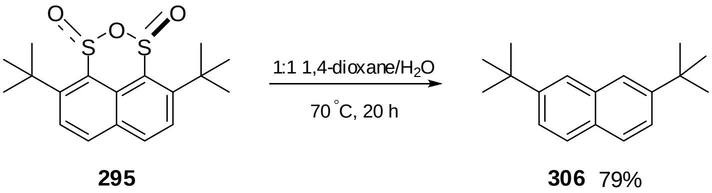
Scheme 3.32 Possible hydrolysis of trioxides **226** and **295**

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.



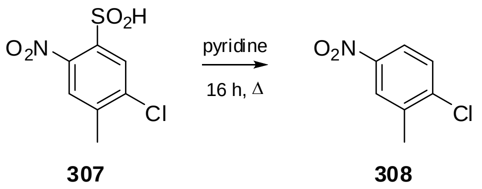
Scheme 3.33 Attempted hydrolysis of sulfinyl sulfone **226**

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]



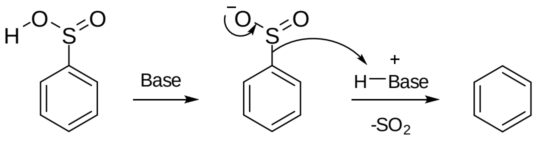
Scheme 3.34 Desulfonylation of sulfinic anhydride **295** in 1,4-dioxane/H_2O

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]



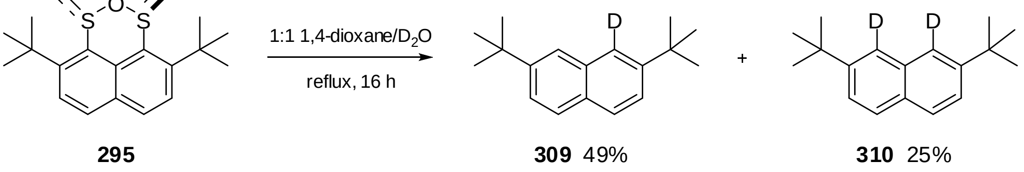
Scheme 3.35 Desulfonylation of *ortho*-nitro benezene sulfinic acid **307**

It is proposed that the base deprotonates the sulfinic acid with a loss of sulfur dioxide followed by protonation (scheme 3.36).



Scheme 3.36 Proposed mechanism for desulfonylation

The desulfonylation reaction was investigated further by reacting sulfinic anhydride **295** in a 1,4-dioxane/D_2O 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_2O mixture for 34 h, unfortunately this failed to result in any desulfonylation. This suggested that the D_2O 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*-butylnaphthalene (**306**) was obtained in good yield (scheme 3.37).



Yields determined by analysis of the mass spectrum

Scheme 3.37 Desulfonylation of sulfinic anhydride **295** in 1,4-dioxane/D_2O

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 $gmol^{-1}$) and the di-deuterated (**310**) (M = 242 $gmol^{-1}$). No peak was observed for **306** (M = 240 $gmol^{-1}$). It is not clear how the mono-deuterated compound **309** is formed in this reaction.

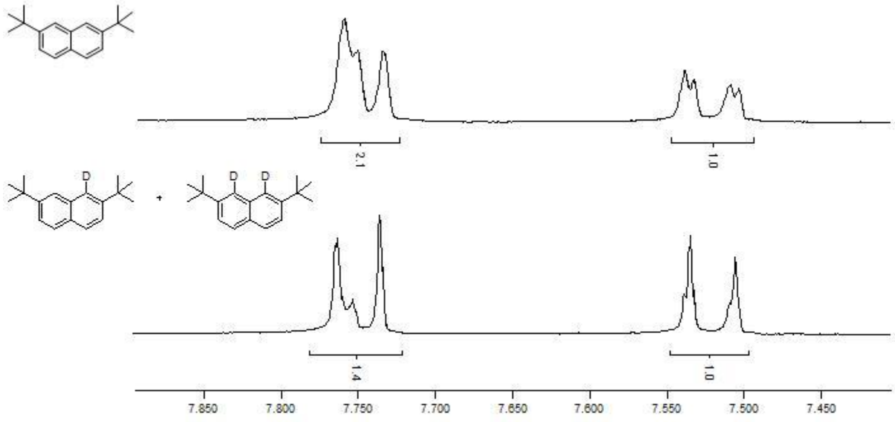
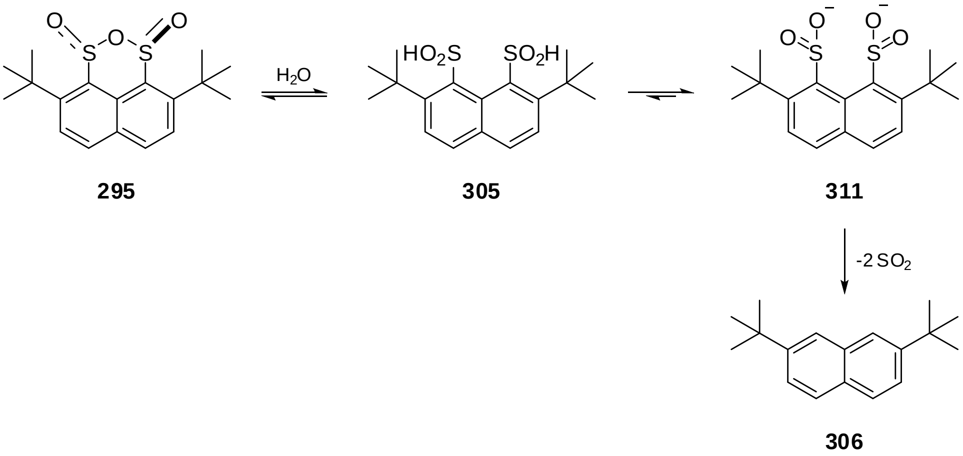


Figure 3.8 ^{1}H-NMR spectra of **306**, and a mixture of **309** and **310**

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 SO_2 resulting in 2,7-di-*tert*-butylnaphthalene (**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.



295

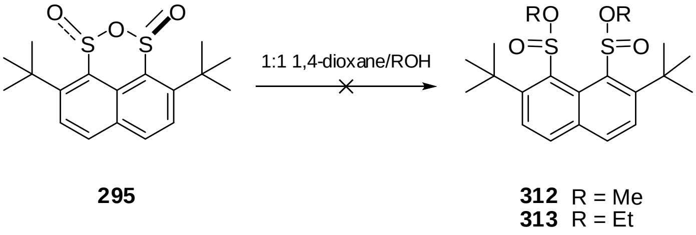
305

311

306

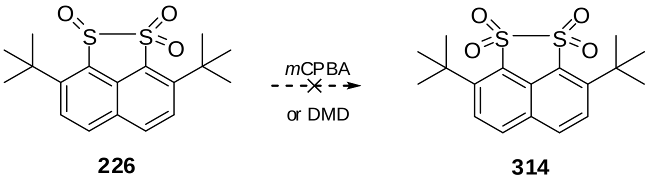
Scheme 3.38 Proposed pathway for the loss of SO_2 from **295**

Efforts to synthesise sulfinic esters **312** and **313** were unsuccessful in 1,4-dioxane/alcohol mixtures (scheme 3.39).



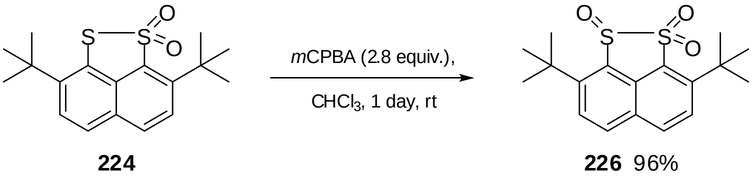
Scheme 3.39 Attempted synthesis of sulfinic esters

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).



Scheme 3.40 Attempted oxidation to bissulfone **314** from sulfinyl sulfone **226**

Conditions used for the oxidation of thiosulfonate **63** 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).

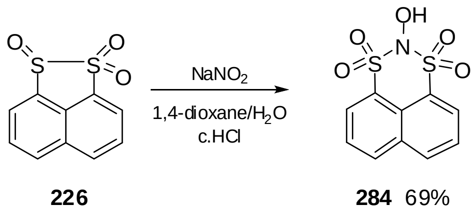


Scheme 3.41 Attempted oxidation of thiosulfonate **224** to bissulfone **314**

3.7 Synthesis of bis(sulfonyl)hydroxylamines

Preliminary studies towards the synthesis of **284** have been carried out in the group.[234] It was shown that the equilibrium shown in scheme 3.10 could be exploited favouring the bissulfinic 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-*1H,3H*-1λ^6,3λ^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**

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

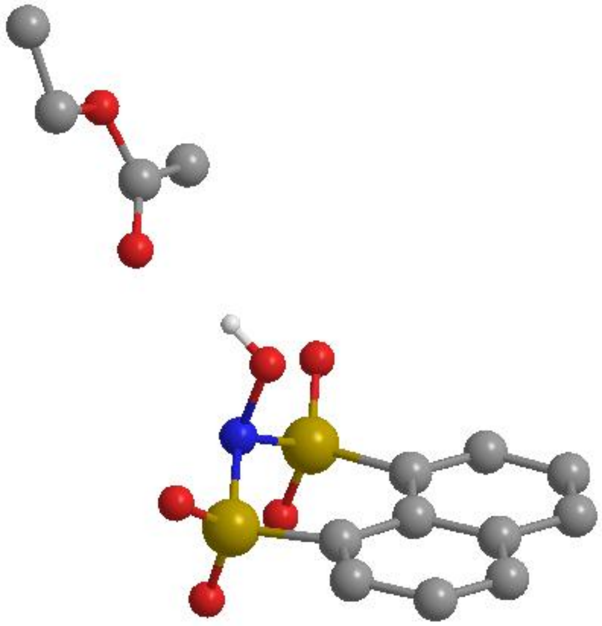
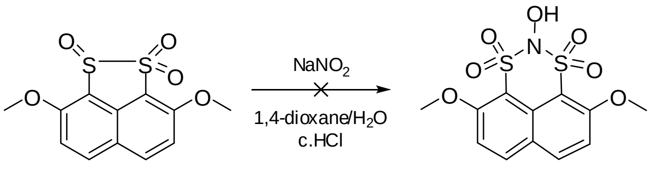


Figure **3.9** X-ray crystal structure of bis(sulfonyl)hydroxylamine **284**

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(O_2) σ* orbital, as is typical for sulfonamides.[235]

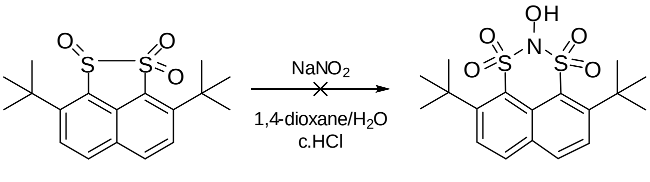
Attempted synthesis of bis(sulfonyl)hydroxylamine **315** from sulfinyl sulfone **207**, using the same conditions as for the synthesis for **284**, resulted in recovery of starting material in 96% yield (scheme 3.43).



207 **315**

Scheme 3.43 Attempted synthesis of bis(sulfonyl)hydroxylamine **315**

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



226 **316**

Scheme 3.44 Unsuccessful synthesis of bis(sulfonyl)hydroxylamine **313**

3.8 Reactions of bis(sulfonyl)hydroxylamine 284

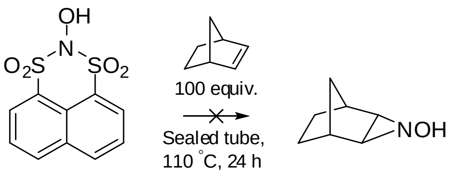
Bis(sulfonyl)hydroxylamine **284** was stable for up to a three month period at room temperature in a DMSO solution. With the addition of D_2O, exchange of the hydroxyl proton was observed, however both samples remained unchanged over the three month period.

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).

Entry	Solvent	Temperature (°C)	**284** (%)
1	*t*-BuOH	82	99
2	DMSO	100	96
3	toluene	108	92
4	octane	125	100
5	PhCl	132	96

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).



284 **317**

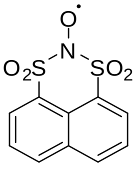
Scheme 3.45 Attempted trapping of reactive species

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).

Entry	Conditions	**284** (%)
1	125 W medium pressure Hg lamp, pyrex filter, MeCN, 48 h	96
2	500 W halogen lamp, MeCN, 48 h	97

Table 3.6 Monitoring the photochemical decomposition of hydroxylamine **284**

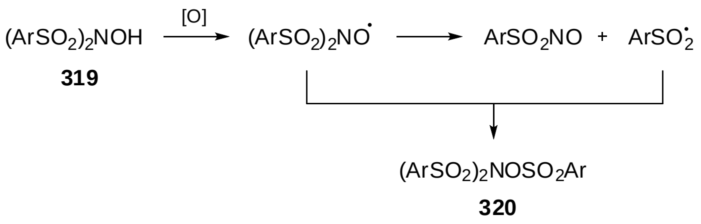
Attention therefore turned to the formation of nitroxide **318** as a compound that could potentially fragment to release NO (figure 3.10).



318

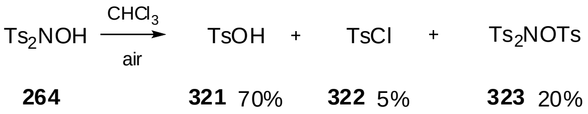
Figure 3.10 Nitroxide **318**

The generation of nitroxides from hydroxylamines has been reported.[175, 211, 236-238] Glidewell described the oxidation of *N*,*N*-bis(arylsulfonyl)hydroxylamines, **319**, using PbO_2.[211] 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

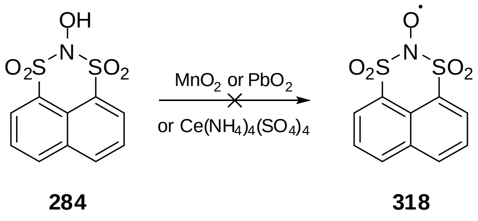
Balakirev investigated the decomposition of *N*,*N*-bis(*p*-tolylsulfonyl)hydroxylamine, **264**, in an air-saturated solution of $CHCl_3$.[175] The products obtained from this reaction were tosic acid (**321**), tosyl chloride (**322**) and *N*,*N*,*O*-trisubstituted hydroxylamine **323** (scheme 3.47), 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 $CHCl_3$

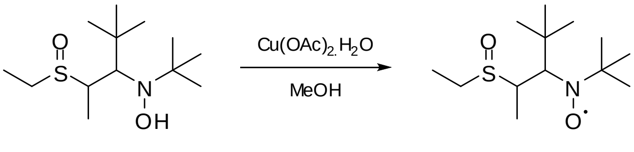
N,*N*-Bis(*p*-tolylsulfonyl)hydroxylamine **264** was treated with ceric ammonium sulfate to form the nitroxide radical. EPR signals of spin trapped sulfonyl radicals were observed, supporting the proposed formation of tosyl chloride and the decomposition pathway proposed by Glidewell.[175]

Hydroxylamine **284** was reacted individually in the presence of MnO_2,[237] PbO_2[238] 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**

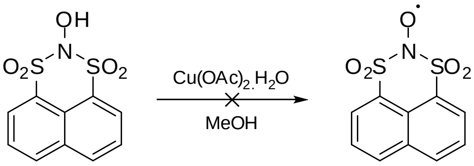
Oxidation of hydroxylamine **324** with $Cu(OAc)_2.H_2O$, conditions reported by Catala, gave nitroxide (scheme 3.49).[236, 239]



324 **325** 49%

Scheme 3.49 Synthesis of *β*-sulfinyl nitroxide

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).

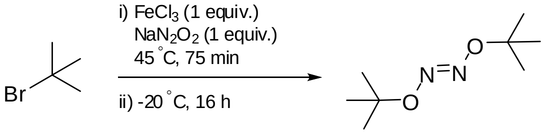


284 **318**

Scheme 3.50 Attempted synthesis of bis(sulfonyl) nitroxide **318**

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 nitroxyl 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).



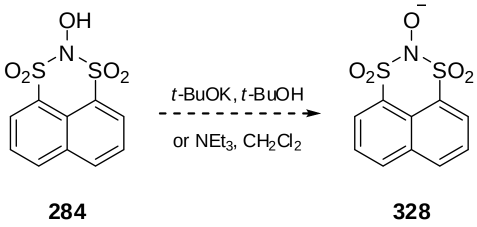
326 **327** 16%

Scheme 3.51 Preparation of di-*tert*-butoxydiazene (**327**)

Entry	Conditions	**284** (%)
1	MnO_2 (4.89 equiv.), $CHCl_3$, 24 h, rt → reflux	92
2	PbO_2 (2.00 equiv.), CH_2Cl_2, O_2, 24 h, rt	98
3	$Ce(NH_4)_4(SO_4)_4.H_2O$ (2.66 equiv.), PhH, 24 h, rt	93
4	$Cu(OAc)_2.H_2O$ (0.016 equiv.), NH_4OH, MeOH, 12 h, rt	90
5	$Cu(OAc)_2.H_2O$ (0.016 equiv.), NH_4OH, MeOH, O_2, 12 h, rt	89
6	**327** (1.20 equiv.), PhH, 24 h, 65 °C	96
7	**327** (1.20 equiv.), MeCN, 24 h, 65 °C	93

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 NEt_3 in CH_2Cl_2 (Scheme 3.52).



Scheme 3.52 Generation of anion **328**

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 CH_2Cl_2. The reaction mixture was then quenched with 1 M HCl. After work-up, the ^{1}H-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 ($C_{10}H_6NO_5S_2.H_2O$) **329** (figure 3.11).

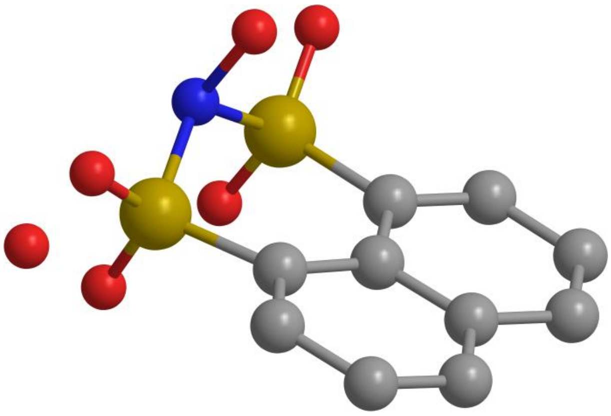


Figure 3.11 Hydrated bis(sulfonyl)hydroxylamine **329** ($C_{10}H_6NO_5S_2.H_2O$)

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.

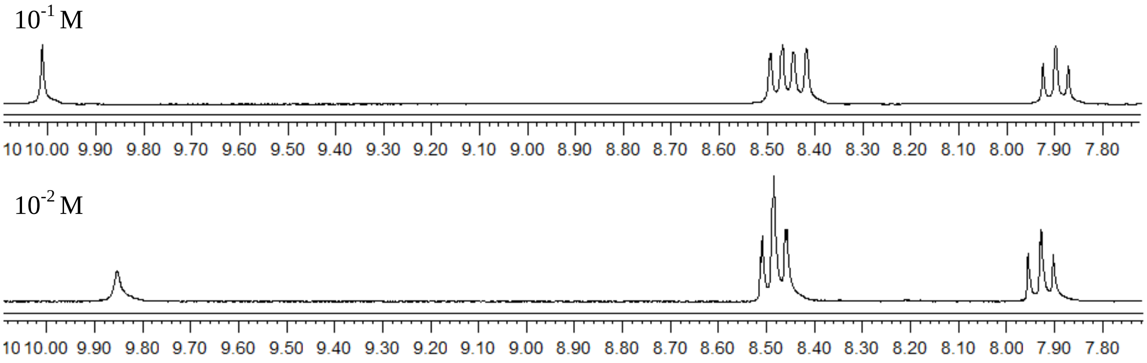


Figure 3.12 Concentration studies of bis(sulfonyl)hydroxylamine **284** in CD_3CN

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.[241] 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).

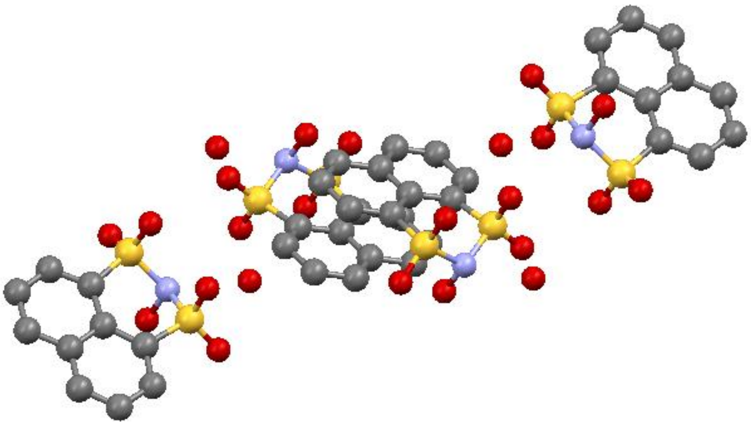


Figure 3.13 X-ray of an unit cell of stacked bis(sulfonyl)hydroxylamine **329**

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).

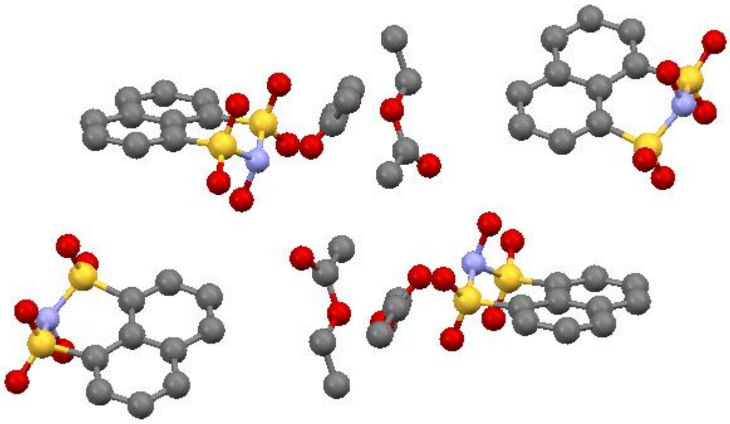
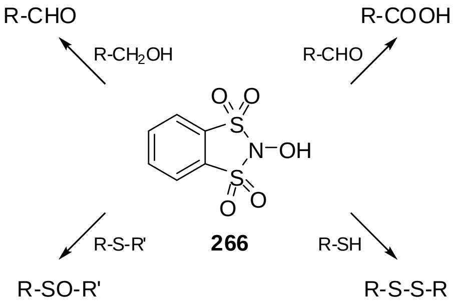


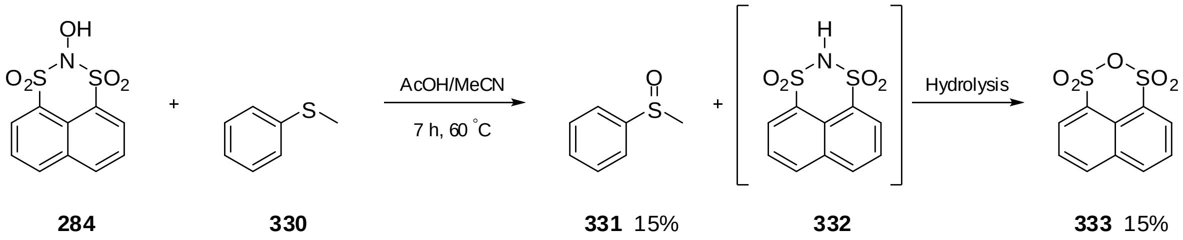
Figure 3.14 Less ordered X-ray of an unit cell of bis(sulfonyl)hydroxylamine **284**

N-Hydroxy-*O*-benzenedisulfonimide (**266**) has been reported by Fochi as a selective oxidising agent (scheme 3.53).[216] 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.



Scheme 3.53 Hydroxylamine **266** as an oxidising agent

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).



Scheme 3.54 Oxidation of thioanisole **330** using hydroxylamine **284**

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 *m*CPBA 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 D_2O. A remarkable deoxygenation of **295** was also observed upon heating in PhCl.

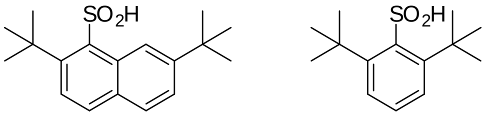
Hydroxylamine **284** has been successfully synthesised from sulfinyl sulfone **228**, yet studies towards the breakdown of **284** have proved to be difficult. Attempts to prepare hydroxylamines **315** and **316** from sulfinyl sulfones **207** and **226** were unsuccessful; this may be due to the 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

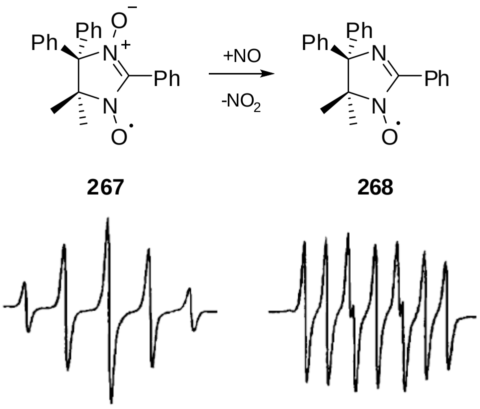
The desulfonylation of sulfinic anhydride **295** has shown deuterium incorporation and this could be further investigated by exploring the reaction in a solution of H_2O and d_8-1,4-dioxane. Sulfinic acids **334** and **335** could also be explored to distinguish whether the desulfonylation is a result of the buttressing of the *ortho tert*-butyl groups (figure 3.15).



334 **335**

Figure 3.15 Buttressed sulfinic acids proposed for desulfonylation

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 of photochemically. EPR studies could also provide evidence of NO by a change in the spectrum upon reaction with nitronyl nitroxide (scheme 3.55).[175]



267 **268**

Scheme 3.55 EPR evidence for the generation of NO

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_2O referenced to residual H_2O (^{1}H, 4.79 ppm; ^{13}C, SR = 161.3, corresponding to external TSP capillary set at 0 ppm), CD_2Cl_2 referenced to residual CH_2Cl_2 (^{1}H, 5.33 ppm; ^{13}C, 53.8 ppm), C_6D_6 referenced to residual C_6H_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_3CN referenced to residual CH_3CN (^{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_3PO_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 (δ) 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),

$KMnO_4$ 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.

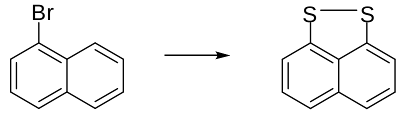
*m*CPBA was purified by washing with a pH 7 phosphate buffer unless otherwise stated:
A buffer solution was prepared from 0.1 M NaOH (154 mL) and 0.2 M KH_2PO_4 (94 mL) and made up to 376 mL with distilled water. *m*CPBA (77% w/w, 10 g) was dissolved in diethyl ether (100 mL) and washed four times with the buffer solution. The organic extract was dried over $MgSO_4$ and carefully evaporated under reduced pressure to yield pure *m*CPBA (7.3 g).

Dimethyl dioxirane (DMD) was prepared using a modified literature procedure:[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_2O (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**)



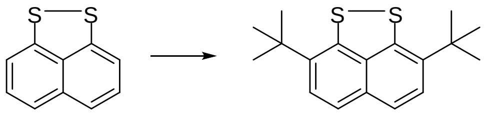
51 **50**

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 Et_2O (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 Et_2O (3 × 30 mL). The combined organic layers were dried over $MgSO_4$ 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. $C_{10}H_6S_2$ requires C, 63.1; H, 3.2%; λ_{max} (MeCN)/nm 366 (ε/dm^3 mol^{-1} cm^{-1} 13 300) and 250 (22 900); ν_{max} (KBr)/cm^{-1} 1544 (aromatic), 1485, 1349 and 1206; δ_H(300 MHz; CDCl$_3$) 7.15 (2 H, d, *J* 7.3, SCC*H*), 7.27 (2 H, t, *J* 7.7, SCCHC*H*) and 7.36 (2 H, d, *J* 7.6, SCCCC*H*); δ_H(300 MHz; C_6D_6) 6.59 (2 H, d, *J* 7.5, Ar*H*), 6.80 (2 H, ap. t, *J* 7.8, Ar*H*) and 6.97 (2 H, d, *J* 8.2, Ar*H*); δ_C(75 MHz, CDCl$_3$) 115.9 (CH, SC*C*H), 121.6 (CH, SCCC*C*H), 127.8 (CH, SCCH*C*H), 134.7 (C, SC*C*), 135.7 (C, SCC*C*) and 144.0 (C, S*C*); δ_C(75 MHz, C_6D_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$^+$, $C_{10}H_6S_2$ 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); ν_{max} (nujol)/cm^{-1} 1605, 1551 (aromatic); δ_H(360 MHz; CDCl$_3$) 7.15 (2 H, d, *J* 8.1, Ar*H*), 7.27 (2 H, t, *J* 7.7, Ar*H*) and 7.35 (2 H, d, *J* 7.4, Ar*H*); δ_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**



50 **65**

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

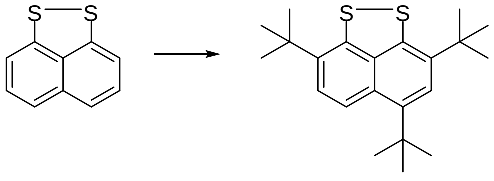
Disulfide **65** was prepared by modification of the literature procedure.[47] FeCl$_3$ (150 mg, 0.920 mmol) was added to a solution of *t*-BuBr (4.15 mL, 36.8 mmol) and disulfide **50** (3.50 g, 18.4 mmol) in CH_2Cl_2 (6.60 mL). The mixture was refluxed for 96 h, allowed to cool to room temperature, 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*-butylnaphtho[1,8-*cd*][1,2]dithiole (**65**) (2.45 g, 44%).

HPLC (t = 0 → 30 min, 80:20 MeCN:CH_2Cl_2): R_t 7.98 min; R_f 0.73 (95:5 hexane:Et_2O); mp 127-130 °C (acetone); ν_{max} (KBr)/cm^{-1} 2949 (CH), 1501, 1477, 1458, 1432, 1363, 1305 (*t*-Bu C-H), 1257, 1198, 1123 and 1007; δ_H(300 MHz; $CDCl_3$) 1.53 (18 H, s, $C(CH_3)_3$), 7.38 (2 H, d, *J* 8.6, Ar*H*) and 7.43 (2 H, d, *J* 8.5, Ar*H*); δ_C(75 MHz; $CDCl_3$) 28.4 (CH_3, $C(CH_3)_3$), 35.6 (C, $C(CH_3)_3$), 121.9 (CH), 125.7 (CH), 132.9 (C), 137.0 (C), 138.9 (C) and 139.4 (C); *m/z* (ESI) 303.1238 ($[M + H]^+$, $C_{18}H_{23}S_2$ requires 303.1241), 303 (100%).

Literature data:[45] mp 129 °C (acetone); found: C, 71.55; H, 7.37. $C_{18}H_{22}S_2$ requires C, 71.47; H, 7.33%; δ_H($CDCl_3$) 1.50 (18 H, s, $C(CH_3)_3$), 7.36 (2 H, d, *J* 8.0, Ar*H*), 7.42 (2 H, d, *J* 8.0, Ar); *m/z* 302.5 (M^+).

Using $AlCl_3$ 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 $AlCl_3$ (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.

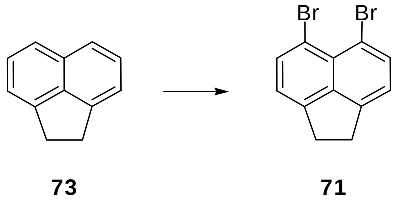


50 **68**

Using $FeCl_3$ and *t*-BuBr (3 equiv.):

Disulfide **65** was prepared by modification of the literature procedure.[47] $FeCl_3$ (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 CH_2Cl_2 (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:CH_2Cl_2): R_t 11.03 min; R_f 0.73 (95:5 hexaneEt_2O); mp 149-150 °C; ν_{max} (KBr)/cm^{-1} 2964, 1504, 1477, 1393, 1363 and 1306; δ_H(300 MHz; $CDCl_3$) 1.51 (9 H, s, C(C*H*$_3$)$_3$), 1.52 (9 H, s, C(C*H*$_3$)$_3$), 1.56 (9 H, s, C(C*H*$_3$)$_3$), 7.43 (1 H, d, *J* 9.1, Ar*H*), 7.47 (1 H, s, CC*H*C) and 7.91 (1 H, d, *J* 9.0, Ar*H*); δ_C(75 MHz; $CDCl_3$) 28.4 (CH_3, 2 × C(*C*H$_3$)$_3$), 31.1 (CH_3, C(*C*H$_3$)$_3$), 35.5 (C, *C*(CH$_3$)$_3$), 35.9 (C, *C*(CH$_3$)$_3$), 36.0 (C, *C*(CH$_3$)$_3$), 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^+, $C_{22}H_{30}S_2$ requires 358.1789), 358 (100%).

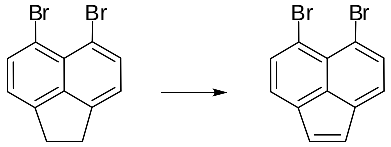
5,6-Dibromo-1,2-dihydroacenaphthylene (**71**)



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. R_f 0.60 (9:1 hexane:Et_2O); mp 167-169 °C (EtOH); δ_H(300 MHz; $CDCl_3$) 3.29 (4 H, s, C*H*$_2$), 7.08 (2 H, d, *J* 7.4, BrCCHC*H*) and 7.78 (2 H, d, *J* 7.4, BrCC*H*); δ_C(75 MHz; $CDCl_3$) 30.0 (CH_2, *C*H_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); ν_{max} (KBr)/μ 6.33, 7.40, 9.12, 11.6 and 12.9; δ_H(270 MHz; $CDCl_3$) 3.28 (4 H, s, CH_2), 7.06 (2 H, d, *J* 7.4, BrCCHC*H*) and 7.76 (2 H, d, *J* 7.4, BrCC*H*); δ_C(68 MHz; $CDCl_3$) 29.99 (CH_2), 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**)

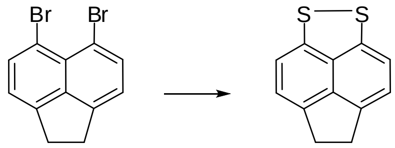


71 **72**

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. $C_{12}H_6Br_2$ requires C, 46.5; H, 1.95%; ν_{max} (KBr)/cm^{-1} 2924, 2854 and 1458; δ_H(300 MHz; $CDCl_3$) 6.93 (2 H, s, BrCCCCC*H*), 7.41 (2 H, d, *J* 7.4, Ar*H*) and 7.87 (2 H, d, *J* 7.3, Ar*H*); δ_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. $C_{12}H_6Br_2$ requires C, 46.50; H, 1.95%; δ_H(250 MHz; $CDCl_3$) 6.85 (2 H, s, BrCCCCC*H*), 7.40 (2 H, d, *J* 7.4, Br$CCCH$) and 7.86 (2 H, d, *J* 7.4, BrCC*H*); δ_C(15 MHz; $CDCl_3$) 121.0 (C, Br*C*), 125.1 (CH, BrCCCH), 125.7 (C, BrCC*C*), 129.1 (CH, BrCCCC*C*H), 135.4 (CH, BrC*C*H), 135.8 (C, BrC*C*) and 140.3 (C, BrCCC*C*); *m/z* (CI) 313 (M^+), 311, 309.

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

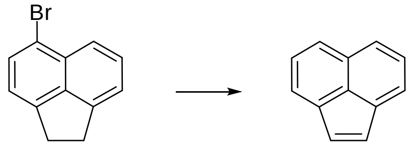


70 **69**

Disulfide **69** was prepared according to the literature procedure.[48] 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 CH_2Cl_2 (3 × 10 mL) and the combined organic phases were dried over $MgSO_4$. 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-d_6) 3.30 (4 H, s, CCH_2), 7.12 (2 H, d, *J* 7.1, Ar*H*), 7.18 (2 H, d, *J* 7.4, Ar*H*); *m/z* (EI) 216.0059 (M^+ - $C_{12}H_8S_2$ requires 216.0067), 152 (13%).

Literature data:[48] mp 190.3 °C; λ_{max} (THF)/nm 250 (ε/dm^3 mol^{-1} cm^{-1}19 600), 351 (11500), 369 (14000) and 422 (99.1); δ_H(CCl_4) 3.25 (4 H, s), 6.90 (4 H, s); *m/z* (M^+ - 216).

Acenaphthylene (**75**)

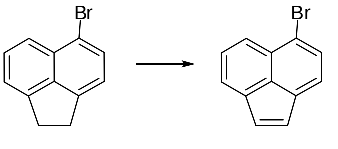


74 **75**

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 Et_2O (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 Et_2O (3 × 3 mL). The combined organic layers were dried over $MgSO_4$ and solvent was removed under reduced pressure. Purification of the residue by column chromatography (hexane) yielded **75** (108 mg, 28%) as a white solid. R_f 0.64 (60-80 pet ether); ν_{max} (KBr)/cm^{-1} 2922, 1597, 1424, 1362 and 1263; δ_H(300 MHz; $CDCl_3$) 7.08 (2 H, s, Ar*H*), 7.55 (2 H, dd, *J* 8.1 and 6.8, CHC*H*CH), 7.69 (2 H, d, *J* 6.8, Ar*H*) and 7.81 (2 H, d, *J* 8.2, Ar*H*); δ_C(75 MHz, $CDCl_3$) 124.1 (CH), 127.1 (CH), 127.6 (CH), 128.0 (C), 128.1 (C), 129.3 (CH) and 139.5 (C).

Literature data:[243-245] ν_{max} (KBr)/cm^{-1} 3060, 3039, 1456, 1447, 1426, 830 and 727; δ_H(500 MHz; CDCl$_3$) 7.09 (2 H, s, Ar*H*), 7.56 (2 H, dd, *J* 8.2 and 6.9, Ar*H*), 7.70 (2 H, dd, *J* 6.8 and 0.6, Ar*H*), 7.82 (2 H, dd, *J* 8.2 and 0.6, Ar*H*); δ_C(125 MHz; CDCl$_3$) 124.1, 127.2, 127.7, 128.0, 128.2, 129.3 and 139.6; *m/z* (CI) 152 (M$^+$).

5-Bromoacenaphthylene (**78**)



74 **78**

Bromide **78** was prepared according to the literature procedure.[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$_f$ 0.53 (hexane); ν_{max} (KBr)/cm^{-1} 2923, 2854, 1473, 1364, 1227, 1207 and 1044; δ_H(300 MHz; CDCl$_3$) 6.98 (1 H, d, *J* 5.3, Ar*H*), 7.02 (1 H, d, *J* 5.3, Ar*H*), 7.44 (1 H, d, *J* 7.3, Ar*H*), 7.57 (1 H, dd, *J* 8.1 and 7.0, Ar*H*), 7.66 (1 H, d, *J* 6.8, Ar*H*), 7.72 (1 H, d, *J* 7.3, Ar*H*) and 7.96 (1 H, d, *J* 8.2, Ar*H*); δ_C(75 MHz; CDCl$_3$) 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* (EI) 231 (M$^+$, 100%), 229 (96), 150 (97), 115 (9), 98 (12), 75 (40), 62 (10) and 44 (6).[i]

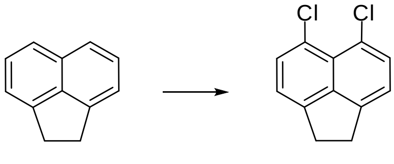
Literature data:[51, 246] mp 53-55 °C; found: C, 62.09; H, 3.22. $C_{12}H_7Br$ requires C, 62.37; H, 3.05%; ν_{max} (KBr)/cm^{-1} 3100, 3070, 3030, 1480, 1420, 1380, 1360, 1210, 1168, 1082, 1071, 1028, 1019, 881, 720-640 and 520; δ_H(60 MHz; CDCl$_3$) 6.78 (2 H, s) and 7.0-7.9 (5 H,

---

[i] Impurity in starting material: *m/z* 309.8 (68%)

m, Ar*H*); δ_C(15 MHz; $CDCl_3$) 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* (CI) 231 (M^+).

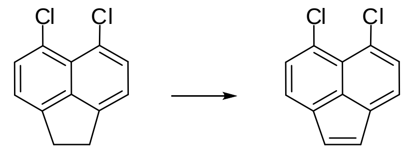
5,6-Dichloro-1,2-dihydroacenaphthylene (**81**)



Dichloride was prepared according to the literature procedure.[57] To a solution of ice-cold acenaphthene (**73**) (6.00 g, 38.9 mmol) and $AlCl_3$ (0.180 g, 1.33 mmol) in CH_2Cl_2 (118 mL) was added SO_2Cl_2 (8.52 mL, 106 mmol) over a period of 5 min. The reaction mixture was stirred for 4 h at 0 ºC. 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. R_f 0.37 (hexane); mp 154-156 ºC (EtOH); ν_{max} (neat)/cm^{-1} 2921, 1600, 1569, 1413, 1332, 1230 and 1111; δ_H(300 MHz; $CDCl_3$) 3.31 (4 H, s, C*H*$_2$), 7.13 (2 H, d, *J* 7.5, Ar*H*) and 7.47 (2 H, d, *J* 7.4, Ar*H*); δ_C(75 MHz; $CDCl_3$) 30.1 (CH_2, *C*H_2), 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 ºC; found: C, 64.48; H, 3.75; Cl, 32.00. $C_{12}H_8Cl_2$ requires C, 64.40; H, 3.62; Cl, 31.78%; ν_{max} (KBr)/cm^{-1} 2920, 1850, 1600, 1570, 1410, 1350, 1330, 1260, 1230, 1110, 1025, 915, 870, 830, 740, 720 and 700; δ_H(500 MHz; $CDCl_3$) 3.27 (4 H, s), 7.09 (2 H, d, *J* 7.5, Ar), 7.44 (2 H, d, *J* 7.5, Ar); δ_C(125 MHz; $CDCl_3$) 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).

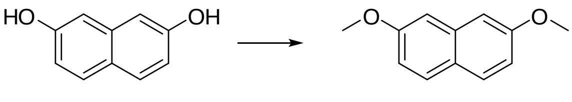
5,6-Dichloroacenaphthylene (**82**)


81 **82**

Dichloride **82** was prepared according to the literature procedure.[57] 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. R_f 0.37 (hexane); mp 153-155 °C (EtOH); ν_{max}(Nujol)/cm^{-1} 2920, 1693, 1564, 1416, 1113 and 1082; δ_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*); δ_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:[57] mp 163-164 ºC; found: C, 65.42; H, 2.64; Cl 31.92. $C_{12}H_6Cl_2$ requires C, 65.18; H, 2.74; Cl, 32.07%; ν_{max} (KBr)/cm^{-1} 3080, 1580, 1485, 1470, 1440, 1420, 1240, 1200, 1110, 1085, 1060, 1030, 900, 830, 745, 730 and 640; δ_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**)

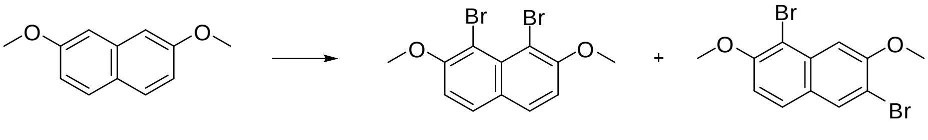

83 **84**

84 was prepared according to the literature procedure.[63] 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, H_2O (30 mL) was added forming a grey precipitate. The solid was filtered and washed with H_2O until a colourless product was obtained, yielding **84** (2.66 g, 91%). R_f 0.23 (9:1 hexane:Et_2O); mp 137-139 ºC; ν_{max} (Nujol)/cm^{-1} 1625, 1606, 1511, 1460, 1384, 1228 and 1210; δ_H(300 MHz; $CDCl_3$) 3.92 (6 H, s, OCH_3), 7.03 (2 H, dd, *J* 8.9 and 2.5, Ar*H*), 7.08 (2 H, d, *J* 2.3, Ar*H*) and 7.68 (2 H, d, *J* 8.9, Ar*H*); δ_C(75 MHz; $CDCl_3$) 55.2 (CH_3, O*C*H_3), 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; ν_{max} (Nujol)/cm^{-1} 1627 and 1228; δ_H(500 MHz; $CDCl_3$) 3.91 (6 H, s, OC*H*$_3$), 6.99 (2 H, d, *J* 8.8, OCC*H*CH), 7.06 (2 H, s, CC*H*C) and 7.65 (2 H, d, *J* 9.0, CCC*H*CH); δ_C(67.8 MHz; $CDCl_3$) 55.4 (CH_3, O*C*H_3), 105.4 (CH, C*C*HC), 116.2 (CH, OC*C*HCH), 124.5 (C, OCCHC*C*), 129.3 (CH, C*C*HCH), 135.6 (C, OCHC*C*) and 158.4 (C, O*C*CH); *m/z* (CI) 189 ($[M + H]^+$, 100%).

Bromination of 2,7-dimethoxynaphthalene

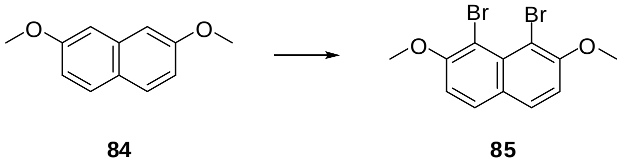


Using bromine:

The bromination of **84** was followed according to the literature procedure.[64] A solution of bromine (0.54 mL, 10.6 mmol) in $CHCl_3$ (4.00 mL) was added dropwise to a solution of 2,7-dimethoxynaphthalene (**84**) (2.00 g, 10.6 mmol) in $CHCl_3$ (10.0 mL) over 2 h at 0 °C. 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 $CHCl_3$ (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 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**: R_f 0.56 (95:5 hexane:EtOAc); mp 125-127 ºC; ν_{max} (KBr)/cm^{-1} 1616, 1595, 1497, 1459, 1397, 1351, 1297, 1261, 1230, 1184, 1156, 1072, and 1035; δ_H(300 MHz; $CDCl_3$) 4.02 (3 H, s, COC*H*$_3$), 4.06 (3 H, s, COC*H*$_3$), 7.14 (1 H, d, *J* 9.0, Ar*H*), 7.51 (1 H, s, Ar*H*), 7.66 (2 H, d, *J* 8.9, Ar*H*) and 7.99 (1 H, s, Ar*H*); δ_H(300 MHz; d_6-DMSO) 3.98 (3 H, s, COC*H*$_3$), 4.00 (3 H, s, COC*H*$_3$), 7.41 (1 H, d, *J* 9.0, Ar*H*), 7.44 (1 H, s, Ar*H*), 7.93 (2 H, d, *J* 9.0, Ar*H*) and 8.29 (1 H, s, Ar*H*); δ_C(75 MHz, $CDCl_3$) 56.2 (CH_3, O*C*H$_3$), 56.8 (CH_3, O*C*H$_3$), 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^+, $C_{12}H_{10}Br_2O_2$ requires 343.9048), 348 (M^+, 48%), 346 (100), 344 (50), 303 (28), 288 (10), 260 (8), and 113 (10).

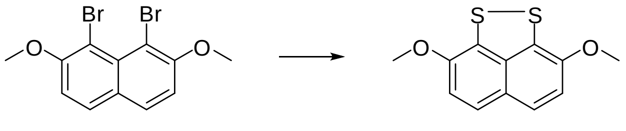
1,8-Dibromo-2,7-dimethoxynaphthalene (**85**)



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%); R_f 0.14 (9:1 hexane:EtOAc); mp 129-130 ºC; ν_{max} (KBr)/cm^{-1} 3008, 2937, 2936, 2838, 1611, 1503, 1459, 1328, 1263, 1163 and 1056; δ_H(300 MHz; $CDCl_3$) 4.02 (6 H, s, COC*H*$_3$), 7.16 (2 H, d, *J* 9.0, Ar*H*) and 7.74 (2 H, d, *J* 9.0, Ar*H*); δ_C(75 MHz, $CDCl_3$) 57.1 (CH_3, O*C*H$_3$), 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^+, $C_{12}H_{10}Br_2O_2$ 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).

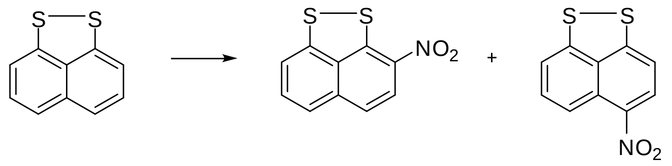
3,8-Dimethoxynaphtho[1,8-*cd*][1,2]dithiole (**87**)



85 **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_2O (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_2O (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); ν_{max} (KBr)/cm^{-1} 2937, 2834 (OCH_3), 1615, 1505, 1427, 1265 and 1061; δ_H(300 MHz; $CDCl_3$) 3.95 (6 H, s, COC*H*$_3$), 7.00 (2 H, d, *J* 8.8, Ar*H*) and 7.39 (2 H, d, *J* 8.8, Ar*H*); δ_H(300 MHz; acetone-d$_6$) 3.97 (6 H, s, COC*H*$_3$), 7.19 (2 H, d, *J* 8.9, Ar*H*) and 7.52 (2 H, d, *J* 8.9, Ar*H*); δ_C(75 MHz, $CDCl_3$) 56.4 (CH_3, O*C*H$_3$), 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^+, $C_{12}H_{10}O_2S_2$ 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).

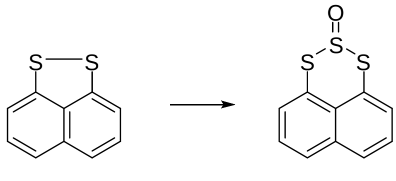
Nitration of disulfide **50**



50 **90** **91**

Disulfide **50** was nitrated by modification of the literature procedure.[66] 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. HNO_3 (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 $NaHCO_3$ (1.02 mL). The resulting solution was extracted with CH_2Cl_2 (3 × 10 mL) and washed with H_2O (3 × 5 mL) and brine (3 × 5 mL). The combined organic layers were dried over Na_2SO_4 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%). R_f 0.29 (9:1 hexane: EtOAc); HPLC (t = 0 → 40 min, 1:1 MeCN:H_2O): **90**: R_t 28.13 min; mp 188-190 °C; ν_{max} (neat)/cm^{-1} 2921, 2849, 1594, 1543 (NO_2), 1497, 1464, 1422, 1325, 1263, 1201, 1160, 1134 and 1058; δ_H(300 MHz; $CDCl_3$) 7.48 (1 H, d, *J* 9.1, Ar*H*), 7.55-7.68 (3 H, m, Ar*H*) and 8.13 (1 H, d, *J* 9.1, Ar*H*); *m/z* (EI) 234.9756 (M^+ - $C_{10}H_5NO_2S_2$ 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**: R_t 25.86 min; mp 180-182 °C; ν_{max} (neat)/cm^{-1} 2918, 2849, 1535 (NO_2), 1493, 1472, 1377 (NO_2), 1279, 1241, 1211, 1164, 1133, 1066 and 1039; δ_H(300 MHz; $CDCl_3$) 7.17 (1 H, d, *J* 8.5, Ar*H*), 7.37 (1 H, d, *J* 7.7, Ar*H*), 7.58 (1 H, dd, *J* 7.7 and 8.6, SCCHC*H*CH), 8.34 (1 H, d, *J* 8.4, Ar*H*) and 8.50 (1 H, d, *J* 9.0, Ar*H*); *m/z* (EI) 234.9769 (M^+ - $C_{10}H_5NO_2S_2$ 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**)

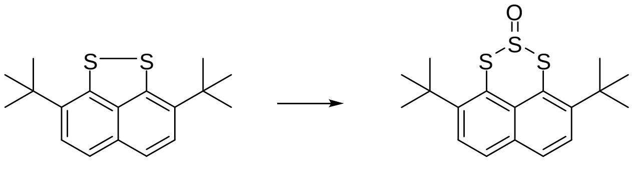


50 **49**

Trisulfide-2-oxide **49** was prepared according to the literature procedure.[42] 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 $NaBH_4$ (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 CH_2Cl_2 (3 × 10 mL) and the combined organic layers were washed with water (3 × 10 mL), dried over $MgSO_4$ and concentrated *in vacuo* to give a white, crystalline solid. The solid was dissolved in Et_2O (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 $SOCl_2$ (0.75 mL, 10.2 mmol) in Et_2O (93.0 mL) at 0 °C and was stirred for 4 h warming to room temperature. The reaction was quenched with 10% H_2SO_4 (35.0 mL), extracted with Et_2O (3 × 10 mL) and washed with brine (3 × 10 mL). The organic layers were combined, dried over $MgSO_4$, 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:Et_2O) afforded the *title compound* which was recrystallised from EtOH to afford **49** (1.01 g, 60%) as a yellow, crystalline solid. R_f 0.31 (7:3 60-80 pet ether:Et_2O); mp 119-121 ºC (EtOH); λ_{max} (MeCN)/nm 364 (ε/dm^3 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; $CDCl_3$) 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; CD_2Cl_2) 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; C_6D_6) 6.84 (2 H, t, *J* 7.8, Ar*H*), 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; $CDCl_3$) 122.3 (C), 124.2 (C), 126.7 (CH), 131.3 (CH), 132.2 (CH) and 134.9 (C); δ_C(75 MHz; CD_2Cl_2) 122.7 (C), 124.5 (C), 127.1 (CH), 131.6 (CH), 132.6 (CH) and 135.1 (C); *m/z* (ESI) 260.9475 ($[M + Na]^+$, $C_{10}H_6OS_3Na$ requires 260.9478), 261.0 (100%).

Literature data:[26] ν_{max} (nujol)/cm^{-1} 1097 (SO); δ_H(360 MHz; $CDCl_3$) 7.56 (2 H, t, *J* 7.6, Ar*H*), 7.60 (2 H, dd, *J* 7.3 and 1.5, Ar*H*) and 7.93 (2 H, dd, *J* 8.0 and 1.5, Ar*H*); δ_C(90 MHz; $CDC1_3$) 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^+, $C_{10}H_6$ OS_3 requires 238.3368), 208 (44%), 134 (55), 106 (100), 102 (65), 76 (23) and 51 (10).

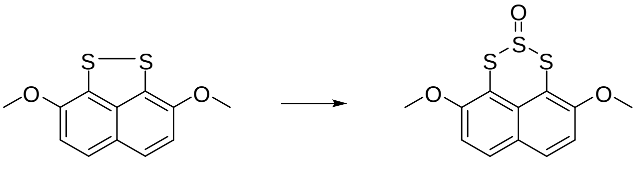
4,9-Di-*tert*-butyl-1,2,3-trithiaphenalene 2-oxide (**58**)



65 **58**

Trisulfide-2-oxide **58** was prepared according to the literature procedure.[42] Disulfide **65** (700 mg, 2.31 mmol) was dissolved in THF (4.05 mL) at room temperature. $LiAlH_4$ (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 H_2O (0.080 mL) and 10 M HCl (0.220 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue (703 mg, 2.31 mmol) was dissolved in Et_2O (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 $SOCl_2$ (0.240 mL, 3.35 mmol) in Et_2O (30.0 mL) at 0 °C and allowed to stir for 4 h warming to room temperature. The reaction was quenched with 10% H_2SO_4 (3.75 mL), extracted with Et_2O (3 × 5 mL) and washed with brine (2 × 5 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. Chromatography on florisil® (98:2 hexane:Et_2O) afforded disulfide **65** (0.607 g, 87%) followed by (95:5 hexane:Et_2O) to afford the *title compound* **58** (0.107 g, 13%) as a yellow, crystalline solid. R$_f$ 0.27 (95:5 hexane:Et_2O); mp 154-156 ºC (CH_2Cl_2/hexane); ν_{max} (KBr)/cm^{-1} 2961 (CH), 1464, 1391, 1360, 1245 and 1106 (SO); δ_H(300 MHz; $CDCl_3$) 1.62 (18 H, s, C(C*H*$_3$)$_3$) and 7.75 (4 H, s, SCCC*H* and SCCCC*H*); δ_C(75 MHz; $CDCl_3$) 31.9 (CH_3, C(*C*H$_3$)$_3$), 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]$^+$, $C_{18}H_{22}OS_3Na$ requires 373.0731), 341 (92%), 319 (15) and 302 (24).

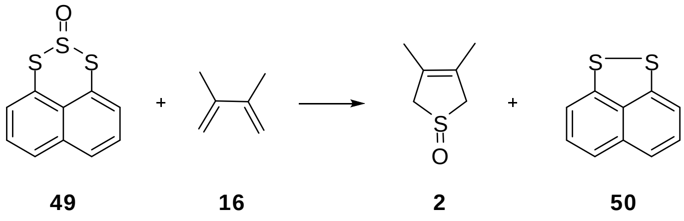
4,9-Dimethoxy-1,2,3-trithiaphenalene 2-oxide (**103**)



87 **103**

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_2Cl_2 (3 × 10 mL) and the combined organic layers were washed with water (3 × 10 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give a white, crystalline solid. The solid was dissolved in Et_2O (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_2O (52.7 mL) at 0 °C and was stirred for 4 h warming to room temperature. The reaction was quenched with 10% H_2SO_4 (35.0 mL), extracted with Et_2O (3 × 10 mL) and washed with brine (3 × 10 mL). The organic layers were combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (9:1 hexane:Et_2O) to afford disulfide **87** (256 mg, 26%). Further elution (1:1 hexane:Et_2O) 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_2O); mp 146-148 ºC (EtOH); ν_{max} (KBr)/cm^{-1} 2933, 1601, 1508, 1455, 1325, 1268, 1163, 1084 (SO) and 1050; δ_H(300 MHz; $CDCl_3$) 4.02 (6 H, s, COC*H*$_3$), 7.26 (2 H, d, *J* 9.0, Ar*H*) and 7.86 (2 H, d, *J* 9.1, Ar*H*); δ_C(75 MHz, $CDCl_3$) 56.0 (CH_3, O*C*H_3), 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^+, $C_{12}H_{10}O_3S_3$ 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**)



Thermally:

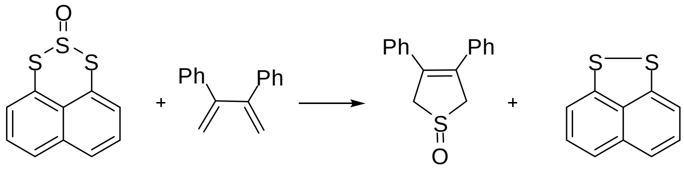
Sulfoxide **2** was prepared according to the literature procedure.[42] A solution of 2,3-dimethyl-1,3-butadiene (**16**) (0.71 mL, 6.30 mmol) and 1,2,3-trithiaphenalene 2-oxide (**49**) (150 mg, 0.630 mmol) in chlorobenzene (63.0 mL) was degassed for 15 min. The solution was refluxed for 10 h, until 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 CH_2Cl_2:EtOH) afforded the sulfoxide **2** (80 mg, 98%) as a pale yellow oil. R_f 0.38 (95:5 CH_2Cl_2:EtOH); ν_{max} (neat)/cm^{-1} 1266 and 1029 (SO); δ_H(300 MHz; $CDCl_3$) 1.77 (6 H, s, CH_3), 3.44 (2 H, d, *J* 16.5, SC*H*) and 3.81 (2 H, d, *J* 17.1, SC*H*); δ_C(75 MHz; $CDCl_3$) 14.4 (CH_3, CCH_3), 64.3 (CH_2, OS*C*) and 126.0 (C, *C*CH_3); *m/z* (EI) 130.0454 (M^+, $C_6H_{10}OS$ requires 130.0452), 114 (11%), 111 (15), 99 (12), 82 (38), 67 (100), 54 (20) and 45 (6).

Literature data:[26] ν_{max} (nujol)/cm^{-1} 1050 (SO); δ_H(400 MHz; $CDCl_3$) 1.71 (6 H, s, CH_3), 3.38 (2 H, d, *J* 16.6, SC*H*) and 3.81 (2 H, d, *J* 17.1, SC*H*); δ_C(100 MHz; CDC1_3) 14.9 (CH_3, CCH_3), 64.6 (CH_2, OS*C*) and 126.4 (C, *C*CH_3); *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 CH_2Cl_2:EtOH) afforded the *title compound* **2** (23.0 mg, 55%).

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

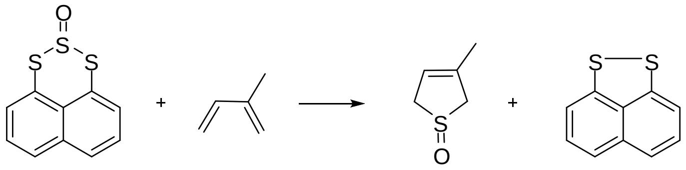


49 **17** **3** **50**

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 CH_2Cl_2:EtOH) afforded sulfoxide **3** (104 mg, 65%) as a white solid. R_f 0.16 (99:1 CH_2Cl_2:EtOH); mp 132-133 °C; ν_{max} (KBr)/cm^{-1} 1025 (SO); δ_H(300 MHz; $CDCl_3$) 4.12 (2 H, d, *J* 16.6, SCH_2), 4.42 (2 H, d, *J* 16.6, SCH_2) and 7.21-7.34 (10 H, m, Ar*H*); δ_C(75 MHz; $CDC1_3$) 64.3 (CH_2, SCH_2), 127.8 (CH), 128.3 (2 × CH), 128.5 (2 × CH), 131.8 (C) and 135.4 (C); *m/z* (EI) 254.0771 (M^+, $C_{16}H_{14}OS$ 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).

Literature data:[15, 26] mp 134-135 °C, v_{max} (nujol)/cm^{-1} 1038 (SO), δ_H(360 MHz; $CDCl_3$) 4.05 (2 H, d, *J* 16.2, SC*H*$_2$), 4.40 (2 H, d, *J* 16.2, SC*H*$_2$) and 7.15-7.25 (10 H, m, Ar*H*); δ_C(90 MHz; $CDC1_3$) 64.8 (CH_2, S*C*H$_2$), 128.4-129.0 (10 × CH), 132.4 (2 × C) and 135.9 (2 × 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**)

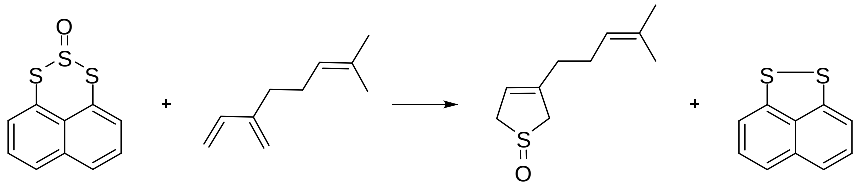


49 **18** **21** **50**

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_2Cl_2:EtOH) afforded **21** (11.9 mg, 98%) as an oil. R$_f$ 0.21 (99:1 CH_2Cl_2:EtOH); v_{max} (neat)/cm^{-1} 1029 (SO); δ_H(300 MHz; $CDCl_3$) 1.92 (3 H, s, CC*H*$_3$), 3.38-3.53 (2 H, m), 3.73-3.87 (2 H, m) and 5.60 (1 H, s, CH$_2$C*H*); δ_C(75 MHz; $CDC1_3$) 16.7 (CH_3, C*C*H$_3$), 59.9 (CH_2), 62.9 (CH_2), 119.0 (CH, CH$_2$*C*H) and 135.5 (C, *C*CH$_3$); *m/z* (EI) 116 (M$^+$, 87%), 99 (8), 85 (4), 67 (100), 53 (38) and 42 (9).

Literature data:[26] v_{max} (CH_2Cl_2)/cm^{-1} 1087 (SO); δ_H(360 MHz; $CDCl_3$) 1.85 (3 H, s, CC*H*$_3$), 3.31-3.46 (2 H, m), 3.66-3.80 (2 H, m) and 5.53 (1 H, s); δ_C(100 MHz; $CDC1_3$) 18.9 (CH_3), 62.2 (CH_2), 65.2 (CH_2), 121.4 (CH) and 137.7 (C, *C*CH$_3$); *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**)

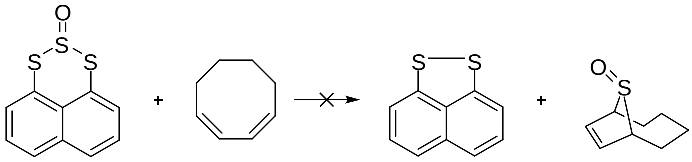


49 **19** **22** **50**

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 CH_2Cl_2:EtOH) afforded sulfoxide **22** (35.2 mg, 91%) as a pale yellow oil. R_f 0.35 (99:1 CH_2Cl_2:EtOH); ν_{max} (neat)/cm^{-1} 1032 (SO); δ_H(300 MHz; $CDCl_3$) 1.59 (3 H, s, CCH_3), 1.66 (3 H, s, CCH_3), 2.17-2.27 (4 H, m, CCH_2CH_2CH), 3.41 (1 H, d, *J* 17.0, SC*H*), 3.50 (1 H, d, *J* 17.1, SC*H*), 3.74 (1 H, d, *J* 17.0, SC*H*), 3.83 (1 H, d, *J* 17.1, SC*H*), 5.07 (1 H, br t, *J* 5.0, CH_3CCH) and 5.59 (1 H, br s, SCH_2CH); δ_C(75 MHz; $CDCl_3$) 17.7 (CH_3), 25.6 (CH_3), 26.2 (CH_2), 31.2 (CH_2), 59.7 (CH_2), 61.6 (CH_2), 117.9 (CH), 123.0 (CH), 132.6 (C) and 139.9 (C); *m/z* (EI) 184.0930 (M^+, $C_{10}H_{16}OS$ 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} (CH_2Cl_2)/cm^{-1} 1032 (SO); δ_H(300 MHz; $CDCl_3$) 1.61 (3 H, s, CCH_3), 1.69 (3 H, s, CCH_3), 2.20-2.29 (4 H, m, CCH_2CH_2CH), 3.43 (1 H, d, *J* 17.0, SC*H*), 3.52 (1 H, d, *J* 17.1, SC*H*), 3.75 (1 H, dd, *J* 16.9 and 1.2, SC*H*), 3.84 (1 H, d, *J* 17.1, SC*H*), 5.09 (1 H, br s, CH_3CCH) and 5.61 (1 H, br s, SCH_2CH); δ_C(90 MHz; $CDCl_3$) 18.1 (CH_3), 26.1 (CH_3), 26.7 (CH_2), 31.7 (CH_2), 60.1 (CH_2), 62.1 (CH_2), 118.4 (CH), 123.4 (CH), 133.0 (C) and 140.3 (C); *m/z* (EI) 184.0921 (M^+, $C_{10}H_{16}OS$ requires 184.0922), 135 (30%), 121 (17), 116 (24), 93 (33) and 69 (100).

Attempted reaction of trisulfide-2-oxide (**49**) with cyclooctadiene

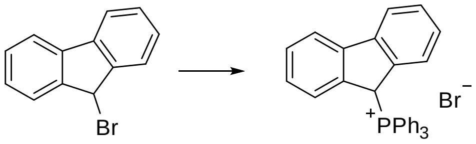


49 **50**

A solution of cyclooctadiene (0.07 mL, 0.525 mmol) and 1,2,3-trithiaphenalene 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 *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-trithiaphenalene 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 *in vacuo* and purification of the residue by column chromatography (60-80 pet ether) yielded disulfide **50** (49.4 mg, 100%).

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

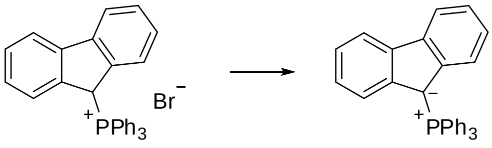


108 **109**

Phosphonium salt **109** was prepared according to the literature procedure.[80] A solution of 9-bromofluorene (**108**) (2.00 g, 8.16 mmol) and PPh_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 (9*H*-fluoren-9-yl)triphenylphosphonium bromide (**109**) (1.82 g, 44%) as a white solid. mp 287-288 °C; ν_{max} (KBr)/cm^{-1} 2995, 2794, 1585, 1434, 1149 and 1109; δ_H(300 MHz; d_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.

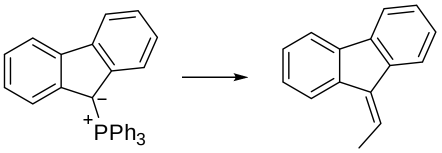
Fluoren-9-ylidene-triphenyl-λ^5-phosphane (**110**)



109 **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_4OH 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; ν_{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, Ar*H*), 6.72-6.78 (2 H, m, Ar*H*), 6.84 (2 H, t, *J* 7.2, Ar*H*), 7.63-7.81 (15 H, m, Ar*H*) and 8.04 (2 H, d, *J* 7.5, Ar*H*); 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-ethylidene-9*H*-fluorene (**111**)

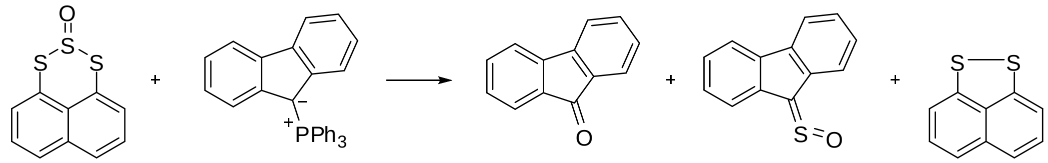


110 **111**

Olefin **111** was prepared by a literature procedure.[81] A solution of ylide **110** (210 mg, 0.491 mmol) and acetaldehyde (0.072 mL, 0.246 mmol) in $CHCl_3$ 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-ethylidene-9*H*-fluorene (**111**) (18.0 mg, 38%). R_f 0.48 (60-80 pet ether); ν_{max} (KBr)/cm^{-1} 2924, 2854, 1648 (C=C) and 1445; δ_H(300 MHz; $CDCl_3$) 2.41 (3 H, d, *J* 7.6, $CHCH_3$), 6.88 (1 H, q, *J* 7.5, $CHCH_3$), 7.29-7.44 (4 H, m, Ar*H*), 7.66 (1 H, d, *J* 6.7, Ar*H*), 7.72 (1 H, d, *J* 6.7, Ar*H*), 7.77 (1 H, d, *J* 6.8, Ar*H*) and 7.91 (1 H, d, *J* 6.9, Ar*H*); δ_C(75 MHz, $CDCl_3$) 15.3 (CH_3), 119.4 (CH), 119.6 (CH), 119.8 (CH), 124.8 (CH), 125.0 (CH), 126.8 (2 × 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^+, $C_{15}H_{12}$ requires 192.0939), 189 (27%), 165 (37), 94 (11) and 82 (7).

Literature data:[82, 249] ν_{max} (CCl_4/CS_2)/cm^{-1} 3065, 1650, 1447, 1294, 1033, 935, 827, 781, 771, 739, 729 and 621; δ_H(400 MHz; $CDCl_3$) 2.26 (3 H, d, *J* 7.6, $CHCH_3$), 6.72 (1 H, q, *J* 7.6, $CHCH_3$), 7.20 (1 H, m, Ar*H*), 7.24 (2 H, m, Ar*H*), 7.28 (1 H, m, Ar*H*), 7.54 (1 H, m, Ar*H*), 7.62 (1 H, m, Ar*H*), 7.67 (1 H, m, Ar*H*) and 7.79 (1 H, br d, *J* 7.1, Ar*H*); δ_C(101 MHz, $CDCl_3$) 15.2 (CH_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^+, 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**



49 **110** **112** **113** **50**

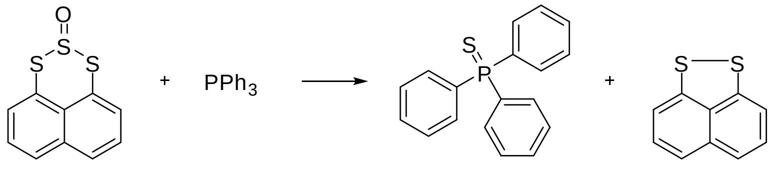
A solution of trisulfide-2-oxide **49** (0.180 mL, 0.756 mmol) and ylide **110** (650 mg, 1.51 mmol) in PhCl (75.6 mL) was degassed for 15 min. The solution was refluxed for 2 h, until disappearance of compound **49** by TLC. The solution was concentrated *in vacuo* and purification of the residue by column chromatography (60-80 pet ether) first yielded disulfide **50** (209 mg, 84%). Further elution (95:5 60-80 pet ether:Et_2O) 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). R_f 0.25 (95:5 60-80 pet ether:Et_2O). Analysis on crude mixture: ν_{max} (KBr)/cm^{-1} 1718, 1686, 1655, 1599, 1560, 1448, 1299, 1120 (CSO), 1087 and 1018 (CSO); HPLC (t = 0 → 40 min, 0 → 100% H_2O in MeCN): Fluorenone **112**: R_t 29.56 min; δ_H(300 MHz; $CDCl_3$) 7.27-7.32 (2 H, m, Ar*H*), 7.46-7.53 (4 H, m, Ar*H*) and 7.66 (2 H, d, *J* 7.3, Ar*H*); *m/z* (EI) 180 (M^+, 100%), 152 (29) and 79 (24). Fluorenethione *S*-oxide **113** and unidentified compound: R_t 32.97 min; peak assignable to **113** δ_H(300 MHz; $CDCl_3$) 8.65 (1 H, d, *J* 7.7, Ar*H*) and 7.16-7.66 (11 H, m, assignable to 7 H for **113**); *m/z* (EI) 212.0288 (M^+, $C_{13}H_8OS$ 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); ν_{max} (KBr)/cm^{-1} 1720 (CO); δ_H($CDCl_3$) 7.25 (2 H, m, Ar*H*), 7.43 (4 H, m, Ar*H*) and 7.63 (2 H, d, *J* 7.6, Ar*H*); δ_C($CDCl_3$) 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); ν_{max} (KBr)/cm^{-1} 1119 (CSO) and 1020 (CSO); δ_H(300 MHz, $CDCl_3$) 7.17 (1 H, m, Ar*H*), 7.30 (1 H, m, Ar*H*), 7.36 (1 H, m, Ar*H*), 7.43 (1 H, m, Ar*H*), 7.56 (1 H, m, Ar*H*), 7.58 (1 H, m, Ar*H*), 7.66 (1 H, dm, J 7.6, Ar*H*) and 8.64 (1 H, dm, J 7.6, Ar*H*); δ_C($CDCl_3$) 179.21 (*C*O); *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:H_2O): **2** R_t 5.65 min, **49** R_t 9.87 min, **16** R_t 12.29 min, **50** R_t 20.60 min.

Triphenylphosphine sulfide (**126**)



49 **126** **50**

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. PPh_3 (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%). R_f 0.23 (95:5 60-80 pet ether:EtOAc); δ_H(300 MHz; $CDCl_3$) 7.42-7.54 (9 H, m, Ar*H*) and 7.69-7.76 (6 H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$) 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 (81), 158 (8), 149 (20), 139 (17), 107 (11), 97 (7), 85 (5), 77 (11), 63 (6), 57 (17) and 43 (14).

Literature data:[254] mp 161-163 °C; found: C, 73.37; H, 5.15. $C_{18}H_{15}PS$ requires C, 73.45; H, 5.14%; ν_{max} (KBr)/cm^{-1} 1440, 1105, 710, 690 and 640; δ_H(300 MHz; $CDCl_3$) 7.25-7.50 (9 H, m) and 7.50-7.80 (6 H, m); δ_C(75 MHz, $CDCl_3$) 128.5 (d, *J* 13), 131.5 (d, *J* 3), 132.2

(d, *J* 11) and 133.0 (d, *J* 85); δ_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 → 100 °C (5×10^{-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. ν_{max} (Ar matrix, ca. 20 K, cm^{-1}) 1137.0 ($^{32}S^{16}O$) and 1125.0 ($^{34}S^{16}O$).

Literature data:[89] ν_{max} (Ar matrix, cm^{-1}) 1136.7 ($^{32}S^{16}O$) and 1125.9 ($^{34}S^{16}O$).

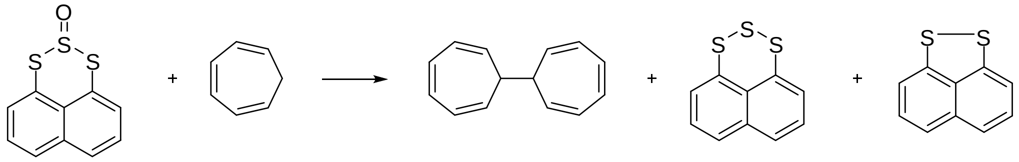
General procedure for the attempted radical trapping of trisulfide-2-oxide **49** thermally:

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).

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

Table 4.1 Attempted radical trapping of trisulfide-2-oxide **49**

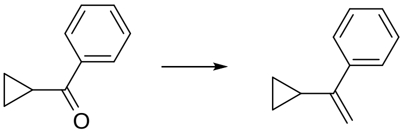
Reaction of 1,2,3-trithiaphenalene 2-oxide (**49**) with cyclohepta-1,3,5-triene (**7**)


49 **7** **8** **138** **50**

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**): δ_H(300 MHz; $CDCl_3$) 1.99 (2 H, s), 5.30 (2 H, d, 3.9), 5.33 (2 H, d, 3.9), 6.27-6.32 (4 H, m) and 6.72 (4 H, t, *J* 3.0); peaks assignable to naphtho[1,8-*de*][1,2,3]trithiine (**138**): δ_H(300 MHz; $CDCl_3$) 7.43 (2 H, t, *J* 7.7, Ar*H*), 7.66 (2 H, dd, *J* 7.2 and 1.1, Ar*H*) and 7.86 (2 H, dd, *J* 8.3 and 1.0, Ar*H*).

Literature data:[26, 255] ditropyl **8**: mp 60-61 °C; ν_{max} (CCl_4)/cm^{-1} 3016 and 2833; δ_H(400 MHz; $CDCl_3$) 1.98 (2 H, br s), 5.30 (2 H, d, *J* 4.03), 5.33 (2 H, d, *J* 4.03), 6.29 (2 H, t, *J* 3.15), 6.30 (2 H, t, *J* 2.67) and 6.72 (4 H, t, *J* 2.97); δ_C(100 MHz, $CDCl_3$) 42.0, 125.0, 125.7 and 131.0; *m/z* (EI) 182 (M$^+$, 0.5%), 165 (8), 152 (4), 104 (16), 91 (100), 78 (19), 65 (15) and 39 (11). naphtho[1,8-*de*][1,2,3]trithiine (**138**): mp 152-154 °C (hex); ν_{max} (CH_2Cl_2)/cm^{-1} 1644; δ_H(360 MHz; $CDCl_3$) 7.42 (2 H, dd, *J* 8.0 and 7.4), 7.64 (2 H, dd, *J* 7.2 and 1.2), 7.85 (2 H, dd, *J* 8.2 and 1.3); δ_C(100 MHz; $CDC1_3$) 116.4, 122.1, 125.2, 128.3, 129.2, 131.2, 133.3, 134.7, 135.8 and 136.1; *m/z* (EI) 221.96316 (M$^+$, $C_{10}H_6S_3$ requires 221.96317), 190 (87), 158 (15), 145 (32), 114 (40) and 95 (59).

(1-Cyclopropylvinyl)-benzene (**140**)



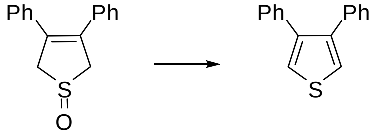
139 **140**

Alkene **140** was prepared according to the literature procedure.[91] A solution of *n*-BuLi in hexanes (2.40 M, 7.48 mL, 17.9 mmol) was added to a solution of PPh_3MeBr (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_2O (~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_f 0.65 (60-80 pet ether); ν_{max} (neat)/cm^{-1} 3083, 3007, 1624 (C=C), 1495 and 1262; δ_H(300 MHz; $CDCl_3$) 0.55-0.60 (2 H, m, $CHCH_2CH_2$), 0.79-0.85 (2 H, m, $CHCH_2CH_2$), 1.59-1.68 (1 H, m, CH_2CHC), 4.92 (1 H, s, $C{=}CH_2$), 5.26 (1 H, s, $C{=}CH_2$), 7.22-7.35 (3 H, m, Ar*H*) and 7.57-7.60 (2 H, m, Ar*H*); δ_C(75 MHz; $CDCl_3$) 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), 141.6 (C) and 149.3 (C, $CHC{=}CH_2$); *m/z* (EI) 144.0945 (M^+, $C_{11}H_{12}$ requires 144.0939), 129 (100%), 115 (28), 103 (42), 91 (17), 77 (30), 71 (6), 66 (12), 63 (14) and 51 (26).

Literature data:[256, 257] ν_{max} (neat)/μ 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; δ_H($CDCl_3$) 0.40-0.49 (2 H, m, cp-*cis*-CH_2), 0.64-0.74 (2 H, m, cp-*trans*-CH_2), 1.47-1.58 (1 H, m, CH_2CHC), 4.79 (1 H, t, *J* 1.2, $C{=}CH_2$), 5.14 (1 H, d, *J* 0.84, $C{=}CH_2$), 7.12-7.24 (3 H, m, Ar*H*) and 7.43-7.48 (2 H, m, Ar*H*);

δ_C($CDCl_3$) 6.6 (CH_2, CCH*C*H_2), 15.6 (CH, C*C*HCH_2), 108.9 (CH_2, C=*C*H_2), 126.0 (CH), 127.4 (CH), 128.1 (CH), 141.5 (C) and 149.3 (C, CH*C*=CH_2); *m/z* (EI) 144 (M^+, 68%).

3,4-Diphenyl-thiophene (**142**)



3 **142**

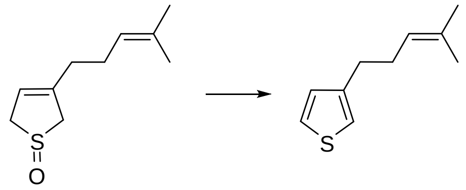
Thiophene **142** was prepared according to the literature procedure.[26] Sulfoxide **3** (80.0 mg, 0.310 mmol) was dissolved in acetic anhydride (12.4 mL) and the resulting solution was refluxed for 3 h. The solution was removed *in vacuo*, the residue was diluted with CH_2Cl_2 (10 mL), washed with saturated aqueous $NaHCO_3$ (3 × 10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were combined, dried over Na_2SO_4 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. R_f 0.47 (60-80 pet ether); mp 112-113 °C; ν_{max}(KBr)/cm^{-1} 3099 and 1437; δ_H(300 MHz; $CDCl_3$) 7.12-7.22 (12 H, m, Ar*H*); δ_C(75 MHz; CDC1_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 °C; ν_{max}(KBr)/cm^{-1} 1460, 850, 795, 770, 750, 730, 720 and 680; δ_H(500 MHz; $CDCl_3$) 7.10-7.20 (12 H, m, Ar*H*); δ_C(90 MHz; CDC1_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_2Cl_2 (23.0 mL) at 0 °C. The mixture was stirred for 5 min, washed with saturated aqueous

$NaHCO_3$ (3 × 10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were combined, dried over Na_2SO_4 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**)

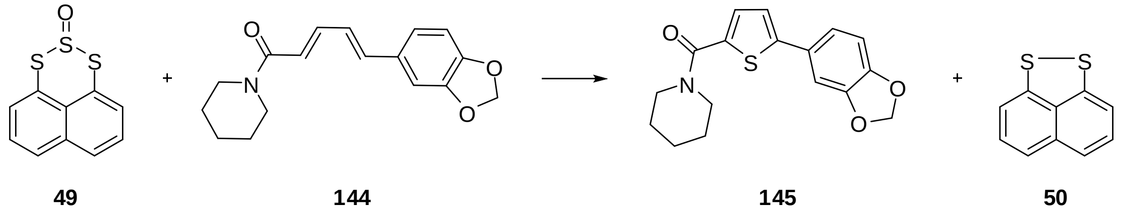


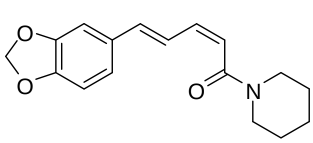
22 **143**

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 CH_2Cl_2 (109 mL) at 0 °C. The mixture was stirred for 10 min at 0 °C, washed with $NaHCO_3$ solution (3 × 5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were combined, dried over Na_2SO_4 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. R_f 0.57 (hexane); ν_{max} (neat)/cm^{-1} 2966, 2924, 2854, 1450 and 1265; δ_H(300 MHz; $CDCl_3$) 1.58 (3 H, s, CCH_3), 1.69 (3 H, s, CCH_3), 2.30 (2 H, ap. q, *J* 7.4, $CHCH_2$), 2.63-2.68 (2 H, m, $CHCH_2CH_2$), 5.17 (1 H, t with unresolved fine coupling, *J* 7.1, $C(CH_3)_2CHCH_2$), 6.94-6.96 (2 H, m, SCHC*H* and SC*H*C) and 7.24 (1 H, dd, *J* 4.8 and 3.0, SC*H*CH); δ_C(75 MHz; $CDC1_3$) 17.7 (CH_3), 25.7 (CH_3), 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^+, $C_{10}H_{14}S$ requires 166.0816), 110 (33%), 97 (100), 69 (69), 53 (10) and 45 (11).

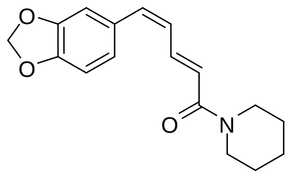
Literature data:[26, 93] ν_{max} (neat)/cm^{-1} 3110, 2980, 2935, 2860, 1442, 1378, 1240, 1104, 1079, 839 and 775; δ_H(360 MHz; $CDCl_3$) 1.49 (3 H, s, CCH_3), 1.60 (3 H, s, CCH_3), 2.18-2.25 (2 H, m, $CHCH_2$), 2.57 (2 H, t, *J* 7.3, $CHCH_2CH_2$), 5.05-5.15 (1 H, m, $C(CH_3)_2CHCH_2$), 6.85 (1 H, d, *J* 3.0, SC*H*C), 6.86 (1 H, d, *J* 4.8, SCHC*H*) and 7.14 (1 H, dd, *J* 4.8 and 3, SC*H*CH); δ_{C}(90 MHz; CDC1$_3$) 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**)

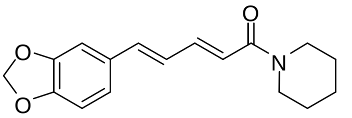




146



147



144

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); ν_{max} (KBr)/cm^{-1} 2924, 2854, 1599 (CO) and 1455; δ_{H}(300 MHz; CDCl$_3$) 1.64-1.71 (6 H, m, NCH$_2$C*H*$_2$C*H*$_2$), 3.68-3.71 (4 H, m NC*H*$_2$), 6.00 (2 H, s, OC*H*$_2$O), 6.83 (1 H, d, *J* 8.0, Ar*H*), 7.07-7.08 (2 H, m, Ar*H*), 7.12 (1 H, d, *J* 1.6, Ar*H*) and 7.20 (1 H, d, *J* 3.8, Ar*H*); δ_{C}(75 MHz; CDC1$_3$) 24.6 (2 × CH$_2$), 26.1 (CH$_2$), 101.3 (CH$_2$,

O*C*H_2O), 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 ($[M + Na]^+$, $C_{17}H_{17}NO_3SNa$ requires 338.0827), 338 (100%). (tentatively assigned as isomers of piperine): HPLC (t = 0 → 40 min, 0 → 100% H_2O 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 and11.5) and 7.73 (dd, *J* 14.7 and 11.8).

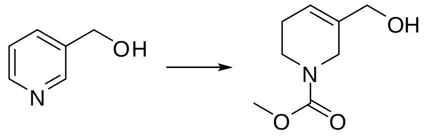
Literature data:[26, 95] **145**: ν_{max} (KBr)/cm^{-1}1606 (CO); δ_H(500 MHz; $CDCl_3$) 1.64-1.72 (6 H, m, $NCH_2CH_2CH_2$), 3.69-3.72 (4 H, m NCH_2), 6.00 (2 H, s, OCH_2O), 6.83 (1 H, d, *J* 8.0, Ar*H*), 7.08-7.09 (2 H, m, Ar*H*), 7.11 (1 H, dd, *J* 8.1 and 1.8, Ar*H*) and 7.21 (1 H, d, *J* 3.8, Ar*H*); δ_C(90 MHz; $CDC1_3$) 25.3 (CH_2), 26.5 (CH_2), 101.8 (CH_2, OCH_2O), 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, *C*O); *m/z* (EI) 315.0883 (M^+, $C_{17}H_{17}NO_3S$ requires 315.0929), 285 (76%), 201 (91), 173 (60), 143(46), 115 (100) and 100 (14). **Piperine** (**144**): δ_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_2O), 6.44 (1 H, d, *J* 14.7, OCC*H*), 6.76 (1 H, dd, *J* 15.0 and 8.5, OCCHCHC*H*), 6.77 (1 H, d, *J* 15.0, ArC*H*), 6.78 (1 H, d, *J* 8.0, Ar*H*), 6.89 (1 H, dd, *J* 8.0 and 1.6, Ar*H*), 6.98 (1 H, d, *J* 1.6, Ar*H*) and 7.40 (1 H, ddd, *J* 14.7, 8.5 and 1.8, OCCHC*H*). **Isopiperine** (**146**): δ_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_2O), 5.99 (1 H, d, *J* 11.2, OCC*H*), 6.50 (1 H, dd, *J* 11.2 and 11.2, OCCHC*H*), 6.61 (1 H, d, *J* 15.6, ArC*H*), 6.75 (1 H, d, *J* 8.0, Ar*H*), 6.90 (1 H, dd, *J* 8.0 and 1.6, Ar*H*), 7.03 (1 H, d, *J* 1.6, Ar*H*) and 7.42 (1 H, ddd, *J* 11.2, 11.2 and 1.0, OCCHCHC*H*). **Isochavicine** (**147**): δ_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_2O), 6.27 (1 H, dd, *J* 11.8 and 11.8, OCCHCHC*H*), 6.48

(1 H, d, *J* 14.7, OCC*H*), 6.60 (1 H, d, *J* 11.8, ArC*H*), 6.82 (3 H, m, Ar*H*) and 7.75 (1 H, ddd, *J* 14.7, 11.8 and 1.1, OCCHC*H*).

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:Et_2O) afforded recovered piperine **144** (0.99 g, 99%).

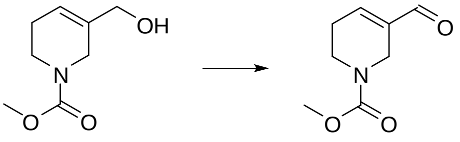
Methyl 3-(hydroxymethyl)-5,6-dihydropyridine-1(2*H*)-carboxylate (**154**)



153 **154**

Alcohol **154** was prepared according to the literature procedure.[101] 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 CH_2Cl_2 (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 $NaBH_4$ (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 Et_2O (3 × 40 mL). The organic layers were combined, dried over $MgSO_4$ 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 $NaHCO_3$ (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 $MgSO_4$, concentrated and purified by column chromatography (Et_2O) to give the allylic alcohol **154** (4.85 g, 31%) as a pale yellow, viscous oil. R_f 0.29 (Et_2O); ν_{max} (neat)/cm^{-1} 3433 (OH), 2998, 2954, 2916, 2859 (CH) and 1703 (CO). The resonances ^{1}H- and ^{13}C-NMR spectra are broad presumably due to a mixture of rotamers δ_H(300 MHz; $CDCl_3$) 1.64-1.98 (1 H, br m, O*H*), 2.15 (2 H, ap. br s, $CH_2C\mathit{H}_2CH$), 3.50 (2 H, br t, *J* 5.7, $NC\mathit{H}_2CH_2$), 3.70 (3 H, s, $OC\mathit{H}_3$), 3.96 (2 H, ap. br s, $NC\mathit{H}_2C$), 4.05 (2 H, ap. br s, $C\mathit{H}_2OH$) and 5.82 (1 H, br s, C*H*=C); δ_C(75 MHz; $CDCl_3$) 24.4 (CH_2, $CH_2\mathit{C}H_2CH$), 40.1 (CH_2, $N\mathit{C}H_2CH_2$), 43.7 (CH_2, $N\mathit{C}H_2C$), 52.5 (CH_3, $O\mathit{C}H_3$), 64.6 (CH_2, $\mathit{C}H_2OH$), 120.8 and 121.5 (CH, C=*C*H), 135.0 and 135.3 (C, *C*=CH) and 156.1 (C, *C*O); *m/z* (EI) 171.0900 (M^+, $C_8H_{13}NO_3$ 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(2*H*)-carboxylate (**152**)

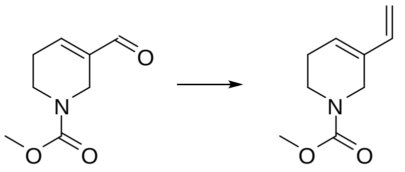


154 **152**

Manganese dioxide (2.99 g, 29.2 mmol) was added to a solution of alcohol **154** (500 mg, 2.92 mmol) in CH_2Cl_2 (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 CH_2Cl_2 (3 × 15 mL) and concentrated under reduced pressure. Purification of the residue by column chromatography (7:3 60-80 pet ether:Et_2O) yielded aldehyde **152** as a white solid (384 mg, 78%) followed by alcohol **154** (100 mg, 20%). R_f 0.52 (Et_2O); mp 81-83 °C; found: C, 57.1; H, 6.7; N, 8.35. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%;

ν_{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 δ_H(300 MHz; CDCl$_3$) 2.45 (2 H, ap. br s, CH$_2$C*H*$_2$CH), 3.58 (2 H, ap. br s, NC*H*$_2$CH$_2$), 3.70 (3 H, s, OC*H*$_3$), 4.13 (2 H, br s, NC*H*$_2$C), 6.92 (1 H, ap. br s, C*H*=C) and 9.42 (1 H, s, C*H*O); δ_C(75 MHz; CDCl$_3$) 26.0 (CH$_2$, CH$_2$*C*H$_2$CH), 39.8 (CH$_2$, N*C*H$_2$CH$_2$), 40.9 (CH$_2$, N*C*H$_2$C), 52.7 (CH$_3$, O*C*H$_3$), 138.8 (C, *C*=CH), 147.3 and 147.8 (CH, C=*C*H), 156.0 (C, *C*O) and 191.6 (C, *C*HO); *m/z* (EI) 169.0740 (M$^+$, $C_8H_{11}NO_3$ 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**)

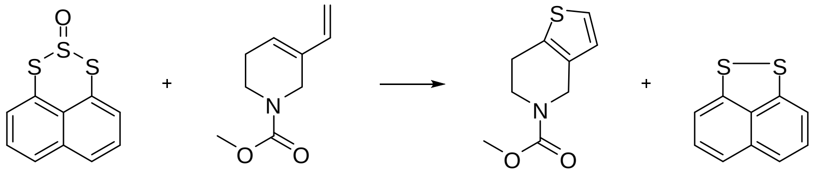


152 **151**

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 × 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); ν_{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 δ_H(400 MHz; CDCl$_3$) 2.21 (2 H, ap. br s, CH$_2$C*H*$_2$CH), 3.51 (2 H, ap. br s, NC*H*$_2$CH$_2$), 3.70 (3 H, s, OC*H*$_3$), 4.06 (2 H, br s, NC*H*$_2$C), 4.95 (1 H, d, *J* 11.0, CCH=C*H*$_2$), 4.19-5.13 (1 H, br m, CCH=C*H*$_2$), 5.83 (1 H, ap. br s, C=C*H*) and 6.27 (1 H, dd, *J* 17.8 and 11.0, CC*H*=CH$_2$); δ_C(75 MHz; CDCl$_3$)

25.2 ($\mathrm{CH_2}$, $\mathrm{CH_2}\mathit{C}\mathrm{H_2CH}$), 40.3 ($\mathrm{CH_2}$, $\mathrm{N}\mathit{C}\mathrm{H_2CH_2}$), 42.7 ($\mathrm{CH_2}$, $\mathrm{N}\mathit{C}\mathrm{H_2C}$), 52.5 ($\mathrm{CH_3}$, $\mathrm{O}\mathit{C}\mathrm{H_3}$), 110.9 and 111.2 ($\mathrm{CH_2}$, $\mathrm{C{=}}\mathit{C}\mathrm{H_2}$), 126.5 and 127.2 (CH, C=*C*H), 133.1 and 133.5 (C, *C*=CH), 136.7 (CH, $\mathrm{C}\mathit{C}\mathrm{H{=}CH_2}$) and 156.0 (C, *C*O); *m/z* (EI) 167.0954 ($\mathrm{M^+}$, $\mathrm{C_9H_{13}NO_2}$ requires 167.0946), 152 (64%), 136 (6), 108 (14), 91 (9), 79 (100), 67 (7) and 53 (13).

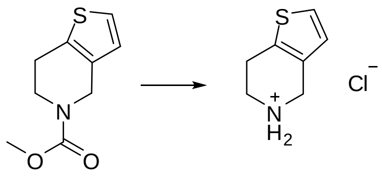
6,7-Dihydro-4*H*-thieno[3,2-*c*]pyridine-5-carboxylic acid methyl ester (**149**)



49 **151** **149** **50**

A solution of diene **151** (100 mg, 0.599 mmol) and 1,2,3-trithiaphenalene 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:$\mathrm{Et_2O}$) afforded diene **151** (25.0 mg, 25%) followed by thiophene **149** (86.0 mg, 73%) as a clear oil. R_f 0.10 (70:30 60-80 pet ether:$\mathrm{Et_2O}$); ν_{max} (neat)/$\mathrm{cm^{-1}}$ 2993, 2953, 2847 and 1701 (CO). The ^{1}H- and ^{13}C-NMR spectra are broad presumably due to a mixture of rotamers δ_{H}(300 MHz; $\mathrm{CDCl_3}$) 2.86 (2 H, ap. br s, $\mathrm{CH_2C}\mathit{H}_2\mathrm{C}$), 3.66-3.85 (5 H, m, $\mathrm{OC}\mathit{H}_3$ and $\mathrm{NC}\mathit{H}_2\mathrm{CH_2}$), 4.55 (2 H, br s, $\mathrm{NC}\mathit{H}_2\mathrm{C}$), 6.78 (1 H, ap. br s, SCHC*H*) and 7.12 (1 H, d, *J* 5.1, SC*H*CH); δ_{C}(75 MHz; $\mathrm{CDCl_3}$) 24.6 and 24.9 ($\mathrm{CH_2}$, $\mathrm{CH_2}\mathit{C}\mathrm{H_2CH}$), 41.5 ($\mathrm{CH_2}$, $\mathrm{N}\mathit{C}\mathrm{H_2C}$), 44.0 ($\mathrm{CH_2}$, $\mathrm{N}\mathit{C}\mathrm{H_2CH_2}$), 52.5 ($\mathrm{CH_3}$, $\mathrm{O}\mathit{C}\mathrm{H_3}$), 123.0 (CH, S*C*H), 124.5 and 124.7 (CH, SCH*C*H), 131.6 and 131.9 (C, S*C*C), 132.7 and 133.2 (C, SC*C*) and 156.0 (C, *C*O); *m/z* (EI) 197.0503 ($\mathrm{M^+}$, $\mathrm{C_9H_{11}NO_2S}$ requires 197.0511), 182 (53%), 166 (6), 138 (15), 110 (100), 84 (6) and 66 (8).

4,5,6,7-Tetrahydro-thieno[3,2-*c*]pyridin-5-ium chloride (**155**)

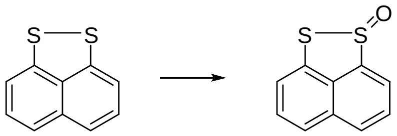


149 **155**

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 Et_2O (3 × 5 mL), dried over Na_2SO_4 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 Et_2O (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); ν_{max} (KBr)/cm^{-1} 2933, 2778, 2706 ($R_2NH_2^+$), 2652, 2615, 2092, 2043, 1933 and 1158; δ_H(300 MHz; D_2O) 3.13 (2 H, t, *J* 6.0, NCH_2CH_2), 3.53 (2 H, t, *J* 6.1, NCH_2CH_2), 4.28 (2 H, s, NCH_2C), 6.88 (1 H, d, *J* 5.2, SCHC*H*) and 7.34 (1 H, d, *J* 5.2, SC*H*CH); δ_C(75 MHz, D_2O) 23.9 (CH_2, NCH_2CH_2), 44.5 (CH_2, NCH_2C), 45.7 (CH_2, NCH_2CH_2), 127.5 (CH, S*C*HCH), 127.6 (CH, SCH*C*H), 129.6 (C, S*C*C) and 134.2 (C, SC*C*); *m/z* (EI) 139.0449 ([M - HCl]$^+$, C_7H_9NS requires 139.0456), 110 (100%), 81 (7), 69 (13), 66 (7), 57 (5) and 43 (5).

Experimental for Chapter Two

Naphtho[1,8-*cd*][l,2]dithiole 1-oxide (**107**)



50 **107**

Using *m*CPBA:

Monoxide **107** was prepared according to the literature procedure.[137] A solution of *m*CPBA (77% w/w, 5.16 g, 23.1 mmol) in CH_2Cl_2 (120 mL) was added dropwise to a stirred solution of naphtho[1,8-*cd*][1,2]dithiole (**50**) (2.96 g, 15.4 mmol) in CH_2Cl_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_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and purified by column chromatography (6:4 hexane:Et_2O) to yield monoxide **107** (3.15 g, 99%) as a yellow solid. R_f 0.29 (6:4 hexane:Et_2O); mp 87-89 °C; ν_{max} (KBr)/cm^{-1} 2361, 1486, 1073 (SO) and 1054; δ_H(300 MHz; $CDCl_3$) 7.60-7.69 (2 H, m, Ar*H*), 7.80-7.85 (2 H, m, Ar*H*), 8.16 (1 H, d, *J* 8.1, Ar*H*) and 8.21 (1 H, d, *J* 7.3, Ar*H*); δ_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^+, $C_{10}H_6OS_2$ requires 205.9860), 190 (14%), 177 (46), 158 (11), 145 (8), 134 (17), 114 (23), 102 (6), 88 (5) and 68 (7).

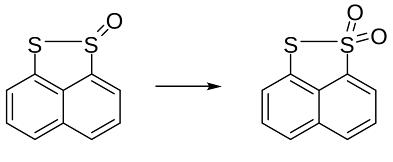
Literature Data:[137, 259] mp 87-89 °C; ν_{max} (KBr)/cm^{-1} 1475, 1390, 1200, 1070 (SO), 800 and 750; δ_H(400 MHz; $CDCl_3$) 7.60 (1 H, dd, *J* 8 and <1), 7.65 (1 H, t, *J* 8) 7.80 (1 H, t, *J* 8), 7.82 (1 H, dd, *J* 8 and <1), 8.14 (1 H, dd, *J* 8 and <1) and 8.19 (1 H, dd, *J* 8 and <1); δ_C(100 MHz, $CDCl_3$)[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^+, $C_{10}H_6OS_2$ requires 205.986), 190 and 158.

[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:Et_2O) to yield monoxide **107** (78.0 mg, 72%) as a yellow solid.

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



107 **63**

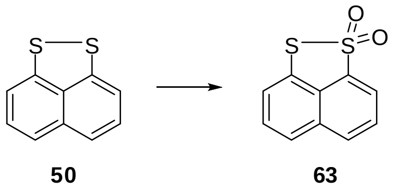
Using *m*CPBA:

Thisulfonate **63** was prepared by modification of the literature procedure.[144] A solution of *m*CPBA (63.0 mg, 0.37 mmol) in CH_2Cl_2 (2.73 mL) was added dropwise to a stirred solution of monoxide **107** (72.0 mg, 0.35 mmol) in CH_2Cl_2 (1.00 mL) at 0 °C over 30 min. The mixture was stirred for 14 h at room temperature, washed with 5% $NaHCO_3$ solution (10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and purified by column chromatography (8:2 CH_2Cl_2:hexane) to yield dioxide **63** (66.0 mg, 85%) as a white solid. R_f 0.61 (8:2 CH_2Cl_2:hexane); mp 147-149 °C; found: C, 54.1; H, 2.5. $C_{10}H_6O_2S_2$ requires C, 54.0; H, 2.7%; ν_{max} (KBr)/cm^{-1} 1487, 1310 (SO_2), 1203, 1165 and 1129 (SO_2); δ_H(300 MHz; $CDCl_3$) 7.51 (1 H, d, *J* 7.3, Ar*H*), 7.66 (1 H, t, *J* 7.9, Ar*H*), 7.77-7.82 (2 H, m, Ar*H*), 8.09 (1 H, d, *J* 7.3, Ar*H*) and 8.17 (1 H, d, *J* 8.1, Ar*H*); δ_C(75 MHz; $CDCl_3$) 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* (EI) 221.9810 (M^+, $C_{10}H_6O_2S_2$ requires 221.9809), 174 (82%), 158 (100), 145 (5), 114 (61), 102 (13), 93 (10), 87 (17), 79 (7), 74 (10), 63 (16) and 50 (5).

Literature data:[40, 260, 261] mp 148-149 °C (methanol); found: C, 54.1; H, 2.8; S, 28.85; O, 14.6. $C_{10}H_6S_2O_2$ 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).

Usinng 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_2Cl_2:hexane) to yield dioxide **63** (80.0 mg, 95%) as a white solid.



Using *m*CPBA:

A solution of *m*CPBA (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_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and purified by column chromatography (8:2 CH_2Cl_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 CH_2Cl_2: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 Na_2.EDTA (0.33 M, 3.99 mL) at room temperature. A mixture of Oxone® (2.10 g, 3.42 mmol) and $NaHCO_3$ (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 $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (8:2 CH_2Cl_2:hexane) afforded dioxide **63** (125 mg, 43%).

Electrochemistry:

Preparation of glassware and solutions for electrochemistry

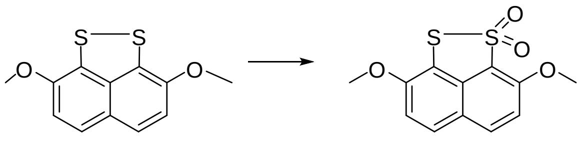
All glassware was cleaned by heating in a 1:1 mixture of concentrated nitric acid and sulfuric acids followed by thorough rinsing with pure water. Glassware was soaked in pure water for several hours and then rinsed and dried overnight in a designated oven. Water used throughout (including solution preparation and rinsing) was purified by a Millipore™ system (resistivity 18.2 MΩ). Electrolytes were made as 0.08 M solutions of Bu_4NClO_4 (Fluka, electrochemical grade) in dry CH_2Cl_2. 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**)



87 **206**

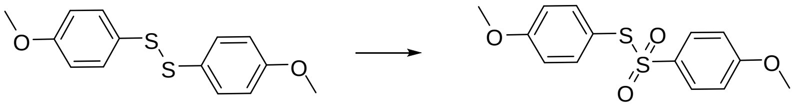
Using *m*CPBA:

A solution of *m*CPBA (314 mg, 1.76 mmol) in Et_2O (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 Et_2O (2.00 mL) at 0 °C over 30 min, which was stirred overnight at room temperature. The mixture was washed with 5% $NaHCO_3$ solution (3 × 5 mL). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (8:2 60-80 pet ether:EtOAc) afforded the *title compound* **206** (204 mg, 90%) as a yellow solid. R_f 0.66 (EtOAc); mp 151-153 °C; ν_{max} (KBr)/cm^{-1} 2938, 2936, 1619, 1505, 1344 (SO_2), 1267, 1171 (SO_2) and 1050; δ_H(300 MHz; $CDCl_3$) 3.99 (3 H, s, OCH_3), 4.08 (3 H, s, OCH_3), 7.47 (1 H, d, *J* 8.9, Ar*H*), 7.55 (1 H, d, *J* 8.9, Ar*H*), 7.96 (1 H, d, *J* 8.9, Ar*H*) and 7.98 (1 H, d, *J* 8.9, Ar*H*); δ_H(300 MHz; acetone-d$_6$) 4.08 (3 H, s, OC*H*$_3$), 4.17 (3 H, s, OC*H*$_3$), 7.47 (1 H, d, *J* 8.9, Ar*H*), 7.55 (1 H, d, *J* 8.9, Ar*H*), 7.96 (1 H, d, *J* 8.9, Ar*H*) and 8.28 (1 H, d, *J* 8.9, Ar*H*); δ_C(75 MHz; CDCl$_3$) 56.5 (CH$_3$, O*C*H$_3$), 56.7 (CH$_3$, O*C*H$_3$), 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 adddition 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**)



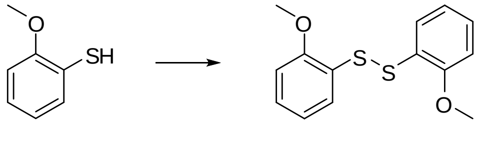
208 **213**

Using *m*CPBA:

A solution of *m*CPBA (52.0 mg, 0.359 mmol) in CH$_2$Cl$_2$ (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$_2$Cl$_2$ (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$_2$Cl$_2$ (3 × 5 mL). The combined organic layers were dried over Na$_2$SO$_4$, concentrated under reduced pressure and the crude mixture was purified by column chromatography (9:1 60-80 pet ether:Et$_2$O) 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. R_f 0.21 (8:2 60-80 pet ether:EtOAc); mp 84-86 °C; ν_{max} (KBr)/cm^{-1} 1590, 1494, 1322 (SO$_2$), 1295, 1261 and 1183 (SO$_2$); δ_H(300 MHz; CDCl$_3$) 3.82 (3 H, s, OC*H*$_3$), 3.85 (3 H, s, OC*H*$_3$), 6.82-6.88 (4 H, m, Ar*H*), 7.24-7.27 (2 H, m, Ar*H*) and 7.47-7.50 (2 H, m, Ar*H*); δ_C(100 MHz, CDCl$_3$) 55.4 (CH$_3$, O*C*H$_3$), 55.7 (CH$_3$, O*C*H$_3$), 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$^+$, $C_{14}H_{14}O_4S_2$ 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. $C_{14}H_{14}O_4S_2$ requires C, 54.2; H, 3.2; S, 20.7%; ν_{max} (KBr)/cm^{-1} 1330 (SO$_2$) and 1142 (SO$_2$); δ_H(400 MHz; CDCl$_3$) 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); δ_C(100 MHz, CDCl$_3$) 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**)



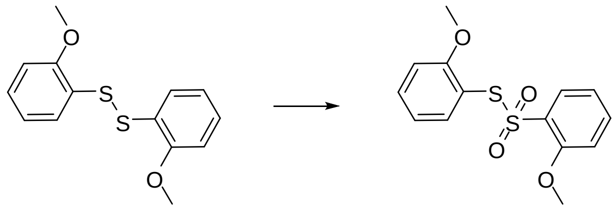
214 **209**

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 × 5 mL), sodium thiosulfate solution (3 × 5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure to afford disulfide **209** (94 mg, 95%). R_f 0.28 (98:2 60-80 pet ether:EtOAc); mp 118-119 °C; ν_{max} (KBr)/cm^{-1} 2966, 2939, 2837, 1578, 1473, 1237 and 1021; δ_H(300 MHz; CDCl$_3$) 3.90 (6 H, s, OC*H*$_3$), 6.84-6.94 (4 H, m, Ar*H*), 7.16-7.22 (2 H, m, Ar*H*) and 7.52 (2 H, dd, *J* 7.8 and 1.5, Ar*H*); δ_C(75 MHz, CDCl$_3$)

55.8 (CH_3, OCH$_3$), 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; ν_{max} ($CHCl_3$)/cm^{-1} 1577, 1471, 1270, 1236, 1021 and 729; δ_H(200 MHz; $CDCl_3$) 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, $CDCl_3$) 56.38, 111.05, 121.83, 128.15, 128.28 and 157.12.

S-2-Methoxyphenyl 2-methoxybenzenesulfonothioate (**215**)

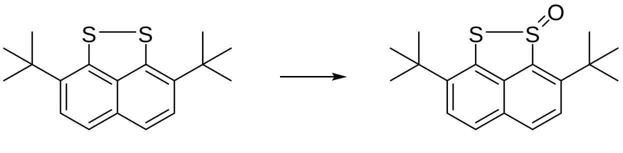


209 **215**

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; ν_{max} (KBr)/cm^{-1} 1585, 1478, 1433, 1320 (SO_2), 1279, 1250, 1145 (SO_2) and 1126; δ_H(300 MHz; $CDCl_3$) 3.45 (3 H, s, OCH_3), 4.03 (3 H, s, OCH_3), 6.76 (1 H, d, *J* 8.3, Ar*H*), 6.85-6.96 (2 H, m, Ar*H*), 7.08 (1 H, d, *J* 8.3, Ar*H*) and 7.38-7.96 (4 H, m, Ar*H*); δ_C(100 MHz, $CDCl_3$) 55.3 (CH_3, OCH$_3$), 56.3 (CH_3, OCH$_3$), 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]$^+$, $C_{14}H_{14}O_4S_2Na$ requires 333.0231), 331.1 (100%).

Literature data:[265] mp 110 °C (ethanol).

3,8-Di-*tert*-butylnaphtho[1,8-*cd*][1,2]dithiole 1-oxide (**216**)



65 **216**

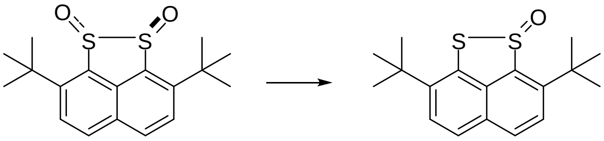
Using *m*CPBA:

To an ice-cold solution of 3,8-di-*tert*-butylnaphtho[1,8-*cd*][1,2]dithiole (**65**) (100 mg, 0.331 mmol) in CH_2Cl_2 (2.60 mL) was added a solution of *m*CPBA (63.0 mg, 0.364 mmol) in CH_2Cl_2 (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% $NaHCO_3$ solution (3 × 5 mL) and extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (CH_2Cl_2) yielded the *title compound* **216** (84.0 mg, 80%) as a white solid. R_f 0.50 (CH_2Cl_2); mp 146-148 °C (EtOAc); ν_{max} (KBr)/cm^{-1} 2963, 1365 and 1071 (SO); δ_H(300 MHz; $CDCl_3$) 1.58 (9 H, s, $C(CH_3)_3$), 1.73 (9 H, s, $C(CH_3)_3$), 7.72 (1 H, d, *J* 8.6, Ar*H*), 7.76 (1 H, d, *J* 8.7, Ar*H*), 7.81 (1 H, d, *J* 8.6, Ar*H*) and 8.01 (1 H, d, *J* 8.6, Ar*H*); δ_C(75 MHz; $CDCl_3$) 30.4 (CH_3), 33.2 (CH_3), 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^+, $C_{18}H_{22}OS_2$ 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_2Cl_2) to yield the *title compound* **216** (53.0 mg, 68%) as a white solid.

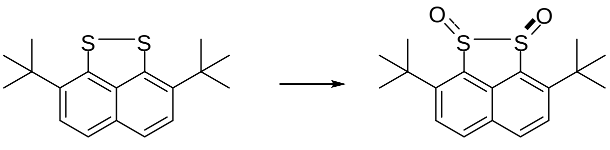
Reduction of *vic*-disulfoxide **217** with 4 M HCl in dioxane



217 **216**

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_2Cl_2 (3 × 3 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (CH_2Cl_2) yielded thiosulfinate **216** (18.0 mg, 94%) as a white solid.

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



65 **217**

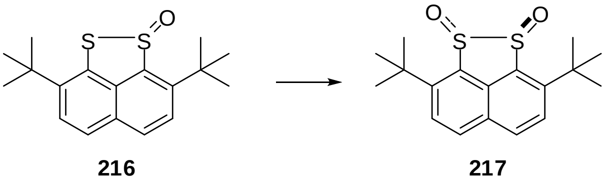
Using *m*CPBA:

To an ice-cold solution of 3,8-di-*tert*-butylnaphtho[1,8-*cd*][1,2]dithiole (**65**) (100 mg, 0.331 mmol) in CH_2Cl_2 (2.59 mL) was added a solution of *m*CPBA (156 mg, 0.694 mmol) in CH_2Cl_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_2Cl_2 (3 × 3 mL). The combined organic layers were dried over Na_2SO_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); λ_{max} (MeCN)/nm 316 (ε/dm^3 mol^{-1} cm^{-1}

74 900) and 231 (67 800); ν_{max} (KBr)/cm^{-1} 2959, 1495, 1367, 1117, 1067 and 1040 (SO); δ_H(300 MHz; CDCl$_3$) 1.70 (18 H, s, C(C*H*$_3$)$_3$), 7.81 (2 H, d, *J* 8.6, Ar*H*) and 8.05 (2 H, d, *J* 8.6, Ar*H*); δ_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$^+$, $C_{18}H_{22}O_2S_2$ 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.



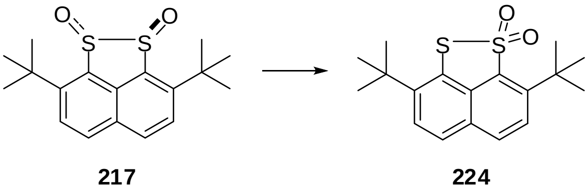
Using *m*CPBA:

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.

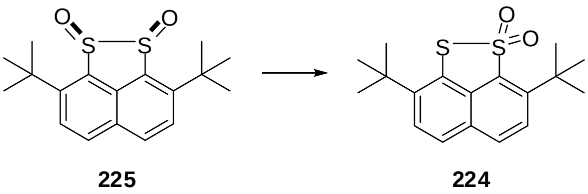
Using DMD:

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*-butylnaphtho[1,8-*cd*][1,2]dithiole 1,1-dioxide (**224**)

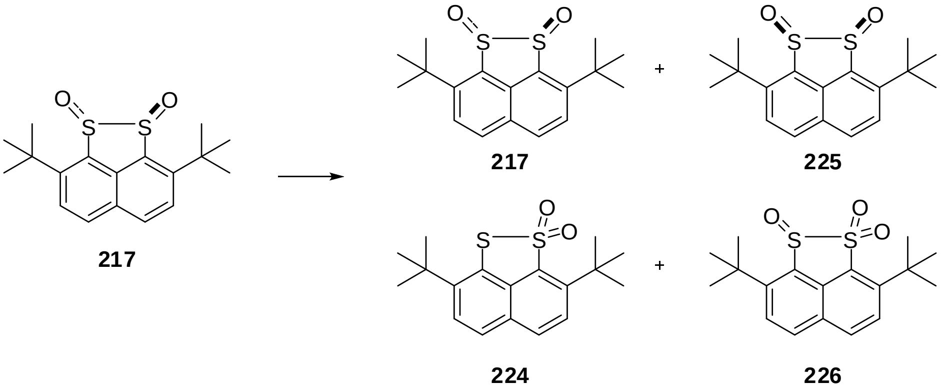


A solution of *trans vic*-disulfoxide **217** (60.0 mg, 0.180 mmol) in mesitylene (18.0 mL) was degassed for 15 min. The mixture was refluxed for 38 h. The solvent was evaporated under reduced pressure and purification by column chromatography (9:1 60-80 pet ether:EtOAc) afforded the *title compound* **224** (55.0 mg, 92%) as a white solid. R$_f$ 0.25 (8:2 60-80 pet ether:CH_2Cl_2); mp 139-140 °C; λ_{max} (MeCN)/nm 249 (ε/dm^3 mol^{-1} cm^{-1} 28 200) and 217 (21 700); ν_{max} (KBr)/cm^{-1} 2964, 1313 (SO_2) and 1138 (SO_2); δ_H(300 MHz; $CDCl_3$) 1.48 (9 H, s, C(C*H*$_3$)$_3$), 1.69 (9 H, s, C(C*H*$_3$)$_3$), 7.68 (1 H, d, *J* 8.9, Ar*H*), 7.72 (1 H, d, *J* 8.9, Ar*H*), 7.84 (1 H, d, *J* 8.6, Ar*H*) and 8.00 (1 H, d, *J* 8.6, Ar*H*); δ_C(75 MHz; $CDCl_3$) 29.8 (CH_3, C*C*H$_3$), 31.9 (CH_3, C*C*H$_3$), 36.3 (C, *C*CH$_3$), 37.5 (C, *C*CH$_3$), 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]$^+$, $C_{18}H_{22}O_2S_2Na$ 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**

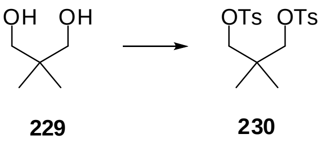


A solution of *trans vic*-disulfoxide **217** (100 mg, 0.299 mmol) in chlorobenzene (30.0 mL) was degassed for 15 min. The mixture was heated at 108 °C for 38 h. The solvent was evaporated under reduced pressure and purification by column chromatography (95:5 60-80 pet ether:EtOAc) afforded sulfinyl 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*-butylnaphtho[1,8-*cd*][1,2]dithiole 1,2-dioxide (**225**) (10.0 mg, 10%) as a white solid. **225**: R_f 0.15 (8:2 60-80 pet ether:EtOAc); mp 172-174 °C; λ_{max} (MeCN)/nm 301 (ε/dm^3 mol^{-1} cm^{-1} 1 200) and 228 (32 400); ν_{max} (KBr)/cm^{-1} 2961, 2925, 1116, 1099, 1068 and 1042 (SO); δ_H(300 MHz; CDCl$_3$) 1.76 (18 H, s, $C(C\mathit{H}_3)_3$), 7.81 (2 H, d, *J* 8.7, Ar*H*) and 7.98 (2 H, d, *J* 8.7, Ar*H*); δ_C(75 MHz; CDCl$_3$) 33.0 (CH$_3$), 38.3 (C), 127.3 (CH), 131.7 (CH), 131.8 (C), 135.9 (C), 137.4 (C) and 154.9 (C); *m/z* (EI) 334.1066 (M^+, $C_{18}H_{22}O_2S_2$ 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**: R_f 0.48 (7:3 60-80 pet ether:EtOAc); mp 199-201 °C (EtOAc); ν_{max} (KBr)/cm^{-1} 2964, 1319 (SO_2), 1141, 1131 and 1074 (SO); δ_H(300 MHz; $CDCl_3$) 1.71 (9 H, s, $C(CH_3)_3$), 1.73 (9 H, s, $C(CH_3)_3$), 7.86 (1 H, d, *J* 8.9, Ar*H*), 7.90 (1 H, d, *J* 8.7, Ar*H*), 8.07 (1 H, d, *J* 8.9, Ar*H*) and 8.08 (1 H, d, *J* 8.7, Ar*H*); δ_C(100 MHz; $CDCl_3$) 31.6 (CH_3), 33.4 (CH_3), 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 ($[M + Na]^+$, $C_{18}H_{22}O_3 S_2Na$ 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 $CDCl_3$ (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**)

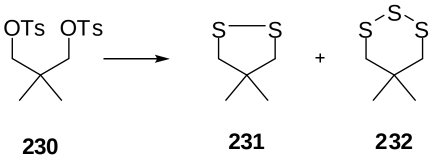


Ditosylate **230** was prepared according to the literature procedure.[163] A solution of 2,2-dimethylpropane-1,3-diol (**229**) (6.24 g, 60.0 mmol) in pyridine (30.0 mL) was added to an ice-cold solution of *p*-TsCl (25.2 g, 132 mmol) in pyridine (100 mL) over 45 min. The solution was stirred for 1 h warming to room temperature and stored in the freezer (-20 °C) overnight. The mixture was extracted with $CHCl_3$ (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 Na_2SO_4 and concentrated under reduced pressure to yield ditosylate **230** (21.8 g, 88%) as a white solid. R_f 0.23

(60-80 pet ether); ν_{max} (KBr)/cm^{-1} 2982, 1598, 1359 (OSO_2), 1177 (OSO_2) and 1096; δ_H(300 MHz; $CDCl_3$) 0.86 (6 H, s, CH_2CCH_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*); δ_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, δ_H(200 MHz; $CDCl_3$) 0.88 (6 H, s, CH_2CCH_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^+, $C_{19}H_{24}O_6S_2$ requires 412.1014).

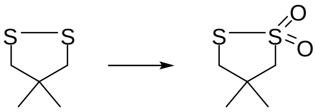
4,4-Dimethyl[1,2]dithiolane (**231**) and 5,5-dimethyl[1,2,3]trithiane (**232**)



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); ν_{max} (neat)/cm^{-1} 2959, 2924, 2867, 1463, 1382 and 1364; δ_H(300 MHz; $CDCl_3$) 1.25 (6 H, s, $C(CH_3)_2$) and 2.88 (4 H, s, SCH_2C); δ_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_2C); *m/z* (EI) 134.0230 (M^+, $C_5H_{10}S_2$ 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); ν_{max} (neat)/cm^{-1} 2954, 2933, 2892, 2864, 1466, 1380 and 1364; δ_H(300 MHz; $CDCl_3$) 1.04 (3 H, br s, $C(CH_3)$), 1.25 (3 H, br s, C(CH_3)), 2.55 (2 H, br s, SCH_2C) and 3.19 (2 H, br s, SCH_2C); δ_C(75 MHz, CDCl$_3$) 26.5 (CH$_3$), 46.2 (CH$_2$) and 56.2 (C); *m/z* (EI) 165.9951 (M$^+$, $C_5H_{10}S_3$ requires 165.9945), 133 (6%), 110 (22), 101 (24), 87 (10), 74 (6), 69 (100), 55 (83) and 45 (57).

Literature data:[267] **231**: ν_{max} (neat)/cm^{-1} 2950, 2870, 1385, 1365, 970 and 895; δ_H(CDCl$_3$) 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**)



231 **233**

Using hν/O$_2$:

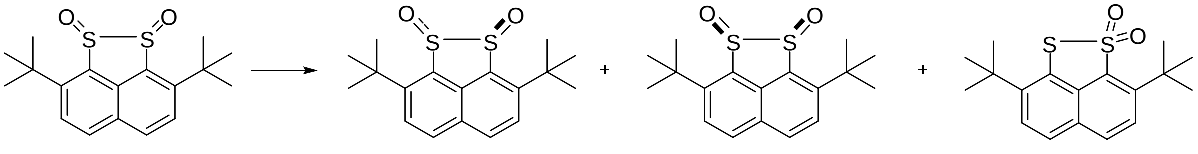
1,1-Dioxide **233** was prepared by a literature procedure.[161] O$_2$ was bubbled into a solution of disulfide **231** (126 mg, 0.940 mmol) and methylene blue (2.40 mg, 0.006 mmol) in acetone (9.40 mL). The solution was irradiated at room temperature for 2 h. The solvent was removed under reduced pressure. 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. R_f 0.35 (8:2 60-80 pet ether:EtOAc); mp 45-47 °C; ν_{max} (KBr)/cm^{-1} 2972, 2936, 1467, 1307 (SO$_2$), 1229, 1166 and 1123 (SO$_2$); δ_H(300 MHz; CDCl$_3$) 1.40 (6 H, s, C(CH_3)), 3.29 (2 H, s, SCH_2C) and 3.45 (2 H, s, O$_2$SCH_2C); δ_C(75 MHz, CDCl$_3$) 27.5 (CH$_3$, 2 × C(*C*H$_3$)$_2$), 40.2 (C, *C*(CH$_3$)$_2$), 49.4 (CH$_2$, S*C*H$_2$C) and 70.0 (CH$_2$, O$_2$S*C*H$_2$C); *m/z* (ESI) 166.0128 (M$^+$, $C_5H_{10}O_2S_2$ requires 166.0122), 69 (15) and 56 (100).

Literature data:[268] mp 49 °C.

Using *m*CPBA:

A solution of *m*CPBA (540 mg, 3.13 mmol) in CH$_2$Cl$_2$ (31.3 mL) was added dropwise to a stirred solution of disulfide **231** (200 mg, 1.49 mmol) in CH$_2$Cl$_2$ (14.9 mL) at room temperature over 20 min. The mixture was stirred for 14 h at room temperature, washed with 5% $NaHCO_3$ solution (10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, 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**



217 **225** **224**

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 $CDCl_3$.

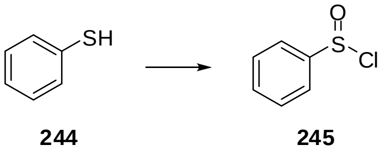
Typical procedure for the attempted spin trapping of *vic*-disulfoxide photochemically:

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*-butylnaphtho[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:

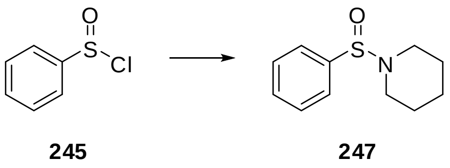
A solution of spin trap (0.149 mmol) and *vic*-disulfoxide **217** or **225** (20.0 mg, 0.059 mmol) in solvent (6.00 mL) was degassed for 15 min. The sample was heated at reflux for 32 h. The solvent was evaporated under reduced pressure and purification by column chromatography (95:5 60-80 pet ether:EtOAc) 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**)



Sulfinyl chloride was prepared by a literature procedure.[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**).

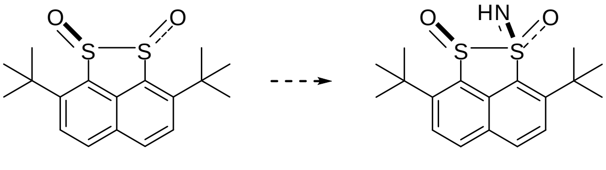
1-(Phenylsulfinyl)piperidine (**247**)



Compound **247** was prepared according to the literature procedure.[152] The crude sulfinyl chloride **245** (200 mg, 1.25 mmol) was dissolved in Et_2O (0.65 mL) and added to a solution of piperidine (0.25 mL, 2.5 mmol) in Et_2O (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 Et_2O (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. R_f 0.33 (1:1 hexane:Et_2O); δ_H(300 MHz; $CDCl_3$) 1.52-1.62 (6 H, m, 2 × NCH_2CH_2 and $NCH_2CH_2CH_2$), 2.91-2.98 (2 H, m, NCH_2), 3.08-3.13 (2 H, m, NCH_2), 7.46-7.53 (3 H, m, Ar*H*) and 7.65-7.67 (2 H, m, Ar*H*); δ_C(75 MHz; $CDCl_3$) 23.8 (CH_2), 26.1 (CH_2), 46.9 (CH_2, NCH_2), 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:[152, 269] mp 84-85 °C, ν_{max} (KBr)/cm^{-1} 2950, 2870, 1435, 1086, 1050, 905, 952 and 868; δ_H(400 MHz; $CDCl_3$) 1.41-1.53 (6 H, m, 2 × NCH_2CH_2 and $NCH_2CH_2CH_2$), 2.83-2.87 (2 H, m, NCH_2), 2.89-3.04 (2 H, m, NCH_2), 7.37-7.42 (3 H, m, Ar*H*) and 7.56-7.59 (2 H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$) 23.8 (CH_2), 26.1 (CH_2), 46.9 (CH_2, NCH_2), 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**



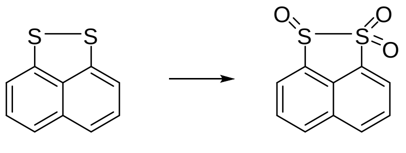
217 **248**

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 $CHCl_3$ (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 $CHCl_3$ (3 × 5 mL). The combined organic layers were dried over

Na_2SO_4 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

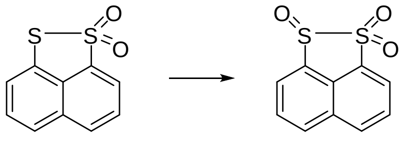
Naphtho[l,8-*cd*][l,2]dithiole l,l,2-trioxide (**228**)



50 **228**

A solution of *m*CPBA (3.18 g, 18.4 mmol) in CH_2Cl_2 (51.0 mL) was added dropwise to a solution of disulfide **50** (1.00 g, 5.26 mmol) in CH_2Cl_2 (41.1 mL) over 30 min. The mixture was stirred for 24 h and then washed with 5% $NaHCO_3$ 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 CH_2Cl_2:hexane to give the pure sulfinyl sulfone **228** (560 mg, 45%) as a white solid. R_f 0.61 (8:2 CH_2Cl_2:hexane); mp 148-150 °C (CH_2Cl_2:hexane); ν_{max} (KBr)/cm^{-1} 3077, 1489, 1404, 1345, 1313 (SO_2), 1182, 1152 (SO_2), 1134 (SO_2) and 1083 (SO); δ_H(300 MHz; $CDCl_3$) 7.85-7.92 (2 H, m, Ar*H*), 8.18 (1 H, d, *J* 7.3, Ar*H*) and 8.25-8.28 (3 H, m, Ar*H*); δ_C(75 MHz; $CDCl_3$) 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 ($[M + Na]^+$, $C_{10}H_6NO_3S_2Na$ requires 260.9656), 260.9 (100%).

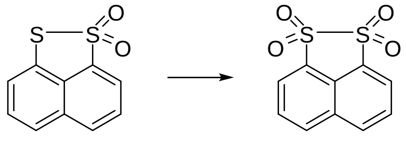
Literature data:[138] mp 168-169 °C; ν_{max} (KBr)/cm^{-1} 1330, 1166, 1136 and 1081.



63 **228**

Sulfinyl sulfone was prepared according to the literature procedure.[138] Thiosulfonate **63** (160 mg, 0.721 mmol) was dissolved in dioxane (4.34 mL) and a solution of H_2O_2 (30%, 0.097 mL, 0.721 mmol) and NaOH (58.0 mg, 1.44 mmol) in water (2.88 mL) was added. The mixture was stirred for 15 min and evaporated to dryness. The resulting disodium salt was dissolved in H_2O (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_2Cl_2:hexane to give sulfinyl sulfone **228** (78.0 mg, 45%).

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

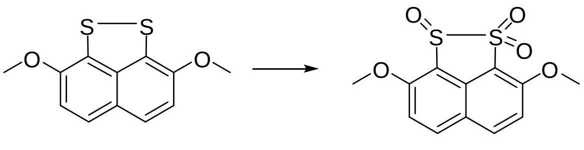


63 **294**

Bissulfone **294** was prepared according to the literature procedure.[230] 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_2Cl_2:60-80 pet ether) to afford bissulfone **294** (58.0 mg, 51%) as a white solid. R_f 0.70 (CH_2Cl_2), ν_{max} (KBr)/cm^{-1} 2924, 2854, 1460, 1350 (SO_2), 1181 (SO_2), 1153 and 1120 (SO_2); δ_H(300 MHz; $CDCl_3$) 7.93 (2 H, t, *J* 7.9, Ar*H*), 8.20 (2 H, d, *J* 7.3, Ar*H*) and 8.31 (2 H, d, *J* 8.4, Ar*H*); δ_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/z* (ES) 276.9598 ($[M + Na]^+$, $C_{10}H_6$ O_4S_2Na requires 276.9605), 277 (100%).

Literature data:[139] mp >200 °C; found: C, 46.91; H, 2.65. $C_{10}H_6O_4S_2$ requires C, 47.23; H, 2.38%; ν_{max} (KBr)/cm^{-1} 1350 (SO_2), 1180 (SO_2) and 1120 (SO_2).

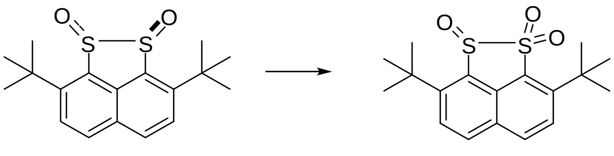
3,8-Dimethoxynaphtho[1,8-*cd*][1,2]dithiole 1,2,2-trioxide (**207**)



87 **207**

A solution of *m*CPBA (214 mg, 1.24 mmol) in CH_2Cl_2 (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 CH_2Cl_2 (3.12 mL) over 10 min at 0 °C and stirred for 16 h at room temperature. The mixture was washed with 5% $NaHCO_3$ solution (3 × 5 mL). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (EtOAc) afforded the *title compound* **207** (49.0 mg, 41%) as a yellow solid. R_f 0.37 (EtOAc); mp 156-158 °C; ν_{max} (KBr)/cm^{-1} 2946, 1616, 1551, 1506, 1462, 1350 (SO_2), 1270, 1159, 1132 (SO_2), 1077 (SO) and 1045; δ_H(300 MHz; $CDCl_3$) 4.14 (3 H, s, OCH_3), 4.15 (3 H, s, OCH_3), 7.27 (1 H, d, *J* 9.2, Ar*H*), 7.30 (1 H, d, *J* 9.4, Ar*H*), 8.06 (1 H, d, *J* 9.0, Ar*H*) and 8.08 (1 H, d, *J* 9.2, Ar*H*); δ_C(75 MHz; $CDCl_3$) 57.0 (CH_3, O*C*H_3), 57.1 (CH_3, O*C*H_3), 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]$^+$, $C_{12}H_{10}O_5S_2Na$ requires 320.9867), 321.0 (100%).

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



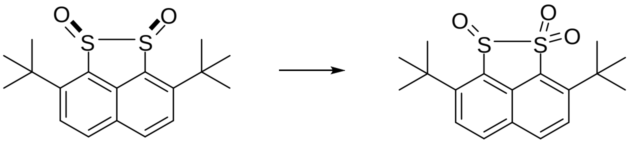
217 **226**

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. R_f 0.48 (7:3 60-80 pet ether:EtOAc); mp 199-201 °C (EtOAc); ν_{max} (KBr)/cm^{-1} 2964, 1319 (SO_2), 1141 (SO_2), 1131 and 1074 (SO); δ_H(300 MHz; $CDCl_3$) 1.71 (9 H, s, $C(CH_3)_3$), 1.73 (9 H, s, $C(CH_3)_3$), 7.86 (1 H, d, *J* 8.9, Ar*H*), 7.90 (1 H, d, *J* 8.7, Ar*H*), 8.07 (1 H, d, *J* 8.9, Ar*H*) and 8.08 (1 H, d, *J* 8.7, Ar*H*); δ_C(100 MHz; $CDCl_3$) 31.6 (CH_3, CCH_3), 33.4 (CH_3, CCH_3), 37.6 (C, CCH_3), 38.6 (C, CCH_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 ($[M + Na]^+$, $C_{18}H_{22}O_3 S_2Na$ requires 373.0908), 373 (100%).

Using *m*CPBA:

A solution of *m*CPBA (28.0 mg, 0.158 mmol) in CH_2Cl_2 (0.44 mL) was added to a solution of *trans vic*-disulfoxide **217** (52.0 mg, 0.150 mmol) in CH_2Cl_2 (1.17 mL) over 10 min. The solution was stirred for 2 h, washed with 5% $NaHCO_3$ solution (3 × 3 mL) and extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried over Na_2SO_4 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.



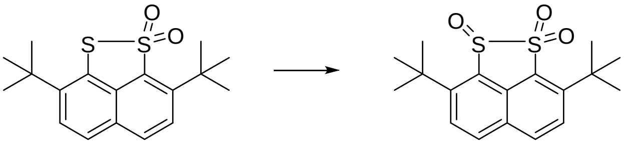
225 **226**

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 *m*CPBA:

A solution of *m*CPBA (19.0 mg, 0.110 mmol) in CH_2Cl_2 (0.30 mL) was added to a solution of *cis vic*-disulfoxide **225** (35.0 mg, 0.105 mmol) in CH_2Cl_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_2Cl_2 (3 × 3 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (8:2 hexane:EtOAc) yielded the *title compound* **226** (28.0 mg, 76%) as a white solid.



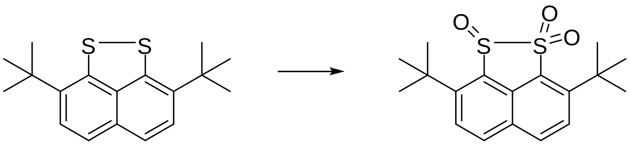
224 **226**

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 *title compound* **226** (48.0 mg, 91%) as a white solid.

Using *m*CPBA:

A solution of *m*CPBA (28.0 mg, 0.165 mmol) in CH_2Cl_2 (0.46 mL) was added to a solution of thiosulfonate **224** (50.0 mg, 0.150 mmol) in CH_2Cl_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_2Cl_2 (3 × 3 mL). The combined organic layers were dried over Na_2SO_4 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.



65 **226**

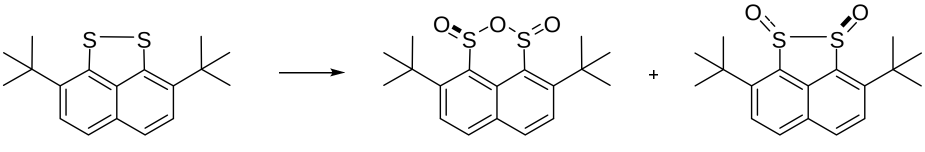
Using DMD:

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 *m*CPBA:

A solution of *m*CPBA (40.0 mg, 0.231 mmol) in CH_2Cl_2 (0.64 mL) was added dropwise to a solution of disulfide **65** (20.0 mg, 0.066 mmol) in CH_2Cl_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_2Cl_2 (3 × 3 mL). The combined organic layers were dried over Na_2SO_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.

trans 4,9-Di-*tert*-butyl-2-oxa-1,3-dithiaphenalene 1,3-dioxide (**295**)



65 **295** **217**

*m*CPBA (5.27 g, 30.6 mmol) was added portionwise over 2 h to disulfide **65** (3.089 g, 10.2 mmol) in CH_2Cl_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_2SO_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; ν_{max} (KBr)/cm^{-1} 2966, 1367 and 1138 (SO); δ_H(300 MHz; CDCl$_3$) 1.68 (18 H, s, C(C*H*$_3$)$_3$), 7.68 (2 H, d, *J* 8.8, Ar*H*) and 7.92 (2 H, d, *J* 8.8, Ar*H*); δ_C(75 MHz; CDCl$_3$) 33.1 (CH$_3$, C*C*H$_3$), 36.8 (C, *C*CH$_3$), 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]$^+$, $C_{18}H_{22}O_3NaS_3$ 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.

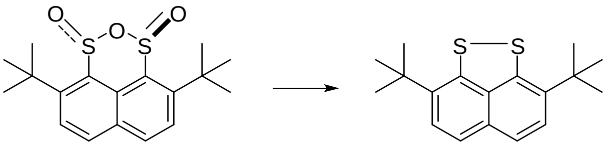
Additives used: *m*CBA (1 equiv.) for 10 h resulted in **217** (96%)

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**)

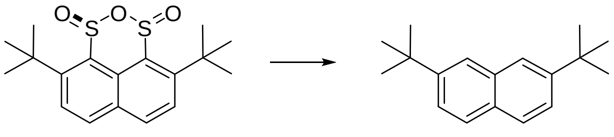


295 **65**

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*-butylnaphthalene (**306**)

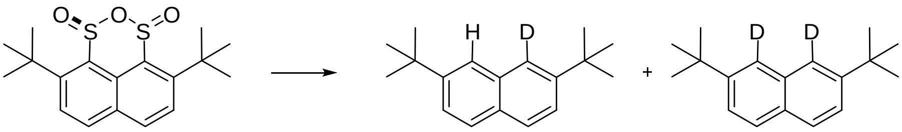


295 **306**

Using 1,4-dioxane/H_2O:

A solution of sulfinic anhydride **295** (13.0 mg, 0.037 mmol) in a 1:1 mixture of 1,4-dioxane:H_2O (0.56 mL:0.56 mL) was heated at 70 °C for 20 h. The mixture was extracted with Et_2O (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*-butylnaphthalene **306** (7.00 mg, 79%) as a white solid. R_f 0.50 (60-80 pet ether); mp 103-105 °C; δ_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, Ar*H*) and 7.73-7.76 (4 H, m, Ar*H*); δ_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).

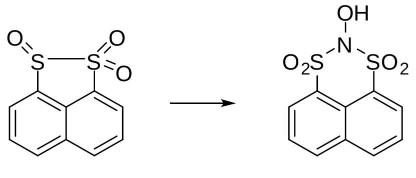
Literature data:[232] mp 103 °C; ν_{max} (KBr)/cm^{-1} 3064, 2990-2840, 1632, 1512, 1472, 1368, 1280, 1210, 904, 840, 632 and 480; δ_H(300 MHz; $CDCl_3$) 1.41 (18 H, s, $C(CH_3)_3$), 7.52 (2 H, dd, *J* 8 and 2, Ar*H*), 7.73 (2 H, d, *J* 8, Ar*H*) and 7.75 (2 H, br s, Ar*H*); δ_C(75 MHz; $CDCl_3$) 28.85 (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_2O:

A solution of sulfinic anhydride **295** (39.0 mg, 0.10 mmol) in a 1:1 mixture of dioxane:D_2O (0.56 mL:0.56 mL) was refluxed for 16 h. The mixture was extracted with Et_2O (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; R_f 0.50 (60-80 pet ether); mp 104-106 °C; ν_{max} (neat)/cm^{-1} 2959, 2965, 1466, 1361 and 847; δ_H(300 MHz; $CDCl_3$) 1.42 (18 H, s, $C(CH_3)_3$), 7.52 (2 H, dd, *J* 8.8 and 1.1, Ar*H*) and 7.73-7.76 (3 H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$) 31.3 (CH_3, $C(CH_3)_3$), 34.8 (CH_3, $C(CH_3)_3$), 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).

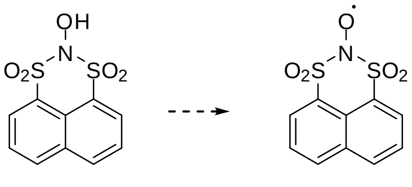
1,1,3,3-Tetraoxo-1*H*,3*H*-1λ^6,3λ^6-dithia-2-azaphenalen-2-ol (**284**)



226 **284**

Naphtho[l,8-*cd*][l,2]dithiole l,l,2-trioxide (**226**) (258 mg, 1.08 mmol) and $NaNO_2$ (75.0 mg, 1.08 mmol) were dissolved in H_2O (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 ºC (EtOAc); R_f 0.33 (7:3 Et_2O:hexane); λ_{max} (MeCN)/nm 298 (ε/dm^3 mol^{-1} cm^{-1} 17 700); ν_{max} (KBr)/cm^{-1} 3535 (OH), 3092 (CH), 2862, 1497, 1380, 1361 (SO_2N), 1220, 1191, 1174 (SO_2N), 1156, 902, 846 (SO_2) and 829; δ_H(300 MHz; CD_3CN, 10^{-1} M) 7.91 (2 H, dd, *J* 8.3 and 7.5, Ar*H*), 8.44 (2 H, dd, *J* 8.5 and 1.0, Ar*H*), 8.49 (2 H, dd, *J* 7.4 and 1.1, Ar*H*) and 9.99 (1 H, s, NO*H*); δ_H(300 MHz; CD_3CN, 10^{-2} M) 7.93 (2 H, dd, *J* 8.3 and 7.4, Ar*H*), 8.47 (2 H, dd, *J* 8.0 and 1.0, Ar*H*), 8.50 (2 H, dd, *J* 7.4 and 1.1, Ar*H*) and 9.85 (1 H, s, NO*H*); δ_H(300 MHz; CD_2Cl_2) 7.90 (2 H, t, *J* 7.8, Ar*H*), 8.37 (2 H, d, *J* 8.4, Ar*H*), 8.49 (2 H, d, *J* 7.4, Ar*H*) and 8.60 (1 H, s, NO*H*); δ_C(100 MHz; CD_3CN) 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]$^+$, $C_{10}H_7NO_5S_2Na$ requires 307.9663), 308 (100%).

Attempted generation of the nitroxide radical **318**



284 **318**

Following a modified literature procedure,[239] NH_4OH (0.053 mL, 0.175 mmol) was added to a stirred solution of hydroxylamine **284** (50.0 mg, 0.175 mmol) and $Cu(OAc)_2.H_2O$ (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%).

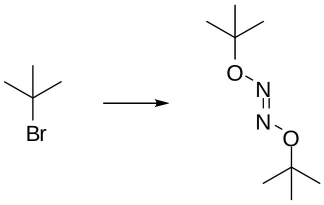
Following a modified literature procedure,[237] MnO_2 (149 mg, 1.71 mmol) was added to a stirred solution of hydroxylamine **284** (100 mg, 0.350 mmol) in $CHCl_3$ (1.49 mL). The reaction was stirred for 4 h at room temperature and then refluxed for a further 8 h. The mixture was allowed to cool to room temperature and then filtered through celite; column chromatography (7:3 Et_2O:hexane) yielded hydroxylamine **284** (92.0 mg, 92%).

Following a modified literature procedure,[238] PbO_2 (47.6 mg, 0.200 mmol) and hydroxylamine **284** (100 mg, 0.350 mmol) was stirred for 4 h in $CHCl_3$ (1.49 mL) at room temperature under an O_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_2O:hexane) yielded hydroxylamine **284** (98.0 mg, 98%).

Following a modified literature procedure,[175] $Ce(NH_4)_4(SO_4)_4.xH_2O$ (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_2O:hexane) yielded hydroxylamine **284** (28.0 mg, 93%).

Following a modified literature procedure,[240] a solution of di-*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_2O:hexane) yielded hydroxylamine **284** (28.0 mg, 93%).

(*E*)-1,2-di-*tert*-butoxydiazene (**327**)

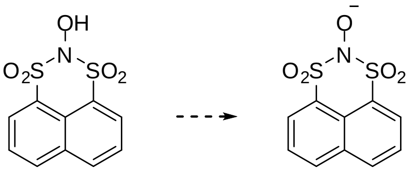


326 **327**

327 was prepared according to the literature procedure.[240] NaN_2O_2 (805 mg, 7.60 mmol) was added over a 5 min period to a mixture of $FeCl_3$ (1.20 g, 7.40 mmol) and *t*-BuBr (8.00 ml, 80.0 mmol) in Et_2O (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 refridgerator. The inorganic precipitate was removed by suction filtration and washed with ice cold Et_2O (3 × 3 mL). The filtrate was washed with water (3 × 3 mL) and extracted with Et_2O (3 × 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Recrystallisation from pentane (7 mL) afforded the *title compound* **327** (201 mg, 16%) as clear crystals. mp 82-83 °C (pentane); δ_H(300 MHz; CDCl$_3$) 1.39 (18 H, s, C(C*H*$_3$)$_3$); δ_C(75 MHz, CDCl$_3$) 27.8 (CH$_3$, C(*C*H$_3$)$_3$) and 81.2 (C, *C*(CH$_3$)$_3$).

Literature data:[270-272] mp 82-83 °C (pentane); ν_{max} (KBr)/cm^{-1} 2959, 1368, 1183 and 995 (NO); δ_H(500 MHz; CDCl$_3$) 1.39 (18 H, s); δ_C(125 MHz; CDCl$_3$) 27.8 and 81.2.

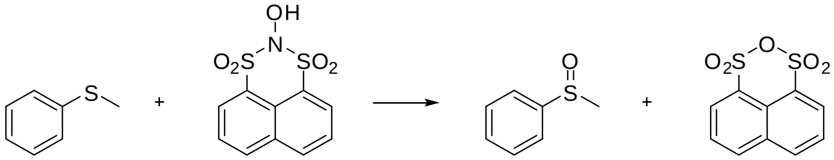
Attempted formation of hydroxylamine anion **328**



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**:



330 **284** **331** **333**

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 $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (7:3 Et_2O:hexane) yielded 3-oxa-1,3-dithiaphenalene 1,1,3,3-tetroxide (**333**) (35.0 mg, 15%) as a white solid. Further elution (Et_2O) afforded sulfoxide **331** (18.0 mg, 15%). **331**: R_f 0.10 (7:3 Et_2O:hexane); mp 29-31 ºC; δ_H(300 MHz; $CDCl_3$) 2.75 (3 H, s, CH_3) and 7.54-7.70 (5 H, m); δ_C(75 MHz; $CDCl_3$) 45.9 (CH_3), 127.4 (2 ×CH), 128.9 (2 × CH), 132.7 (CH) and 143.2 (C). **333**: R_f 0.58 (7:3 Et_2O:hexane); mp 211-213 °C; v_{max} (KBr)/cm^{-1} 1400, 1384, 1370, 1344, 1180 and 1147; δ_H(300 MHz; $CDCl_3$) 7.89 (2 H, dd, *J* 8.3 and 7.5, Ar*H*) and 8.35 (2 H, dd, *J* 8.5 and 1.0, Ar*H*) and 8.43 (2 H, dd, *J* 7.4 and 1.1); δ_C(100 MHz; $CDCl_3$) 119.9 (C), 127.0 (CH), 128.5 (CH), 130.5 (C), 133.1 (C), and 135.4 (CH); *m/z* (ESI) 292.9551 ($[M + Na]^+$, $C_{10}H_6O_5S_2Na$ requires 292.9554), 292.8 (100%). **Literature data**:[273-275] mp 29.5-30 °C, v_{max} ($CHCl_3$)/cm^{-1} 749, 1041 and 3013; δ_H(300 MHz; $CDCl_3$) 2.73 (3 H, s, CH_3) and 7.45-7.75 (5 H, m); δ_C(100 MHz; $CDCl_3$) 43.83, 123.36, 139.24, 130.92 and 145.51.

Chapter Five: References

1. Hartzell, G. E.; Paige, J. N. *J. Org. Chem.* **1967**, *32*, 459-460.
2. Schenk, P. W.; Steudel, R. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 402-409.
3. Nakayama, J.; Aoki, S.; Takayama, J.; Sakamoto, A.; Sugihara, Y.; Ishii, A. *J. Am. Chem. Soc.* **2004**, *126*, 9085-9093.
4. Steudel, R.; Steudel, Y. *Eur. J. Inorg. Chem.* **2004**, 3513-3521.
5. Dodson, R. M.; Sauers, R. F. *Chem. Commun.* **1967**, 1189-1190.
6. Saito, S. *Tetrahedron Lett.* **1968**, *9*, 4961-4964.
7. Ishikawa, Y.; Gong, Y. C.; Weiner, B. R. *Phys. Chem. Chem. Phys.* **2000**, *2*, 869-876.
8. Chao, P.; Lemal, D. M. *J. Am. Chem. Soc.* **1973**, *95*, 920-922.
9. Lemal, D. M.; Chao, P. *J. Am. Chem. Soc.* **1973**, *95*, 922-924.
10. Dodson, R. M.; Nelson, J. P. *J. Chem. Soc. D.* **1969**, 1159-1160.
11. Abuyousef, I. A.; Harpp, D. N. *Tetrahedron Lett.* **1995**, *36*, 201-204.
12. Heyke, O.; Neher, A.; Lorenz, I. P. *Z. Anorg. Allg. Chem.* **1992**, *608*, 23-27.
13. Schenk, W. A.; Leissner, J.; Burschka, C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 806-807.
14. Chow, Y. L.; Tamm, J. N. S.; Blier, J. E.; Szmant, H. H. *J. Chem. Soc. D.* **1970**, 1604-1605.
15. AbuYousef, I. A.; Harpp, D. N. *J. Org. Chem.* **1997**, *62*, 8366-8371.
16. Bonini, B. F.; Maccagnani, G.; Mazzanti, G. *J. Chem. Soc., Chem. Commun.* **1976**, 431-431.
17. Bonini, B. F.; Maccagnani, G.; Mazzanti, G. *Tetrahedron Lett.* **1977**, *18*, 1185-1186.
18. Bonini, B. F.; Maccagnani, G.; Mazzanti, G.; Pedrini, P.; Piccinelli, P. *J. Chem. Soc., Perkin Trans. 1.* **1979**, 1720-1722.
19. Blake, A. J.; Cooke, P. A.; Kendall, J. D.; Simpkins, N. S.; Westaway, S. M. *J. Chem. Soc., Perkin Trans. 1.* **2000**, 153-163.
20. Kendall, J. D.; Simpkins, N. S. *Synlett.* **1998**, 391-392.

21. Huang, R. L.; Espenson, J. H. *J. Org. Chem.* **1999**, *64*, 6374-6379.

22. Ishii, A.; Ohishi, M.; Matsumoto, K.; Takayanagi, T. *Org. Lett.* **2006**, *8*, 91-94.

23. Huang, R. L.; Guzei, I. A.; Espenson, J. H. *Organometallics* **1999**, *18*, 5420-5422.

24. Nakayama, J.; Tajima, Y.; Xue-Hua, P.; Sugihara, Y. *J. Am. Chem. Soc.* **2007**, *129*, 7250-7251.

25. Suwabe, S.; Okuhara, A.; Sugahara, T.; Suzuki, K.; Kunimasa, K.; Nakajima, T.; Kumafuji, Y.; Osawa, Y.; Yoshimura, T.; Morita, H. *Tetrahedron Lett.* **2009**, *50*, 1381-1384.

26. Procopio, A. *Ph.D Thesis. University of London*, 2003.

27. Grainger, R. S.; Procopio, A.; Steed, J. W. *Org. Lett.* **2001**, *3*, 3565-3568.

28. Balasubramaniyan.V *Chem. Rev.* **1966**, *66*, 567-641.

29. Glass, R. S.; Adamowicz, L.; Broeker, J. L. *J. Am. Chem. Soc.* **1991**, *113*, 1065-1072.

30. Glass, R. S.; Broeker, J. L. *Tetrahedron* **1991**, *47*, 5087-5098.

31. Glass, R. S.; Broeker, J. L. *Tetrahedron* **1991**, *47*, 5077-5086.

32. Glass, R. S.; Broeker, J. L.; Firouzabadi, H. *J. Org. Chem.* **1990**, *55*, 5739-5746.

33. Glass, R. S.; Adamowicz, L.; Broeker, J. L. *J. Mol. Struct. (THEOCHEM)* **1989**, *55*, 273-291.

34. Glass, R. S.; Andruski, S. W.; Broeker, J. L.; Firouzabadi, H.; Steffen, L. K.; Wilson, G. S. *J. Am. Chem. Soc.* **1989**, *111*, 4036-4045.

35. Fujii, T.; Kusanagi, H.; Takahashi, O.; Horn, E.; Furukawa, N. *Tetrahedron* **1999**, *55*, 5027-5046.

36. Kobayashi, K.; Shinhara, S.; Moriyama, M.; Fujii, T.; Horn, E.; Yabe, A.; Furukawa, N. *Tetrahedron Lett.* **1999**, *40*, 5211-5214.

37. Alder, R. W. *Chem. Rev.* **1989**, *89*, 1215-1223.

38. Pozharskii, A. F.; Ryabtsova, O. V.; Ozeryanskii, V. A.; Degtyarev, A. V.; Kazheva, O. N.; Alexandrov, G. G.; Dyachenko, O. A. *J. Org. Chem.* **2003**, *68*, 10109-10122.

39. Ozeryanskii, V. A.; Pozharskii, A. F.; Milgizina, G. R.; Howard, S. T. *J. Org. Chem.* **2000**, *65*, 7707-7709.

40. Zweig, A.; Hoffmann, A. K. *J. Org. Chem.* **1965**, *30*, 3997-4001.

41. Neugebauer, W.; Clark, T.; Schleyer, P. V. *Chem. Ber.* **1983**, *116*, 3283-3292.

42. Patel, B. *MSci Thesis. University of London*. 2005.

43. Wakamiya, A.; Nishinaga, T.; Komatsu, K. *J. Am. Chem. Soc.* **2002**, *124*, 15038-15050.

44. Ashe, A. J.; Kampf, J. W.; Savla, P. M. *Heteroat. Chem.* **1994**, *5*, 113-119.

45. Tesmer, M.; Vahrenkamp, H. *Eur. J. Inorg. Chem.* **2001**, 1183-1188.

46. Aucott, S. M.; Milton, H. L.; Robertson, S. D.; Slawin, A. M. Z.; Woollins, J. D. *Dalton Trans.* **2004**, 3347-3352.

47. Carpino, L. A.; Gao, H. S.; Ti, G. S.; Segev, D. *J. Org. Chem.* **1989**, *54*, 5887-5897.

48. Aso, Y.; Yui, K.; Miyoshi, T.; Otsubo, T.; Ogura, F.; Tanaka, J. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2013-2018.

49. Chiang, L. Y.; Meinwald, J. *Tetrahedron Lett.* **1980**, *21*, 4565-4568.

50. Neudorff, W. D.; Lentz, D.; Anibarro, M.; Schluter, A. D. *Chem. Eur. J.* **2003**, *9*, 2745-2757.

51. Mitchell, R. H.; Chaudhary, M.; Williams, R. V.; Fyles, R.; Gibson, J.; Ashwoodsmith, M. J.; Fry, A. J. *Can. J. Chem.* **1992**, *70*, 1015-1021.

52. Aucott, S. M.; Kilian, P.; Milton, H. L.; Robertson, S. D.; Slawin, A. M. Z.; Woollins, J. D. *Inorg. Chem.* **2005**, *44*, 2710-2718.

53. Letsinger, R. L.; Gilpin, J. A.; Vullo, W. J. *J. Org. Chem.* **1962**, *27*, 672-674.

54. House, W. T.; Orchin, M. *J. Am. Chem. Soc.* **1960**, *82*, 639-642.

55. Silverwood, H. A.; Orchin, M. *J. Org. Chem.* **1962**, *27*, 3401-3404.

56. Gamage, S. A.; Smith, R. A. J. *Tetrahedron* **1990**, *46*, 2111-2128.

57. Koziar, J. C.; Cowan, D. O. *J. Am. Chem. Soc.* **1976**, *98*, 1001-1007.

58. Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385-391.

59. Bartl, A.; Fröhner, J.; Kniess, T.; Domschke, G.; Mayer, R.; Roth, S. *Synth. Met.* **1992**, *51*, 115-119.

60. Yui, K.; Aso, Y.; Otsubo, T.; Ogura, F. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 953-959.

61. Tucker, J. H. R.; Gingras, M.; Brand, H.; Lehn, J. M. *J. Chem. Soc., Perkin Trans. 2.* **1997**, 1303-1307.

62. Thirsk, C.; Hawkes, G. E.; Kroemer, R. T.; Liedl, K. R.; Loerting, T.; Nasser, R.; Pritchard, R. G.; Steele, M.; Warren, J. E.; Whiting, A. *J. Chem. Soc., Perkin Trans. 2.* **2002**, 1510-1519.

63. Blair, P. A.; Chang, S. J.; Shechter, H. *J. Org. Chem.* **2004**, *69*, 7123-7133.

64. Adams, R.; Miller, M. W.; McGrew, F. C.; Anderson, A. W. *J. Am. Chem. Soc.* **1942**, *64*, 1795-1801.

65. Oae, S.; Nabeshima, T.; Takata, T. *Heterocycles* **1982**, *18*, 41-44.

66. Liu, S. Q.; Brown, C. W.; Berlin, K. D.; Dhar, A.; Guruswamy, S.; Brown, D.; Gardner, G. J.; Birrer, M. J.; Benbrook, D. M. *J. Med. Chem.* **2004**, *47*, 999-1007.

67. Ghosh, T.; Bartlett, P. D. *J. Am. Chem. Soc.* **1988**, *110*, 7499-7506.

68. Yomoji, N.; Takahashi, S.; Chida, S.; Ogawa, S.; Sato, R. *J. Chem. Soc., Perkin Trans. 1.* **1993**, 1995-2000.

69. Field, L.; Lacefield, W. B. *J. Org. Chem.* **1966**, *31*, 3555-3561.

70. Nakayama, J.; Masui, N.; Sugihara, Y.; Ishii, A. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1181-1186.

71. Ogawa, S.; Ohmiya, T.; Kikuchi, T.; Kawaguchi, A.; Saito, S.; Sai, A.; Ohyama, N.; Kawai, Y.; Niizuma, S.; Nakajo, S.; Kimura, T.; Sato, R. *J. Organomet. Chem.* **2000**, *611*, 136-145.

72. Xu, H.; Yip, J. H. K. *Inorg. Chem.* **2003**, *42*, 4492-4494.

73. Kim, Y. H.; Shin, J. M. *Tetrahedron Lett.* **1985**, *26*, 3821-3824.

74. Allin, S. M.; Page, P. C. B., *Organosulfur Chemistry, Synthetic and Stereochemical Aspects*. Academic Press: San Diego, CA: 1998; Vol. 2.

75. Harpp, D. N.; Gleason, J. G. *J. Org. Chem.* **1971**, *36*, 1314-1316.

76. Bass, S. W.; Evans, S. A. *J. Org. Chem.* **1980**, *45*, 710-715.

77. Kimura, T.; Hanzawa, M.; Horn, E.; Kawai, Y.; Ogawa, S.; Sato, R. *Tetrahedron Lett.* **1997**, *38*, 1607-1610.

78. Watson, W. H.; Krawiec, M.; Ghosh, T.; Bartlett, P. D. *Acta Cryst.* **1992**, *48*, 2092-2094.

79. Rayner, D. R.; Gordon, A. J.; Mislow, K. *J. Am. Chem. Soc.* **1968**, *90*, 4854-4860.

80. Johnson, A. W.; Lee, S. Y.; Swor, R. A.; Royer, L. D. *J. Am. Chem. Soc.* **1966**, *88*, 1953-1958.

81. Fletcher, T. L.; Namkung, M. J.; Dice, J. R.; Schaefer, S. K. *J. Med. Chem.* **1965**, *8*, 347-350.

82. Ibrom, K.; Kohn, G.; Boeckmann, K. U.; Kraft, R.; Holba-Schulz, P.; Ernst, L. *Org. Lett.* **2000**, *2*, 4111-4113.

83. Sheppard, W. A.; Diekmann, J. *J. Am. Chem. Soc.* **1964**, *86*, 1891-1892.

84. Braverman, S.; Grinstein, D.; Gottlieb, H. E. *Tetrahedron Lett.* **1997**, *53*, 13933-13944.

85. Derbesy, G.; Harpp, D. N. *J. Org. Chem.* **1995**, *60*, 4468-4474.

86. Derbesy, G.; Harpp, D. N. *J. Org. Chem.* **1996**, *61*, 991-997.

87. Jones, R. A. Y., *Physical and Mechanistic Organic Chemistry*. Cambridge University Press: Cambridge: 1979.

88. Maskill, H., *The Physical Basis of Organic Chemistry*. Oxford University Press: Oxford: 1989.

89. Hopkins, A. G.; Brown, C. W. *J. Chem. Phys.* **1975**, *62*, 2511-2512.

90. Carpino, L. A.; Chen, H. W. *J. Am. Chem. Soc.* **1979**, *101*, 390-394.

91. Okamoto, T.; Kobayashi, K.; Oka, S.; Tanimoto, S. *J. Org. Chem.* **1988**, *53*, 4897-4901.

92. Feldman, K. S. *Tetrahedron* **2006**, *62*, 5003-5034.

93. Araki, S.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1446-1449.

94. Epstein, W. W.; Netz, D. F.; Seidel, J. L. *J. Chem. Ed.* **1993**, *70*, 598-599.

95. Ternes, W.; Krause, E. L. *Anal. Bioanal. Chem.* **2002**, *374*, 155-160.

96. Ishii, A.; Oshida, H.; Nakayama, J. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 319-328.

97. Ishii, A.; Kawai, T.; Tekura, K.; Oshida, H.; Nakayama, J. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 1924-1926.

98. Ishii, A.; Oshida, H.; Nakayama, J. *Tetrahedron Lett.* **2001**, *42*, 3117-3119.

99. Herbert, J. M.; Frehel, D.; Vallee, E.; Kieffer, G.; Gouy, D.; Berger, Y.; Necciari, J.; Defreyn, G.; Maffrand, J. P. *Cardiovasc. Drug Rev.* **1993**, *11*, 180-198.

100. Rogers, E.; Araki, H.; Batory, L. A.; McInnis, C. E.; Njardarson, J. T. *J. Am. Chem. Soc.* **2007**, *129*, 2768-2769.

101. Winkler, J. D.; Axten, J.; Hammach, A. H.; Kwak, Y. S.; Lengweiler, U.; Lucero, M. J.; Houk, K. N. *Tetrahedron* **1998**, *54*, 7045-7056.

102. Robichaud, J.; Tremblay, F. *Org. Lett.* **2006**, *8*, 597-600.

103. Harirchian, B.; Bauld, N. L. *J. Am. Chem. Soc.* **1989**, *111*, 1826-1828.

104. Minakata, S.; Komatsu, M.; Ohshiro, Y. *Synthesis* **1992**, 661-663.

105. Folkins, P. L.; Harpp, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 8998-9000.

106. Folkins, P. L.; Harpp, D. N. *J. Am. Chem. Soc.* **1993**, *115*, 3066-3070.

107. Lacombe, S. M. *Rev. Heteroat. Chem.* **1999**, *21*, 1-41.

108. Field, L. *Synthesis* **1978**, 713-740.

109. Block, E.; Oconnor, J. *J. Am. Chem. Soc.* **1974**, *96*, 3921-3929.

110. Block, E.; Oconnor, J. *J. Am. Chem. Soc.* **1974**, *96*, 3929-3944.

111. Freeman, F. *Chem. Rev.* **1984**, *84*, 117-135.

112. Ishii, A. *J. Synth. Org. Chem, Japan* **2006**, *64*, 395-405.

113. Freeman, F.; Lee, C. S. *J. Org. Chem.* **1988**, *53*, 1263-1266.

114. Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1983**, *105*, 4039-4049.

115. Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1982**, *104*, 5766-5774.

116. Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1981**, *103*, 6232-6235.

117. Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827-1836.

118. Gregory, D. D.; Jenks, W. S. *J. Phys. Chem. A* **2003**, *107*, 3414-3423.

119. Ishii, A.; Nakabayashi, R.; Nakayama, J. *J. Am. Chem. Soc.* **1999**, *121*, 7959-7960.

120. Ishii, A.; Nakabayashi, M.; Jin, Y. N.; Nakayama, J. *J. Organomet. Chem.* **2000**, *611*, 127-135.

121. Oshida, H.; Ishii, A.; Nakayama, J. *Tetrahedron Lett.* **2002**, *43*, 5033-5037.

122. Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2.* **1987**, S1-S19.

123. Oshida, H.; Ishii, A.; Nakayama, J. *J. Org. Chem.* **2004**, *69*, 1695-1703.

124. Ishii, A.; Kashiura, S.; Oshida, H.; Nakayama, J. *Org. Lett.* **2004**, *6*, 2623-2626.

125. Ishii, A.; Ohishi, M.; Nakata, N. *Eur. J. Inorg. Chem.* **2007**, 5199-5206.

126. Petzold, H.; Brautigam, S.; Gorls, H.; Weigand, W.; Celeda, M.; Mloston, G. *Chem. Eur. J.* **2006**, *12*, 8090-8095.

127. Wunsch, R.; Bosl, G.; Robl, C.; Weigand, W. *J. Organomet. Chem.* **2001**, *621*, 352-358.

128. Weigand, W.; Bosl, G.; Robl, C.; Amrein, W. *Chem. Ber.* **1992**, *125*, 1047-1051.

129. Ishii, A.; Saito, M.; Murata, M.; Nakayama, J. *Eur. J. Org. Chem.* **2002**, 979-982.

130. Ishii, A.; Kawai, T.; Noji, M.; Nakayama, J. *Tetrahedron* **2005**, *61*, 6693-6699.

131. Ishii, A.; Murata, M.; Oshida, H.; Matsumoto, K.; Nakayama, J. *Eur. J. Inorg. Chem.* **2003**, 3716-3721.

132. Aucott, S. M.; Milton, H. L.; Robertson, S. D.; Slawin, A. M. Z.; Walker, G. D.; Woollins, J. D. *Chem. Eur. J.* **2004**, *10*, 1666-1676.

133. Aucott, S. M.; Kilian, P.; Robertson, S. D.; Slawin, A. M. Z.; Woollins, J. D. *Chem. Eur. J.* **2006**, *12*, 895-902.

134. Ishii, A.; Kashiura, S.; Hayashi, Y.; Weigand, W. *Chem. Eur. J.* **2007**, *13*, 4326-4333.

135. Anderson, J. E.; Jorgensen, F. S. *J. Chem. Soc., Perkin Trans. 2.* **1988**, 469-471.

136. Aucott, S. M.; Milton, H. L.; Robertson, S. D.; Slawin, A. M. Z.; Woollins, J. D. *Heteroat. Chem.* **2004**, *15*, 530-542.

137. Boduszek, B.; Kice, J. L. *J. Org. Chem.* **1982**, *47*, 3199-3207.

138. Chau, M. M.; Kice, J. L. *J. Org. Chem.* **1977**, *42*, 3265-3270.

139. Chau, M. M.; Kice, J. L.; Margolis, H. C. *J. Org. Chem.* **1978**, *43*, 910-914.

140. Grainger, R. S. *Ph.D Thesis. University of Sheffield*, 1996.

141. Levai, A. *Arkivoc* **2003**, 14-30.

142. Sherlock, A. E. *Ph.D Thesis. University of Nottingham*, 2006.

143. Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377-2377.

144. Peduli, G. F.; Vivarelli, P.; Dembech, P.; Ricci, A.; Secondi, G. *Int. J. Sulfur Chem.* **1973**, *3*, 255-260.

145. Yang, D.; Yip, Y. C.; Jiao, G. S.; Wong M, K. *Org. Synth.* **2002**, *78*, 255.

146. Sato, R.; Takeda, E.; Nakajo, S.; Kimura, T.; Ogawa, S.; Kawai, Y. *Heteroat. Chem.* **2001**, *12*, 209-216.

147. Bramwell, F. B.; Haddon, R. C.; Wudl, F.; Kaplan, M. L.; Marshall, J. H. *J. Am. Chem. Soc.* **1978**, *100*, 4612-4614.

148. Carrasco, M.; Jones, R. J.; Kamel, S.; Rapoport, H.; Truong, T. *Org. Synth.* **1992**, *70*, 29-32.

149. Barnard, D.; Percy, E. J. *Chem. Ind. London* **1960**, 1332-1333.

150. Koch, P.; Ciuffari.E; Fava, A. *J. Am. Chem. Soc.* **1970**, *92*, 5971-5977.

151. Kice, J. L.; Venier, C. G.; Large, G. B.; Heasley, L. *J. Am. Chem. Soc.* **1969**, *91*, 2028-2035.

152. Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015-9020.

153. Crich, D.; Smith, M. *Org. Lett.* **2000**, *2*, 4067-4069.

154. Yamamoto, K.; Yoshida, S.; Nishide, H.; Tsuchida, E. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3655-3660.

155. Mislow, K.; Melillo, J. T.; Simmons, T.; Ternay, A. L. *J. Am. Chem. Soc.* **1964**, *86*, 1452-1453.

156. Yoshida, H.; Numata, T.; Oae, S. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2875-2876.

157. Madesclaire, M. *Tetrahedron* **1988**, *44*, 6537-6580.

158. Block, E.; Bayer, T.; Naganathan, S.; Zhao, S. H. *J. Am. Chem. Soc.* **1996**, *118*, 2799-2810.

159. Santaniello, E.; Manzocchi, A.; Farachi, C. *Synthesis* **1980**, 563-565.

160. Khan, S. A.; Lambert, J. B.; Hernandez, O.; Carey, F. A. *J. Am. Chem. Soc.* **1975**, *97*, 1468-1473.

161. Clennan, E. L.; Wang, D.; Zhang, H.; Clifton, C. H. *Tetrahedron Lett.* **1994**, *35*, 4723-4726.

162. Clennan, E. L.; Zhang, H. W. *J. Org. Chem.* **1994**, *59*, 7952-7954.

163. Desper, J. M.; Gellman, S. H.; Wolf, R. E.; Cooper, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 8663-8671.

164. Eliel, E. L.; Rao, V. S.; Smith, S.; Hutchins, R. O. *J. Org. Chem.* **1975**, *40*, 524-526.

165. Darmanyan, A. P.; Gregory, D. D.; Guo, Y. S.; Jenks, W. S. *J. Phys. Chem. A* **1997**, *101*, 6855-6863.

166. Iino, M.; Matsuda, M. *J. Org. Chem.* **1983**, *48*, 3108-3109.

167. Leaver, I. H.; Ramsay, G. C. *Tetrahedron* **1969**, *25*, 5669-5675.

168. Flesia, E.; Surzur, J. M. *Tetrahedron Lett.* **1974**, 123-126.

169. Gilbert, B. C.; Gill, B.; Sexton, M. D. *J. Chem. Soc., Chem. Commun.* **1978**, 78-79.

170. Nishizawa, M.; Kohno, M.; Nishimura, M.; Kitagawa, A.; Niwano, Y. *Chem. Pharm. Bull.* **2005**, *53*, 714-716.

171. Crich, D. *Helv. Chim. Acta* **2006**, *89*, 2167-2182.

172. Markovic, D.; Varela-Alvarez, A.; Sordo, J. A.; Vogel, P. *J. Am. Chem. Soc.* **2006**, *128*, 7782-7795.

173. Gilbert, B. C.; Kirk, C. M.; Norman, R. O. C.; Laue, H. A. H. *J. Chem. Soc., Perkin Trans. 2.* **1977**, 497-501.

174. Josephy, P. D.; Rehorek, D.; Janzen, E. G. *Tetrahedron Lett.* **1984**, *25*, 1685-1688.

175. Balakirev, M. Y.; Khramtsov, V. V. *J. Org. Chem.* **1996**, *61*, 7263-7269.

176. Naghipur, A.; Reszka, K.; Lown, J. W.; Sapse, A. M. *Can. J. Chem.* **1990**, *68*, 1950-1960.

177. Davies, M. J.; Forni, L. G.; Shuter, S. L. *Chem.-Biol. Interact.* **1987**, *61*, 177-188.

178. Reggelin, M.; Zur, C. *Synthesis* **2000**, 1-64.

179. Enders, D. J., K-E., *Asymmetric Synthesis with Chemical and Biological Methods*. Wiley-VCH, Weinheim: 2007.

180. Bentley, H. R.; McDermott, E. E.; Pace, J.; Whitehead, J. K.; Moran, T. *Nature* **1949**, *163*, 675-676.

181. Cren, S.; Kinahan, T. C.; Skinner, C. L.; Tye, H. *Tetrahedron Lett.* **2002**, *43*, 2749-2751.

182. Gryglewski, R. J.; Palmer, R. M. J.; Moncada, S. *Nature* **1986**, *320*, 454-456.

183. Morris, S. M. *J. Nutr.* **2004**, *134*, 2743S-2747S.

184. Hrabie, J. A.; Keefer, L. K. *Chem. Rev.* **2002**, *102*, 1135-1154.

185. Miranda, K. M. *Coord. Chem. Rev.* **2005**, *249*, 433-455.

186. Fukuto, J. M.; Switzer, C. H.; Miranda, K. M.; Wink, D. A. *Annu. Rev. Pharmacol. Toxicol.* **2005**, *45*, 335-355.

187. Bartberger, M. D.; Fukuto, J. M.; Houk, K. N. *Proc. Natl. Acad. Sci. U. S. A.* **2001**, *98*, 2194-2198.

188. Fukuto, J. M.; Chiang, K.; Hszieh, R.; Wong, P.; Chaudhuri, G. *J. Pharmacol. Exp. Ther.* **1992**, *263*, 546-551.

189. DeMaster, E. G.; Redfern, B.; Quast, B. J.; Dahlseid, T.; Nagasawa, H. T. *Alcohol* **1997**, *14*, 181-189.

190. Shoeman, D. W.; Shirota, F. N.; DeMaster, E. G.; Nagasawa, H. T. *Alcohol* **2000**, *20*, 55-59.

191. Wilson, E. K. *Chem. Eng. News* **2004**, *82*, 39-44.

192. Mordaunt, D. H.; Flothmann, H.; Stumpf, M.; Keller, H. M.; Beck, C.; Schinke, R.; Yamashita, K. *J. Chem. Phys.* **1997**, *107*, 6603-6615.

193. Maier, G.; Reisenauer, H. P.; De Marco, M. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 108-110.

194. Wang, P. G.; Xian, M.; Tang, X. P.; Wu, X. J.; Wen, Z.; Cai, T. W.; Janczuk, A. J. *Chem. Rev.* **2002**, *102*, 1091-1134.

195. Hartung, J. *Chem. Rev.* **2009**, *ASAP*.

196. Butler, A. *Chem. Br.* **2003**, *39*, 32-34.

197. Engelhardt, F. C.; Shi, Y. J.; Cowden, C. J.; Conlon, D. A.; Pipik, B.; Zhou, G.; McNamara, J. M.; Dolling, U. H. *J. Org. Chem.* **2006**, *71*, 480-491.

198. Zhao, Y. L.; McCarren, P. R.; Houk, K. N.; Choi, B. Y.; Toone, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 10917-10924.

199. Miura, M.; Sakamoto, S.; Yamaguchi, K.; Ohwada, T. *Tetrahedron Lett.* **2000**, *41*, 3637-3641.

200. Reynolds, M. M.; Zhou, Z. R.; Oh, B. K.; Meyerhoff, M. E. *Org. Lett.* **2005**, *7*, 2813-2816.

201. Pavlos, C. M.; Xu, H.; Toscano, J. P. *Free Radical Biol. Med.* **2004**, *37*, 745-752.

202. Miranda, K. M.; Katori, T.; de Holding, C. L. T.; Thomas, L.; Ridnour, L. A.; MeLendon, W. J.; Cologna, S. M.; Dutton, A. S.; Champion, H. C.; Mancardi, D.; Tocchetti, C. G.; Saavedra, J. E.; Keefer, L. K.; Houk, K. N.; Fukuto, J. M.; Kass, D. A.; Paolocci, N.; Wink, D. A. *J. Med. Chem.* **2005**, *48*, 8220-8228.

203. Alston, T. A.; Porter, D. J. T.; Bright, H. J. *J. Biol. Chem.* **1985**, *260*, 4069-4074.

204. Fukuhara, K.; Kurihara, M.; Miyata, N. *J. Am. Chem. Soc.* **2001**, *123*, 8662-8666.

205. Hwang, K. J.; Kim, S. K.; Shim, S. C. *Chem. Lett.* **1998**, 859-859.

206. Bauer, J. A.; Fung, H. L. *Life Sci.* **1994**, *54*, PL1-PL4.

207. Callari, F. L.; Sortino, S. *Chem. Commun.* **2008**, 1971-1973.

208. Caruso, E. B.; Petralia, S.; Conoci, S.; Giuffrida, S.; Sortino, S. *J. Am. Chem. Soc.* **2007**, *129*, 480-481.

209. Rothrock, A. R.; Donkers, R. L.; Schoenfisch, M. H. *J. Am. Chem. Soc.* **2005**, *127*, 9362-9363.

210. Etchenique, R.; Furman, M.; Olabe, J. A. *J. Am. Chem. Soc.* **2000**, *122*, 3967-3968.

211. Birchall, J. D.; Glidewell, C. *J. Chem. Soc., Dalton Trans.* **1977**, 10-14.

212. Birchall, J. D.; Glidewell, C. *J. Chem. Soc., Dalton Trans.* **1977**, 1976-1980.

213. Birchall, J. D.; Glidewell, C. *Inorg. Chim. Acta* **1977**, *25*, L67-L68.

214. Birchall, J. D.; Glidewell, C. *J. Chem. Soc., Dalton Trans.* **1978**, 604-607.

215. Birchall, J. D.; Glidewell, C. *Inorg. Chim. Acta* **1978**, *28*, 103-106.

216. Barbero, M.; Degani, I.; Fochi, R.; Perracino, P. *J. Org. Chem.* **1996**, *61*, 8762-8764.

217. Miranda, K. M.; Dutton, A. S.; Ridnour, L. A.; Foreman, C. A.; Ford, E.; Paolocci, N.; Katori, T.; Tocchetti, C. G.; Mancardi, D.; Thomas, D. D.; Espey, M. G.; Houk, K. N.; Fukuto, J. M.; Wink, D. A. *J. Am. Chem. Soc.* **2005**, *127*, 722-731.

218. Gladwin, M. T.; Schechter, A. N.; Kim-Shapiro, D. B.; Patel, R. P.; Hogg, N.; Shiva, S.; Cannon, R. O.; Kelm, M.; Wink, D. A.; Espey, M. G.; Oldfield, E. H.; Pluta, R.

M.; Freeman, B. A.; Lancaster, J. R.; Feelisch, M.; Lundberg, J. O. *Nat. Chem. Biol.* **2005**, *1*, 308-314.

219. Sha, X.; Isbell, T. S.; Patel, R. P.; Day, C. S.; King, S. B. *J. Am. Chem. Soc.* **2006**, *128*, 9687-9692.

220. Xu, Y. P.; Alavanja, M. M.; Johnson, V. L.; Yasaki, G.; King, S. B. *Tetrahedron Lett.* **2000**, *41*, 4265-4269.

221. Adachi, Y.; Nakagawa, H.; Matsuo, K.; Suzuki, T.; Miyata, N. *Chem. Commun.* **2008**, 5149-5151.

222. Pennington, R. L.; Sha, X.; King, S. B. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2331-2334.

223. Kice, J. L.; Margolis, H. *J. Org. Chem.* **1975**, *40*, 3623-3624.

224. Kice, J. L.; Ikura, K. *J. Am. Chem. Soc.* **1968**, *90*, 7378-7379.

225. Oae, S.; Takata, T. *Chem. Lett.* **1981**, 845-848.

226. Mueller, W. H.; Dines, M. B. *J. Chem. Soc. D.* **1969**, 1205-1206.

227. Derbesy, G.; Harpp, D. N. *J. Org. Chem.* **1995**, *60*, 1044-1052.

228. Swern, D., *Organic Peroxides*. Wiley-Interscience: London; New York: 1970.

229. Legros, J.; Bolm, C. *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 5487-5489.

230. Kice, J. L.; Krowicki, K. *J. Org. Chem.* **1981**, *46*, 4894-4898.

231. Ronan, B.; Kagan, H. B. *Tetrahedron-Asymmetry* **1992**, *3*, 115-122.

232. Takimiya, K.; Aso, Y.; Otsubo, T.; Ogura, F. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2091-2102.

233. Dann, A. T.; Davies, W. *J. Chem. Soc.* **1929**, 1050-1055.

234. Grainger, R. S.; Carlisle, J. *Unpublished work*, 2005.

235. Bharatam, P. V.; Amita, A. G.; Kaur, D. *Tetrahedron* **2002**, *58*, 1759-1764.

236. Drockenmuller, E.; Catala, J. M. *Macromolecules* **2002**, *35*, 2461-2466.

237. Kirilyuk, I. A.; Bobko, A. A.; Grigorev, I. A.; Khramtsov, V. V. *Org. Biomol. Chem.* **2004**, *2*, 1025-1030.

238. Kirilyuk, I. A.; Bobko, A. A.; Khramtsov, V. V.; Grigorev, I. A. *Org. Biomol. Chem.* **2005**, *3*, 1269-1274.

239. Flakus, S.; Mandel, K.; Bartsch, M.; Schmidt-Naake, G. *Macromol. Rapid Commun.* **2005**, *26*, 1698-1703.

240. Mendenhall, G. D. *Tetrahedron Lett.* **1983**, *24*, 451-452.

241. Yamada, S.; Morimoto, Y.; Misono, T. *Tetrahedron Lett.* **2005**, *46*, 5673-5676.

242. Mallory, F. B.; Mallory, C. W.; Butler, K. E.; Lewis, M. B.; Xia, A. Q.; Luzik, E. D.; Fredenburgh, L. E.; Ramanjulu, M. M.; Van, Q. N.; Francl, M. M.; Freed, D. A.; Wray, C. C.; Hann, C.; Nerz-Stormes, M.; Carroll, P. J.; Chirlian, L. E. *J. Am. Chem. Soc.* **2000**, *122*, 4108-4116.

243. Baranovic, G.; Jordanov, B.; Schrader, B. *J. Mol. Struct.* **1994**, *323*, 103-115.

244. Iida, Y.; Daishima, S. *Chem. Lett.* **1983**, 273-276.

245. Lutnaes, B. F.; Luthe, G.; Brinkman, U. A. T.; Johansen, J. E.; Krane, J. *Magn. Reson. Chem.* **2005**, *43*, 588-594.

246. Ferree, W. I.; Plummer, B. F. *J. Am. Chem. Soc.* **1973**, *95*, 6709-6717.

247. Seiders, T. J.; Elliott, E. L.; Grube, G. H.; Siegel, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 7804-7813.

248. Kuhnert, N.; Burzlaff, N.; Patel, C.; Lopez-Periago, A. *Org. Biomol. Chem.* **2005**, *3*, 1911-1921.

249. Neuenschwander, M.; Vogeli, R.; Fahrni, H. P.; Lehmann, H.; Ruder, J. P. *Helv. Chim. Acta* **1977**, *60*, 1073-1086.

250. Ibrahim, Y. A.; Al-Awadi, N. A.; Kual, K. *Tetrahedron* **2003**, *59*, 5425-5430.

251. Bergmann, E. D.; Solomonovici, A. *Synthesis* **1970**, 183-189.

252. Machiguchi, T.; Hasegawa, T.; Otani, H.; Yamabe, S.; Mizuno, H. *J. Am. Chem. Soc.* **1994**, *116*, 407-408.

253. Jeanes, A.; Adams, R. *J. Am. Chem. Soc.* **1937**, *59*, 2608-2622.

254. Baccolini, G.; Boga, C.; Mazzacurati, M. *J. Org. Chem.* **2005**, *70*, 4774-4777.

255. Badejo, I. T.; Karaman, R.; Pinkerton, A. A.; Fry, J. L. *J. Org. Chem.* **1990**, *55*, 4327-4332.

256. Olah, G. A.; Reddy, V. P.; Prakash, G. K. S. *Synthesis* **1991**, 29-30.

257. Ketley, A. D.; McClanah, J. L. *J. Org. Chem.* **1965**, *30*, 942-943.

258. Grunwell, J. R.; Foerst, D. L.; Sanders, M. J. *J. Org. Chem.* **1977**, *42*, 1142-1145.

259. Oxelbark, J.; Thunberg, L.; Andersson, A.; Allenmark, S. *Acta Chem. Scand.* **1999**, *53*, 710-713.

260. Kice, J. L.; Kang, Y. H.; Manek, M. B. *J. Org. Chem.* **1988**, *53*, 2435-2439.

261. Meinwald, J.; Knapp, S.; Obendorf, S. K.; Hughes, R. E. *J. Am. Chem. Soc.* **1976**, *98*, 6643-6649.

262. Chemla, F. *Synlett.* **1998**, 894-896.

263. Bell, K. H. *J. Chem. Soc., Perkin Trans. 1.* **1988**, 1957-1960.

264. Barton, D. H. R.; Chen, C.; Michael Wall, G. *Tetrahedron* **1991**, *47*, 6127-6138.

265. Leandri, G.; Mangini, A.; Tundo, A. *J. Chem. Soc.* **1957**, 52-57.

266. Brown, H. C.; Peters, E. N.; Ravindranathan, M. *J. Am. Chem. Soc.* **1977**, *99*, 505-509.

267. Dhar, P.; Chidambaram, N.; Chandrasekaran, S. *J. Org. Chem.* **1992**, *57*, 1699-1702.

268. Goethals, E. J.; Huylebro.J; Smolders, W. *Bull. Soc. Chim. Belg.* **1969**, *78*, 191-196.

269. Wudl, F.; Lee, T. B. K. *J. Am. Chem. Soc.* **1973**, *95*, 6349-6358.

270. Kiefer, H.; Traylor, T. G. *Tetrahedron Lett.* **1966**, *7*, 6163-6168.

271. Thompson, R. A.; Francisco, J. S.; Grutzner, J. B. *Phys. Chem. Chem. Phys.* **2004**, *6*, 756-765.

272. Walling, C.; McGuinne.Ja *J. Am. Chem. Soc.* **1969**, *91*, 2053-2058.

273. Price, C. C.; Hydock, J. J. *J. Am. Chem. Soc.* **1952**, *74*, 1943-1946.

274. Shukla, V. G.; Salgaonkar, P. D.; Akamanchi, K. G. *J. Org. Chem.* **2003**, *68*, 5422-5425.

275. Kim, S. S.; Nehru, K.; Kim, D. W.; Jung, H. C. *Synthesis* **2002**, 2484-2486.

Appendix

X-ray for data for 86

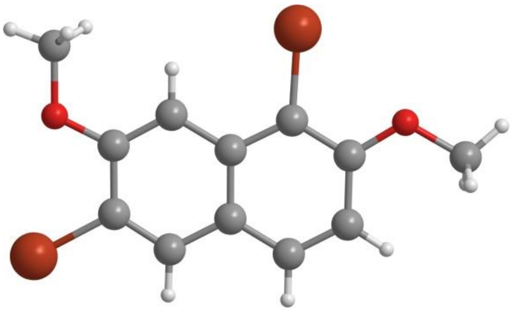
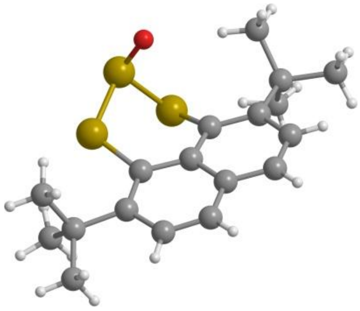


Table 1. Crystal data and structure refinement for BP83.

Identification code	BP83, 2009src0360r	
Empirical formula	$C_{12} H_{10} Br_2 O_2$	
Formula weight	346.02	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.3022(2) Å	α = 84.2050(10)°.
	b = 7.6899(2) Å	β = 89.146(2)°.
	c = 21.1997(7) Å	γ = 85.231(2)°.
Volume	1180.22(6) $Å^3$	
Z	4	
Density (calculated)	1.947 Mg/m^3	
Absorption coefficient	6.849 mm^{-1}	
F(000)	672	
Crystal size	0.16 x 0.05 x 0.04 mm^3	
Theta range for data collection	3.14 to 27.46°.	
Index ranges	-9<=h<=9, -9<=k<=9, 0<=l<=27	
Reflections collected	5376	
Independent reflections	5376 [R(int) = 0.0000]	
Completeness to theta = 27.46°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7713 and 0.4070	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5376 / 0 / 294	
Goodness-of-fit on F^2	1.159	
Final R indices [I>2sigma(I)]	R1 = 0.0594, wR2 = 0.1650	
R indices (all data)	R1 = 0.0645, wR2 = 0.1733	
Largest diff. peak and hole	1.417 and -2.144 e.$Å^{-3}$	

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, α = 99.464(3), β = 108.734(2), γ = 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**: $C_{12}H_{10}O_3S_3$: Monoclinic, $P2_1/n$, FW = 298.38, T = 273, *a* =10.1383(18), *b* =6.9855(13), *c* = 17.520(3)Å, β =95.936(9), V = 1234.1(4), *Z* = , Final residuals (2σF), wR2 = 0.387, R1 = 0.157, with goodness of fit 1.421 on F^2.

X-ray for data for 90

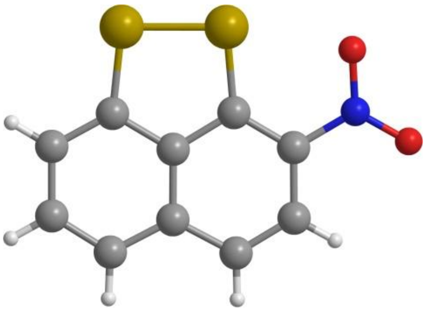


Table 1. Crystal data and structure refinement for s101f2m.

Identification code	s101f2	
Empirical formula	C10 H5 N O2 S2	
Formula weight	235.27	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 4.0018(3) Å	α = 90°.
	b = 12.8838(9) Å	β = 94.511(5)°.
	c = 18.0222(14) Å	γ = 90°.
Volume	926.32(12) Å^3	
Z	4	
Density (calculated)	1.687 Mg/m^3	
Absorption coefficient	5.019 mm^{-1}	
F(000)	480	
Crystal size	0.50 x 0.10 x 0.05 mm^3	
Theta range for data collection	4.22 to 65.36°.	
Index ranges	-4<=h<=4, -14<=k<=13, -21<=l<=18	
Reflections collected	5487	
Independent reflections	1530 [R(int) = 0.0414]	
Completeness to theta = 65.36°	96.2 %	
Max. and min. transmission	0.7874 and 0.1881	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1530 / 0 / 136	
Goodness-of-fit on F^2	1.041	
Final R indices [I>2sigma(I)]	R1 = 0.0378, wR2 = 0.0963	
R indices (all data)	R1 = 0.0482, wR2 = 0.1028	
Largest diff. peak and hole	0.322 and -0.273 e.Å^{-3}	

X-ray for data for 91

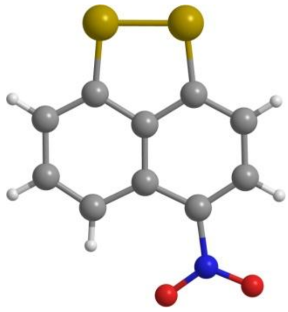


Table 1. Crystal data and structure refinement for s101f1m.

Identification code	s101f1	
Empirical formula	C10 H5 N O2 S2	
Formula weight	235.27	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2$_1$/c	
Unit cell dimensions	a = 12.4427(6) Å	α = 90°.
	b = 9.9312(5) Å	β = 93.499(3)°.
	c = 7.3694(4) Å	γ = 90°.
Volume	908.95(8) Å^3	
Z	4	
Density (calculated)	1.719 Mg/m^3	
Absorption coefficient	5.115 mm^{-1}	
F(000)	480	
Crystal size	0.50 x 0.05 x 0.05 mm^3	
Theta range for data collection	3.56 to 65.70°.	
Index ranges	-14<=h<=14, -11<=k<=10, -8<=l<=8	
Reflections collected	5727	
Independent reflections	1501 [R(int) = 0.0323]	
Completeness to theta = 65.70°	95.2 %	
Max. and min. transmission	0.7840 and 0.1841	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1501 / 0 / 136	
Goodness-of-fit on F^2	1.064	
Final R indices [I>2sigma(I)]	R1 = 0.0325, wR2 = 0.0850	
R indices (all data)	R1 = 0.0422, wR2 = 0.0913	
Largest diff. peak and hole	0.293 and -0.181 e.Å^{-3}	

X-ray for data for 103

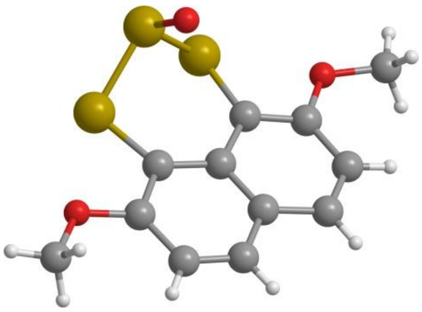
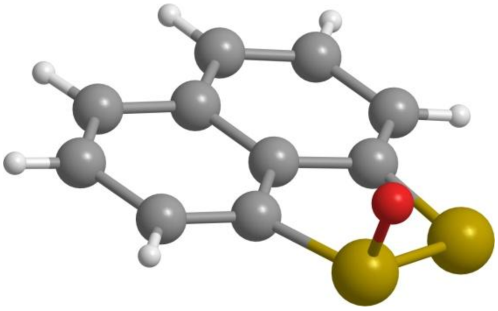


Table 1. Crystal data and structure refinement for dmto.

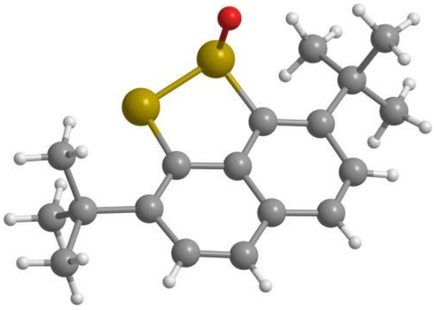
Identification code	dmto	
Empirical formula	C12 H10 O3 S3	
Formula weight	298.38	
Temperature	273(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P21/n	
Unit cell dimensions	a = 10.1383(18) Å	α = 90°.
	b = 6.9855(13) Å	β = 95.936(9)°.
	c = 17.520(3) Å	γ = 90°.
Volume	1234.1(4) Å^3	
Z	4	
Density (calculated)	1.606 Mg/m^3	
Absorption coefficient	5.480 mm^{-1}	
F(000)	616	
Crystal size	0.30 x 0.08 x 0.08 mm^3	
Theta range for data collection	4.83 to 65.96°.	
Index ranges	-11<=h<=10, -6<=k<=7, -17<=l<=20	
Reflections collected	5842	
Independent reflections	1869 [R(int) = 0.0842]	
Completeness to theta = 65.96°	86.8 %	
Absorption correction	Empirical	
Max. and min. transmission	0.6683 and 0.2902	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1869 / 0 / 165	
Goodness-of-fit on F^2	1.421	
Final R indices [I>2sigma(I)]	R1 = 0.1570, wR2 = 0.3872	
R indices (all data)	R1 = 0.1807, wR2 = 0.3997	
Largest diff. peak and hole	1.870 and -0.658 e.Å^{-3}	

X-ray for data for 107



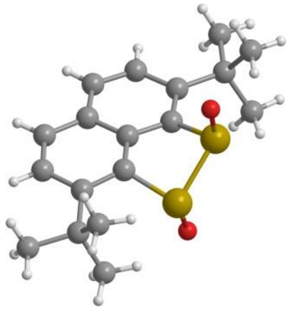
(bxp1): $C_{10}H_6OS_2$, M_r = 206.27, T = 296(2) K, λ = 1.54178 Å, Triclinic, P-1, a = 7.629(15) Å, b = 8.665(14) Å, c = 14.72(2) Å, α = 91.55(9)°, β= 99.73(10)°, γ = 110.05(10)°, V = 897(3) Å^3, Z = 4, σ_{cal} = 1.527 Mg/m^3, μ = 4.970 mm^{-1}, Crystal size = 0.50 x 0.15 x 0.15 mm^3, θ_{max}= 64.84°, Reflections collected = 5035, Independent reflections = 2574, R(int) = 0.0496, Final R1 [I>2σ(I)] = 0.0534, Final wR2 [I>2σ(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



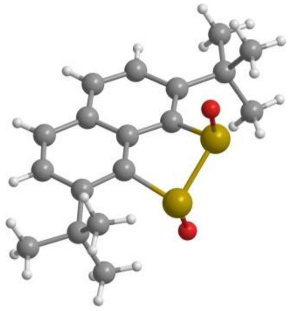
(bp365): $C_{18}H_{22}OS_2$, M_r = 318.48, T = 293(2) K, λ = 1.54178 Å, Monoclinic, P2$_1$/c, a = 8.1614(2) Å, b = 20.1864(7) Å, c = 10.1344(3) Å, β = 94.359(2)°, V = 1664.81(9) Å^3, Z = 4, σ_{cal} = 1.271 Mg/m^3, μ = 2.854 mm^{-1}, Crystal size = 0.25 x 0.20 x 0.10 mm^3, θ_{max} 66.50°, Reflections collected = 11086, Independent reflections = 2830, R(int) = 0.0378, Final R1 [I>2σ(I)] = 0.0436, Final wR2 [I>2σ(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



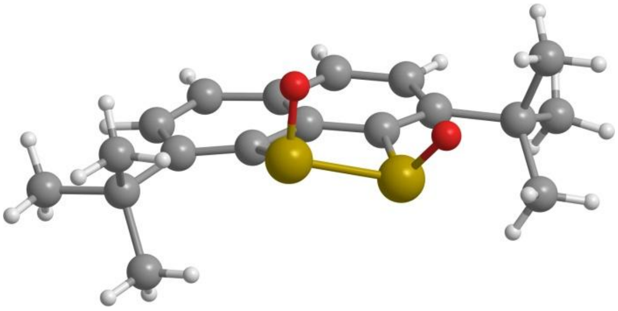
(bp395): $C_{18}H_{22}O_2S_2$, M_r = 334.48, T = 200(2) K, λ = 0.67030 Å, Triclinic, P-1, a = 8.7247(16) Å, b = 9.4724(18) Å, c = 10.642(2) Å, α = 97.649(3)°, β = 107.070(2)°, γ = 92.469(3)°, V = 830.1(3) Å^3, Z = 2, σ_{cal} = 1.338 Mg/m^3, μ = 0.325 mm^{-1}, Crystal size = 0.10 x 0.10 x 0.05 mm^3, θ_{max} 30.06°, Reflections collected = 10683, Independent reflections = 5577, R(int) = 0.0680, Final R1 [I>2σ(I)] = 0.0711, Final wR2 [I>2σ(I)] = 0.1793, R1 (all data) = 0.0964, wR2 (all data) = 0.2017, Residual electron density = 0.595 e.Å^{-3}. The S_2O_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



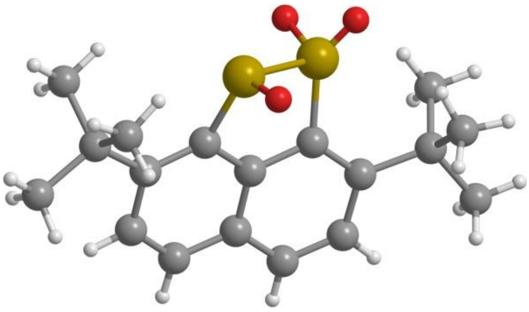
(bp376f1): $C_{18}H_{22}O_2S_2$, M_r = 334.48, T =296(2) K, λ = 1.54178 Å, Monoclinic, P2$_1$/n, a = 12.1098(5) Å, b = 12.1134(5) Å, c = 12.6884(5) Å, β = 114.400(2)°, V = 1695.03(12) Å^3, Z = 4, σ_{cal} = 1.311 Mg/m^3, μ = 2.874 mm^{-1}, Crystal size = 0.23 x 0.20 x 0.10 mm^3, θ_{max} = 66.50°, Reflections collected = 11118, Independent reflections = 2865, R(int) = 0.0532, Final R1 [I>2σ(I)] =0.0484, Final wR2 [I>2σ(I)] = 0.1238, R1 (all data) = 0.0585, wR2 (all data) = 0.1290, Residual electron density = 0.318 e.Å^{-3}. The S_2O_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): $C_{18}H_{22}O_2S_2$, M_r = 334.48, T = 296(2) K, λ = 1.54178 Å, Triclinic, P-1, a = 8.6970(4) Å, b = 9.5037(4) Å, c = 10.6581(4) Å, α = 97.635(3)°, β = 107.551(2)°, γ = 91.727(3)°, V = 830.18(6) Å^3, Z = 2, σ_{cal} = 1.338 Mg/m^3, μ = 2.934 mm^{-1}, Crystal size = 0.30 x 0.20 x 0.20 mm^3, θ_{max} 65.74°, Reflections collected = 5460, Independent reflections = 2557, R(int) = 0.0267, Final R1 [I>2σ(I)] = 0.0429, Final wR2 [I>2σ(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): $C_{18}H_{22}O_3S_2$, M_r = 350.48, T = 296(2) K, λ = 1.54178 Å, Monoclinic, $P2_1/n$, a = 8.396(4) Å, b = 20.943(11) Å, c = 9.891(5) Å, β= 94.459(16)°, V = 1734.0(15) Å^3, Z = 4, σ_{cal} = 1.343 Mg/m^3, μ = 2.880 mm^{-1}, Crystal size = 0.15 x 0.13 x 0.10 mm^3, θ_{max} 65.74°, Reflections collected = 6613, Independent reflections = 2128, R(int) = 0.0710, Final R1 [I>2σ(I)] = 0.0591, Final wR2 [I>2σ(I)] = 0.1007, R1 (all data) = 0.1128, wR2 (all data) = 0.1181, Residual electron density = 0.158 e.Å^{-3}. The S_2O_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).

X-ray for data for 295

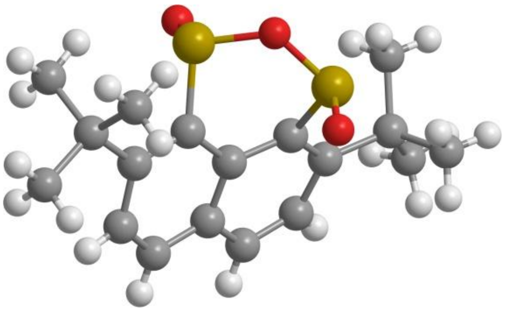


Table 1. Crystal data and structure refinement for bp516.

Identification code	bp516	
Empirical formula	C19 H23 Cl3 O3 S2	
Formula weight	469.84	
Temperature	293(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.0991(6) Å	α = 107.604(4)°.
	b = 11.3796(7) Å	β = 108.300(4)°.
	c = 12.7428(8) Å	γ = 102.799(4)°.
Volume	1118.64(12) Å^3	
Z	2	
Density (calculated)	1.395 Mg/m^3	
Absorption coefficient	5.595 mm^{-1}	
F(000)	488	
Crystal size	0.25 x 0.20 x 0.20 mm^3	
Theta range for data collection	3.99 to 65.94°.	
Index ranges	-10<=h<=9, -13<=k<=12, -14<=l<=14	
Reflections collected	7293	
Independent reflections	3418 [R(int) = 0.0399]	
Completeness to theta = 65.94°	87.6 %	
Absorption correction	Empirical	
Max. and min. transmission	0.4008 and 0.3352	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3418 / 0 / 250	
Goodness-of-fit on F^2	1.057	
Final R indices [I>2sigma(I)]	R1 = 0.0862, wR2 = 0.2113	
R indices (all data)	R1 = 0.1087, wR2 = 0.2284	
Largest diff. peak and hole	0.886 and -1.048 e.Å^{-3}	

X-ray for data for 284

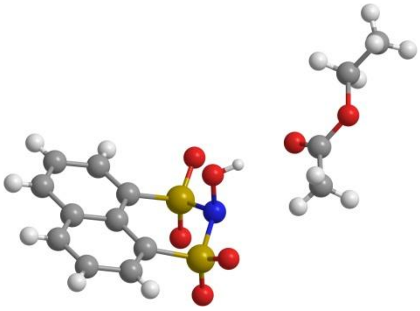


Table 1. Crystal data and structure refinement for bp2.

Identification code	bp2	
Empirical formula	C14 H15 N O7 S2	
Formula weight	373.39	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P21/n	
Unit cell dimensions	a = 14.1894(3) Å	α = 90°.
	b = 7.1236(2) Å	β = 112.6270(10)°.
	c = 18.0588(4) Å	γ = 90°.
Volume	1684.87(7) Å^3	
Z	4	
Density (calculated)	1.472 Mg/m^3	
Absorption coefficient	3.207 mm^{-1}	
F(000)	776	
Crystal size	0.30 x 0.20 x 0.20 mm^3	
Theta range for data collection	3.40 to 70.87°.	
Index ranges	-15<=h<=17, -7<=k<=8, -19<=l<=22	
Reflections collected	10441	
Independent reflections	3067 [R(int) = 0.0385]	
Completeness to theta = 70.87°	94.3 %	
Absorption correction	Empirical	
Max. and min. transmission	0.5664 and 0.4462	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3067 / 0 / 221	
Goodness-of-fit on F^2	1.040	
Final R indices [I>2sigma(I)]	R1 = 0.0388, wR2 = 0.0992	
R indices (all data)	R1 = 0.0515, wR2 = 0.1083	
Extinction coefficient	0.0105(5)	
Largest diff. peak and hole	0.257 and -0.271 e.Å^{-3}	

X-ray for data for 329

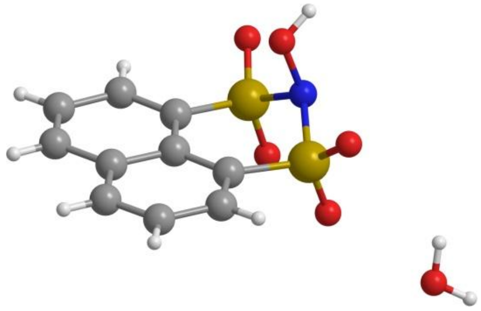


Table 1. Crystal data and structure refinement for BP886.

Identification code	BP886	
Empirical formula	$C_{10} H_7 N O_5 S_2$, $H_2 O$	
Formula weight	303.30	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 2(1)/n	
Unit cell dimensions	a = 6.9698(2) Å	α = 90°.
	b = 9.4671(3) Å	β = 94.399(2)°.
	c = 17.7500(4) Å	γ = 90°.
Volume	1167.76(6) Å^3	
Z	4	
Density (calculated)	1.725 Mg/m^3	
Absorption coefficient	0.479 mm^{-1}	
F(000)	624	
Crystal size	0.54 x 0.16 x 0.13 mm^3	
Theta range for data collection	3.07 to 27.48°.	
Index ranges	-8<=h<=9, -12<=k<=12, -22<=l<=23	
Reflections collected	16422	
Independent reflections	2668 [R(int) = 0.0898]	
Completeness to theta = 27.48°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9403 and 0.7819	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2668 / 3 / 179	
Goodness-of-fit on F^2	1.082	
Final R indices [I>2sigma(I)]	R1 = 0.0552, wR2 = 0.1506	
R indices (all data)	R1 = 0.0645, wR2 = 0.1599	
Largest diff. peak and hole	0.773 and -0.973 e.Å^{-3}	