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Nitroso Derivatives of 1,3-Dithiol-2-ylidenes, and Related Systems

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A thesis submitted for the degree of Doctor of Philosophy at the University of
Durham

May 1996

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Declaration

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Abstract

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by

Michael Allen Chalton, B.Sc. (Hons.)

A thesis submitted for the degree of Doctor of Philosophy at the University of Durham
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A range of substituted 1,3-dithiol-2-ylidene systems have been prepared. These species have, subsequently, been converted to nitroso derivatives. The role of the 4-, 5- and ylidene substituents in stabilising the nitroso-alkene moiety thus obtained has been investigated. X-ray molecular crystal data which show that these species are stabilised by intramolecular interactions are presented. Conversion of the nitroso derivatives to their thionitroso analogues has been attempted, but was unsuccessful.

A selection of 1-(1,3-dithiol-2-ylidene)-prop-2-ene systems have been prepared. These systems have been shown to be sufficiently activated to undergo nitrosation reactions at the 3-vinyl position, though the nitroso-alkenes thus formed are unstable.

A new route to 4,5-dicarbomethoxy-2-(tributylphosphino)-1,3-diselenolium tetrafluoroborate utilising hydrogen selenide as the source of selenium has been detailed. This Wittig reagent has been employed in the synthesis of various 1,3-diselenol-ylidene systems. Conversion to nitroso derivatives has been accomplished and X-ray data shows that the resultant nitroso-alkenes are stabilised by an intramolecular oxygen---selenium interaction.
Acknowledgments

I would like to thank my supervisor, Prof. Martin Bryce for his help and encouragement during the last three years that I spent in Durham.

Thanks to Ciba-Geigy (Basel) for generous funding of this work and to Dr. Jean-Claude Gehret for helpful discussions, and for arranging my three month stay in Switzerland. My thanks to Dr. Tony O’Sullivan for his ideas, encouragement, and ability to translate Schwyzerdütsch during the time that I spent in Basel.

Thanks to the technical staff in Durham for providing Mass specs, CHN analyses, NMR spectra and for fixing all the expensive glassware that I managed to break. Thanks to the crystallographers: Dr. A. Batsanov, Dr C. Lehmann and Prof. J. A. K. Howard for solving the crystal structures.

Thanks to the members of the Bryce group (and lab. 29) who have come and gone during the last three years, but especially Ade, Alex, Andy, Chez, Graham, Pete and Steve for the regularity of their trips to the ‘New Inn’. Special thanks to Ade and Chez for their help in the dithiole and diselenole chemistry and for checking the relevant chapters in this thesis.

Thanks to my parents for providing support, both moral and financial when things got tough.

Thanks and love to Helen for being there when I needed cheering up.
“I had obtained good results in such cases by the inhalation of nitrite of amyl and the present seemed an admirable opportunity of testing its virtues.”

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Chapter 1

Introduction
1.1 Introduction

1.1.1 Thionitroso compounds

Thionitroso species 1 are highly reactive intermediates whose presence normally can only be identified by a trapping reaction, with a suitable diene in a Diels-Alder reaction. Typically, the dienes used are buta-1,3-diene, 2-methylbuta-1,3-diene or 2,3-dimethylbuta-1,3-diene which form the 1,2-thiazine ring system, 2 as products (Scheme 1.1).

Since their discovery in 1966, thionitroso species have been isolated only under special circumstances. Highly sterically hindered examples have been isolated below 110K in an argon matrix by Okazaki et al. and N-thionitrosoamines have been prepared by Middleton.

The thionitrosamines were isolated as purple solids in low yields (ca. 15-30%) from either the reaction of 1,1-dialkylhydrazines with elemental sulfur, or by the lithium aluminium hydride reduction of thionyldimethylhydrazine (Scheme 1.2). At temperatures above -30°C, the thionitrosamines were unstable, and led to decomposition products with a tendency to explode. N-thionitrosoamines are acid sensitive and the methyl signals in the proton NMR spectrum of compound, 5a are inequivalent, suggesting some double bond character in the nitrogen-nitrogen bond. Middleton accounted for both these facts by suggesting that the thionitrosoamines were stabilised by the resonance form 5a'.
Recently, work has been carried out on C-thionitroso compounds and much information about the generation of such thionitroso compounds has been gained.\(^4\) To date, no isolable C-thionitroso compound has been prepared, and only recently have shelf-stable Diels-Alder adducts 6-8 been reported.\(^5\) In compounds 6 and 7 the adducts are stabilised by a non-bonded sulfur-sulfur (X=S) or sulfur-oxygen (X=O) interaction (Figure 1.1), the former leading to greater stability. Stabilisation of the thiazine ring system has also been reported to occur on chromium complexation; the X-ray crystal structure of 8 has been solved.\(^6\)

**Figure 1.1: Stabilised Diels-Alder Adducts of Thionitroso Intermediates**
Two of the most common and useful synthetic routes to thionitroso compounds are outlined in Scheme 1.3. The first route, known as the phthalimide route was developed by Taylor and Bryce. Reaction of the silylated amine, $\text{9}$ with phthalimide sulfenyl chloride led to the formation of phthalimide derivatives, $\text{10}$. These compounds were shelf-stable for extended periods of time (> 3 years). The derivatives are sparingly soluble in acetone and, therefore, reaction with a base yielded the thionitroso intermediate $\text{1}$ in only a low concentration which facilitated efficient trapping reactions with dienes and minimised the formation of other products. The second route, developed by Markovskii et al., was initially reported for the formation of alkylthionitroso species ($R =$ alkyl chain). The authors claimed that the reaction failed in the preparation of aryl thionitroso ($R =$ aryl group) species; however, recent work has shown that the route is equally useful in the synthesis of aryl derivatives. The reaction of the silylated amine, $\text{9}$ with sulfur dichloride yielded the unstable $N$-chlorothio-$N$-trimethylsilyl amines $\text{11}$. These were immediately reacted with a base to induce a 1,2-elimination reaction which formed the required thionitroso intermediate $\text{1}$.

![Scheme 1.3: Convenient Methods of Generating Thionitroso Intermediates](image)

Reagents and Conditions i) $\text{Et}_3\text{N}$, $\text{Me}_3\text{SiCl}$, Ether; ii) Phthalimide sulfenyl chloride, chloroform; iii) $\text{Et}_3\text{N}$, Acetone; iv) $\text{SCl}_2$, Ether; v) heat
1.1.2 The utilisation of a 1,3-dithiol-2-ylidene system to stabilise a thioaldehyde

At the outset of the present work Bryce et al had prepared and isolated the stable thioaldehyde 12 and X-ray data (Figure 1.2) showed a sulfur-sulfur non-bonded distance of 2.9 Å,\(^9\) which is significantly closer than the sum of the Van der Waals radii of the two sulfur atoms (3.6 Å).\(^{10}\) Thioaldehydes are normally highly unstable and reactive intermediates whose presence, like that of thionitroso species, may be confirmed only by trapping reactions.\(^1\) The X-ray data showed that this reactive moiety in 12 was stabilised by both a dipolar form and a non-bonded sulfur-sulfur interaction.

\[\text{Figure 1.2: X-Ray Molecular Structure of Thioaldehyde 12}\]

\[\text{Figure 1.3: A Resonance Stabilised Thioaldehyde}\]
This close S–S interaction is due to the formation of the dipolar structure 12', (Figure 1.3) the stability of which is increased by the formation of the 6π aromatic 1,3-dithiolium cation.\(^{11}\) We reasoned that if a structurally related thionitroso compound, 13 could be prepared, then a similar dipolar form 13' might stabilise the thionitroso moiety (Figure 1.4).

![Diagram showing the structures 13 and 13'](image)

*Figure 1.4: The Target C-Thionitroso Species*

### 1.1.3 Nitroso species as models for, and precursors to, thionitroso compounds

Cava *et al* reported the isolation of 1,3-dithiol-2-ylidene-nitroso species 16 as green solids by reaction of the corresponding 1,3-dithiol-2-ylidene system 14 with isoamyl nitrite at room temperature in dichloromethane.\(^{12}\) The reaction was found to be promoted by the presence of acids and inhibited by the presence of tertiary amines. Hence Cava suggested that the weakly electrophilic NO\(^+\) cation was not producing the nitrosation, but rather a radical mechanism (Scheme 1.4) accounted for the formation of the nitroso-alkene, making use of the well known ability of dithiole rings to stabilise positive charge as a dithiolium cation-radical e.g. as 15.\(^{13}\) Surprisingly, however, the nitroso compound 16 was represented as a transoid structure, *i.e.* 16, and there was no mention of the possibility of a non-bonded interaction stabilising the usually highly reactive nitroso-alkene moiety (structure 16'). During the course of our work, Cava published some NMR studies on these nitroso-alkenes,\(^{14}\) which provided evidence for a low barrier to rotation about the exocyclic double bond. This was interpreted as inferential evidence for an intramolecular interaction, and, hence, the cisoid nature, 16' of the nitroso-alkene in solution. However, they reported no crystallographic evidence to support this structure in the solid state. We recognised that further examination...
of the chemistry and scope of the nitrosation reaction, coupled with possible X-ray crystallographic studies, should identify whether or not the nitroso-alkene was stabilised by the envisaged intramolecular interaction.

\[
\text{Am-O-N=O} + \text{H}^+ \rightarrow \text{Am-OH} + \text{NO}^0
\]

\[
\text{NO}^0 + \text{MeCbC} \rightarrow \text{MeCbC} \quad \text{14 IS}
\]

\[
\text{MeO_C} \quad \text{NO} \quad \text{AmONO} \quad \text{NO}
\]

\[
\text{AmOR} \quad \text{N=O}
\]

\[
\text{AmOR} = \quad \text{C} \quad \text{O}
\]

**Scheme 1.4: Nitrosation Mechanism According to Cava**

The nitroso species **17** may also be considered as interesting models for their thionitroso counterparts **19** and could be used to determine the most favourable substituents for both the ylidene, and 4- and 5- dithiole substituents. The polarisation of the nitrogen-oxygen double bond in a nitroso-alkene is opposite to that of the nitrogen-sulfur bond in the thionitroso analogues, but, nonetheless, we considered that the nitroso species were good models for the thionitroso compounds.

We hoped to convert a nitroso species to the corresponding thionitroso analogue. Two possible routes were envisaged (Scheme 1.5). Firstly, the reduction of the nitroso group to an amine **18**, followed by the use of conventional thionitroso chemistry, or secondly, a more direct thionation route using phosphorus pentasulfide.
Scheme 1.5: Possible Pathways for the Conversion of Nitroso Species to Thionitroso Analogues

It was noted that Barton et al had previously investigated the use of phosphorus pentasulfide in the thionation of arylnitroso compounds and found that the reactions yielded dithionitrites (Scheme 1.6) indicating that sulfur-nitrogen double bonds could be formed this way. We hoped that in our system the intramolecular sulfur-sulfur interaction would prevent thionation proceeding beyond the thionitroso stage.

Scheme 1.6: Thionation of Aryl-Nitroso Species

1.2 1,3-Dithiole Systems

1.2.1 Introduction to 1,3-dithioles

The chemistry of dithiole rings has been much studied since the first synthesis of a benzo-fused dithiole reported by Hurtley and Smiles in 1926. Interest in dithiole containing systems has increased significantly in the last 25
years, due to the discovery in the 1970’s, that tetrathiafulvalene (TTF) 23 formed a charge transfer (CT) complex with tetracyano-p-quinodimethane (TCNQ) 24, which was found to exhibit unusually high conductivity.\textsuperscript{18} X-ray crystal structure analysis of the CT salt showed that the TTF and TCNQ units formed separate stacks in the crystal, a stacking motif which has been found to be necessary for a CT salt to be superconducting, and many research groups have attempted to increase the conductivity by modification of the basic TTF unit. Although many modifications have been attempted, the common feature of a 1,3-dichalcogen ring has remained in most cases.\textsuperscript{19} The modifications made to the TTF structure include: varying the 4- and 5- substituents, extending the dimensionality present in the structure,\textsuperscript{20} and separating the two dithiole rings with conjugated spacer units.\textsuperscript{21}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure1.5.png}
\caption{Important Compounds in the Development of Dithiole Chemistry}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure1.6.png}
\caption{Applications of the 1,3-Dithiole Unit in a Post-TTF Era}
\end{figure}
Recently Becher and Hansen reviewed the applications of 1,3-dithioles in a post-TTF era, which highlights the wide ranging uses of the 1,3-dithiol-2-ylidene unit. (Figure 1.6).\textsuperscript{13}

The applications rely on the electron-donating nature of the 1,3-dithiole ring \textsuperscript{25}. This donating ability is due to the system forming a 6\pi aromatic 1,3-dithiolium cation \textsuperscript{26}.(Scheme 1.7)\textsuperscript{13}

\begin{equation}
\chem{\begin{array}{c}
\text{S} \\
\text{S} \\
\end{array} \xrightleftharpoons{\text{e}^+} \begin{array}{c}
\text{S} \\
\text{S} \\
\end{array}}
\end{equation}

Scheme 1.7: Reversible Oxidation of a Dithiol-ylidene ring

1.2.3 Synthetic routes to the 1,3-dithiole system

The 1,3-dithiole ring system can be built up in several ways:

(a) Formation of 1 bond: Intramolecular Cyclisation
(b) Formation of 2 bonds: [4+1] atom fragments
(c) Formation of 2 bonds: [3+2] atom fragments
(d) Formation from heterocycles

each of these methods has found use in the synthesis of various dithiole systems

(a) Formation of 1 bond

The most widely used type of dithiole synthesis is the acid catalysed cyclisation of compounds containing a ketone and thione group or two thione groups. Compounds, such as \textsuperscript{27}, are readily prepared by the reaction of carbamic acid salts with \(\beta\)-chloroketones. Reaction with an acid for molecules with at least 1 thione group,\textsuperscript{22} or with hydrogen sulfide for molecules with two ketonic groups,\textsuperscript{23} leads to the required cyclisation step in high yield to give the 1,3-dithiolium system \textsuperscript{28}. (Scheme 1.8)
**Scheme 1.8: Typical Dithiolium Cation Formation by Acid Catalysed Cyclisation**

This method of dithiole formation is still widely used for the synthesis of dithiole derivatives with a range of 4- and 5- substituents, including 4,5-dimethyl, 4,5-dihydro, and fused ring groups. Recently this type of cyclisation has been utilised by Moore and Bryce in the large-scale synthesis of both trimethyltetrathiafulvalene and tetrathiafulvalene.

**Figure 1.7: Trimethyltetrathiafulvalene**

Iodine catalysed cyclisation of trithiocarbonates onto alkynes has also been utilised in the synthesis of dithiole systems. Haley showed that trithiocarbonates, or dithiocarbonates prepared by the action of sodium di- (Z = OMe) or trithiocarbonates (Z = tBuS) and allyl halides cyclised in the presence of iodine, to form the dithiolanes. Sequential treatment of with pyridine and trifluoroacetic acid induced elimination of hydrogen iodide, to produce, followed by isomerisation to afford the desired 1,3-dithiole system (Scheme 1.9)
Haley also reported a similar bromine induced cyclisation to yield a 1,3-dithiole system.\textsuperscript{28} Reaction of sodium t-butyl-trithiocarbonate with propargyl halides led to the compounds \textsuperscript{36}. Reaction of \textsuperscript{36} with bromine induced a cyclisation reaction to form a dithiolane structure \textsuperscript{37}; elimination of 2-methylpropene, yielding \textsuperscript{38} and an isomerisation afforded the required 1,3-dithiole system \textsuperscript{39}. (Scheme 1.10)

More recently Zard and Poelert have demonstrated that heating S-propargyl dithiocarbonates \textsuperscript{40} leads, \textit{via} the intermediate structure \textsuperscript{41}, to the dithiole betaines \textsuperscript{42} and \textsuperscript{43} (Scheme 1.11) which can be trapped with acid chlorides.\textsuperscript{29} The nature of the dithiole betaine (\textsuperscript{42} or \textsuperscript{43}) determined which of the two 1,3-dithiole-2-one structures \textsuperscript{44} or \textsuperscript{45} was formed; if \( R^2 \) is a proton, the dithiolane structure \textsuperscript{45} is able to isomerise, in a manner similar to that shown by Haley,\textsuperscript{27} to afford the 1,3-dithiole structure \textsuperscript{46}.
Scheme 1.10: Dithiole Systems from Propargyl Halides

Scheme 1.11: Dithiole Systems from Thermal Rearrangements
(b) Formation of 2 bonds: [4+1] atom fragments

Under this category comes the initial synthesis of a dithiole ring, 48 by Hurtley and Smiles by the reaction of 1,2-dimercaptobenzene 47 with various aldehydes.\(^\text{17}\) Oxidation of these systems leads to the formation of the benzo-fused dithiolium salt 49 (Scheme 1.12).

\[
\begin{align*}
\text{Scheme 1.12: The First Dithiole Synthesis Reported by Hurtley and Smiles}
\end{align*}
\]

Synthetically more useful dithiole ring systems, with thione substituents in the 2-position may also be produced in this manner. Reaction of the dithiolates 50 with thiophosgene 51 led to the formation of the 4,5-dicyano substituted system 52, which was subsequently converted to acid or amide substituted derivatives.\(^\text{30}\) Reaction of 52 with concentrated hydrochloric acid led to amide 53; treatment of 53 with aqueous acid afforded the di-carboxylic acid substituted 1,3-dithiole-2-thione 54 (Scheme 1.13).

\[
\text{Scheme 1.13: Dithiole Synthesis from Dithiolates}
\]

Since the work of Hurtley and Smiles, 1,2-dimercaptobenzenes 47 have found uses in other schemes which afford 1,3-dithioles (Scheme 1.14). Their
reaction with tetrachloroethene forms the benzofused TTF 56, albeit in modest yield.\textsuperscript{31} Reaction with carbon disulfide under basic conditions affords 1,3-dithiole-2-thione 55,\textsuperscript{32} and reaction with 57 affords the 2-methylthio-1,3-dithiolium salts 58.\textsuperscript{33}

\[ \text{Scheme 1.14: Formation of Dithioles from 1,2-Dimercaptobenzene} \]

(c) Formation of 2 bonds: [3+2] atom fragments

Under this methodology is, possibly, the simplest route to the dithiole ring system. In 1979 Cava \textit{et al} reported that the complex formed between carbon disulfide and alkyl phosphites, notably n-butyl phosphine, underwent a [3+2] cycloaddition reaction with dimethyl acetylenedicarboxylate (DMAD) to produce an ylide, which, upon, protonation with tetrafluoroboric acid could be isolated as its salt, 59 (Scheme 1.15).\textsuperscript{34} This ‘one pot’ synthesis was carried out under mild conditions and led to a high yield of the 2-phosphorane substituted system 59. Compound 59 has enjoyed use as a building block in dithiole chemistry primarily due to its versatility as a Wittig reagent.\textsuperscript{21,34,35} The ester groups in 60, which are undesirable in the field of electrical conductors, can be removed to yield the 4,5-unsubstituted system, 61 by reaction with wet lithium bromide in HMPA.\textsuperscript{36}
Scheme 1.15: Dithiole Synthesis from a Phosphine-Carbon Disulfide Complex

In 1976 Chen reported a method of forming dithioles from 1,2-dichloroethyl-1-ethoxyethane 62 and potassium trithiocarbonate 63, via formation of the 4-ethoxy substituted dithiolane 64 (Scheme 1.16).\(^{37}\) Acid catalysed elimination of ethanol forms the 1,3-dithiole-2-thione 65 in 89% yield.

Scheme 1.16: Two Step Dithiole Synthesis from 1,2-Dichloroethyl-1-ethoxyethane

The reaction of benzyne intermediate 66 with carbon disulfide, documented by Nakayama (Scheme 1.17) led to the formation of 67 with a carbene at the 2-position of the dithiole ring; this carbene dimerises to form benzo-fused TTF 56, via reaction of the tautomeric dipolar form.\(^{38}\) If the dithiole carbene intermediate was trapped with an alcohol then a 2-alkoxy derivative was obtained.
Scheme 1.17: A Benzo-fused TTF from the Reaction of Benzyne with Carbon Disulfide

(d) Formation from heterocycles

Dithiole derivatives have also been prepared from other heterocycles in pericyclic reactions (Scheme 1.18). The most commonly used of these techniques is that first described by Easton and Leaver in 1965; the reaction of dimethyl acetylenedicarboxylate with ethylene trithiocarbonate 66 (X=S) at elevated temperature yielded 4,5-dicarbomethoxy-1,3-dithiole-2-thione 67 (X=S) and ethene.\(^{39}\) This cycloaddition has since been accomplished with several other electron-deficient alkynes e.g. methyl propiolate, to produce substituted dithiole-2-thiones, although the method is not applicable to ethyne or electron donating alkynes e.g. diphenylethyne.\(^{40}\) The cycloaddition reaction also proceeds between 1,3-thiaoxolane-2-thione 66 (X=O) and electron-deficient alkynes to afford 1,3-dithiol-2-ones.

Scheme 1.18: Dithiole Synthesis via Cycloadditions of DMAD
1,2-Dithiole-3-thiones have been utilised in the preparation of 1,3-dithiole systems. Reaction of systems 68 with DMAD, at elevated temperature, lead to a cycloaddition to produce the dithiol-ylidene species with the other ring sulfur atom becoming a thiocarbonyl substituent. This approach was successfully employed by Bryce and Gorgues in the preparation of the stable thioaldehyde 12 (Section 1.1.2).

Noel and Vialle reported the thermal reaction of 1,3,4-dithiazoles 70 with DMAD to yield 4,5-dicarbomethoxy-1,3-dithiole-2-thione 67, and although this reaction was reported as irreproducible by Behringer and Deichmann, the results were confirmed in 1985 by Paton et al.

In 1961 Huisgen and Weberndörfer reported that the thermolysis of 1,2,3-benzothiadiazole 71 led to the elimination of nitrogen and the formation of the dipolar intermediate, which, when intercepted with carbon disulfide formed the benzo-fused 1,3-dithiole-2-thione 55 (Scheme 1.19). Cava and Spencer showed that although this reaction proceeded in very low yield for the parent 1,2,3-thiadiazole, reaction of other fused ring 1,2,3-thiadiazoles 73 in a similar manner gave the corresponding fused ring 1,3-dithiole-2-thiones 74 in ca. 40% yield.

\[
\begin{align*}
&\text{Scheme 1.19: Dithiole Synthesis from 1,2,3-Thiadiazoles} \\
&\end{align*}
\]

1.2.4 Chemistry of the 1,3-dithiol-2-ylidene system

The dithiol-ylidene system 77 is usually formed by either a Wittig or Emmons-Horner reaction (Scheme 1.20). Most of the methods of producing the dithiole ring system yield a product which can be 'slotted' somewhere in the scheme to produce these reagents. Both Wittig and Emmons-Horner reagents are
prepared from 2\textit{H}-dithiolium salts 74, which in turn are formed by the reaction of a strong acid with the dithioles possessing hetero-linked substituents at the 2-position, resulting in the liberation of the hetero-substituent.\textsuperscript{49} Dithiole species containing heterolinked 2- substituents are readily produced by reduction of dithiolium salts produced either in the dithiole forming reaction or by the methylation of dithiole-thiones.\textsuperscript{22b, 49a, 50}

\begin{center}
\textbf{Scheme 1.20: 1,3-Dithiol-2-ylidene Derivatives from Wittig and Emmons-Horner Chemistry}
\end{center}

Wittig reagents 76 are produced by the reaction of the dithiolium salt with an alkyl or aryl phosphine,\textsuperscript{47} to afford the phosphonium salt in high yield. Emmons-Horner reagents 75 are produced by the reaction of trialkylphosphites with dithiolium salts (if iodide is not the counter ion, then sodium iodide is added to remove the methyl group). The Emmons-Horner 75 reagents are more reactive than their Wittig counterparts and have, therefore, been utilised in reactions with less reactive substrates, e.g. ketones\textsuperscript{48}, rather than aldehydes.\textsuperscript{34}
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Introduction

Scheme 1.21: 1,3-Dithiol-2-ylidene Derivatives from Dithiolium Salts

The 1,3-dithiol-2-ylidene functionality can also be introduced into molecules via a reaction with dithiolium salt 78 (Scheme 1.21). Gompper and Kutter have produced benzo-fused dithiol-ylidene derivatives by this method, and Bryce and Moore have synthesised the anthrone derivatives 80 (R = Me, SMe) via reaction of dithiolium salts 78 with anthrone 79 in refluxing pyridine/acetic acid.

The dithiole-ylidene sub-unit may also be formed from a dithiolium salt 82 and dicyanomethylene anion in a Knoevenagel-type reaction, a process which has been utilised to form compounds 83 (Scheme 1.22).

Scheme 1.22: 1,3-Dithiol-2-ylidene Species via Knoevenagel Methodology

1.2.4 Reactions of the 1,3-dithiol-2-ylidene system

The most relevant reaction of the 1,3-dithiol-2-ylidene system in terms of this thesis is the nitrosation reaction reported by Cava and Lakshmikantham (see Section 1.1.3). They also reported some other interesting reactions of 1,3-dithiol-2-ylidenes. System 84 was found to be unreactive towards a benzylation reaction using benzoyl chloride in pyridine (Scheme 1.23), which suggested that the earlier reported reaction between 84 and phenyl isocyanate, was not, as postulated, a nucleophilic reaction, but rather a cycloaddition involving the ylidene bond and
the nitrogen-carbon double bond of the isocyanate to afford 85, followed by fragmentation of the lactam ring to yield the amide 86.

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{84} & \quad \text{PhNCO} \\
& \quad \text{Et}_3\text{N} \\
\text{PhCOCl} & \quad \text{Pyridine} \\
\text{Ph} & \quad \text{H} \\
\text{85} & \quad \text{Proton transfer} \\
\text{Ph} & \quad \text{Ph} \\
\text{86} & \quad \text{Ph} \quad \text{NHPh}
\end{align*}
\]

**Scheme 1.23: Reactions of the 1,3-Dithiol-2-ylidene System**

Cava reported that reaction of 87 with bromine led to a bromination to afford 89, the ease of reaction was consistent with the radical nature via 88 as suggested for the nitrosation reaction (Scheme 1.24). Reaction of 87 with benzene diazonium tetrafluoroborate in DMF solution again resulted in a substitution process, for which the initially formed 1,3-dithiol-2-ylidene radical could couple with the diazo radical to afford the product 90.

The ability of the 1,3-dithiol-2-ylidene system e.g. 84 to react through its oxidised radical cation form e.g. 91 is well documented and the resulting dimer e.g. 92 has been known for many years.\textsuperscript{53, 54} (Scheme 1.25) A related electrochemical synthesis of extended tetrathiafulvalenes via molecules of the type 84 has recently been reported (see section 2.3.4).\textsuperscript{55}
Scheme 1.24: Radical Bromination of a 1,3-Dithiol-2-ylidene and Reaction of a 1,3-Dithiol-2-ylidene with a Diazonium Salt

Scheme 1.25: Dimerisation of an Oxidised 1,3-Dithiol-2-ylidene

An unexpected reaction of the 1,3-dithiol-2-ylidene system was observed by Hansen and Bryce.\(^{56}\) Compound 93 was readily prepared by reaction of the Wittig reagent 59, and paraformaldehyde in the presence of triethylamine. However, 93 was found to be unstable with respect to a cycloaddition, as described earlier in the reaction of a 1,3-dithiol-2-ylidene with phenyl isocyanate.\(^{53}\) The cycloaddition product 94 was, itself unstable and decomposed to give a product which is suspected to be 95.
1.3 Nitroso-alkenes

1.3.1 Introduction

The chemistry of the nitroso group has developed mainly around the use of aryl and saturated aliphatic nitroso compounds, and their chemistry is well documented in the literature. Three further examples of conjugated nitroso species were reported in the late 1970’s viz. nitroso-carbonyls, nitrosyl cyanide and C-nitroso imines. All of these were shown to act as dienophiles; nitrosoalkenes are a further example of conjugated nitroso species.

\[
\begin{align*}
F & \quad N=O \\
\text{F} & \quad \text{F}
\end{align*}
\]

Figure 1.27: 1,1,2-Trifluoro-2-nitroso ethene

The first example of an isolable nitroso-alkene, 96 was reported by Griffin and Haszeldine in 1960. Many further examples of nitroso-alkenes with various \( \beta \)-substituents including alkyl, aryl, dialkylamino or halogen substituents have been reported, but these usually exist in solution as transient intermediates, their presence determined, either spectroscopically, or more conveniently, by the appearance of a characteristic blue colour in solution. The lifetime of nitroso-alkene species varies from short periods at low temperature (ca. -50 °C) to
several weeks at room temperature. Further examples of nitroso-alkenes, including all examples of terminal alkenes \(i.e.\) containing the unit \(\text{CH}_2=\text{C}(\text{R})\text{NO}\) can only be inferred by the presence of trapped products.

1.3.2 Formation of nitroso alkenes

The synthesis of nitroso-alkenes can be divided into two main types: (a) elimination methods and (b) the combination of nitric oxide with vinyl radicals. Other methods of generating nitroso-alkenes exist, although these are less general and depend on the presence of particular functional groups.

Elimination reactions provide the most important method of accessing nitroso-alkenes \(98\), viz. the reaction between \(\alpha\)-halo-oximes \(97\) and non-nucleophilic bases (Scheme 1.28).

\[ \text{H } \xrightarrow{\text{:Base}} \text{Hal} \xrightarrow{\text{R}_1 \text{R}_2 \text{R}_3 } \xrightarrow{\text{R}_1 \text{R}_2 \text{R}_3 } \]

\(97\)

\[ \xrightarrow{\text{N}=\text{O}} \]

\(98\)

\(\text{Scheme 1.28: Nitroso-alkenes from } \alpha\text{-Halo oximes}\)

The susceptibility of nitroso-alkenes to nucleophilic attack at the \(\beta\)-carbon necessitates the use of a non-nucleophilic solvent as well as a non-nucleophilic base for efficient generation. In the case of stable nitroso-alkene derivatives, tertiary amines will deprotonate the oxime, although for highly reactive species the use of an inorganic base is preferable, since it leads to a lower concentration of the reactive moiety, thereby limiting by-products. The preparation of \(\alpha\)-halo oximes \(97\) is documented in the literature and three methods are detailed in Scheme 1.29.
A second method of forming nitroso-alkenes (and the more relevant in terms of the present study) is the addition of nitric oxide to radical species. This was the postulated process in the formation of the nitroso-alkene 96, by the irradiation of iodo-trifluoroethene 98 in the presence of nitric oxide (Scheme 1.30). Irradiation of 98 formed the trifluoroethene radical 99 which combined with the radical nitric oxide to afford 96.

Other attempts to combine radicals in this way has failed to afford stabilised nitroso-alkenes. The reaction of ethyne with atomic hydrogen in the presence of nitric oxide afforded hydrogen cyanide and formaldehyde: ethane radical 100, nitroso-alkene 101 and oxazete 102 were postulated as intermediates (Scheme 1.31).
Scheme 1.31: Postulated Nitroso-Alkene Intermediate for the Reaction of Ethyne with Atomic Hydrogen and Nitric Oxide

An analogous reaction pathway was suggested for the formation of lactone 104 and hydrogen cyanide from 103 (Scheme 1.32).^{71}

Scheme 1.32: Combination of Radicals to Produce a Transient Nitroso-Alkene

Cava and Lakshmikantham reported the formation of stable nitrosoalkenes 16 by the reaction of isoamyl nitrite and 1,3-dithiol-2-ylidene species and postulated that these were formed by the reaction of a dithiol-2-ylidene radical cation and the nitric oxide radical (see Section 1.1).^{12}
Other methods exist for the preparation of nitroso-alkenes but these invariably require the presence of specific functional groups. An example of this is outlined in Scheme 1.33. Thermolysis, or irradiation, of 2-azidopyridine-1-oxides 104 leads to the formation of a dienyl-nitroso species which are transient intermediates and rapidly undergo an intramolecular reaction to produce the cyclic compounds, 6$H$-1,2-oxazines, 106, or 2$H$-pyrrole-1-oxides 107.

### 1.3.3 Reactions of nitroso-alkenes

As previously mentioned, (Section 1.3.3), transient nitroso-alkenes are liable to form oxazetes which are able to breakdown to form nitriles and carbonyl containing molecules.\(^{70}\)\(^{71}\) Investigation of the chemistry\(^{62}\) (Scheme 1.34) of the stable nitroso-alkene 108 has shown that at high temperature (220°C), 108 will also undergo the intramolecular cyclisation reaction to afford oxazete 109, which under controlled conditions can be isolated.

If the temperature of the reaction was raised to 240°C, oxazete 109 fragmented to afford ketone 110 and hydrogen cyanide. This provided confirmation of the
intermediacy of nitroso-alkenes in the previously described reactions where ketones and nitriles were isolated (Schemes 1.31 and 1.32).

Compounds such as 111, with a \( \beta \)-methyl group, have shown that nitroso-alkenes are also able to undergo a \([1,5]\)-hydrogen shift reaction to form \( \beta \)-unsaturated oximes, 112 e.g. Scheme 1.35.\(^{73}\)

![Scheme 1.35: 1,5 Hydrogen Shift in a \( \beta \)-methyl Substituted Nitroso-Alkene](image)

Nitroso-alkenes are highly susceptible to nucleophilic attack at the \( \beta \)-carbon in a Michael-addition fashion (Scheme 1.36). Thus the reaction of \( \beta \)-chloro-oximes 113, as nitroso-alkene precursors, in the presence of a strong nucleophile leads to an overall substitution reaction via 114 whereby the chlorine is replaced by the nucleophile affording 115.\(^{74}\) This elimination-addition mechanism is, however, not thought to occur with a weak nucleophile e.g. CN\(^{-}\),\(^{75}\) where conventional substitution reactions are favoured to yield 116.

![Scheme 1.36: Nucleophillic addition to \( \alpha \)-Chloro-oximes](image)

Investigation of reactions of nitroso-alkene dimers 117 in the presence of both sodium methoxide and piperidine has determined that the major product is
the piperidine substituted derivative 118 and not methoxy derivative 119.\(^{76}\) (Scheme 1.37) The dimers 117 are known to react faster with methoxide ions than with piperidine. Hence, reaction in the mixed system indicates that the reaction with the more nucleophilic piperidine occurs in the non rate determining step, and that the rate determining step must be the formation of the nitroso-alkene 98 from its dimer 117.

\[
\begin{align*}
\text{Piperidine (i) and Sodium Methoxide (ii) } & \text{In equi-molar amounts} \\
\text{(i) } & \text{NNOH MeO NOH} \\
\text{(ii) } & \text{NNOH MeO NOH}
\end{align*}
\]

Scheme 1.37 Reaction of Nitroso-Alkene Dimers in a Mixed Methoxide/Pyridine System

Reaction of both anti- 120 and syn - 122 \(\alpha\)-bromo-acetophenone oximes with morpholine, led to the formation of anti- \(\alpha\)-morpholino-acetophenone oxime 124.\(^{74}\) This provides evidence of nitroso-alkene intermediacy in the reaction, deprotonation of both syn- and anti- compounds leading to the formation of nitroso-alkene intermediates 121 and 123. The nitroso-alkene intermediate will exist primarily in its more stable transoid form 121 and, therefore, preferentially react in this configuration, affording the anti- product 124 (Scheme 1.38).
Scheme 1.38: Preferential Nucleophilic Attack upon the Anti- Configuration of Nitroso-Alkenes

Nitroso-alkenes react with a variety of nucleophiles e.g. primary and secondary amines,\textsuperscript{77} alcohols\textsuperscript{76} and thiols\textsuperscript{77}, in either reactions to give only the Michael-type addition products, or in other cases further reactions may occur.\textsuperscript{78} The reaction of nitroso-alkenes with carbon nucleophiles has found use in the alkylation of nucleophilic carbon centres under mild conditions.\textsuperscript{79} The reaction of an $\alpha$-chloro oxime with two equivalents of a reactive nucleophile, leads, firstly to the formation of a nitroso-alkene, which reacts with the second equivalent of the nucleophile to give, overall, a substitution of the halogen with the carbon nucleophile.

Nitroso-alkenes are potentially excellent reagents to effect electrophilic aromatic substitution under mild conditions, although in practice the reaction is limited to only the most nucleophilic of aromatic e.g. \textsuperscript{125} to afford \textsuperscript{127} and \textsuperscript{128} and heteroaromatic systems and the most electrophilic of nitroso-alkenes e.g. \textsuperscript{126}, the reaction with heteroaromatics being the more successful of the two (Scheme 1.39).\textsuperscript{80} However, the alkylation of pyrrole has, recently been shown by Gilchrist, not to occur via a direct substitution reaction, but rather a cycloaddition-ring opening reaction mechanism (Scheme 1.40).\textsuperscript{81} Reaction of pyrrole \textsuperscript{129} with a nitroso-alkene resulted in the [4+2] cycloaddition product \textsuperscript{130} which, when $R^1$ was a proton, underwent a proton shift to afford the oxime \textsuperscript{131}. 
Chapter 1  

Scheme 1.39: Alkylation of Aromatic Rings via Nitroso-alkenes

Scheme 1.40: Alkylation of Pyrroles with Nitroso-Alkenes

Cycloaddition reactions are a major feature in the chemistry of nitroso-alkenes, and, indeed, the existence of the more reactive examples can be inferred only by the isolation of the cycloadducts. There are 4 types of thermally allowed nitroso-alkene cycloaddition reactions (Scheme 1.41, paths A-D), and there are two thermally allowed interconversions (Scheme 1.41, paths E and F) between the adducts from the reactions.
Reactions where the nitroso group acts as a $2\pi$ unit, although common in other nitroso containing functionalities, are more unusual in nitroso-alkenes.\textsuperscript{65} They are usually only encountered with halogenated nitroso-alkenes, or in the case of [2+2] cycloadditions, if the second $2\pi$ component is a ketene.

It has been shown that reaction of nitroso-alkene 132 (path A) with cyclic dienes leads to an unstable reaction product 133 which thermally rearranges to an epoxy-aziridine 134 (Scheme 1.42).\textsuperscript{65}
Chapter 1  

Introduction

Faragher in the cycloaddition between α-nitrosostyrene and cyclopentadiene and has since been extended to other nitroso-alkenes, mainly those unsubstituted in the β-position. A wide variety of conjugated-alkenes, both cyclic and acyclic, react with β-unsubstituted nitroso-alkenes to produce 1,2-oxazine rings. These [4+2] cycloadditions are stereoselective and are, therefore, considered not to be stepwise reactions, but rather as concerted reactions with an unsymmetrical transition state, in which the formation of the carbon-oxygen bond lags behind the formation of the carbon-carbon bond: there is no evidence for the existence of long-lived dipolar intermediates. Reactions with simple alkenes (Scheme 1.43) are harder to accomplish although they have been encountered for nitroso-alkenes possessing a conjugated highly electron withdrawing group e.g. a carbonyl group as in 135 (X = COR).

\[
\begin{align*}
\text{135} & \quad \text{N=O} \\
\text{136} & \quad \text{H} \\
\rightarrow & \quad \text{R}_1 \text{R}_2 \\
\text{137} & \quad \text{H} \quad \text{H} \\
\end{align*}
\]

**Scheme 1.43: Formation of 1,2 Oxazines from Nitroso-alkenes**

[4+2] Cycloadditions of nitroso-alkenes show the expected characteristics of ‘inverse electron demand’ cycloaddition i.e. reactions with electron deficient heterodienes and electron rich dienophiles, although no rate studies have been performed on the transient nitroso-alkenes. No examples of cycloadditions with ‘normal electron demand’ involving nitroso-alkenes as the 4π component have been reported.

1.3.4 Stabilised nitroso-alkenes

Since the report that nitroso-alkene 96 was stable, several other stable nitroso-alkenes have been synthesised, two of which are shown in Figure 1.8. A common feature of these compounds is the presence of bulky aryl or alkyl groups or halogen substituents on the β-carbon. The presence of these groups stabilises the nitroso-alkene moiety by hindering the decomposition pathways.
Figure 1.8 Representative Stable Nitroso-alkenes

There have been several reports of heteropentalene structures, e.g., 140-142 which can formally be considered as nitroso-alkenes. Reaction of 6a-thiathiophens 138 (Z = S) or oxadithiapentalenes 138, (Z = O) with nitrous acid, affects a nitrosation reaction, followed by a rearrangement to produce the species 140-142. 86

Scheme 1.44: Nitrosation and Isomerisation of Heteropentalene Structures
Interestingly, studies on 138 where there is the possibility of a heteropentalene involving the nitroso or carbonyl group, showed that the system involving the nitroso group was preferred *i.e.* upon nitrosation, compound 138, having a carbonyl oxygen---sulfur interaction expelled the carbonyl group and formed a heteropentalene involving the nitroso group. The mechanism was postulated (Scheme 1.44) by Reid to involve addition of the nitrosonium cation to the pentalene system followed by cleavage of a heteroatom-heteroatom bond to form the 6π monocyclic system 139. This intermediate could lose a proton and reform a heteropentalene system. The strength of the possible hypervalent bonds determine whether the system reverts to the initial system, or forms a new system with a hypervalent bond to the nitroso oxygen, as was the case where the displaced group was a carbonyl functionality.

Reid *et al* mentioned that the nitrosation reaction with nitrous acid resulted in the production of a small amount of the nitro derivative. Treatment of authentic samples of the nitrosated species 141 with the nitrosation conditions failed to accomplish an oxidation, hence, nitro species 143 was accounted for by a direct nitration, rather than an oxidation of the major, nitrosated products 141.

![Scheme 1.45: Possible Structures for a Nitro-substituted Heteropentalene](image)

In these heteropentalene structures the nitroso-alkene moiety is stabilised by the formation of a hypervalent system 141. The X-ray crystal structure for compound 141 shows a very close S---O interaction (2.03Å) between the nitroso oxygen and the 1,2-dithiole sulfur atom. A study of the similar nitro substituted system 144 indicated that there was far less interaction between the nitro oxygen and the dithiole sulfur.

Systems where the nitroso-alkene is stabilised by a non-bonded interaction between nitroso groups and other chalcogen atoms have been reported. Reid *et al*
have reported the selenium analogues of their heteropentalene systems,\textsuperscript{89} and Cava has reported similar systems where the nitroso-alkene is stabilised by a non-bonded interaction with a chalcogen atom of a 1,3-diselenole, \textsuperscript{145} or 1,3-ditellurole ring, \textsuperscript{146}. In neither of these papers does Cava comment on the unusual stability of the nitroso-alkene, or the possibility of a stabilising interaction between a chalcogen atom and the nitroso group.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure19.png}
\caption{Nitroso-alkenes Stabilised by Intramolecular Interactions to Selenium or Tellurium Atoms}
\end{figure}

Perrier and Vialle have similarly reported the formation of nitroso-alkenes by stabilised formation of intramolecular interactions with chalcogen atoms;\textsuperscript{92} the reaction of the di-oxime \textsuperscript{147} with sulfur mono- or di-chloride afforded the heteropentalene system \textsuperscript{148a}, containing two nitroso-alkene functionalities. Reaction of \textsuperscript{147} with selenium (or tellurium) dioxide (Scheme 1.46) afforded the structurally similar heteropentalene systems where the two nitroso-alkene functionalities were stabilised by oxygen---selenium \textsuperscript{148b} (or tellurium \textsuperscript{148c}) intramolecular interactions.

\begin{scheme}[h]
\centering
\begin{align*}
\text{OH} & \text{OH} & \text{OH} & \text{OH} \\
\text{Nitroso-alkene} & \text{XO}_2 & \text{Heteropentalene} & \text{X} = \text{S} \\
\text{147} & \text{148a} & \text{148b} & \text{148c}
\end{align*}
\caption{Synthesis of a Heteropentalene Containing Two Nitroso Groups}
\end{scheme}
Chapter 2

\(1-(1,3\text{-Dithiol-2-ylidene})\) methane systems
2.1 Introduction

In order to determine the effects that the various substituents in our 1,3-dithiole compounds were having on the stability of the nitroso alkenes we decided to prepare a series of derivatives. In these derivatives we could incorporate various substituents with differing electronic characteristics and by determining whether or not the nitroso-alkene was isolable, we could discover the optimum substituents for nitroso-alkene stability and also the effect of the inter-play between substituents at both the 4- and 5- dithiole sites and the ylidene site.

2.2 Investigation of the Ylidene Substituent

2.2.1 Introduction

Initially, it was decided to investigate the effect of the ylidene substituent.

The ylidene substituent could be altered by simple variation of the aldehyde used in the Wittig reaction to form the 1,3-dithiol-2-ylidene species 151. The reactions utilise the readily accessible Wittig reagent 150, 34 prepared by the reaction of the tributylphosphine complex 149 with dimethyl acetylenedicarboxylate in a [3+2] cycloaddition reaction. The isolable Wittig salt 59, was formed in 50-60% yield by protonation of 150 with tetrafluoroboric acid (Scheme 2.1). This Wittig reagent is available in bulk quantities (ca. 40g) and is
the most conveniently prepared of all the dithiole Wittig reagents, the others requiring multi-step reactions.\textsuperscript{47}

### 2.2.2 Hydrocarbon ylidene substituents

Cava's initial paper on nitroso-alkenes\textsuperscript{12} mentioned only one ylidene substituent, namely a phenyl group: we therefore, investigated whether a simple alkyl chain would similarly produce a stable nitroso-alkene. The Wittig reaction of 150 with butanal proceeded cleanly to afford compound 151\textit{a} in 80\% yield as a viscous orange oil. It was, however, impossible to isolate the corresponding nitroso-alkene 153\textit{a}. The nitrosation reaction, as described by Cava\textsuperscript{12} proceeded as expected to produce a green colouration of the reaction mixture, which has been characteristic of these monomeric nitroso species. All attempts to isolate a product from this green solution led rapidly to the solution changing to yellow. Preliminary characterisation of the resultant yellow product was consistent with the formation of the nitro-alkene [m/z (Cl) 291, fragment 152 (M\textsuperscript{+}+1)]. It was concluded, therefore that saturated ylidene substituents disfavour the stability of the nitroso-alkenes.

![Mass Spectral Fragment from Compound 153a](image)

**Figure 2.1: Mass Spectral Fragment from Compound 153a**

In order to determine the degree of unsaturation necessary in the ylidene substituent, compound 151\textit{b} was prepared and isolated as an orange solid in 61\% yield. Nitrosation of 151\textit{b} yielded a green solid ca. 50\% yield The product was highly insoluble and could not be characterised. A proton spectrum was unobtainable due to the insolubility of the compound and the mass spectrum indicated that a mass ion 2 mass units lower than that of 153\textit{b} as well as ion peaks at greater mass; an IR spectrum showed carbonyl, alkene and ether stretches. It is possible that the compound had polymerised upon nitrosation due to the ability of the radical formed in the nitrosation step to initiate a polymerisation of the double bond (Scheme 2.2).
Scheme 2.2: Possible Polymerisation Mechanism For Compound 153b

We then turned our attention to the investigation of various aromatic substituents to discover if electron withdrawing or donating substituents favoured the stability of the nitroso-alkenes.

Table 2.1: Summary of products for sections 2.2.2 & 2.2.3

<table>
<thead>
<tr>
<th>R</th>
<th>Non-nitrosated</th>
<th>Nitrosated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Compound</td>
<td>Nature</td>
</tr>
<tr>
<td>C₃H₇</td>
<td>151a</td>
<td>Orange oil</td>
</tr>
<tr>
<td>CH=CH₂</td>
<td>151b</td>
<td>Orange solid</td>
</tr>
<tr>
<td>Ph(OMe)₂</td>
<td>151c</td>
<td>Impure</td>
</tr>
<tr>
<td>Ph-NO₂</td>
<td>151d</td>
<td>Yellow Crystals</td>
</tr>
<tr>
<td>Ph-(NO₂)₂</td>
<td>151e</td>
<td>Orange crystals</td>
</tr>
<tr>
<td>Ph-CF₃</td>
<td>151f</td>
<td>Yellow Crystals</td>
</tr>
<tr>
<td>Ph(Cl)₂</td>
<td>151g</td>
<td>Yellow oil</td>
</tr>
</tbody>
</table>
2.2.3 Substituted Aromatic Ylidene substituents

Compounds 151c and 151d were prepared by the reaction of the Wittig reagent 150 with 3,4-dimethoxybenzaldehyde and 2-nitrobenzaldehyde, respectively. The reaction with dimethoxybenzaldehyde failed to proceed to completion, despite the use of extended reaction times, presumably due to the donating substituents reducing the electrophilicity of the aldehyde carbonyl group. The product 151c was inseparable from the aldehydic starting material. The reaction to form the 2-nitrophenyl substituted 1,3-dithiol-2-ylidene 151d proceeded in 82% yield and the product isolated as bright yellow crystals. Nitrosation reactions were attempted on both compound 151d and the impure compound 151c. Unfortunately, neither reaction yielded the expected green solid. The 2-nitro compound, 151d yielded a green oil which was unstable to column chromatography (on both silica gel and alumina). The product retained its green colouration for a considerable time, consistent with the electron-withdrawing nitro-substituent stabilising the nitroso-alkene 153d. The 3,4-dimethoxy compound yielded a yellow oil which was tentatively assigned as being the corresponding nitro-alkene. The instability of the compound 153c is most likely due to the donating character of the substituents on the phenyl ring. The incompatibility of the nitrosation reaction with an aldehyde functionality (from the unreacted dimethoxybenzaldehyde) is less likely, as further work (Section 2.5) has shown that the nitrosation reaction results in stable nitroso-alkene moieties in the presence of both aldehydes and ketones.

Preparation of the 2,4-dinitrophenyl compound 151e, was attempted to determine if the compound would form an isolable nitroso-alkene species. The Wittig reaction proceeded in 80% yield to form 151e as orange crystals. Nitrosation proceeded smoothly to afford the desired compound 153e as a stable bright green solid in 48% yield. This clearly established that the presence of electron-withdrawing groups increased the stability of the nitroso-alkenes. Nitroso-alkene 153e has proved to be air-stable for greater than 2 years.

Our initial aim of producing thionitroso analogues from the nitroso compounds led to the investigation of other electron-withdrawing groups, since it was possible that nitro groups on the phenyl ring may interfere with either the
reduction step or the direct thionation (Scheme 1.5). The Wittig reaction with 2,6-dichlorobenzaldehyde produced 151g, in 90% yield as a viscous yellow oil, nitrosation of which produced compound 153f in 27% yield as bright green crystals. Similarly a Wittig reaction with 2-trifluoromethylbenzaldehyde produced 151f in 64% yield. The proton NMR spectrum of 151f showed the vinyl peak as a quartet ($J_{HF} = 4\text{Hz}$) (Figure 2.2) rather than the usual singlet, probably due to through bond coupling to the 3 fluorine nuclei in the trifluoromethyl group. Nitrosation of 151f yielded a green oil presumably 153f, which, though stable to air was unstable to purification by column chromatography on either silica gel or alumina.

![Figure 2.2: Comparison of the Vinyl Peaks in the $^1H$ NMR spectra of Compounds 151f and 151g](image)

Attempted nitrosation of compound 14 a 1,3-dithiol-2-ylidene with a phenyl ylidene substituent, using excess nitrosonium tetrafluoroborate yielded a very intense green coloured solution in either dichloromethane or acetonitrile at 0°C, from which no pure product could be isolated.

This failure of nitrosonium tetrafluoroborate to effect a clean nitrosation is possibly due to there being too high a concentration of nitrosonium ions. This
would lead to a high concentration of NO radicals which would be more likely to undergo unwanted side reactions than react with the dithiol-2-ylidene species.

### 2.2.4 Heterocycles as ylidene substituents

In a parallel study we attempted to prepare stable 1,3-dithiol-2-ylidene-nitroso compounds with heterocycles as ylidene substituents. The compounds 151h-l were prepared in ca. 90% yield by a Wittig reaction between 150 and the appropriate heterocyclic aldehyde. Nitrosation reactions of the compounds 151h-k failed to afford stable nitroso-alkenes, but rather yellow oils which were tentatively identified as the corresponding nitro-alkenes on the basis of mass spectral evidence. This showed that the inherent electron rich nature of the 5 membered heterocycles was too great to stabilise the nitroso-alkenes, and that the inclusion of a highly electron withdrawing substituent in 153j and 153k was insufficient to counter this effect. Nitrosation of the 2-pyridyl substituted 1,3-dithiol-2-ylidene afforded the nitroso-alkene 153l in 50% yield as emerald green pinnacoidal crystals, which were suitable for single crystal X-ray analysis.

**Table 2.2: Summary of compounds for section 2.2.4**

<table>
<thead>
<tr>
<th>R</th>
<th>Non-nitrosated</th>
<th>Nitrosated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Compound</td>
<td>Nature</td>
</tr>
<tr>
<td>2-Thienyl</td>
<td>151h</td>
<td>Brown Solid</td>
</tr>
<tr>
<td>5-Nitro-2-thienyl</td>
<td>151j</td>
<td>Orange Crystals</td>
</tr>
<tr>
<td>5-Nitro-2-furyl</td>
<td>151k</td>
<td>Dark red crystals</td>
</tr>
<tr>
<td>2-Pyridyl</td>
<td>151l</td>
<td>Orange Crystals</td>
</tr>
</tbody>
</table>
The X-ray structure was solved by Dr. A. Batsanov and several interesting structural features were highlighted. The crystal structure has two independent molecules in the unit cell, and this initially led to difficulties in the refinement (Figure 2.3). The structure provides, for the first time, direct evidence of the expected cisoid nature of the nitroso-alkene moiety of the molecules in the solid state. Both independent molecules (A and B) exhibited the predicted close S—O interaction between the nitroso oxygen and a sulfur atom in the dithiole ring. The inter-atomic distances were 2.36Å (molecule A) and 2.35Å (molecule B), which are both considerably shorter than the sum of the sulfur and oxygen Van der Waals radii (3.25Å).

![Figure 2.3: X-Ray Molecular Structure of Nitroso-alkene 153](image)

Figure 2.3: X-Ray Molecular Structure of Nitroso-alkene 153
Examination of the bond lengths indicates that the C-N [1.345Å (A), 1.336Å (B)] and C=C [1.385Å (A), 1.409Å (B)] bonds are respectively shorter and longer than the expected values (C-N, 1.47Å; C=N, 1.28Å and C=C, 1.34Å respectively), suggesting a contribution from the dipolar form 153'. The crystal structure shows that the molecules are essentially flat, with the ester groups inclined to the plane of the molecule, and the nitroso group slightly displaced from the plane of the ring. These data proved that the reactive nitroso-alkenes are stabilised by the dipolar resonance form 153' and a close S—O interaction. The ester groups on the dithiole ring prevented efficient stacking of the dithiole units which is seen in many other dithiole derivatives.

2.2.5 Carbonyl containing groups as ylidene substituents

In the field of extended tetrathiafulvalene (TTF) analogues, there have been reports of the reaction of Wittig reagent 150 with glyoxal (Scheme 2.3).\cite{47b}

The isolable intermediate 155, in the reaction scheme to produce 156 retains the 1,3-dithiol-2-ylidene unit and also possesses an ylidene electron withdrawing group that could to stabilise a derivative nitroso-alkene.

\[ \text{Scheme 2.3: Preparation of Extended Tetrathiafulvalene Analogues for Organic Conductors} \]

Utilising the literature procedure, described by Yoshida, compounds 157a and 157b were prepared in 70% and 89% yield respectively, as yellow solids.\cite{47b} Both the reactions led only to the mono-reacted product, and with methylglyoxal it is notable that reaction occurred exclusively with the aldehydic carbonyl group;
both these facts can be explained by the fact the both the dithiole substituent and
the methyl group are electron donating, thereby deactivating the carbonyl group
towards nucleophilic attack. Nitrosation of both compounds \textbf{157a} and \textbf{157b}
proceeded to give the expected green coloured solution from which
nitroso-alkenes \textbf{158a} and \textbf{158b} were isolated as green solids in 45\% and 70\%
yield respectively. At this point during our study, Cava reported the preparation
of compound \textbf{158b} in good yield, although the melting point he reported is
markedly different from that we obtained (Mp 127-128\degree C, lit. 116\degree C). All other
data indicate the two compounds are identical.\textsuperscript{14}

\begin{center}
\textbf{Scheme 2.4: Preparation of Dithiole Systems with Ylidene Carbonyl Groups}
\end{center}

\begin{table}
\centering
\begin{tabular}{|c|c|c|c|c|c|}
\hline
R & Non-nitrosated & & Nitrosated & \\
 & Compound & Nature & Yield / \% & Compound & Nature & Yield / \% \\
\hline
Me & \textbf{157a} & Yellow & solid & 70 & \textbf{158a} & Green & Crystals & 45 \\
\hline
H & \textbf{157b}\textsuperscript{17b} & Yellow & solid & 89 & \textbf{158b}\textsuperscript{14} & Green & Crystals & 70 \\
\hline
\end{tabular}
\caption{Summary of Compounds for Section 2.2.5}
\end{table}

Recrystallisation of compound \textbf{158a} from dichloromethane/hexane
1:10 \textsuperscript{v/v} led to the growth of crystals suitable for single crystal analysis (Figure
2.4). The structure revealed many similarities with the structure of the pyridyl
derivative, \textbf{1531}. Again the structure is essentially flat, with the dithiole ring, the
nitroso and carbonyl groups lying in the same plane. The oxygen atoms of both
the nitroso and carbonyl groups show close contacts with the dithiole ring (S---O
distances of 2.43Å & 2.68Å respectively). The nitroso oxygen is more closely bound than the carbonyl oxygen, this is in accordance with the results reported by Reid et al (see section 1.3.4). As found with the pyridyl derivative 1531 the presence of the ester groups prevented efficient stacking of the molecules.

We investigated the formation of imines from compounds 157a and 157b using the route reported by Boger et al for the production of α-β unsaturated imines (scheme 2.5).

Thus compound 157b was stirred in refluxing toluene with the appropriate amine, together with a large excess of magnesium sulfate. The required imines were isolated in reasonable yield with extended reaction times (typically 72h), which could be substantially reduced (to 16h) by the substitution of xylenes for toluene. It was not possible to form imines from the reaction of amines with 157a, this probably due to the deactivating nature of the ketonic methyl group.

Figure 2.4: X-ray Crystal Structure of Nitroso-alkene 158a
Scheme 2.5: Generation of Dithiol-Ylidene Systems with Conjugated Imino Substituents

Table 2.4: Summary of Imine Derivatives

<table>
<thead>
<tr>
<th>R</th>
<th>Non-nitrosated</th>
<th>Nitrosated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Compound</td>
<td>Nature</td>
</tr>
<tr>
<td>4-Tolyl</td>
<td>159a</td>
<td>Orange</td>
</tr>
<tr>
<td></td>
<td>159b</td>
<td>Orange</td>
</tr>
</tbody>
</table>

Nitrosation of compound 159a, under standard conditions afforded the required nitroso substituted imine in 23% yield as a buff coloured powder, although in dichloromethane or chloroform solution this acquired the expected green colouration. Attempted nitrosation of imine 159b, led to production of an oil which was unstable to column chromatography and was not isolated.

2.3 Investigation of the 4- & 5- substituents on the dithiole ring.

2.3.1 Introduction

Having determined the optimum nature of the ylidene substituent our attention turned to investigating the role that the substituents in the 4- and 5-positions on the dithiole ring were playing in stabilising the nitroso-alkenes. The
only other 4- or 5- dithiole substituent previously prepared was a 4-phenyl derivative 161 reported by Cava.12

![Figure 2.6: 4-Phenyl Dithiole Derivative Described by Cava](image)

2.3.2 Preparation of the mono-ester substituted dithiole ring analogues.

![Scheme 2.6: Preparation of 1-(4-Carbomethoxy)-1,3-dithiole-2-ylidene)-1-(2-pyridyl) nitroso methane](image)

Rather than make a radical departure from the electronic characteristics of the molecules studied in Section 2.2 preparation of the mono ester version, 163 was attempted.

The cycloaddition of the tributylphosphine-carbon disulfide adduct with other dipolarphiles eg.methyl propiolate is well documented.96 It is not possible to isolate the Wittig reagent 162 (in contrast to 150) which was reacted with pyridine-2-carboxaldehyde in situ (scheme 2.6) to produce 163 in 33% yield. Examination of the proton spectrum of 163 indicated that as expected both the s-cis and s-trans isomers were formed in equimolar amounts. Both the dithiole ring proton and the vinyl proton appear as two distinct singlets, separated by 0.01 ppm: although no attempt was made to separate the isomers or to assign the
peaks to the specific isomers (Figure 2.7). Nitrosation of 163 afforded the required nitroso compound 164 as a sparingly soluble green solid (54% yield).

![Proton NMR Spectrum of 163](image)

**Figure 2.7: Section of the Proton NMR Spectrum of 163 Showing the Two Peaks Due to the Mixture of s-cis and s-trans isomers**

### 2.3.3 Preparation of 4,5 di(methylthio) derivatives.

Methylthio substituents on the 1,3-dithiole ring are less electron withdrawing than ester groups, acting as both d-acceptors and π-donators with an overall electron-withdrawing effect.\(^{97}\) The starting material for the preparation of the 4,5-di(methylthio) derivatives is the tetraethylammonium zinc bis-dithiolate (zincate) complex, 165 which is prepared by a chemical reduction of carbon disulfide with metallic sodium.\(^{98}\) The reaction was first investigated by Fetkenheuer in 1927,\(^{99}\) although it was not until 1974 that the product obtained by trapping with methyl iodide was correctly assigned as 4,5-dimethylthio-1,3-dithiole-2-thione 166 by Wawzonek.\(^{98}\) Methylthio substituted dithiol-2-ylidene derivatives are readily prepared from the highly versatile zincate salt 165 (scheme 2.7).\(^{100}\) Methylation of salt 165 with methyl iodide, affords 166 in excellent yield. A second methylation with neat dimethyl sulfate (or methyl triflate in dichloromethane) followed by an anion exchange with tetrafluoroboric acid in ether led to the production of the dithiolium cation 167. Compound 167 could be reduced with sodium borohydride to afford product 168, which, upon reaction
with tetrafluoroboric acid led to the elimination of methanethiol and the formation of the 2H-dithiolium cation salt 169.

Scheme 2.7: Preparation of 4,5-Dimethylthio-1,3-dithiolium Tetrafluoroborate

There are two possible methodologies to assemble the desired 1,3-dithiol-2-ylidene systems from 169, viz either the preparation of a) a Wadsworth-Emmons reagent\textsuperscript{101} 171, or b) the preparation of a Wittig salt 170\textsuperscript{a} or 170\textsuperscript{b}\textsuperscript{101} (scheme 2.8).

The Wadsworth-Emmons reagents are easily prepared following the procedure outlined by Moore and Bryce.\textsuperscript{101} Thus, reaction of 169 with trimethyl phosphite in the presence of sodium iodide, led to the Wadsworth-Emmons reagents in high yields as dark red, unstable oils, reaction of 171 with a base followed by the appropriate aldehyde, in tetrahydrofuran at -78°С, afforded the required 1-(4,5-methylthio-1,3-dithiol-2-ylidene) methane derivatives 172\textsuperscript{a} and 172\textsuperscript{b} in 30% and 33% yields respectively, as yellow oils.

The routes utilising the Wittig reagents 170\textsuperscript{a} and 170\textsuperscript{b} were also attempted; reaction of the dithiolium cation 169, with triphenyl phosphine or tributyl phosphine led to the generation of the Wittig reagents 170\textsuperscript{a} and 170\textsuperscript{b} as white crystalline solids in excellent yields (ca. 90%).\textsuperscript{102} Reaction of the tributyl phosphine Wittig salt with aldehydes led to the formation of the required systems 172 in good yields.
Chapter 2

1-(1,3-Dithiol-2-yldene) methane systems

Scheme 2.8: Routes to 4,5-Di(methylthio)-1,3-dithiol-2-yldene Systems

However, reaction with the triphenylphosphine Wittig reagent 170b led to the formation of the tetra(methylthio)tetrathiafulvalene 173. This is in contrast to the results of the reaction with glyoxal as reported by Moore and Bryce whereby the 1,3-dithiol-2-yldene is formed in good yield and also the results found by Hansen and Bryce whereby the thiobenzoyl substituted dithiole triphenyl phosphine Wittig reagent 174 leads to the production of the compounds 175 in high yield (scheme 2.9).

Scheme 2.9: Use of a Triphenyl Wittig Reagent in Forming 1,3-Dithiol-2-yldene Systems
The dimerisation reaction of 169 to 173 is well known in the literature, and extensively utilised in the preparation of tetrathiafulvalene derivatives.\textsuperscript{104} The formation of product 173 may be accounted for by the sequence outlined in scheme 2.10. The Wittig salt 170b is in equilibrium with both the dithiolium cation 169 and the Wittig reagent 176b. If the rate of reaction between the aldehyde and Wittig reagent is slow compared with the deprotonation of the dithiolium cation 169, then the carbene 177 will exist in a concentration high enough to lead to the reaction of 177 with the dithiolium cation 169 to produce 178. The species 178 will then be deprotonated by a further mole of base to form the tetrathiafulvalene 173.

\begin{center}
\begin{tikzpicture}
\node[below] at (0,0) {169};
\node[below] at (0,-1) {170b};
\node[below] at (0,-2) {177};
\node[below] at (0,-3) {173};
\node[below] at (1.5,-1) {172};
\node[below] at (1.5,-2) {178};
\path[draw] (0,0) edge (0,-1) edge (1.5,-1) (0,-1) edge (1.5,-2) (1.5,-1) edge (1.5,-2);
\draw[thick] (0.5,-1) -- (1,0) -- (1.5,-0.5);
\draw[thick] (0.5,-2) -- (1,0) -- (1.5,-1.5);
\node at (0,0) {MeS} node at (1,0) {PPh\textsubscript{3}} node at (0,-1) {MeS} node at (1,-1) {Et\textsubscript{3}N} node at (0,-2) {MeS} node at (1,-2) {H} node at (1.5,-1) {170b} node at (1.5,-2) {177};
\end{tikzpicture}
\end{center}

\textit{Scheme 2.10: Formation of Tetra(methylthio)tetrathiafulvalene}

The fact that the tributylphosphine Wittig reagent 170a will undergo a Wittig reaction under the same conditions, indicates that there is a further factor, probably electronic, to be considered when deciding which Wittig reagent to prepare. In the presence of a base there are two possible equilibria for the phosphonium salt 170, the equilibrium between the salt and the Wittig reagent...
176 and the equilibrium between the phosphonium salt and the dithiolium salt 169 (Scheme 2.11). There are two possible explanations for the difference in reaction products:

(a) If the equilibria favour formation of the Wittig reagent, then a Wittig reaction will result, whereas if the equilibria favour formation of the dithiolium salt the substituted tetrathiafulvalene will result. The results obtained would indicate that for R = butyl the Wittig reagent predominates, but for R = phenyl the dithiolium salt predominates.

(b) The distribution of the products at equilibrium is unimportant, but rather the relative rates of reaction of the species 176 and 169 influence the products. The results obtained would indicate that if R = butyl then $k_1 > k_2$, but if R = phenyl then $k_1 < k_2$.

The fact that the phenyl Wittig reagent reacts with glyoxal to produce the desired Wittig product, suggests that the second explanation is the more plausible, since the balance of the equilibrium is unlikely to be moved by the presence of glyoxal rather than benzaldehyde. The highly electron deficient nature of the carbonyl groups in glyoxal render it more susceptible to the
nucleophilic attack necessary for the Wittig reaction to occur. A possible explanation for the discrepancy in the reaction products is the donating nature of the butyl groups, which will stabilise a greater positive charge on the phosphorus atom and hence allow a greater negative charge on the carbon atom rendering it more nucleophilic.

**Table 2.5: Summary of Compounds for Section 2.3.3**

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>R</th>
<th>Non-nitrosated</th>
<th>Nitrosated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Compound</td>
<td>Nature</td>
</tr>
<tr>
<td>Phenyl</td>
<td>172a</td>
<td>Yellow Oil</td>
</tr>
<tr>
<td></td>
<td>172b</td>
<td>Yellow Oil</td>
</tr>
<tr>
<td></td>
<td>172c</td>
<td>Black Solid</td>
</tr>
<tr>
<td>Pyridyl</td>
<td>172a</td>
<td>Yellow Oil</td>
</tr>
<tr>
<td></td>
<td>172b</td>
<td>Yellow Oil</td>
</tr>
<tr>
<td></td>
<td>172c</td>
<td>Black Solid</td>
</tr>
<tr>
<td>2,4-(NO₂)₂ Phenyl</td>
<td>172a</td>
<td>Black Solid</td>
</tr>
<tr>
<td></td>
<td>172b</td>
<td>Yellow Oil</td>
</tr>
<tr>
<td></td>
<td>172c</td>
<td>Black Solid</td>
</tr>
</tbody>
</table>

Nitrosation reactions of 172a-c were attempted. Derivative 172a reacted (t.l.c. evidence) but yielded a dark red/brown oil which was unstable to column chromatography, and was not purified. Compounds 172a and 172b nitrosated smoothly to produce a dark brown solution, from which the dark brown nitroso-derivatives 179a and 179b could be isolated (82% and 35% yields). The startling difference in colour between the ester substituted derivatives and these methylthio derivatives is possibly explained by a greater intramolecular donor-acceptor nature of the latter system. The UV spectra of three pyridyl systems are detailed in table 2.6. Each compound shows two characteristic absorptions at ca. 302-313 nm and ca. 441-466 nm which are not present in the parent dithiol-2-ylidene system. The absorptions for the strongly electron withdrawing
subsituents (mono and diesters) are both within experimental error (2nm) of each other and significantly lower than those for the less electron withdrawing methylthio derivitives. The difference in wavelength suggests a more aromatic system in the methylthio case indicating that there is greater cyclisation of the nitroso group. Both the diester 1531 and methylthio 179a nitroso species show the characteristic weak nitroso-alkene absorption at about 650 nm.

**Table 2.6: U.V. Data for Pyridyl Substituted Nitroso-alkenes**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Colour</th>
<th>Absorbance 1 (MeCN)</th>
<th>Absorbance 2 (MeCN)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>( \lambda / \text{nm} )</td>
<td>( \varepsilon / \text{1 mol}^{-1} \text{ cm}^{-1} )</td>
</tr>
<tr>
<td>1511</td>
<td>Green</td>
<td>302</td>
<td>1.60 x 10^4</td>
</tr>
<tr>
<td>164</td>
<td>Green</td>
<td>304</td>
<td>1.53 x 10^4</td>
</tr>
<tr>
<td>179b</td>
<td>Brown</td>
<td>313</td>
<td>4.45 x 10^3</td>
</tr>
</tbody>
</table>

Crystals of 179b were suitable for single crystal X-ray analysis. The structure of 179b was solved by Dr. A. Batsanov and the key features are shown in figure 2.13. As was found for 1511 and 158a molecules of 179b exhibited a S—O close interaction of 2.359Å which is almost indentical to the S—O distance in the ester substituted system (see section 2.2.4) the C=C, C-N, and N=O bond lengths are different from those expected, the double bonds being slightly longer and the single bond slightly shorter. As shown in figure 2.13 there is slight disorder in one of the methyl groups. The packing diagram indicates that the molecules stack in the direction of the x-axis with almost maximum (head to tail) overlap. The interlayer spacing is ca. 3.55Å.
2.3.4 Preparation of 4,5-dimethyl derivatives

Having determined that the nitroso-alkenes could be stabilised by an intramolecular interaction with a dithiole ring substituted with electron withdrawing groups, attention turned to studying dithiole rings substituted with electron donating groups, specifically the 4,5-dimethyl species 188, the preparation of which is outlined in Scheme 2.12.

Reaction of the sodium salt of piperidinodithiocarbamate 180 with 3-chloro-2-butanone to afford 181, followed by acid catalysed cyclisation leads to the formation of iminium salt 182. Iminium salt 182 was reduced to 183 by reaction with sodium borohydride, acidification with hexafluorophosphoric acid afforded the dithiolium hexafluorophosphate salt 184. Conversion to the iodide salt 185, was achieved by dissolving 184 in a minimum volume of acetone, to
which an excess of sodium iodide in acetone was added to precipitate 185 as a bright yellow solid.26

Scheme 2.12: Preparation of 4,5-Dimethyl-1,3-Dithiolium Systems

Wittig reagent 186 was found to be preferable to the Wadsworth-Emmons reagent as the former was stable under argon for a significantly longer period than the latter. The derivative 188a with the phenyl ylidene substituent
was prepared in 50% yield in both the Wadsworth-Emmons and Wittig procedures. Compound 188a was found to be less stable than the ester and methylthio substituted analogues 14 and 172a discussed earlier, and decomposed to a red compound in ca 1-2 weeks. The product from this decomposition is unknown, but the cyclic voltamograms of compound 188a indicate (Figure 2.9) that it undergoes the dimerisation process (189 to 191) reported by Lorcy et al who also mention that the species 189 decompose on standing (Scheme 2.13).55

\[
\begin{align*}
2 \begin{array}{c}
\text{Me} \\
\text{MeS} \\
\text{H}
\end{array}
\begin{array}{c}
\text{S} \\
\text{Me} \\
\text{MeS}
\end{array}
\begin{array}{c}
\text{R} \\
\text{H}
\end{array}
& \xrightarrow{-1e^0} \begin{array}{c}
\text{Me} \\
\text{MeS} \\
\text{H}
\end{array}
\begin{array}{c}
\text{S} \\
\text{Me} \\
\text{MeS}
\end{array}
\begin{array}{c}
\text{R} \\
\text{H}
\end{array} \\
\text{189} & \rightarrow \text{190}
\end{array}
\]

\[
\begin{array}{c}
\text{Me} \\
\text{MeS} \\
\text{MeS}
\end{array}
\begin{array}{c}
\text{S} \\
\text{Me} \\
\text{MeS}
\end{array}
\begin{array}{c}
\text{R} \\
\text{R}
\end{array}
& \xrightarrow{-2H^0} \begin{array}{c}
\text{Me} \\
\text{MeS} \\
\text{MeS}
\end{array}
\begin{array}{c}
\text{S} \\
\text{Me} \\
\text{MeS}
\end{array}
\begin{array}{c}
\text{R} \\
\text{R}
\end{array} \\
\text{191}
\end{array}
\]

**Scheme 2.13: Radical Dimerisation Reported By Lorcy et al**

This dimerisation is reported as a radical process, and hence the decomposition maybe due to the formation of radicals on standing. The dimerisation is not encountered for the diester, or the monoester case probably due to the reduced stability of the radical cation analogous to 190.

Nitrosation of compound 188a, failed to lead to the formation of a stable nitroso-alkene; the transient green colour indicating the formation of nitroso-alkene rapidly changed to a yellow colour indicating oxidation to a nitro-alkene. This indicates that the electron-donating groups on the dithiole ring destabilise the nitroso-alkene with respect to the electron-withdrawing ester substituents.
Chapter 2  \(1\)-(1,3-Dithiol-2-ylidene) methane systems

![Cyclic Voltamogram](image)

**Figure 2.9:** Cyclic Voltamogram for compound 188a in Acetonitrile at 20°C with Tetrabutylammonium Hexafluorophosphate as Electrolyte.

**Table 2.6: Summary of compounds for Section 2.3.4**

<table>
<thead>
<tr>
<th>R</th>
<th>Non-nitrosated</th>
<th>Nitrosated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Compound</td>
<td>Nature</td>
</tr>
<tr>
<td>Phenyl</td>
<td>188a</td>
<td>Off-white solid</td>
</tr>
<tr>
<td>2,4-(NO(_2))(_2) phenyl</td>
<td>188b</td>
<td>Dark purple solid</td>
</tr>
</tbody>
</table>

To investigate further whether the ylidene substituent, or the 4- and 5-dithiole substituents played the dominant role in stabilising the nitroso-alkene species, compound 188b was prepared in 87% yield as a purple-black solid. The darker colour possibly being due to intramolecular charge transfer.\(^{105}\) Nitrosation
of the compound 188b proceeded smoothly to afford 192b (85%), as a green-black solid. We conclude therefore that the electronic characteristics of the ylidene substituent dominate in stabilising the nitroso-alkene.

2.4 Conjugated Bis(1,3-dithiol-2-ylidene) systems

2.4.1 Introduction

As illustrated in scheme 2.11, bis-dithiole systems are easily prepared from readily available starting materials.

\[
\begin{align*}
\text{Scheme 2.14: Vilsmeier Reaction of 1,2-bis-(1,3-dithiol-2-ylidene) Ethane Systems}
\end{align*}
\]

One reaction of these systems is a Vilsmeier formylation with a dimethyl formamide / oxalyl chloride complex to form 193 (scheme 2.14). Only monoformylation occurred according to Yoshida,\textsuperscript{106} even though a large excess of formylating agent was used, although recent results suggest that this may not be the case with the methylthio substituted systems.\textsuperscript{107} We investigated whether nitrosation would occur in these compounds, and whether the system would react once or twice.

2.4.2 1,2-Bis(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-ethane

Compound 196a was prepared by the literature method:\textsuperscript{47b} compound 157b was isolated then reacted with another equivalent of the Wittig reagent 150 at higher temperature to produce the required compound as a dark purple crystalline solid (37% yield over both steps). The nitrosation of compound 196a proceeded smoothly to generate the characteristic green solution from which the dinitroso compound 196b could be isolated as a green solid in 53% yield. This appears to contradict earlier results, since the electron donating 1,3-dithiole ring
should destabilise the nitroso-alkene. This contradiction can be explained in two possible ways. Firstly, the nitrosations are probably sequential. After the first nitrosation has occurred, the mono nitrosated product is destabilised by the electron donating character of the dithiole ring. The second nitrosation must occur more rapidly, to form the bis-nitrosated product 196b before oxidation to the nitro alkene can occur.

\[
\text{MeCbC} \quad \text{NO} \quad X \quad \text{S NO} \quad \text{ON} \quad \text{CCbMe} \quad \text{MeCbC} \quad \text{ON} \quad \text{CCbMe}
\]

\[
\text{MeCbC} \quad \text{MeCbC} \quad \text{N=O}
\]

\[
\text{MeCbC} \quad \text{MeCbC} \quad \text{N=O} \quad \text{N CO^Me} \quad \text{CCbMe}
\]

\[
\text{MeCbC} \quad \text{MeOi}
\]

\[
\text{Or}^®
\]

\[
\text{196b}'
\]

\[
\text{196b}''
\]

**Figure 2.10:** Possible Explanations for the Unexpected Stability of 196b

After this second nitrosation, the donating nature of both the dithiole rings is 'tied up' in stabilising the closer nitroso-alkene and is therefore unable to destabilise the other nitroso-alkene moiety (Figure 2.10, 196b'). Another possibility is that there are two possible S—O interactions which can stabilise the nitroso-alkene, the 5-membered interaction encountered in the systems discussed earlier, or a 6-membered interaction with a sulfur atom in the more remote dithiole ring 196b''. Experiments to test these hypotheses are reported below.

2.4.3 1,4-*Bis-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-benzene

To explore further if the unexpected stability of 1,2-dinitroso-1,2-bis-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-ethane we prepared the phenyl spaced analogue, 194a, by the Wittig reaction of 150 with terephthalaldehyde proceeded which proceeded twice in 50% yield without need to isolate the mono Wittig product.\(^{35}\) Nitrosation of 194a proceeded smoothly and bis-nitroso-alkene 194b could be isolated as a green solid in 36% yield.
This result suggested that the 6-membered interactions, did not play a part in stabilising the nitroso-alkene, and indicated that the first explanation above (see section 2.4.2) was the more reasonable. To confirm this we aimed to prepare a mono-nitrosated version of the form of a bis-1,3-dithiole.

The attempt to form compound 198 by a Wittig reaction between compounds 150 and 158b (Scheme 2.16) was unsuccessful; the reaction led to decomposition of the starting nitroso-alkene. This failure was due either to the incompatibility of the nitroso-alkene with the conditions needed to generate the Wittig reagent, or that the Wittig reagent was insufficiently reactive to react with the aldehydic functionality in compound 158b. Further attempts at Wittig reactions of 158b with the 4-nitrophenyl Wittig 199 reagent to produce 200 also led to decomposition of starting materials. It became apparent that this route would be unsuccessful and that a fresh approach was necessary.
2.4.4 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-2-[4,5-di(methylthio)-1,3-dithiol-2-ylidene]-propane.

The compound 197 with a methyl group at one of the vinyl positions would allow the formation of a mono-nitrosated system. Attempts to prepare 197 from 157a were unsuccessful, and is probably due to two factors; firstly the donating nature of both the dithiole ring and the methyl group reducing the electrophilicity of the carbonyl group, and secondly a steric influence of the methyl group had to be considered. It was decided that a more reactive Wadsworth-Emmons reagent would alleviate this deactivated carbonyl problem, but the 4,5-dicarbomethoxy-1,3-dithiole Wadsworth-Emmons reagent is unstudied. It was thought that the mixed compound 195a would alleviate this problem since the di(methylthio) Wadsworth-Emmons reagent is well documented. The target compound was synthesised in low yield (14%), by reaction of the known, 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-propanone, 157a with the di(methylthio)-dithiole Wadsworth-Emmons reagent in tetrahydrofuran at -78°C. This low yield was probably due to the competing reaction between the Wadsworth-Emmons reagent and the ester carbonyl group, this has been encountered before and is why the Wadsworth-Emmons chemistry of the 4,5-dicarbomethoxy system has not been studied.
Nitrosation of compound 195a failed to lead to stable nitroso-alkene products, but to a yellow oil which is tentatively assigned as the nitro-derivative. This result confirms that hypothesis that unexpected stability of these systems is due to the donating character of the dithiole ring being unable to destabilise the one nitroso-alkenes as it is 'tied up' in stabilising the other with an S—O interaction.

2.5 Conclusions

We have investigated the effect of the ylidene and 4- and 5- substituents in stabilising the nitroso-alkene moiety, and shown that the stability is enhanced by the use of electron-withdrawing substituents. It has been shown that the effect of the exo-cyclic substituent has the greater bearing on the stability of the nitroso-alkene. X-ray analysis has confirmed the idea that the originally suggested transoid nature of the nitroso-alkenes is incorrect and they are actually a cisoid structure with the nitroso oxygen atom in close contact with a sulfur in the dithiole ring. Examination of the bond lengths in the X-ray structures have shown that there is a major contribution to the structure from a dipolar resonance form, which is exactly what is required for stabilisation of the thionitroso target molecules. Work into organic conductors has shown that dithiole rings substituted with electron-donating groups are more readily oxidised than those with electron deficient ones. It is, therefore, possible that the same oxidation procedure manifests itself as the oxidation of the nitroso group to the nitro species as encountered in these systems.

2.6 Investigation of Diels-Alder Reactions of the Nitroso-Alkenes.

2.6.1 Introduction

As mentioned previously, (see section 1.3.3) many nitroso-alkene species are usually so unstable the their presence can only be inferred by the isolation of trapped Diels-Alder products. We attempted to determine if the unusually stable nitroso-alkenes which we had prepared, would undergo Diels-Alder reactions.
There are two common types of Diels-Alder reactivity of nitroso-alkenes (Scheme 2.17).\textsuperscript{60} Firstly the nitroso group can act as a hetero-dieneophile and react with a diene to form the adducts of general type 201, and secondly, the nitroso-alkene can act as heterodiene and undergo reactions with dieneophiles to produce systems of type 202.

\textit{Scheme 2.17: Usual Diels-Alder Reactions of Nitroso-Alkenes}

2.6.2 Attempted Diels-Alder reactions

Compound 153e was heated in refluxing toluene for 4h together with an excess of dimethylbutadiene, during which time the reaction was monitored by withdrawing samples for NMR analysis. The spectra indicated gradual decomposition of the nitroso-alkene and showed no evidence of the trapped products (broad CH\textsubscript{2}O & CH\textsubscript{2}N peaks) suggesting that the nitroso group is unreactive as a dienophile. Compound 153e was also shown to decompose on heating in neat toluene.

Nitroso-alkenes are known to undergo cycloaddition reactions utilising the C=C-N=O moiety as a heterodiene. Three reactions were attempted utilising compound 153l, in refluxing chloroform. Reactions with cyclohexene, dimethyl acetylenedicarboxylate and 2H-pyran as an alkene, an electron deficient alkene and an electron rich alkene respectively, all led to no reaction (t.l.c. evidence). The reaction using 2H-pyran was repeated in refluxing toluene, but these conditions led simply to decomposition. This indicates that these highly stable nitroso-alkenes are also unreactive as hetero dienes.

2.6.4 Conclusions

Attempts to utilise the nitroso-alkene in Diels-Alder reactions as either a diene or dieneophile failed, most likely because of the resonance stabilised nature
of the nitroso-alkene and also the intramolecular S---O interactions discussed earlier (see sections 2.2.4, 2.2.6 & 2.3.3).

2.7 Attempted Generation of Thionitroso Species

2.7.1 Introduction

As discussed earlier (section 1.1.3) it was intended to use the nitroso species as both models for, and precursors to, thionitroso species. Two methods were considered for the transformation to thionitroso species. Firstly, a direct thionation method, and, secondly the reduction of the nitroso species to yield an amine, which could be used in conventional thionitroso chemistry as described earlier (section 1.1.1).

2.7.2 Direct Thionation method

The direct thionation method was attempted using phosphorus pentasulfide, which is a well known reagent for creating thiones from ketones via two [2+2] pericyclic reactions, firstly to form a 4 membered heterocycle, which breaks down to form sulfur-carbon and phosphorus-oxygen double bonds.¹⁵

![Scheme 2.18: Attempted Thionation with Phosphorus Pentasulfide](image)

The thionation reaction was attempted with compound 14, (Scheme 2.18) which was chosen since it had the minimal number of functional groups to interfere with the thionation. No reaction occurred at room temperature. The temperature was increased stepwise (increments of 10°C) to 70°C whereupon a reaction occurred (t.l.c. evidence) to yield a multitude of uncharacterised decomposition products. Hence this route to thionitroso species was abandoned.
2.7.3 Thionitroso Species by the Use of Conventional Thionitroso Chemistry

In order to utilise conventional thionitroso chemistry, it was necessary to prepare the corresponding amine, which could be reacted in either of the reaction schemes indicated in Scheme 1.3. Alternatively because one of the amine hydrogen atoms may be closely associated by a non-bonded interaction to the dithiole ring, a modified procedure could be attempted, whereby the amine could be reacted with sulfur dichloride, to produce $205$, followed by reaction with a base strong enough to remove the H-bonded proton (scheme 2.19). This would lead to the 1,2-elimination of HCl to form the thionitroso species $206$.

$$
\text{Ri} \quad \text{R} \quad \text{X} \\
\text{Ri} \quad \text{R} \quad \text{X} \quad \text{N} \quad \text{S} \\
\text{204} \quad \text{205} \\
\text{Base} \quad \text{Base} \\
\text{206}
$$

Scheme 2.19: Postulated Route to Thionitroso Systems

2.7.3.1 Preparation of Amines by Reduction of Nitroso Species

It is known that nitroso compounds are intermediates in the reduction of nitro species to amines, and that nitroso species are more easily reduced than the nitro analogues, and hence the conditions which will reduce nitro species will also reduce a nitroso compound. Two methods were tried (Scheme 2.20): firstly reduction of the nitroso compound 14 by sodium borohydride. In this case a reaction occurred (t.l.c. evidence) but preliminary characterisation indicated the loss of the ester groups, suggesting that the borohydride reagent had reduced the esters. Since this work was done it has been reported that borohydride reagents do reduce the ester groups on 1,3-dithioles to the corresponding alcohols, and this reaction is now used regularly in synthetic schemes. A second method
which was attempted was a catalytic reduction of 14 using hydrogen with palladium on carbon, this reduction yielded a multitude of uncharacterised products. To circumvent problems associated with ester reduction we reacted 179a with sodium borohydride in anhydrous propan-2-ol at room temperature which led to a rapid reaction (Scheme 2.21). The sparingly soluble nitroso derivative disappeared and a lighter brown solution was formed. Aqueous work-up of this solution led to the production of a light brown solid (90%).

Scheme 2.20: Attempted reductions of 4,5-dicarbomethoxy-1,3-dithiol-yldenes

The proton spectrum showed a broad singlet at 9.65ppm and a sharp singlet at 6.30ppm, (each integrating for 1H). This could be due to the amine groups of 207 with a strong sulfur-hydrogen interaction explaining why one proton was exchangeable and broad while the other not exchangeable and hence sharp.

Scheme 2.21: Borohydride Reduction of Compound 179a

The proposed route to the thionitroso species was that outlined in Scheme 2.28. For reaction of 207, the base initially chosen was LDA, followed by the addition of sulfur dichloride, however these reaction conditions failed to yield the required thionitroso species and t.l.c. indicated that the reaction had yielded a multitude of uncharacterised products. A further attempt using butyl lithium,
(which had the advantage over LDA that the by-products were either gaseous or ionic) again failed to yield an isolable thionitroso species and an attempt to generate (using butyl lithium), then trap in situ the thionitroso species with dimethylbutadiene failed to produce the characteristic adduct CH$_2$N & CH$_2$S peaks [typically $\delta_H$ 4.0 ppm, (broad s, 2H) and 3.0 ppm, (broad s, 2H) respectively$^7$] in the proton NMR spectrum.

2.7.3.2 Preparation of Amines from Dithiole anions

At the outset of this study there was a literature report by Page et al of the generation of the structurally similar primary aminoketene dithioacetals, 210.$^{112}$ These species were formed by the reaction of the dithiane anion 208 with various nitriles, to form the imino species 209, which on work up isomerised to the required ene-amines 210 in 55-87% yield.

$$\begin{array}{c}
\text{S} \text{S} \text{BuLi} \rightarrow \text{S} \text{S} \text{Li} \text{R-CN} \\
\text{208} \\
\rightarrow \text{S} \text{S} \text{Li} \text{NH} \text{H}_2 \text{O}^+ \\
\text{209} \rightarrow \text{S} \text{S} \text{NH}_2 \\
\text{210}
\end{array}$$

Scheme 2.22: Formation of the Dithiane Ene-amine reported by Page et al

We considered that the 1,3-dithiole anion may undergo a similar reaction with nitriles to form ene-amines 213. The analogous benzodithiole anion has been reported previously, originally by Ncube et al$^{113}$ although its chemistry is not as widely developed as that of the structurally similar dithiane anion 208. It was chosen to utilise the di(methylthio)-dithiole species 213 as our targets, since we had already noted that these substituents stabilise the nitroso analogues.
The dithiole anion is prepared as outlined in Scheme 2.23. The dithiolium cation, 169 (section 2.3.2) can be further reduced with sodium borohydride in tetrahydrofuran/propan-2-ol to yield the 4,5-di(methylthio)-2-dihydro-1,3-dithiole 211, (57%). However, attempts to generate the anion and react it with benzonitrile failed to yield the required amine: an intractable mixture was obtained. This lack of success reflects the fact that anion 212 is not as stable as a dithiane anion 208, since the stabilising effect of the two α-sulfur atoms is counteracted by the formation of an 8π dithiole system.

2.7.4 Conclusions

We have attempted several methods towards the generation of thionitroso species, however we have been unsuccessful in isolating them. Further work is needed to determine if the thionitroso species can be prepared and, indeed whether they are stable.
Chapter 3

1-(1,3-Dithiol-2-ylidene)-prop-2-ene Systems
3.1 Introduction

During the course of the work described in Chapter 2, compound 214 was prepared in 82% yield by the Wittig reaction between 150 and the α,β-unsaturated aldehyde, para-nitro-cinnamaldehyde. Upon nitrosation (Scheme 3.1), rather than obtaining the expected green solution, the reaction mixture merely darkened and a dark orange solid was isolated.

![Proton NMR Spectrum of Compound 215](image)

**Figure 3.1: Proton NMR Spectrum of Compound 215**

Proton NMR analysis (Figure 3.1) indicated that the solid was a mixture of two compounds, one of which was a disubstituted product as indicated by the appearance of four signals due to ester protons, and the pattern of peaks between δH 5.8 and 8.4 ppm.

Mass spectral evidence, was, however, inconclusive since it only showed a mass peak corresponding to the mono-nitro product [m/z (CI) 425 (M⁺+1)]. This suggested either that the mono-nitrosated product was unstable or that the disubstituted product fragmented in the mass spectrometer. This indication that reaction could occur at the similar, but more remote, secondary vinyl site (Scheme 3.1) led to the investigation of ‘blocking’ the primary reaction site, to effect nitrosation only at the secondary site.
Chapter 3  l-(1,3-Dithiol-2-ylidene)-prop-2-ene systems

3.2 Reaction of Wittig reagent 150 with Simple ketones

3.2.1 Introduction

The most convenient way to block the primary reaction site would be to react the Wittig reagent with α,β-unsaturated ketones, leading to molecules such as 216. The Wittig reagent 150, is known to react with ketones as described by Cava\textsuperscript{34} in the initial paper on the generation and reactivity of this reagent, and also with α,β-unsaturated aldehydes.\textsuperscript{34} However, there has been no report of the Wittig reagent reacting with α,β-unsaturated ketones. Therefore, it was necessary to determine whether the reagent was reactive towards α,β-unsaturated ketones. If the compounds 216 were generated a subsequent investigation into the possible scope of the nitrosation reaction, and stability of the products derived therefrom, was possible.
3.2.2 Use of Methyl and Phenyl substituents as 'blocking groups'

Initial attempts to effect the Wittig reaction of 150 with trans-4-phenyl-3-butene-2-one 217 focused on the procedure utilised for the reaction with simple aldehydes. However, these attempts in which triethylamine in tetrahydrofuran or acetonitrile was used to deprotonate the phosphonium salt and then trap the ylide with the ketone were unsuccessful. This was attributed to the reduced reactivity of the carbonyl moiety of 217 when compared to that of an aldehyde. This reduced reactivity is presumably due to two factors: the steric effect of the increased bulk of the group at the carbonyl position, and secondly, and probably more importantly, the donating effect of the alkyl group reducing the electrophilicity of the carbonyl carbon atom. A similar effect was shown earlier (Section 2.2.5) when Wittig reagent 150 was found to react exclusively with the aldehydic carbonyl group of methyl glyoxal, to form 157a. In the presence of triethylamine, the phosphonium salt 59 will be in equilibrium with ylide 150; the use of butyl lithium, however, should effect an irreversible deprotonation and lead to the ylide being forced into a reaction.\(^{35}\) Indeed the use of butyl lithium at low temperature (-78°C) led to the formation of the desired Wittig product 218 as a red/orange crystalline solid, albeit in low yield (15%). The proton NMR spectrum showed the expected pattern for the vinyl peaks, which subsequently was used to allow rapid identification of products during this series of reactions. Compound 218 was now set up for nitrosation of the more remote vinyl site since the primary site of nitrosation was blocked by the methyl group.
The previous nitrosation procedure (section 2.2.1) was performed with 218 and after one hour t.l.c. investigation indicated that a reaction had occurred. Removal of the solvent gave a red product (ca. 18% yield) which was isolated by repeated recrystallisation. Proton NMR analysis showed the disappearance of the characteristic vinyl pattern of compound 218, and the appearance of a single vinyl peak which clearly suggested that it was possible to effect a substitution reaction at the secondary vinyl site. The mass spectrum showed fragments which corresponded to both the nitroso [m/z (CI) 378 (M⁺+1)] and the nitro [m/z (CI) 394 (M⁺+1)] species 219 and 220 respectively. To determine whether the nitroso species was merely a fragment from the nitro species, a parent-daughter scan was performed on both the species and a different breakdown pattern was exhibited for each, suggesting that both the compounds existed separately. The nitro species in the mixture was presumably being formed by the oxidation of the initial nitroso product.

Although compound 218 possessed a blocking group occupying the primary vinyl site, it lacked the electron withdrawing groups at the site of nitrosation which had been found to stabilise the nitroso-alkene system. Attempts were, therefore, made to prepare compound 222 by a Wittig reaction with 4-nitro-chalcone 221, since this would retain the blocked primary vinyl site, and also introduce an electron withdrawing group on the phenyl ring directly attached to the new site of nitrosation.

![Scheme 3.3: Introduction of an Electron Withdrawing Group at the Site of Nitrosation](image)

Utilising the procedure optimised for the formation of 218 and despite repeated attempts, compound 222 was not obtained in a yield greater than 3%. This lack of reactivity was attributed to the sterically hindered nature of the carbonyl group: the activating effect of the para-nitro group on the phenyl ring is
obviously too remote in this case to counter this. Wittig reagent 150 has been shown by Cava not to react with benzophenone and attributes this to steric hindrance. \(^{34}\) Due to the small amount of the Wittig product obtained and the expected low yield of the nitrosation reaction, nitrosation of 222 was not attempted.

### 3.3 Highly electron deficient 'blocking groups' for the vinyl site

#### 3.3.1 Introduction

In order to increase the yields of the Wittig reactions, it was decided to investigate the use of electron withdrawing substituents, viz. nitrile and trifluoromethyl groups as 'site blockers'. These electron deficient groups would have the advantages of helping the Wittig reaction, and, by extension of the work described in Chapter 2, assist in the stabilisation of the nitroso-alkenes.

#### 3.3.2 Use of a Nitrile Functionality as a 'Blocking Group'

We needed to establish conditions under which acyl cyanides would react with Wittig reagent 150, so as a model reaction benzoyl cyanide was used.

\[ \text{Scheme 3.4: Test Reaction to Determine the Reactivity of the Wittig Reagent 150} \]

Towards Acyl Cyanides

The reaction conditions previously employed in the Wittig reaction with simple aldehydes, were found to lead to the required product 224 in 64% yield. X-ray quality crystals were grown and single crystal analysis by Dr. A. Batsanov confirmed the nature of the product.\(^ {93, 94}\)
Structural analysis also indicated that there is essentially no intramolecular donor-acceptor nature in the species (bond alternation shown in 224' is not seen in the structural data), the C(1)-N(1) bond being essentially the expected length for a triple bond. It has been shown in our research group by X-ray analysis that the conjugated system 225 (Figure 3.5) containing both the dithiol-2-ylidene and dicyanomethylene moieties exhibits a high degree of intramolecular charge transfer (i.e., it exists in the form 225'). In the case of species 226, however, with the cyano groups directly attached to the ylidene double bond, there is thought to be little donor-acceptor nature due to the white colour of the product.

Figure 3.3: X-ray Molecular Structure of Compound 224

Figure 3.4: Possible Donor-Acceptor Nature of the 1-(Dithiol-2-ylidene)-1-cyano methane Systems
Having determined that simple acyl cyanides successfully underwent Wittig reactions with reagent 150, the preparation of a molecule which could subsequently be utilised in a nitrosation reaction at the more remote vinyl site was attempted. Following the procedure of Koenig and Weber,\textsuperscript{116} reaction of cinnamoyl chloride 227 with sodium cyanide in water, in the presence of a phase transfer catalyst, 228 was obtained in 98% yield. The product was sufficiently pure to use without the need for further purification. Acyl cyanide 228 was reacted in the manner developed for the simple unsaturated ketones (section 3.2.2), and led to the formation of the dithiol-2-ylidene 229, in 22% yield as a yellow crystalline solid. This reaction confirmed, as expected, enhanced reactivity of the systems substituted with electron-withdrawing groups over the simple ketones used in section 3.2.2.

Nitrosation of 229 was attempted via the usual procedure and after two hours t.l.c. indicated that a reaction had occurred. The proton NMR spectrum of the reaction product showed the loss of the characteristic vinyl pattern, and mass spectrometric analysis again indicated the presence of both nitro [m/z (Cl) 405 (M$^+$+1)] and nitroso [m/z (Cl) 389 (M$^+$+1)] groups and a parent-daughter scan showed that the two molecules 230 and 231 existed independently of each other.
Separation of compounds 230 and 231 was attempted by flash column chromatography on silica gel. It has previously been noted that these conditions led to decomposition of the simpler nitroso species (section 2.2). Indeed, chromatography led to the isolation solely of the nitro compound as proved by the disappearance of the peak corresponding to the nitroso species 230 in the mass spectrum.

3.3.3 The use of a trifluoromethyl functionality as a ‘blocking group’

The use of an acyl cyanide led to much improved yields in the Wittig reaction, although the electron-withdrawing nitrile group in 230 had failed to enhance the stability of the nitroso alkene. It was, therefore, decided to utilise the commercially available 1,1,1-trifluoromethyl-4-phenyl-but-3-ene-2-one 232 to prepare compound 234, which would also possess the electron withdrawing trifluoromethyl group to enhance the Wittig reaction.

Since the trifluoromethyl group is very electron withdrawing, we were able to use triethylamine as the base. This would allow the use of milder and more convenient conditions than the use of butyl lithium at -78°C. The reaction of phosphonium salt, 59 and the trifluoromethylketone with triethylamine proceeded well at room temperature to afford product 234 in 80% yield as a red crystalline solid.
Scheme 3.6: Use of a Trifluoromethyl Functionality as a 'Blocking Group'

The presence of three fluorine atoms in 234 led to the usual $AB$ vinyl pattern in the $^1H$ NMR spectrum being further split into a doublet of doublets of quartets, the coupling constants of which were dependent on the number of bonds between the proton and the fluorine group (Figure 3.6). By comparison of the $J_{H-F}$ values, the vinyl protons can be assigned, since $^3J_{H-F}$ will be greater than $^4J_{H-F}$. In this case, the $J_{H-F}$ values are 1.62 and 0.92 Hz, thus the proton with the $J_{H-F}$ value of 1.62 Hz is that lying closest to the trifluoromethyl group, in this case the peak at $\delta$ 6.77 ppm. The proton decoupled fluorine spectrum showed as expected, a singlet due to the three equivalent fluorine nuclei.

Figure 3.6: $H---F$ Coupling Interactions in Compound 234

Nitrosation of compound 234 was attempted utilising the standard procedure and led to a yellow product in 52% yield. This was shown to be solely the nitro derivative 236 [m/z (Cl) 448 (M^+=1)], both before and after chromatographic purification.

3.3.4 Systems based around the mono-ester substituted dithiole ring.

We had discovered two species 229 and 234 which provided the factors necessary for this area of work to be investigated. These were a carbonyl compound which was reactive enough for the Wittig reaction, and also one
which would afford a product with a ‘blocking group’ at the primary nitrosation site. Attention turned to discover whether nitrosation could be affected in these extended systems with only one ester substituents on the dithiole ring.

As mentioned previously (Section 2.3.2), the mono-ester Wittig reagent 162 cannot be isolated as its fluoroboric acid salt, and it is generated and trapped in ‘one pot’. Initial attempts showed that the acyl cyanide, 228 was insufficiently reactive for the ‘one pot’ reaction and no Wittig reaction had occurred. This effect is attributed to the reduced reactivity of the \( \alpha,\beta \)-unsaturated derivatives in these Wittig reactions.

\[
P_{Bu_3} + CS_2 \rightarrow \text{MeO}_2\text{C} = \text{S} = \text{PBu}_3
\]

Attention, therefore, turned to trifluoromethylketone, 232 which had been found to be more reactive in the Wittig reactions described above (Section 3.3.3). Generation of the mono-ester Wittig reagent and \textit{in situ} trapping afforded the desired system 238 in 47% yield as yellow needles. The NMR spectrum of this mono-ester derivative confirmed that 238 was an equimolar mixture of isomers (see also section 2.3.2), which complicated the spectrum. For example, the ester group appeared as two distinct singlets one for the \( s\text{-cis} \) isomer and the other for the \( s\text{-trans} \) isomer.

\textit{Scheme 3.7: Mono-Ester Extended Systems}
Nitrosation of 238, yielded an oil which was purified by chromatography to afford the nitro derivative 240 in 76% yield. Presumably the nitroso derivative 239 is an unstable precursor to nitro-alkene 240.

### 3.4 Conclusions

The work investigating nitrosation reactions at the secondary vinyl site rather than the usual primary nitrosation site has highlighted two main areas;

Firstly reactions with α,β-unsaturated ketones seem to be at the limit of the reactivity of the versatile Wittig reagent 150. This is illuminated by the fact that unless strongly electron withdrawing groups are attached to the carbonyl carbon the yields of the Wittig reactions are very low.

Secondly, with regard to nitrosation reactions, it appears that the more remote vinyl sites are sufficiently activated to undergo a nitrosation reaction, although the nitroso-alkenes which are formed are not stable. This in turn illustrates the importance of the intramolecular interaction in stabilising the more simple structures discussed previously in Chapter 2, and that it is not solely the dipolar nature of these compounds which impart stability to the nitroso-alkene systems.
Chapter 4

1-(1,3-Diselenol-2-ylidene) methane Systems
4.1 Introduction

4.1.1 Comparison of sulfur and selenium interactions

The use of sulfur-oxygen interactions to stabilise the nitroso-alkene moieties in the 1-(1,3-dithiol-2-ylidene)-1-nitroso methane systems has been detailed in Chapter 2. A selenium atom which possesses substantially more diffuse p- and d- orbitals than a sulfur atom, will emphasise the disparity in size in the atoms utilised in an intra-molecular selenium-oxygen interaction\textsuperscript{10}. We reasoned that this size mis-match could lead to a decrease in the strength of any intramolecular interaction and, therefore, the synthesis of selenium containing systems, analogous to the dithiole systems studied in Chapter 2, should, therefore, determine to what extent weaker Se---O interactions are able to stabilise the nitroso-alkene moiety.

The 1,3-selenathiole system has been widely documented in the literature relating to the synthesis of organic metals.\textsuperscript{117} However this system would be expected to lead to inseparable cis and trans isomers \textsuperscript{241a} and \textsuperscript{241b} in which there could be the possibility of the nitroso-alkene being stabilised by either an Se---O or an S---O interaction. This problem would be alleviated by the use of 1,3-diselenole systems, which were, therefore, chosen as our targets.

![Figure 4.1: Isomers of 1,3-Selenathiol-2-ylidene Systems](image)

4.1.2 1-(1,3-Diselenol-2-ylidene) methane systems

1,3-Diselenole derivatives are known in the literature relating to the synthesis of organic metals.\textsuperscript{117} Established routes to the systems, involved the use of the noxious, fetid and commercially unavailable reagent, carbon diselenide.\textsuperscript{47b,118}

Synthesis of the systems \textsuperscript{242} and \textsuperscript{243} was via an analogous reaction (Scheme 4.2) to that used to prepare the 4,5-dicarbomethoxy-1,3-dithiole system...
(Section 2.1). In order to investigate selenium interactions stabilising nitroso-alkenes, a route to the 4,5-diester substituted diselenole system that utilised a more practical form of selenium needed to be developed.

\[
\text{PBU}_3 + \text{CSe}_2 \xrightarrow{\text{DMAD}} \text{MeO}_2\text{C} - \text{Se} - \text{MeO}_2\text{C} \xrightarrow{\text{HBF}_4 \text{ Ether}} \text{MeO}_2\text{C} - \text{Se} - \text{PBu}_3 \text{BF}_4
\]

**Scheme 4.1: Preparation of 4,5-Dicarbomethoxy-1,3-diselenole Wittig reagent**

### 4.2 Ethane triselenocarbonate

#### 4.2.1 Introduction

Much work on the dithiole system 244 has stemmed from the known [3+2] cycloaddition between electron deficient alkynes and ethane trithiocarbonate to produce the substituted 1,3-dithiole-2-thione unit 244 (scheme 4.3).

\[
\text{CH}_2=\text{CH}_2
\]

**Scheme 4.2: Preparation of 1,3-Dithiole-2-thione Systems with Electron-withdrawing 4- and 5- Substituents**

The preparation of ethane triselenocarbonate 249, utilising hydrogen selenide as a commercially available source of selenium has been reported independently by Chakroune and Wudl; its reaction with alkynes, including dimethyl acetylenedicarboxylate has also been investigated.
4.2.2 Synthesis of 4,5-dicarbomethoxy-1,3-diselenole-2-selone

\[
\text{Et}_3\text{N} \xrightarrow{\text{H}_2\text{Se}} \text{Et}_3\text{NH}.\text{SeH} \xrightarrow{\text{Et}_3\text{N} \text{ 1 Equiv.}} \text{Me} \xrightarrow{\text{Me}^+ \text{Se}^-} \text{Me} \xrightarrow{\text{Et}_3\text{N} \text{ 1 Equiv.}} \text{Me} \xrightarrow{\text{Br} \text{ 2 Equiv.}} \text{Me} \xrightarrow{\text{HPF}_6} \text{Me} \xrightarrow{\text{DMAD} \text{ Toluene Reflux}} \text{Me} \xrightarrow{\text{DMAD} \text{ Toluene Reflux}} \text{Me}
\]

**Scheme 4.3: Preparation of 4,5-Dicarbomethoxy-1,3-diselenole-2-selone**

Ethane triselenocarbonate was readily prepared by the reaction sequence detailed in scheme 4.4. Reaction of triethylamine with gaseous hydrogen selenide in dry chloroform led to the production of triethylammonium hydrogen selenide salt 245. Reaction of this salt 245 with \(N,N\)-dimethyl-phosgene iminium chloride led to the substitution of both chlorine atoms with selenium to yield salt 246 which reacted with an equivalent of 1,2-dibromoethane to afford species 247. Acidification with hexafluorophosphoric acid led to ion exchange affording the hexafluorophosphate salt 248 as a white solid. Reaction of 248 with either hydrogen selenide or sodium hydrogen selenide afforded the desired product 249 in good yield.

Having prepared the ethane triselenocarbonate 249, the cycloaddition with dimethyl acetylenedicarboxylate in refluxing toluene proceeded as reported to afford the desired compound 250 in 89% yield. The cycloaddition reaction presumably proceeds in a stepwise manner as detailed in Scheme 4.2 for the sulfur analogue.
4.3 Generation of the 1,3-diselenole Wittig reagent

4.3.1 Introduction

The use of thiones as starting materials for the preparation of 1,3-dithiol-2-ylidene systems is well documented for systems incorporating a range of substituents, including di(methylthio) and ethanedithio at the 4- and 5- positions on the dithiole ring.\(^{100, 101}\) This route has not been extended to the diester substituted systems due the greater convenience of the tributyl phosphine, carbon disulfide and dimethyl acetylenedicarboxylate route (scheme 2.1).\(^{34}\) The preparation of Emmons-Horner reagents could increase the interest in the diester substituted dithiole-thione; however the ester functionalities are not compatible with Emmons-Horner reagents. Further investigation into this methodology was undertaken to find a convenient route to a diester substituted selenole Wittig reagent \(^{254}\).

4.3.2 Generation of a diselenole Wittig reagent

The reaction sequence employed for preparation of 4,5-di(thiomethyl)-1,3-dithiole Wittig reagents outlined earlier (section 2.3) appeared to be applicable for the preparation of the diselenole Wittig reagent \(^{254}\). The only two modifications deemed necessary would be:

a) The use of less harsh conditions in the methylation of selone \(^{250}\), since the ring system may be unstable in neat dimethylsulfate at 90°C. The use of methyl trifluoromethanesulfonate as a methylating agent has previously been described for the methylation of dithiole-thiones at low temperature.\(^{122}\) The fact that only one equivalent of this stronger methylating agent would be necessary should effect methylation under milder conditions.

b) Replacement of sodium borohydride with a more selective reducing agent for the reduction of the diselenolium cation \(^{251}\). Sodium cyanoborohydride was thought to be sufficient to alleviate the problem of accomplishing the reduction in the presence of the ester groups.
Thus, methylation of selone 250 with methyl trifluoromethylsulfonate in anhydrous dichloromethane, afforded the required diselenolium cation salt 251 in excellent yield (93%). The salt 251 was stable for several days if stored under argon at 0°C. Reduction of the salt with sodium cyanoborohydride in anhydrous propan-2-ol afforded the required selenoether in 91% yield. No reduction of the ester functionalities was observed, indicating that the reducing reagent is, as anticipated, more selective than sodium borohydride. The selenoether 252 thus obtained, was isolated as an unstable orange oil and characterised only by its proton NMR spectrum. Due to its instability the selenoether was immediately dissolved in dry acetonitrile and cooled to 0°C. The sequential addition of tetrafluoroboric acid and triphenylphosphine, led to the formation of the desired Wittig reagent 254. Attempts to isolate and characterise the Wittig salt at this stage were unsuccessful, the usual method of isolating 4,5-dithiole Wittig salts (concentration of the solution in vacuo and addition of a large excess of dry ether) led to the formation of a ‘tacky’ oil. Yoshida isolated the tributyl phosphine Wittig reagent as its hexafluorophosphate salt\cite{47b} when it was prepared by the sequence outlined in Scheme 4.2, however, substitution of
tributylphosphine for triphenylphosphine failed to facilitate isolation of the analogous butyl-phosphino Wittig reagent. The Wittig reagent was, therefore, reacted as a crude solution, addition of an excess of triethylamine at room temperature was sufficient to liberate the Wittig reagent from its tetrafluoroborate salt \(254\). The resultant ylide was trapped with an appropriate aldehyde to afford \(255_{a-e}\) in useful yields (21-36%); the choice of aldehydes was made in the light of those derivatives which had led to interesting chemistry in the sulfur analogues.

Surprisingly, in all cases 4,5-dicarbomethoxy-2-dihydro-1,3-diselenole \(256\) was isolated as a malodorous orange oil in a yield comparable to the yield of the desired 1,3-diselenol-2-ylidene systems \(255\) (Table 4.1). The preparation of the corresponding 2-dihydro-1,3-dithiole derivatives by borohydride reduction of 1,3-dithiolium salts have been previously known. However, in our reactions, although a slight excess of hydride source was used, there was insufficient cyanoborohydride to account fully for the amount of the dihydro derivative obtained. In the light of the exhaustive aqueous work up used to purify the selenoether it is highly unlikely that any residual sodium cyanoborohydride remained. Indeed, the proton NMR spectrum of selenoether \(252\) failed to show the presence of the dihydro compound \(256\). Further investigations into the mechanism of formation of the dihydro species have failed to yield a definitive explanation, although the use of a radical inhibitor (hydroquinone) failed to decrease the amount of the dihydro derivative isolated, suggesting that the reaction pathway is not radical in nature. It appears that the quality of the tetrafluoroboric acid utilised in the elimination of methane selenol influences the amount of the dihydro compound formed, older samples leading to a greater yield of the dihydro by-product. This suggests that some unidentified decomposition product from the tetrafluoroboric acid is instrumental in the formation of the dihydro species. We have shown that \(256\) is not formed by fluoride induced elimination of MeSeCl from the seleno-ether \(252\). In view of the greater success encountered in Chapter 2, employing tributyl Wittig reagents over triphenyl reagents, the use of a tributyl reagent was investigated in the formation of the 1,3-selenol-2-ylidenes; however, this led to increased amounts
(ca. 50%) of the by-product 256 a significantly reduced yield of the desired system being isolated and so was not pursued further.

**Table 4.1: Yields of 2-Ylidene- and 2-Dihydro-1,3-diselenoles 255 and 256, Respectively**

<table>
<thead>
<tr>
<th>R</th>
<th>Yield of 255 (^a)</th>
<th>Yield of 256 (^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-CF(_3)-C(_6)H(_4) (a)</td>
<td>31</td>
<td>24</td>
</tr>
<tr>
<td>2-Pyridyl (b)</td>
<td>21</td>
<td>42(^b)</td>
</tr>
<tr>
<td>2,4-Di-NO(_2)-C(_6)H(_3) (e)</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>C(O)Me (d)</td>
<td>34</td>
<td>16</td>
</tr>
<tr>
<td>CHO (e)(^{47})</td>
<td>36</td>
<td>32(^b)</td>
</tr>
</tbody>
</table>

\(^a\) Yields quoted are of isolated products purified by column chromatography

\(^b\) Yields are based on \(^1\)H NMR analysis of the crude reaction mixture

### 4.4 Nitrosation reactions of 1,3-diselenol-2-ylidene systems

Having identified a new, and synthetically viable route to the desired 1,3-dithiol-2-ylidene systems, attention turned to the preparation of novel nitroso derivatives. The 1,3-diselenol-2-ylidene derivatives possessed electron-withdrawing groups at both the 4- and 5- diselenole positions as well the ylidene substituent and were ideal candidates. The reaction of systems 255a, d and e with isoamyl nitrite (Scheme 4.6) as described by Cava, successfully accomplished the desired transformation to green nitroso derivatives.\(^{12}\) Concentration of the reaction solvent *in vacuo* followed by the addition of cold methanol allowed isolation of the compounds 257 in 34-55% yield as green solids. Two recrystallisations from dichloromethane / hexane were necessary to purify the nitroso-alkenes.

![Scheme 4.5: Nitrosation of 1,3-diselenol-2-ylidene](image-url)
Table 4.2: Nitroso Derivatives of 1,3-Diselenol-2-ylidenes

<table>
<thead>
<tr>
<th>R</th>
<th>Compound</th>
<th>Nature</th>
<th>Yield / %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-CF₃-C₆H₄</td>
<td>257a</td>
<td>Green Solid</td>
<td>37</td>
</tr>
<tr>
<td>C(O)Me</td>
<td>257d</td>
<td>Green Crystals</td>
<td>55</td>
</tr>
<tr>
<td>CHO</td>
<td>257e</td>
<td>Green Crystals</td>
<td>34</td>
</tr>
</tbody>
</table>

Crystals of 257e were suitable for X-ray crystallographic investigation to determine the nature of any Se---O interactions.

Figure 4.1: X-ray Molecular Structure of Nitroso-alkene 257e

The X-ray molecular structure (Figure 4.1) was solved by Dr. A. Batsanov and showed many structural similarities with those discussed in Chapter 2 in which the nitroso-alkene moiety was stabilised by an S---O interaction. The diselenole ring of 257e is planar with the ylidene group and its substituents inclined at an angle of 3.5° to the plane of the ring. Both the nitroso group and carbonyl group are in a cisoid conformation and both groups
Chapter 4  1-(1,3-Diselenol-2-ylidene) methane systems

exhibit a close Se---O interaction with a selenium atom in the diselenene ring. In accordance with earlier results (see section 2.2) and those found by Reid et al\textsuperscript{86} the nitroso oxygen atom is more closely bound (Se---O 2.51Å) than the carbonyl (Se---O 2.73Å). Interestingly, the interatomic distances are larger than those in the dithiole case by the difference between the atomic radii of sulfur and selenium, indicating that there is a substantial amount of interaction between the nitroso oxygen atom and a selenium in the diselenene ring. Such Se---O interactions are less widely documented than the analogous S---O interactions; some examples are given in figure 4.2. The hypervalent bonding in the heteropentalene structure 258, is, as encountered with this type of S---O system, a far stronger interaction, the Se---O distance\textsuperscript{124} of 2.04Å being significantly closer to the Se-O covalent bond length of 1.91Å than the 1,3-diselenene system studied. Structures 259\textsuperscript{125} and 260\textsuperscript{126} also possess a very close interaction (2.08Å) although in this case the formation of a Se---O interaction is favoured by the presence of a heteroatom, (eg. chlorine in 259) in particular a strongly electronegative one.

The molecules of 257e are packed in parallel layers, though the presence of the out-of-plane methoxycarbonyl group prevents efficient overlap of the molecules, as seen with the diester substituted dithiole systems. In 257e, however, the selenium atoms participate in intermolecular contacts between Se(1)---Se(2) of independent molecules, the interatomic distances of 3.72 and 3.77Å being slightly less than the sum of the Van der Waals radii (4Å).\textsuperscript{10}

A solitary example of a related nitroso-alkene appeared during the course of our work; Cava et al prepared the 4-phenyl derivative 261 and proposed a cisoid nature for the nitroso-alkene on the basis of VT-NMR studies,\textsuperscript{14} although no crystallographic evidence for the cisoid nature of the nitroso-alkenes was presented.
4.5 Conclusion

The investigation of the use of Se---O interactions in stabilising a nitroso-alkene has led us to develop a synthetically useful route to a 4,5-dicarbomethoxy-1,3-diselenole Wittig reagent. This methodology will facilitate easier preparation of 1,3-diselenole derivatives and reopens avenues of research neglected due to the inaccessibility of reagents derived from carbon diselenide.

We have shown that nitroso-alkenes can indeed be stabilised by a Se---O interaction with a diselenole ring and that the selenium---oxygen interaction is of a comparable strength to that in the dithiole cases and also to other documented Se---O interactions.
Chapter 5

Experimental Details
5.1 General Methods

Melting points were recorded on a Reichert-Kofler hot-stage microscope apparatus and are uncorrected.

Infra-red spectra were recorded on a Perkin-Elmer 1720 FT-IR spectrophotometer: samples were either embedded in KBr discs or analysed neat between KBr plates, as indicated.

Proton NMR spectra were recorded on Varian Gemini-200, XL-200 or Varian VXR-200 operating at 199.9 Hz, $^{13}$C NMR were recorded on a Varian-400 instrument, fluorine Spectra were obtained on a Brucker AC250 spectrometer. Chemical shifts are quoted in ppm, relative to tetramethylsilane as an internal standard (0 ppm).

Mass spectra were recorded on a VG 7070E instrument, with ionisation modes as indicated; ammonia was used as the impinging gas in chemical ionisation mode.

Elemental analyses were obtained on a Carlo-Erba Strumentazione instrument.

Column chromatography was carried out using Merck silica gel (70-230 mesh or Merck alumina (activity II to III 70-230 mesh), the latter was neutralised by presoaking basic alumina in ethyl acetate for 24 h. Solvents were distilled prior to use for column chromatography.

Nitrogen gas was dried by passing it through a column of phosphorus pentoxide. Reaction solvents were dried over, and distilled from the following reagents under an inert atmosphere; ether, tetrahydrofuran and toluene (sodium metal / benzophenone), acetonitrile and dichloromethane (calcium hydride), acetone (potassium carbonate), triethylamine (3Å molecular sieves). All other reagents were reagent grade and used as supplied. Ether refers to ethoxyethane.

Cyclic voltammetry experiments were performed in a one-compartment cell with platinum working and counter electrodes. The reference electrode was a silver / silver chloride electrode. Electrochemical measurements were carried out using a BAS 100 electrochemical analyser and were compensated for internal resistance. The cell contained the test compound (ca. $1 \times 10^{-5}$ M) with dry
tetrabutylammonium hexafluorophosphate (ca. 70 mg) as the supporting electrolyte in acetonitrile (ca. 10 ml); all solutions were purged with argon and retained under the inert atmosphere whilst measurements were carried out.
Chapter 5  
Experimental Details

5.2  
Experimental Details for Chapter 2

5.2.1  
Experimental details for section 2.2.2

4,5-Dicarbomethoxy-2-(tributylphosphino)-1,3-dithiolium tetrafluoroborate, 59.

This was prepared by the method described by and Cava subsequently modified by Hansen. To a stirring solution of carbon disulfide (6 ml, 96 mmol) in dry methanol (130 ml) at 0°C was added tributylphosphine (25 ml, 100 mmol). To the resulting red solution was added an ethereal solution (85.5 ml) of dimethylacetylenedicarboxylate (13.5 ml, 110 mmol) and tetrafluoroboric acid (ca. 54% in ether) (20 ml, 120 mmol) at -30°C. White crystals, (25.5 g) which precipitated out on cooling were recrystallised from acetonitrile/ether to yield 59 (25.5 g, 53% Yield) m.p. 121-122.5 °C (lit. 120-121 °C).

5.2.2  
Experimental details for sections 2.2.2 & 2.2.3

Preparation of 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene) methane derivatives. General procedure:

To a stirring solution of Wittig reagent 59 (2.0 g, 3.96 mmol) and the appropriate aldehyde (3.96 mmol) in dry tetrahydrofuran (50 ml) was added triethylamine (5 ml, excess), and the mixture stirred at 0 °C for 18h. The solvent was then removed in vacuo, the resulting product was purified by column chromatography on silica gel using a dichloromethane/hexane mixture as eluent, and recrystallised from dichloromethane: methanol (1:10 v/v). The following derivatives were thereby obtained.

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-phenyl-methane, 14, from benzaldehyde.

Red Solid (68%). m.p. 89-90 °C (lit. 90-91 °C), $E_{ox}=1.01$ V.
1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-butane, 151a from butanal.
Orange oil (80% yield) m/z (EI) 274(M⁺); HRMS Found: 274.0035; C₁₁H₁₄O₄S₂ requires 274.0334; ν_max(neat) 2958, 2936, 2876, 1744, 1716 and 1270 cm⁻¹; δ_H (CDCl₃) 5.38 (t, J= 7.3 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H) 1.92 (dt, J=7.3 and 7.3 Hz, 2H), 1.42 (tq, J= 7.3 and 7.3 Hz, 2H) and 0.93 (t, J=7.3 Hz, 3H).

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-prop-2-ene, 151b from acrolein.
Orange solid (61% yield) m.p. 43-45 °C m/z (Cl) 259(M⁺+1); HRMS Found 258.9871; C₁₀H₁₁O₄S₂ requires 259.0098; ν_max(KBr) 3026, 2962, 1762, 1724, 1609, 1579, 1424 and 1230 cm⁻¹; δ_H(CDCl₃) 5.9-6.2 (m, 2H), 5.0-5.2(m, 2H), 3.84 (s, 3H) and 3.83 (s, 3H).

1-(4,5-Dicarbomethoxy-1,3-dithioI-2-ylidene)-1-(2-nitrophenyl)-methane, 151d from 2-nitrobenzaldehyde.
Yellow crystals (82% yield) m.p. 115.5-116 °C [Found: C, 47.2; H, 3.1; N, 4.0; C₁₄H₁₈NO₃S₂ requires C, 47.6; H, 3.1; N, 4.0%] m/z (EI) 353(M⁺); ν_max(KBr) 1737, 1716, 1592, 1571, 1543, 1522, 1343 and 1257 cm⁻¹; δ_H(CDCl₃) 7.37 (m, 4H), 6.94 (s, 1H), 3.87 (s, 3H) and 3.83 (s, 3H).

1-(4,5-Dicarbomethoxy-1,3-dithioI-2-ylidene)-1-(2,4-dinitrophenyl)-methane, 151e from 2,4-dinitrobenzaldehyde.
Orange crystals (80% yield) m.p. 156-157°C [Found: C, 42.5; H, 2.5, N, 7.0; C₁₄H₁₀N₂O₈S₂ requires C, 42.1; H, 2.5; N, 7.0%] m/z (EI) 398(M⁺); ν_max(KBr) 1733, 1726, 1588, 1540, 1530, 1512, 1335 and 1257 cm⁻¹; δ_H(CDCl₃) 8.83 (d, J= 3 Hz, 1H), 8.43 (dd, J= 11 and 3 Hz, 1H), 7.70 (d, J= 11 Hz, 1H), 7.08 (s, 1H), 3.91 (s, 3H) and 3.88 (s, 3H).
1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-[2-(trifluoromethyl)phenyl] methane, 151f from 2-(trifluoromethyl)benzaldehyde.

Yellow crystals (64% yield), m.p. 117.5-118.5°C. [Found: C, 47.7; H, 2.9; C_{15}H_{11}F_3O_4S_2 requires C, 48.0; H, 3.0%] m/z (EI) 376(M^+); ν_{max}(KBr) 1730, 1658, 1309, 1260, 1222 and 1029 cm\(^{-1}\); δ_{H}(CDCl_3) 7.32-7.65 (m, 4H), 6.67(q, J_{H,F} = 2.0 Hz, 1H), 3.89 (s, 3H) and 3.84 (s, 3H).

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2,6-dichlorophenyl) methane, 153g from 2,6-dichlorobenzaldehyde.

Yellow oil (87% yield) m/z (EI) 377(M^+); HRMS Found: 375.9393 C_{14}H_{10}Cl_2O_4S_2 requires 375.9398; ν_{max}(neat) 1728, 1591, 1433 and 1258 cm\(^{-1}\); δ_{H}(CDCl_3) 7.25 (m, 3H), 6.33 (s, 1H) 3.87 (s, 3H) and 3.80 (s, 3H).

Preparation of 1,3-dithiol-2-ylidene-1-nitroso methane derivatives: General procedure:

To a stirring solution of the appropriate 1,3-dithiol-2-ylidene methane derivative (200 mg) in dichloromethane at 0 °C was added isoamyl nitrite (3-methyl-butyl nitrite) (2 ml, 15 mmol, excess). The solution was stirred at 0 °C for 5 min, then allowed to warm to 20 °C and stirring continued for a further 45 min. The solution was concentrated in vacuo and the addition of cold methanol precipitated the product. Analytically pure samples were obtained by recrystallisation from dichloromethane/methanol (1:10\%/v). The following products were thereby obtained:

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-phenyl-1-nitroso-methane, 16. 12

Green solid (50 %) m.p. 164-165°C (lit. 12 165°C).
Attempted preparation of 1-(4,5-Dicarbomethoxy-1,3-dithio-2-ylidene)-prop-2-ene, 153b.

This reaction yielded a bright green solid, which was insoluble in all NMR solvents. (ca 50% yield) m.p. >250 °C m/z (Cl) 285 [expected m/z (El) 287] νₘₐₓ(KBr) 2955, 1635, 1588, 1435, 1256.

1-(4,5-Dicarbomethoxy-1,3-dithio-2-ylidene)-1-(2,4-dinitrophenyl)-1-nitroso-methane 153c.

Green crystals (48% yield) m.p. 156-157°C [Found: C, 39.0; H, 2.0, N, 9.6; C₁₄H₉N₂O₇S₂ requires C, 39.3; H, 2.1; N, 9.8%] m/z (El) 428(M⁺); νₘₐₓ(KBr) 1749, 1734, 1538, 1349 and 1264 cm⁻¹; δₜ(H(CDC₁₃)) 8.82 (d, J= 3 Hz, 1H) 8.43 (dd, J= 11 and 3 Hz, 1H) 7.70 (d, J= 11 Hz, 1H) 3.91 (s, 3H) 3.88 (s, 3H).

1-(4,5-Dicarbomethoxy-1,3-dithio-2-ylidene)-1-(2,6-dichlorophenyl)-1-nitroso-methane 153g.

Green crystals (27% yield) m.p. 179-180°C [Found: C, 41.4; H, 2.2, N, 3.3; C₁₄H₁₂Cl₂NO₅S₂ requires C, 41.4; H, 2.2; N, 3.5%] m/z (El) 407(M⁺); νₘₐₓ(neat) 1749, 1734, 1608, 1538 and 1193 cm⁻¹; δₜ(H(CDC₁₃)) 7.60 (m, 3H), 4.02 (s, 3H), 3.94 (s, 3H).

5.2.3 Experimental details for section 2.2.4

For General methods see section 5.2.2

1-(4,5-Dicarbomethoxy-1,3-dithio-2-ylidene)-1-(5-nitro-2-thiophene) methane, 151h from thiophene-2-carboxaldehyde.

This compound was kindly supplied by Dr. T. Hansen.
1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(5-nitro-2-thiophene) methanone, 151j from 5-nitrothiophene-2-carboxaldehyde.

Orange crystals (87%) m.p. 200-201°C [Found: C, 40.1; H, 2.5; N, 4.2; C_{12}H_9NO_6S_3 requires C, 40.1; H, 2.5; N, 3.9%] m/z (EI) 359(M^+); δ_{max}(KBr) 3106, 2959, 1739, 1584, 1418, 1343, 1302 and 1252 cm⁻¹; δ_{H}(CDCl_3) 7.89 (d, J= 4 Hz, 1H), 6.80(dd, J= 4 and 1 Hz, 1H), 6.71 (d, J= 1 Hz , 1H), 3.92 (s, 3H) and 3.90 (s, 3H).

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(5-nitro-2-furyl) methane, 151k from 5-nitro-2-furfuraldehyde.

Orange solid (90% yield) m.p. 111-112°C [Found: C, 41.8; H, 2.7, N, 4.0; C_{12}H_9NO_7S_2 requires C, 42.0; H, 2.6; N, 4.1%] m/z (EI) 343(M^+); δ_{max}(KBr) 1731, 1716, 1595, 1363 and 1255 cm⁻¹; δ_{H}(CDCl_3) 7.39 (d, J= 4 Hz, 1H), 6.41 (s, 1H), 6.30 (d, J= 4 Hz, 1H), 3.91 (s, 3H) and 3.89 (s, 3H).

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl) methane, 151l from pyridine-2-carboxaldehyde.

Orange crystals (89% yield) m.p. 145.5-146.5°C [Found: C, 50.5; H, 3.6, N, 4.6; C_{13}H_{11}NO_4S_2 requires C, 50.5; H, 3.6; N, 4.5%] m/z (EI) 338(M^+); δ_{max}(KBr) 1739, 1716, 1582, 1523, 1467 and 1226 cm⁻¹; δ_{H}(CDCl_3) 8.64 (dd, J= 4 and 1 Hz, 1H), 7.60 (td, J= 4 and 2 Hz, 1H), 7.00 (m, 2H), 6.63 (s, 1H) 3.89 (s, 3H) and 3.86 (s, 3H).
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1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso methane, 153L.

Green crystals (50% yield) m.p. 214-215°C [Found: C, 46.4; H, 2.9, N, 8.3; C_{13}H_{10}N_{2}O_{5}S_{2} requires C, 46.2; H, 3.0; N, 8.3%] m/z (EI) 338(M^+); \nu_{max} (KBr) 1840, 1740, 1536, 1514, 1503 and 1269 cm^{-1}; \delta_{H}(CDCl_3) 8.80 (m, 2H), 7.95 (m, 1H), 7.35 (m, 1H), 4.04 (s, 3H), 4.01 (s, 3H); \lambda_{max}(MeCN)(\epsilon/ mol l^{-1} cm^{-1}) 302 (1.60x10^4), 443 (1.44x10^4), 642 (117).

X-ray quality crystals were grown from dichloromethane/methanol (1:10\nu).  

5.2.4  Experimental details for section 2.2.5.

For General methods see section 5.2.2

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-ethanal, 157b from glyoxal.

This compound was prepared by the route described by Yoshida\textsuperscript{47b}. Yellow solid (yield 70%) m.p. 110-111°C (lit\textsuperscript{47b} 111-112°C).

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-propan-2-one, 157a from methyl glyoxal.

This was prepared analogously to 157b. Yellow solid (89% yield) m.p. 134-135°C. [Found: C, 43.7; H, 3.4; C_{10}H_{10}O_{5}S_{2} requires C, 43.8; H, 3.7%] m/z (EI) 274(M^+); \nu_{max}(KBr) 1735, 1711, 1636, 1580, 1490, 1433 and 1250 cm^{-1}; \delta_{H}(CDCl_3) 6.67 (s, 1H), 3.90 (s, 3H), 3.88 (s, 3H) and 2.46 (s, 3H).

Preparation of 1-imino-2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-ethane derivatives; General procedure\textsuperscript{95}:

To a stirring solution of 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-ethanal (300 mg, 1.1 mmol) in xylenes (30 ml) with magnesium sulfate (2g, excess) was
added the required amine (1.1 mmol). The solution was heated to reflux for 48h during which the reaction turned from a yellow colour to a dark orange / red shade. Column chromatography on silica gel eluting with dichloromethane/hexane mixtures followed by freeze drying (from benzene) yielded the following derivatives.

1-[(4-Methylphenyl)-imino]-2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-ethane, 159a from 1-amino-4-methylbenzene.

Dark orange powder (40%) m.p. 109-111°C m/z (Cl) 350(M^+1); νmax(KBr) 2949, 1720, 1579, 1476, 1432 and 1259 cm⁻¹; δH(CDCl₃) 8.15 (d, J=4.3 Hz, 1H), 7.16 and 7.07 (AB, J= 8.5 Hz, 4H), 6.48 (d, J= 4.3 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H) and 2.35 (s, 3H).

1-[(2-Thiazolyl)-imino]-2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-ethane, 159b from 2-aminothiazole.

Orange powder (59%) m.p. 107-109°C [Found: C, 42.6; H, 3.1; N, 8.3: C₁₂H₁₀N₂O₄S₃ requires C, 42.1; H, 2.9; N, 8.2%] m/z (Cl) 343(M^+1); νmax(KBr) 3853, 1726, 1587, 1486 and 1261 cm⁻¹; δH(CDCl₃) 8.58 (d, J= 4.5 Hz, 1H), 7.60(d, J= 3.5 Hz, 1H), 7.12 (d, J= 3.5 Hz, 1H), 6.52 (d, J= 4.5 Hz, 1H), 3.92 (s, 3H) and 3.89 (s, 3H).

2-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-2-nitroso ethanal, 158b.

Green crystals (70% yield) m.p. 127-128°C [Found: C, 37.2; H, 2.3, N, 4.9; C₉H₇NO₆S₂ requires C, 37.4; H, 2.4; N, 4.9%] m/z (EI) 289(M^⁺); νmax (KBr) 1744, 1735, 1651, 1400, 1268, and 1221 cm⁻¹; δH(CDCl₃) 11.05 (s, 1H) 4.04 (s, 6H).
1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-nitroso propan-2-one 158a.
Green crystals (45% yield) m.p. 118-118.5°C. [Found: C, 39.4; H, 2.9, N, 4.4; C_{10}H_{18}NO_{6}S_{2} requires C, 39.6; H, 3.0; N, 4.6%] m/z (EI) 303(M^{+}), \nu_{\text{max}}(\text{KBr}) 1752, 1734, 1718, 1700, 1653 , 1541 . 1534 and 1261 cm\(^{-1}\); \delta_{\text{H}(\text{CDCl}_{3})} 4.03 (s, 3H) 4.02 (s, 3H) 3.10 (s, 3H).

1-[(4-Methylphenyl)-imino]-2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-2-nitroso-ethane, 160a.
Buff solid (23% yield) m.p. 138-140°C m/z (CI) 379(M^{+}+1); \nu_{\text{max}}(\text{KBr}) 2960, 1734, 1728, 1619, 1507, 1430, 1260 and 1224 cm\(^{-1}\); \delta_{\text{H}(\text{CDCl}_{3})} 9.80 (s, 1H), 4.04 (s, 6H) and 2.44 (s, 3H).

5.2.5 Experimental details for section 2.3.2.

For General methods see section 5.2.2

s-cis & s-trans 1-(4-Carbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-methane 163 from pyridine-2-carboxaldehyde.

To a stirring solution of tributylphosphine (1.23 ml, 4.9 mmol) and carbon disulfide (0.3 ml, 4.9 mmol) in dry methanol (40 ml) at 0 °C was added a mixture of methyl propiolate (0.45 ml, 5.0 mmol) and pyridine-2-carboxaldehyde (0.48 ml, 5.0 mmol) in methanol at -30 °C. The resultant solution was stirred for 2h during which time the colour changed from orange/red to yellow, and a yellow precipitate formed. The solution was concentrated in vacuo, the precipitate filtered and washed with cold methanol to afford 163 as a Yellow solid (400 mg, 33% yield) m.p. 147-149° C(sub.) [Found: C, 52.8; H, 3.6; N, 5.8; C_{11}H_{9}NO_{2}S_{2} requires C, 52.6; H, 3.6; N, 5.6%] m/z (EI) 251(M^{+}); \nu_{\text{max}}(\text{KBr})
3047, 2946, 1583 and 1283 cm\(^{-1}\); \(\delta_{\text{H}} (\text{CDCl}_3) \text{ } ^{1} 8.63 \text{ (m, 2H), 7.60 (td, } J=7.5, 1.5 \text{ Hz, 2H)}, 7.51^* \text{ (s, 1H), 7.50^* (s, 1H), 7.06-6.86 (m, 4H), 6.69^* (s, 1H)}

\(6.68^* \text{ (s, 1H) and 3.84 (s, 6H).}

**s-cis & s-trans 1-(4-Carbomethoxy-1,3-dithiol-2-ylidene)-1-nitroso-1-(2-pyridyl)-methane 164.**

Green solid (54% yield) m.p. 201-203°C. [Found: C, 46.9; H, 2.9; N, 10.1: \(C_{11}H_{8}N_{2}O_{3}S_{2}\) requires C, 47.1; H, 2.9; N, 10.0%] \(m/z \text{ (EI) 280 (M})^+\); \(\nu_{\text{max}}\) (KBr) 3094, 3051, 1727, 1587, 1554, 1449 and 1244 cm\(^{-1}\); \(\delta_{\text{H}} \text{ (CDC}_3\text{)} 8.70-8.85 \text{ (m, 2H), 8.55 and 8.15 (both s, together 1H), 7.8-8.0 (m, 1H) 7.28-7.38 (m, 1H) and 4.03 and 4.00 (both s, together 3H); } \lambda_{\text{max}}\text{(MeCN)(ε/mol l}^{-1}\text{ cm}^{-1}) 304 (1.53 \times 10^4), 441 (1.72 \times 10^4).

### 5.2.6 Experimental details for section 2.3.3

*For General methods see section 5.2.2*

**Tetraethylammonium bis-(1,3-dithiole-2-thione-4,5-dithio) zincate salt, 165.**

This was prepared by the literature method\textsuperscript{98} and isolated as a red solid in 83% yield.

**4,5-(Dimethylthio)-1,3-dithiole-2-thione, 166.**

This was prepared by the literature method\textsuperscript{98} from the zincate salt 165. (95%). m.p. 99-100°C (lit.\textsuperscript{98} 100-101°C).

\textsuperscript{1} The appearance of 2 peaks for the vinyl\textsuperscript{2} and 5-substituent on the dithiole ring\textsuperscript{*} was due to the presence of equal amounts of s-cis & s-trans isomers; no attempt was made to separate the isomers or to assign the peaks.
**4,5-Di(methylthio)-1,3-dithiolium tetrafluoroborate 169.**

This was prepared from thione 166 by the literature method (69%).

**4,5-Di(methylthio)-2-(tributylphosphino)-1,3-dithiolium tetrafluoroborate, 170a.**

To a stirring solution of 4,5-di(methylthio)-1,3-dithiolium tetrafluoroborate (3.38 g, 12 mmol) in acetonitrile (80 ml) was added tributyl phosphine (3.07 ml, 12 mol) and the solution stirred for 1 h, during which time the solution turned from yellow to colourless. The solution was concentrated almost to dryness, addition of cold ether (80 ml) afforded 170a as white crystals (4.54 g, yield 90%) m.p. 143-145 °C. (lit. 128 146-147°C)

**General procedure for the preparation of 4,5-di(methylthio)-1,3-dithiol-2-ylidene derivatives (Method 1).**

To a stirring solution of the Wittig reagent 170a (2.0 mmol) in THF (40 ml) at -78 °C was added butyl lithium (2.2 mmol) and the solution stirred for 1 h. The required aldehyde (2.0 mmol) was added in tetrahydrofuran solution (10 ml) and the reaction allowed to warm to 20 °C over 16 h. The reaction was poured into water (150 ml) and extracted with chloroform (3 x 30 ml), the combined organic phases were washed with water then dried (MgSO₄). The solvent was removed in vacuo and the resultant oil chromatographed on silica gel with dichloromethane as eluent to yielded the following derivatives:

1-(4,5-Dimethylthio-1,3-dithiol-2-ylidene)-1-(phenyl)-methane 172a from benzaldehyde.

Yellow oil (55% yield), m/z (EI) 284(M⁺), HRMS Found: 283.9865 C₁₂H₁₂S₄; requires 283.9822; \( v_{\text{max}} \)(neat) 2916, 2848, 1595, 1578, 1496, 1441 and 1427 cm⁻¹; \( \delta_{\text{H}}(\text{CDCl}_3) \) 7.28 (m, 5H), 6.49 (s, 1H) 2.45 (s, 3H) and 2.43 (s, 3H).
1-(4,5-Dimethylthio-1,3-dithiol-2-ylidene)-1-(pyridyl)-methane 172b from pyridine-2-carboxaldehyde.

Yellow oil (60% yield) \( m/z \) (EI) 285(\( M^+ \)), HRMS Found: 284.9770 \( C_{11}H_{11}NS_4 \) requires 284.9774; \( \nu_{\text{max}} \) (neat) 2917, 1582, 1532, 1494, 1465, 1421, 1314, 1216 and 1147 cm\(^{-1}\); \( \delta_{\text{H}}(\text{CDCl}_3) \) 8.62 (m, 1H), 7.51 (td, \( J=8 \) and 2 Hz, 1H), 6.90-7.05 (m, 2H) 6.95 (s, 1H), 2.46 (s, 3H) and 2.41 (s, 3H).

1-(4,5-Dimethylthio-1,3-dithiol-2-ylidene)-1-(2,4-dinitrophenyl) methane, 172c from 2,4-dinitrophenylbenzaldehyde.

Recrystallisation from dichloromethane/methanol (1:10 \(^7\)) gave 172c as black crystals (82% yield) m.p. 177-179°C [Found: C, 38.7; H, 2.8; N, 7.4; \( C_{12}H_{10}N_2O_4S_4 \) requires C, 38.5; H, 2.7; N, 7.5%] \( m/z \) (Cl) 375(\( M^+\pm1 \)) \( \nu_{\text{max}} \)(KBr) 1600, 1581, 1533, 1507, 1482 and 1332 cm\(^{-1}\); \( \delta_{\text{H}}(\text{CDCl}_3) \) 8.78 (d, \( J=2.3 \) Hz, 1H), 8.38 (dd, \( J=2.0 \) and 8.9 Hz, 1H), 7.70 (d, \( J=8.9 \) Hz, 1H), 7.13 (s, 1H), 2.49 (s, 3H) and 2.44 (s, 3H).

Preparation of 1-(4,5-dimethylthio-1,3-dithiol-2-ylidene)-methane derivatives (Method 2).

Compounds 172a & 172b were prepared by the Emmons-Horner methodology described by Moore\(^{101}\) as yellow oils (30 & 32% yields, respectively). Both samples were identical to those prepared by Wittig methodology (See above).
1-(4,5-Dimethylthio-1,3-dithiol-2-ylidene)-1-(phenyl)-1-nitroso methane

179a.

Brown crystals (82% yield) m.p. 167-169°C. [Found: C, 45.7; H, 3.5, N, 4.3; C_{12}H_{11}NOS_{4} requires C, 46.0; H, 3.5; N, 4.5%] m/z (CI) 314(M^{+}+1), ν_{max}(KBr) 2992, 2115, 1495, 1458, 1158 and 1120 cm\(^{-1}\); δ_{H}(CDCl\(_3\)) 7.90-7.50 (m, 5H) 2.66 (s, 3H) 2.53 (s, 3H).

1-(4,5-Dimethylthio-1,3-dithiol-2-ylidene)-1-(pyridyl)-1-nitroso methane

179b.

Brown crystals (35% yield) m.p. 165-166°C m/z (EI) 314(M^{+}); ν_{max} (KBr) 1589, 1564, 1476, 1461, 1444 and 1222 cm\(^{-1}\); δ_{H} (CDCl\(_3\)) 8.73 (m, 2H) 7.87 (td, J=8, 2 Hz, 1H) 7.30 (m, 1H) 2.67 (s, 3H) 2.68 (s, 3H); λ_{max} (MeCN)(ε/mol l\(^{-1}\) cm\(^{-1}\)) 313 (4.45x10\(^3\)), 4.66 (4.76x10\(^3\)), 609 (26). X-ray quality crystals grown from dichloromethane / methanol 1:10 (v/v).

5.2.7 Experimental details for section 2.3.4

For General methods see section 5.2.2

4,5-Dimethyl-1,3-dithiolium hexafluorophosphate 184.

This was prepared by the literature method\(^{26}\) (75%) m.p. 125-126 °C (lit\(^{26}\) 123-125 °C).

4,5-Dimethyl-1,3-dithiolium iodide 185.

This was prepared by the route described by Moore and Bryce.\(^{26}\)
4,5-Dimethyl-2-tributylphosphino-1,3-dithiolium iodide, 186.

To a stirring solution of 4,5-dimethyl-1,3-dithiolium iodide (3.22g, 12 mmol) in acetonitrile (80 ml) was added tributyl phosphine (3.07 ml, 12mol) and the solution stirred for 1h, during which time the solution turned from yellow to colourless. The solution was concentrated in vacuo almost to dryness, addition of cold ether (80 ml) afforded reagent 186 as white crystals (5.26g, 91%).

General method for the preparation of 4,5-dimethyl-1,3-dithiole derivatives. (Method 1).

To a stirring solution of the Wittig reagent 186 (2.0 mmol) in tetrahydrofuran (40 ml) at -78 °C was added n-butyl lithium (2.2 mmol) and the solution stirred for 1h. The required aldehyde (2.0 mmol) was added in tetrahydrofuran solution (10 ml) and the reaction allowed to warm to 20 °C over 16h. The reaction was poured into water (150 ml) and extracted with chloroform (3x30 ml), the combined organic phases were washed with water and dried (MgSO4). The solvent was removed in vacuo and the resulting oil dissolved in dichloromethane, addition of methanol and the removal of dichloromethane in vacuo yielded the following derivatives. Recrystallisation from dichloromethane / hexane (1:10 v/v) afforded analytically pure samples.

1-(4,5-Dimethyl-1,3-dithiol-2-ylidene)-1-phenyl methane, 188a from benzaldehyde.

Off white solid (50% yield) m.p. 60-62 °C. [Found: C, 65.1; H, 5.5 C12H12S2 requires C, 65.4; H, 5.5%] m/z (EI) 220(M+); νmax(KBr) 2913, 2850, 1596,1576, 1551 and 1440 cm⁻¹; δH (CDCl3) 7.2 (m, 5H) 6.46 (s, 1H) 1.99 (s, 3H) 1.98 (s, 3H); Eox(1st cycle) = 0.74, Ered (1st Cycle) = 0.24, Eox (2nd and 3rd cycles) = 0.39 ,0.72 Ered (2nd and 3rd cycles) = 0.28 V.
1-(4,5-Dimethyl-1,3-dithiole-2-ylidene)-1-(2,4-dinitrophenyl) methane, 188b from 2,4-dinitrobenzaldehyde.

Dark purple solid (87% yield) m.p. 198-200 °C(sub.). [Found: C, 46.5; H, 3.4, N, 9.2; C_{12}H_{10}N_2O_4S_2 requires C, 46.4; H, 3.3 N, 9.0%] m/z (CI) 311(M^+1); v_{max}(KBr) 1597, 1576, 1500, 1453, 1320, 1300 and 1259 cm^{-1}; \delta_\text{H} (CDCl_3) 8.76(d, J= 2 Hz, 1H), 8.34 (dd, J= 9 and 2 Hz, 1H) 7.73 (d, J= 9 Hz, 1H) 7.15 (s, 1H) 2.10 (s, 3H), 2.08 (s, 3H); E_{ox}(1st cycle) = 0.92; E_{red} (1st Cycle) = 0.44; E_{ox} (2nd and 3rd cycles) = 0.52, 0.93; E_{red} (2nd and 3rd cycles) = 0.45 V.

Diethyl-4,5-dimethyl-1,3-dithiol-2-ylphosphonate 187.

This was prepared analogously to diethyl-4,5-diethyl-1,3-dithiole-2-ylphosphonate described by Moore and Bryce\textsuperscript{48} to yield 187 as an unstable dark red hygroscopic oil (90% yield); \delta_\text{H}(CDCl_3) 4.46 (d, J_{HP}= 4.5 Hz, 1H), 3.96 (m, 4H) 1.54 (s, 6H), 1.07 (t, J= 3.4 Hz, 6H).

4,5-(Dimethyl-1,3-dithiol-2-ylidene)-1-phenyl methane, 188a (Method 2).

Compound 118a was prepared by the Horner-Emmons methodology described by Moore\textsuperscript{101}. Off-white solid 0.62g, (52% yield), identical to the sample prepared by Wittig methodology.

1-(4,5-Dimethyl-1,3-dithiole-2-ylidene)-1-(2,4-dinitrophenyl)-1-nitroso methane 192b.

Dark green crystals (85% yield) m.p. 172-173°C m/z (CI) 340 (M^+1); HRMS Found: 338.9980; C_{12}H_{13}N_2O_5S_2 requires 338.9984; v_{max} (KBr) 3111, 1602, 1540, 1530, 1355 and 1190 cm^{-1}; \delta_\text{H}(CDCl_3) 9.04 (d, J= 2 Hz, 1H), 8.64 (dd, J= 8 and 2 Hz, 1H), 8.06 (d, J=8 Hz, 1H) and 2.41 (s, 6H).
5.2.8 Experimental details for section 2.4.2.

*For General methods see section 5.2.2*

1,2-Bis(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-ethane, 196a.

Prepared by the route described by Yoshida.\(^{47b}\) (62% yield) m.p. 183-184 °C (lit. \(^{47b}\) 184-185 °C).

1,2-Bis(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1,2-dinitroso-ethane, 196b.

Green solid, (53%) m.p. 166-168°C. \(m/z\) (D.C.I.) no mass or characteristic peaks found; \(v_{\text{max}}(\text{KBr})\) 2955, 1754, 1740 1722, 1577, 1501 and 1257 cm\(^{-1}\); \(\delta_{\text{H}}(\text{CDCl}_3)\) 3.99 (s, 6H) and 3.86 (s, 6H).

5.2.9 Experimental details for section 2.4.3.

*For General methods see section 5.2.2*

1,4-Bis[(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-methyl]-benzene, 194a from terephthalaldehyde.

Prepared by the literature route.\(^{35}\) (50% yield) m.p. 234-236 °C. (lit.\(^{35}\) 234-235 °C).

1,4-Bis[(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-nitroso-methyl]-benzene, 194b.

Green solid (36%) m.p. 185-187 °C. [Found: C, 43.3; H, 2.7; N, 4.7: \(C_{22}H_{16}N_2O_{10}S_4\) requires C, 43.3; H, 2.7; N, 4.3%] \(m/z\) (D.C.I.) No mass or
characteristic peaks Found; $v_{\text{max}}$(KBr) 2955, 1745, 1569, 1435, 1268 and 1178 cm$^{-1}$; $\delta_{\text{H}}$(CDCl$_3$) 8.13 (s, 4H) and 4.00 (s, 12H).

**Attempted preparation of 1,2-bis(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-nitroso-ethane 198.**

To a stirring solution of 2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-2-nitroso ethanal, 158b (50 mg, 0.17 mmol) and Wittig reagent 59 (100 mg, 20 mmol) in dry acetonitrile (30 ml) was added triethylamine (0.5 ml, excess). After 1h the solvent was removed in vacuo and the residue dissolved in dry dichloromethane (1 ml) addition of cold methanol failed to yield any precipitate and t.l.c. indicated the presence of a multitude of uncharacterised compounds.

**Attempted preparation of 1-(dicarbomethoxy-1,3-dithiol-2-ylidene)-1-nitroso-3-(2-nitrophenyl) prop-2-ene, 199.**

To a stirring solution of 2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-2-nitroso ethanal, 158b (40 mg, 0.14 mmol) and (2-nitrobenzyl)-triphenylphosphino tetrafluoroborate (80 mg, 1.68 mmol) in dry acetonitrile (20 ml) was added triethylamine (1 ml, excess). The solution was stirred for 1h, during which the solution changed from green to yellow. The solvent was removed in vacuo and the residue dissolved in dry dichloromethane (1 ml) addition of cold methanol failed to yield any precipitate and t.l.c. indicated the presence of a multitude of uncharacterised compounds, which were inseparable on an alumina column.
1-(4,5-di(methylthio)-1,3-dithiol-2-ylidene)-2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-propane, 195a.

To a stirring solution of dimethyl-4,5-dimethylthio-1,3-dithiol-2-ylphosphonate, 187 (1.10g, 3.6 mmol) in dry tetrahydrofuran (50 ml) at -78 °C was added n-butyl lithium (2.25 ml, 3.6 mmol) (1.6M in hexanes) and the solution stirred for 0.5h. To this mixture was added a solution of 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-propan-2-one, 157a (1.0g, 3.6 mmol) in dry tetrahydrofuran (10 ml), the temperature was maintained at -78 °C for a further 1h, then allowed to warm to 20 °C over 16h. The reaction was poured in water (100 ml) and extracted with chloroform (3x40 ml), the combined organic phases were washed with water and dried (MgSO₄). The solvent was removed in vacuo and the resulting oil chromatographed on a neutral alumina column with dichloromethane as eluent, to afford a crude product which was recrystallised from dichloromethane/methanol (1:10 V/V) to give 195a as red/brown needles (220 mg, 14%) m.p. 106-108°C [Found: C, 39.5; H, 3.6; C₁₅H₁₆O₄S₆ requires C, 39.8; H, 3.6%] m/z (D.C.I.) 452(M⁺+1), νₘₐₓ(KBr) 2948, 1731, 1712, 1578, 1436, 1291, 1263 and 1035 cm⁻¹; δ(H(CDCl₃)) 5.82 (s, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 2.41 (s, 6H) and 1.27 (s, 3H).

5.2.10 Experimental details for section 2.6.2.

Attempted Cycloaddition reaction between 4,5-dicarbomethoxy-1,3-dithiole-2-ylidene)-1-(2,4-dinitrophenyl)-1-nitroso-methane, 153e and dimethyl-butadiene.

To a stirring solution of 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2,4-dinitrophenyl)-1-nitroso-methane (60 mg, 0.14 mmol) in dry toluene (30 ml) was added 2,3-dimethylbutadiene (5.0 ml, excess) and the solution heated to reflux. NMR samples were taken after 2h, 4h and 2 days and showed gradual decomposition and no cycloaddition products.
5.2.11 Experimental details for section 2.6.3.

**Attempted Cycloaddition reaction between 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso-methane, 1531 and cyclohexene.**

To a stirring solution of 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso-methane (60 mg, 0.17 mmol) in dry chloroform (30 ml) was added cyclohexane (0.1 ml, 0.98 mmol, excess) and the solution heated to reflux for 3 days during which no reaction occurred.

**Attempted Cycloaddition reaction between 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso-methane, 1531 and dimethyl acetylenedicarboxylate.**

To a stirring solution of 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso-methane (60 mg, 0.17 mmol) in dry chloroform (30 ml) was added dimethyl acetylenedicarboxylate (0.1 ml, excess) and the solution heated to reflux for 3 days during which no reaction occurred.

**Attempted Cycloaddition reaction between 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso-methane, 1531 and 2H-dihydropyran.**

To a stirring solution of 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso-methane (60 mg, 0.17 mmol) in dry chloroform (30 ml) was added 2H-dihydropyran (0.1 ml, 1.1 mmol, excess) and the solution heated to reflux for 3 days during which no reaction occurred. The reaction repeated in toluene at 110 °C led to decomposition products.
5.2.12 Experimental details for section 2.7.2.

**Attempted preparation of 1-(4,5-dicarbomethoxy-1,3-dithole-2-ylidene)-1-phenyl-thionitrosomethane, 203.**

To a stirring solution of 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-phenyl-1-nitrosomethane (100 mg, 0.30 mmol) in toluene (50 ml) at 20°C was added phosphorus pentasulfide (30 mg, 67 μmol). The reaction temperature was increased stepwise to 70°C when a reaction started to occur. The reaction was stirred for 3 h and then the solvent removed in vacuo. T.l.c. analysis showed the presence of a multitude of unidentified products.

5.2.13 Experimental details for section 2.7.3.

**Attempted preparation of 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-phenyl-aminomethane, 206 (Method 1).**

To a stirring solution of 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-phenyl-1-nitroso-methane (100 mg, 0.30 mmol) in dry ethanol (60 ml) at 20°C was added sodium borohydride (16 mg, 42 mmol) and the solution stirred for 16 h, during which time the solution turned orange. The reaction was poured into water (100 ml) and extracted with dichloromethane (3x30 ml), the combined organic phases were washed with water and dried (MgSO₄). T.l.c. analysis indicated the presence of a multitude of uncharacterised products.

**Attempted preparation of 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-phenyl-aminomethane, 206 (Method 2).**

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-phenyl-1-nitroso-methane 179a (100 mg, 0.30 mmol) was dissolved in ether (150 ml) and palladium on carbon (10 mg) was added. The suspension was then hydrogenated for 16 h with 1 atm.
of hydrogen at \( ca \) 0 °C, after which time the catalyst was filtered off. The solvent was removed \textit{in vacuo} to yield a dark brown, unidentifiable mixture.

1-[4,5-di(methylthio)-1,3-dithiol-2-ylidene]-1-phenyl-aminomethane, 207.

To a stirring solution of 1-(4,5-dimethylthio-1,3-dithiol-2-ylidene)-1-(phenyl)-1-nitroso-methane, 179a (320 mg, 1.0 mmol) in anhydrous propan-2-ol (30 ml) was added sodium borohydride (150 mg, excess) and the solution stirred for 2h. After this time the reaction was poured into water (150 ml) and extracted with chloroform (4x20 ml) the combined organic phases were dried (MgSO\(_4\)). Removal of the solvent in vacuo afforded the required compound as a pale brown solid (280 mg, 91%). m.p. 103-105°C \( m/z \) (Cl) 300(M\(^+\)+1); \( \nu_{\text{max}} \)(KBr) 3256, 2988, 2962, 2920, 1497, 1417, 1302 and 1261 cm\(^{-1}\); \( \delta_{\text{H}} \)(CDCl\(_3\)) 9.65 (broad s, 1H), 7.6-7.3(m, 5H), 6.30 (s, 1H) and 2.04 (s, 6H).

Attempted preparation of 1-[4,5-di(methylthio)-1,3-dithiol-2-ylidene]-1-phenyl-1-thionitroso methane, 208.

To a stirring solution of 1-(4,5-di(methylthio)-1,3-dithiol-2-ylidene)-1-phenyl-aminomethane in dry tetrahydrofuran at -30 °C was added LDA (0.4 mmol) and the temperature maintained for 15min. Sulfur dichloride (0.4 mmol, 1 ml of 0.4M solution in tetrahydrofuran) was added and the reaction stirred for 1h. The temperature was raised to -10 °C and LDA (0.4 mmol) was added and the reaction stirred for 1h, t.l.c. indicated a multitude of products and attempts to precipitate a product by addition of methanol or ether were unsuccessful. A repeat reaction using butyl lithium as the base instead of LDA similarly failed to yield any characterisable products. When this reaction was carried out in the presence of dimethyl butadiene (1.5 ml, excess), added before the second equivalent of LDA, a multitude of unidentified compounds were obtained and no product from a Diels-Alder trapping of a thionitroso intermediate was isolated.
4,5-Di(methylthio)-2-dihydro-1,3-dithiole 211.

This compound was prepared as described by Moore and Bryce\textsuperscript{5} and was identical to an authentic sample.

1-(4,5-di(methylthio)-1,3-dithiol-2-ylidene)-1-phenyl-aminomethane, 213.

To a stirring solution of 4,5-di(methylthio)-2-dihydro-1,3-dithiole, 211 (670 mg, 3.41 mmol) in dry tetrahydrofuran (40 ml) at -78 °C was added BuLi (1.6M in hexanes) (2.56 ml, 4.09 mmol) and the temperature maintained at -78° C for 15min. To the solution at -78 °C was added benzonitrile (0.42 ml, 4.09 mmol) and the reaction allowed to warm to ambient temperature over 16h. The reaction was poured into water (150 ml) and extracted with ether (3x30 ml). The combined organic phases were washed with brine and dried (MgSO$_4$). Preliminary characterisation (t.l.c.) indicated that the reacton had produced a multitude of compounds, and work-up was, therefore, halted.

5.3 Experimental Details for Chapter 3

1-Cyano-3-phenyl-prop-2-eneone, 228.

This compound was prepared by the method described by Koenig and Weber\textsuperscript{116} to afford 228 as light brown solid. (5.59g, 98% yield), m.p. 58-62°C. This reagent was used without further purification for any subsequent reactions.

1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-3-(4-nitrophenyl) propene 214.

Prepared as described in the general method for the preparation of 1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-methane systems (section 5.2.1)
Red solid (81% yield) m.p. 162-163°C [Found C, 50.1; H, 3.5; N, 3.4; C_{16}H_{13}NO_{6}S_{2} requires C, 50.6; H, 3.5; N, 3.4%] m/z (EI) 379(M^+), \nu_{\text{max}}(\text{KBr}) 1735, 1711, 1577, 1508, 1335 and 1287 cm^{-1}; \delta_{\text{H}}(\text{CDCl}_3) 8.16 (d, J= 8.8 Hz, 2H), 7.47 (d, J=8.6 Hz, 2H), 6.71 (dd, J= 15.2, 11.0 Hz, 1H), 6.37 (d, J=15.2 Hz, 1H), 6.21 (d, J= 10.9 Hz, 1H), 3.87(s, 3H), and 3.86 (s, 3H)

Attempted preparation of 1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-3-(4-nitrophenyl) 1-nitrosopropene 215a.

Under the usual nitrosation conditions the reaction solution failed to go green, however a orange brown solid was precipated, preliminary characterisation indicated that it was a mixture of a mono- and di-substituted compounds.

Mono-substituted: \delta_{\text{H}}(\text{CDCl}_3) 8.33 (d, J= 6.8Hz, 2H), 7.96 (d, J= 12.5Hz, 1H), 7.51 (d, J= 6.8Hz, 2H), 3.91 (s, 3H), 3.88 (s, 3H)

Di-substituted: \delta_{\text{H}}(\text{CDCl}_3) 8.26 (d, J= 8.9Hz, 2H), 7.66 (d, J= 8.9Hz, 2H) 7.30 (s, 1H), 3.96 (s,3H),3.99 (s, 3H)

2-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-4-phenyl-but-3-ene, 218.

To a stirring solution of Wittig reagent 59 (510 mg, 1 mmol) in dry tetrahydrofuran (50 ml) at -78°C was added, dropwise, n-butyl lithium (1.6M in hexanes) (0.63 ml, 1 mmol). During this time the solution turned deep red then 4-phenyl-but-3-en-2-one (152 mg, 1 mmol) was added dropwise. The reaction temperature was maintained at -78°C for 1.5 h then allowed to warm to ambient temperature over 2.5 h. The reaction was poured into water (20 ml) and extracted with dichloromethane (3 x 10 ml). The combined organic phases were washed with water and dried (MgSO_4). The solvent was removed in vacuo to yield a deep red oil, which was purified by recrystallisation from dichloromethane/methanol (1:10 v/v) to yield 218 as an orange solid (53 mg, 15% yield) m.p. 130-132°C. [Found C, 58.3; H, 4.5; C_{17}H_{16}O_{4}S_{2} requires C, 58.6; H, 4.6; %] m/z (CI) 349(M^{+}+1); \nu_{\text{max}}(\text{KBr}) 3054, 2986, 1736 and 1235 cm^{-1}:
1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-phenyl-3-(4-nitrophenyl)-prop-2-ene, 222.

To a stirring solution of Wittig reagent 59 (512 mg, 1 mmol) in dry tetrahydrofuran at -78°C (50 ml) was added, dropwise, n-butyl lithium (1.6 M in hexanes) (0.06 ml, 1 mmol). To this solution was added, dropwise, a solution of 4-nitrochalcone 221 (255 mg, 1 mmol) in tetrahydrofuran (10 ml) and the resultant mixture allowed to warm to 20°C overnight. The solvent was removed in vacuo to afford an orange/red solid, which was purified by column chromatography on silica gel with dichloromethane / hexane (1:1 v/v) as eluent, followed by recrystallisation from methanol to yield 222 as a deep red solid. (12 mg, 3% yield) m.p. >250°C. m/z (Cl) 456 (M+1); $\delta_{\text{H}}$(CDCl$_3$) 8.12 (d, $J$= 8.9 Hz, 2H), 7.45 (m, 7H), 7.08 (d, $J$= 16.0 Hz, 1H), 5.97 (d, $J$= 15.5 Hz, 1H), 3.87 (s, 3H) and 3.78 (s, 3H)

1-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-cyano-methane, 224.

To a stirring solution of Wittig reagent 59 (400 mg, 0.79 mmol) in dry tetrahydrofuran (40 ml) was added, sequentially, triethylamine (1 ml, excess) and benzoyl cyanide (100 mg, 0.76 mmol) and the solution stirred for 1 h. After this time the solvent was removed in vacuo and the resulting oil dissolved in dichloromethane (10 ml); methanol (60 ml) was added to induce precipitation of compound 224 as yellow crystals. Recrystallisation from dichloromethane / methanol (1:10 v/v) afforded an analytically pure sample 160 mg, 64% yield) m.p. 146-148°C. [Found C, 53.8; H, 3.3; N, 4.1: C$_{15}$H$_{11}$NO$_4$S$_2$ requires C, 54.0; H, 3.3; N, 4.2%] m/z (EI) 333(M$^+$); $\nu_{\text{max}}$(KBr) 2187, 1755, 1728, 1582, 1508, 1430 and 1240 cm$^{-1}$; $\delta_{\text{H}}$(CDCl$_3$) 7.6-7.3 (m, 5H), 3.91 (s, 3H) and 3.87 (s, 3H); $\delta_{\text{C}}$(CDCl$_3$) 158.8, 158.7, 152.5, 133.1, 132.1, 130.8, 129.1, 126.3, 128.5, 117.2, 96.1, 53.7, 53.6
2-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-cyano-3-phenyl-prop-2-ene, 229.

To a stirring solution of Wittig reagent 59 (1.05 g, 2.0 mmol) in dry tetrahydrofuran (50 ml) at -78°C was added n-butyl lithium (1.6 M in hexanes)(2 ml, 3.6 mmol). 1-Cyano-3-phenyl-prop-2-enone (0.33 g, 2 mmol) in dry tetrahydrofuran (10 ml) was added after 1h and the reaction was allowed to warm to 20°C and then stirred for 3 days. The solution was poured into water (80 ml) then extracted with dichloromethane (3 x 20 ml), the combined organic phases were washed then dried (MgSO4). The solvent was removed in vacuo to yield a yellow solid which was purified by chromatography on silica gel with dichloromethane as eluent to afford 229 as yellow crystals (160 mg, 22% yield) m.p. 161-162°C. [Found C, 56.8; H, 3.3; N, 4.0: C17H13NO4S2 requires C, 56.8; H, 3.6; N, 3.9%] m/z (Cl) 360(M+1); νmax(KBr) 3054, 2986, 2211, 1738 and 1265 cm⁻¹; δH(CDC13) 7.34 (m, 5H), 6.76(d, J= 15.5 Hz, 1H), 6.38 (d, J= 16 Hz, 1H) 3.89 (s, 3H) and 3.88 (s, 3H)

1,1,1-trifluoro-2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-4-phenyl-but-3-ene, 234.

To a stirring solution of Wittig reagent 59 (250 mg, 0.5 mmol) in dry tetrahydrofuran (50 ml) at 20°C was added triethylamine (3 ml, excess). To this mixture was added trans-1,1,1-trifluoro-4-phenyl-3-buten-2-one (110 mg, 0.5 mmol) and the solution stirred for 18h. The solvent was removed in vacuo and the resulting oil purified by column chromatography on silica gel with dichloromethane as eluent to afford 235 as red crystals (160 mg, 80% yield) m.p. 124-125°C. [Found C, 51.0; H, 3.3: C17H13F3O4S2 requires C, 50.8; H, 3.2%] m/z (Cl) 403(M+1); δH(CDC13) 7.38 (m, 5H), 6.77(dq, JHH= 16Hz, 3JHF= 1.6Hz, 1H), 6.51 (dq, JHH= 16.5Hz, 4JHF= 0.9Hz, 1H) and 3.87 (s, 6H), δF(CDC13) -58.5 (s, 3F)
1,1,1-Trifluoro-2-(4-carbomethoxy-1,3-dithiol-2-ylidene)-4-phenyl-but-3-ene, 238.

To a stirring solution of tributylphosphine (0.12 ml, 0.5 mmol) and carbon disulfide (0.03 ml, 0.5 ml) in methanol (20 ml) at 0°C was added methyl propiolate (0.05 ml, 0.5 mmol) followed by trans-1,1,1-trifluoro-4-phenyl-3-buten-2-one (113 mg, 0.5 mmol). The solution was stirred at this temperature for 5 min then allowed to warm to ambient temperature and stirred for 18 h. The solvent was removed in vacuo to produce an oily crude product which was recrystallised from methanol to afford 238 as yellow needles (43 mg). The mother liquor was concentrated in vacuo and chromatography on silica gel with dichloromethane as eluent afforded a second crop of 238 (Combined yield 81 mg, 47% yield) m.p. 119°C. m/z (CI) 345(M+1); HRMS Found: 344.01544; C_{15}H_{11}F_{3}O_{2}S_{2} requires 344.01523; v_{\text{max}}(KBr) 3155, 1720 and 1257 cm⁻¹; δ_{H}(CDCl₃) † 7.35 (m, 10H+2H), 6.8-6.45(m, 4H), 3.84(s, 3H) and 3.83(s, 3H) δ_{F}(CDCl₃) -58.3 (s, 3F), -58.7 (s, 3F)

Nitrosation reactions of extended 1,3-dithiol-2-ylidene systems, General procedure:

To a stirring solution of the required 1,3-dithiole derivative (ca 0.1 mmol) in dry dichloromethane (5 ml) at 0°C was added isoamyl nitrite (0.5 ml, excess). The solution was stirred at this temperature for 15 min then allowed to warm to ambient temperature and stirred for a further 15 min. After this time the solvent was removed in vacuo and the resulting oil either (method a) recrystallised from methanol or (method b) chromatographed on silica gel with dichloromethane as eluent to yield an inseparable mixture of the nitro and nitroso species.

† The appearance of 2 ester peaks is due to the presence of equal amounts of s-cis and s-trans isomers, no attempt was made to separate the compounds or assign the peaks.
Chapter 5 Experimental Details

Preparation of 2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-3-nitroso-4-phenyl-but-3-ene, 219 and 2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-3-nitro-4-phenyl-but-3-ene 220.

(method a) An inseparable mixture of the nitro 220 and nitroso 219 species was obtained \( m/z \) (CI) 378(M\(^+\)+1)[nitroso], \( m/z \) (CI) 394(M\(^+\)+1)[nitro]; \( \delta_H(\text{CDCl}_3) \) 8.94 (s, 1H), 7.35 (m, 5H), 3.89 (s, 3H), 3.88 (s, 3H) and 1.25 (s, 3H)

2-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-cyano-3-nitro-3-phenyl-prop-2-ene, 231.

(method b) Pale yellow solid (62% yield) m.p. 32-34°C. \( m/z \) (CI) 405(M\(^+\)+1); \( \delta_H(\text{CDCl}_3) \) 7.46 (m, 5H), 4.79 (s, 1H) and 3.80 (s, 6H)

1,1,1-Trifluoro-2-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-3-nitro-4-phenyl-but-3-ene, 236.

(method b) Yellow solid (50% yield) m.p. 88-90°C. \( m/z \) (CI) 448(M\(^+\)+1); HRMS Found: 447.0088; \( \text{C}_{17}\text{H}_{12}\text{F}_3\text{NO}_5\text{S}_2 \) requires 447.0058; \( \nu_{\text{max}}(\text{KBr}) \) 3155, 1735, 1561 and 1383 cm\(^{-1}\); \( \delta_H(\text{CDCl}_3) \) 7.41 (m, 5H), 5.01 (m, 1H), 3.92 (s, 3H) and 3.88 (s, 3H)

1,1,1-Trifluoro-2-(4-carbomethoxy-1,3-dithiol-2-ylidene)-3-nitro-4-phenyl-but-3-ene, 240.

(method b) Red/orange oil (76% yield) \( m/z \) (CI) 390(M\(^+\)+1); HRMS Found: 388.97898; \( \text{C}_{15}\text{H}_{10}\text{F}_3\text{NO}_5\text{S}_2 \) requires 388.98033; \( \nu_{\text{max}}(\text{neat}) \) 3155, 1712, 1573 and 1366 cm\(^{-1}\); \( \delta_H(\text{CDCl}_3) \) 7.43 (m, 5H), 5.07 (m, 1H), 3.85 (s, 3H) and 3.85 (s, 3H)
5.4 Experimental Details for Chapter 4

4,5-Dicarbomethoxy-vinylene triselenocarbonate 250. 121

To a solution of ethane triselenocarbonate119 (1.81 g, 6.5 mmol) in dry toluene (125 ml) was added dimethyl acetylenedicarboxylate (0.96 g, 6.8) and the resulting solution was refluxed under Argon for 1h. The solvent was removed in vacuo to afford a red solid which was recrystallised from methanol to afford the required compound as red needles (2.26 g, 89% yield) m.p. 126-127 °C (lit.36 127-129 °C)

Preparation of 4,5-dicarbomethoxy-2-(tributylphosphino)-1,3-diselenolium tetrafluoroborate 254.

To a stirring solution of 4,5-dicarbomethoxy-vinylene triselenocarbonate 250 (250 mg, 0.63 mmol) in dry dichloromethane (5ml) was added methyl trifluoromethyl sulfonate (0.1 ml, 0.66 mmol) and the resulting mixture stirred under an argon atmosphere for 2h. Addition of dry ether (40 ml) led to the precipitation of a solid, which was filtered, washed with ether and dried to yield the salmon-pink triflate salt 251 (320 mg, 93% yield) m.p. 109-112 °C; δ_1H(CDCl3) 4.05 (s, 6H), 3.05 (s, 3H)

The salt 251 was dissolved in anhydrous propan-2-ol (5ml) and sodium cyanoborohydride (40 mg, 0.63 mmol) was added. The suspension of the salt was stirred for 10 min, during which time the salt dissolved, and the solution became orange. The solution was poured into diethyl ether (100 ml) and then washed with water (6 x 50 ml) and brine (50 ml). The ethereal phase was dried (MgSO₄), removal of the solvent in vacuo yielded the selenoether 252, as an unstable orange oil (235 mg, 91% yield), [δ_1H(CDCl3) 6.24 (s, 1H) 3.78 (s, 6H), 2.31 (s, 3H)]
The crude selenoether 252 was immediately dissolved in dry acetonitrile (15 ml) and cooled to 0 °C under argon. To this stirring solution was added, dropwise, tetrafluoroboric acid (54% in ether) (0.5 ml, 3.15 mmol), the temperature was maintained at 0 °C for 1 hour during which time the reaction turned deep red. Triphenylphosphine (180 mg, 0.68 mmol) was added and the reaction stirred at ambient temperature overnight. The resultant solution was used in the subsequent reactions without isolation of the product 254.

1-(4,5-Dicarbomethoxy-1,3-diselenol-2-ylidene)-1-(2-trifluoromethyl-phenyl) methane 255a from 2-(trifluoromethyl)benzaldehyde.

To a pre-prepared solution of Wittig reagent 254 in acetonitrile was added 2-trifluoromethyl benzaldehyde (120 mg, 0.69 mmol) and triethylamine (1 ml, excess) and the mixture was stirred at room temperature for 3h. Removal of the solvent in vacuo yielded a dark brown oil which was chromatographed on silica gel using dichloromethane/hexane (1:1 v/v) as eluent to afford 255a as an orange solid (92 mg, 31% yield) m.p. 125.5-126.5°C. [Found C, 38.4; H, 2.33; C_{15}H_{11}F_{3}O_{4}S_{2}e_{2} requires C, 38.3; H, 2.36 %]; m/z (Cl_{80}Se) 473(M^{+}+1); v_{max}(KBr) 1727, 1584, 1433, 1310, 1244, 1168 and 1120 cm^{-1}; δ_{H}(CDCl_{3}) 7.70 (m, 1H), 7.58 (m, 1H), 7.40 (m,2H), 7.10 (q, J_{HF} = 4 Hz, 1H), 3.83 (s, 3H) and 3.79 (s, 3H)

1-(4,5-Dicarbomethoxy-1,3-diselenol-2-ylidene)-1-(2-pyridyl)-methane, 255b from pyridine-2-carboxaldehyde.

To a pre-prepared solution of Wittig reagent 254 in acetonitrile was added 2-pyridene carboxaldehyde (73 mg, 0.69 mmol) and triethylamine (1 ml, excess) and the mixture was stirred at room temperature for 3h. Removal of the solvent in vacuo yielded a dark brown oil which was chromatographed on silica gel using dichloromethane/hexane (3:1 v/v) as eluent to afford 255b as a pale yellow solid.
(50 mg, 21% yield) m.p. 127-129 °C. [Found C, 38.5; H, 2.7; N, 3.2; 
C_{13}H_{11}NO_4Se_2 \text{ requires C, 38.7; H, 2.8; N, 3.5%}; m/z (Cl, ^{80}\text{Se}) 406 (M^+1); 
\delta_{H}(\text{CDCl}_3) 8.67 (m, 1H), 7.65 (td, J= 4.5 and 1.6 Hz, 1H), 7.18 (s, 1H) 7.05(m, 2H), 3.89 (s, 3H), and 3.84 (s, 3H)

1-(4,5-Dicarbomethoxy-1,3-diselenol-2-ylidene)-1-(2,4-dinitrophenyl)-methane 255c from 2,4-dinitrobenzaldehyde.

To a pre-prepared solution of Wittig reagent 254 in acetonitrile was added 2,4-dinitrobenzaldehyde (124 mg, 0.69 mmol) and triethylamine (1 ml, excess) and the mixture was stirred at room temperature for 30 min. Removal of the solvent in vacuo yielded a yellow oil which was chromatographed on silica gel using dichloromethane/hexane (1:1 v/v) as eluent to afford 255c as an orange solid. (93 mg, 30% yield) m.p. 142 °C. [Found C, 34.4; H, 2.0; N, 5.7; C_{14}H_{10}N_2O_6Se_2 \text{ requires C, 34.2; H, 2.1; N, 5.7%}; m/z (Cl, ^{80}\text{Se}) 494(M^+1); v_{\text{max}}(\text{KBr}) \text{ 1740}, 
1718, 1624, 1533, 1434 and 1245 cm^{-1}; \delta_{H}(\text{CDCl}_3) 8.82 (d, J= 2.8Hz, 1H), 8.45 
(dd, J= 10, 3 Hz, 1H), 7.70 (d, J= 10Hz, 1H), 7.20 (s, 1H), 3.85 (s, 3H) and 3.81 
(s, 3H)

1-(4,5-Dicarbomethoxy-1,3-diselenol-2-ylidene)-propan-2-one, 225d from methyl glyoxal.

To a pre-prepared solution of Wittig reagent 254 in acetonitrile was added Methyl glyoxal (1 ml of a 40% solution in water, excess) and triethylamine (1ml, excess) and the mixture was stirred at room temperature for 1h. The solution was poured into water (50 ml), extracted with dichloromethane (2 x 50 ml) and the combined organic phases were dried (MgSO_4). The solvent was removed in vacuo and the residue chromatographed on silica gel using dichloromethane/hexane (1:1 v/v), followed by dichloromethane as eluent to afford 255d as a yellow solid (80 mg, 34% yield) m.p. 117-119 °C. [Found
C, 32.6; H, 3.0; C_{10}H_{10}O_5Se_2 requires C, 32.6; H, 2.7 %]; m/z (Cl, ^{80}\text{Se}) 371(M^{+}+1); \nu_{\text{max}}(\text{KBr}) 1734, 1701, 1625, 1577, 1475, 1434 and 1231 cm^{-1}; \delta_{H} (d_6\text{-acetone}) 7.46 (s, 1H), 3.73 (s, 3H), 3.72 (s, 3H) and 2.10 (s, 3H)

1-(4,5-Dicarbomethoxy-1,3-diselenol-2-ylidene)-ethanal 255e\textsuperscript{47b} from glyoxal.

To a pre-prepared solution of Wittig reagent 254 in acetonitrile was added glyoxal (1 ml of a 40% solution in water, excess) and triethylamine (1 ml, excess) and the mixture was stirred at room temperature for 1h. The solution was poured into water (50ml), extracted with dichloromethane (2 x 50 ml) and the combined organic phases were dried (MgSO_4). The solvent was removed \textit{in vacuo} and the residue chromatographed on silica gel using dichloromethane/hexane (1:1 v/v) as eluent to afford 255e as a yellow solid, (67 mg, 36% yield). m.p. 108-110 °C (lit.\textsuperscript{47b} 108-109 °C)

4,5-Dicarbomethoxy-2,2-dihydro-1,3-diselenole 256.

Isolated from the above reactions by column chromatography as the first product to elute in the aforementioned solvent systems in the yields stated in table 4.1 as a malodorous orange oil. m/z (Cl, ^{80}\text{Se}) 317(M^{+}+1); HRMS Found 315.8757 C_7H_8O_4Se_2 requires 315.8753; \nu_{\text{max}}(\text{neat}) 1716, 1567, 1431 and 1239 cm^{-1}; \delta_{H} (CDCl_3) 4.52 (s, 2H), 3.80 (s, 6H). \delta_{C} (CDCl_3) 163.66, 134.55, 53.61, 14.02.

\textbf{Preparation of the nitrosated derivitives 257, General Procedure:}

To a stirring solution of the appropriate 1,3-diselenol-2-ylidene derivative 255 (\textit{ca.} 50 mg) in dichloromethane at 0°C was added isoamyl nitrite (0.5 ml, 3.75 mmol, excess). The mixture was maintained at 0°C for 15 min then stirred at ambient temperature for 16 h. The solvent was removed \textit{in vacuo} and cold
methanol (3 ml) was added to induce precipitation. The resulting nitrosoalkenes were purified by crystallisation from dichloromethane/hexane.

1-(4,5-Dicarbomethoxy-1,3-diselenol-2-ylidene)-1-(2-trifluoromethylphenyl)-1-nitroso methane 257a.

Green crystals (37% yield). m.p. 148-150 °C. m/z (Cl, $^{80}$Se) 502 (M$^+$+1); HRMS Found 500.8840 C$_{15}$H$_{10}$F$_3$NO$_2$Se$_2$ requires 500.8841; $\delta$H (CDCl$_3$) 8.1 (m, 1H) 7.8 (m, 1H) 7.6-7.5 (m, 2H) 3.99 (s, 3H) 3.89 (s, 3H); $\delta$C (CDCl$_3$) 163.27, 162.95, 155.58, 134.63, 133.03, 132.19, 131.59, 129.93, 129.56, 129.37, 128.71, 127.31, 126.46, 54.71, 53.18

1-(4,5-Dicarbomethoxy-1,3-diselenol-2-ylidene)-1-nitroso-propan-2-one, 257d.

Green crystals (55% yield) m.p 119-120 °C. [Found C, 30.4; H, 2.4; N, 3.3; C$_9$H$_7$NO$_6$Se$_2$ requires C, 30.2; H, 2.3; N, 3.5 %]; m/z (Cl, $^{80}$Se) 400 (M$^+$+1); $\nu$$_{max}$(KBr) 1741, 1703, 1641, 1400, 1283 and 1223; $\delta$H(CDCl$_3$) 4.00 (s, 3H), 3.99 (s,3H), 3.10 (s, 3H)

1-(4,5-dicarbomethoxy-1,3-diselenol-2-ylidene)-1-nitroso-ethanal 257e.

Green crystals, (34% yield). m.p. 132-133 °C. [Found C, 28.4; H, 2.0, N, 3.5; C$_9$H$_7$NO$_6$Se$_2$ requires C, 28.2; H, 1.8; N, 3.7 %]; m/z (Cl, $^{80}$Se) 386 (M$^+$+1); $\nu$$_{max}$(KBr) 1734, 1653, 1396, 1281, 1247 and 1211cm$^{-1}$; $\delta$H(CDCl$_3$) 11.12 (s,1H), 3.99 (s, 3H), 3.90 (s,3H).
References
References


References


94. G. M. Sheldrick, SHEXL-93, Program for the refinement of crystal structures, Univ. Gottingen, Germany, 1993.


References


107. M. R. Bryce, A. Green, Unpublished Results.


111. A. Gorgues, Personal Communication.


Appendix 1

*Crystal Data*
A1.1 Crystallographic data for 1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-nitroso-1-(2-pyridyl)-methane

Crystal Data

Empirical Formula \( \text{C}_{13}\text{H}_{10}\text{N}_{2}\text{O}_{5}\text{S}_{2} \)

Formula Weight 338.35

Crystal Colour Green

Crystal dimensions/ mm 0.25 x 0.40 x 0.50

Crystal system Monoclinic

Unit cell parameters

\[
a = 22.551 (9) \, \text{Å} \quad \alpha = 90^\circ
\]

\[
b = 9.512 (4) \, \text{Å} \quad \beta = 107.53 (1)^\circ
\]

\[
c = 13.669 (6) \, \text{Å} \quad \gamma = 90^\circ
\]

Space group \( \text{P2} (1)/c \) (No. 14)

Z value 8

Density (calculated) 1.565 Mgm\(^{-3}\)

\( F_{000} \) 1392

\( \mu / \text{cm}^{-1} \) 4.1

Intensity Measurements

Radiation Mo-K\( \alpha \)

Temperature 20\(^\circ\)C

\( 2\theta_{\text{max}} \) 46.5\(^\circ\)

No. of reflections measured Total: 10766

Independent: 3983
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A1.2 Crystallographic data for 1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene)-1-nitroso-propan-2-one

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Intensity Measurements

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A1.3 Crystallographic data for 1-(4,5-Di(methylthio)-1,3-dithiol-2-ylidene)-1-nitroso-1-(2-pyridyl)-methane

Crystal Data

- **Empirical Formula**: $\text{C}_{11}\text{H}_{10}\text{N}_{2}\text{OS}_4$
- **Formula Weight**: 314.45
- **Crystal Colour**: Brown
- **Crystal dimensions/mm**: 0.54 x 0.20 x 0.10
- **Crystal system**: Triclinic
- **Unit cell parameters**: $a = 7.6895 (6)$ Å, $\alpha = 103.641 (5)^\circ$
  $b = 8.6368 (5)$ Å, $\beta = 92.427 (6)^\circ$
  $c = 10.5357 (6)$ Å, $\gamma = 98.716 (6)^\circ$
- **Space group**: P-1
- **Z value**: 2
- **Density (calculated)**: 1.559 g cm$^{-3}$
- **$F_{000}$**: 324
- **$\mu / \text{cm}^{-1}$**: 7.0

Intensity Measurements

- **Radiation**: Mo-$K_\alpha$
- **Temperature**: 20°C
- **$2\theta_{\text{max}}$**: 50
- **No. of reflections measured**: Total: 2894
  Independent: 2334
Appendix 1

Crystal Data

Structure Solution and Refinement

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A1.4 Crystallographic data for l-(4,5-Dicarbomethoxy-1,3-dithiole-2-ylidene)-1-phenyl-ethanenitrile

Crystal Data

Empirical Formula: C₁₆H₁₁NO₄S₂
Formula Weight: 333.37
Crystal Colour, habit: Orange, block
Crystal dimensions/ mm: 0.5 x 0.4 x 0.25
Crystal system: Monoclinic
Unit cell parameters:
\[ a = 12.944(4) \text{ Å} \]
\[ b = 7.391(3) \text{ Å} \]
\[ c = 16.178(8) \text{ Å} \]
\[ \alpha = 90^\circ \]
\[ \beta = 103.07(3)^\circ \]
\[ \gamma = 90^\circ \]
Space group: P2₁/n
Z value: 4
Density (calculated) / Mgm⁻³: 1.469
F₀₀₀: 688

Intensity Measurements

Radiation: Mo-Kα
Temperature: 293(2)
2θ_max: 50.04
No. of reflections measured:
Total: 3535
Independent: 2655
Appendix J Crystal Data

Structure Solution and Refinement

Structure solution
Refinement
Goodness of Fit Indicator

Direct methods
Full-matrix least-squares
0.798

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Structure Solution and Refinement

Structure solution
Refinement
Goodness of Fit Indicator

Direct methods
Full-matrix least-squares
0.798

Bond lengths / Å

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A1.5 Crystallographic data for 2-(4,5-Dicarbomethoxy-1,3-diselenol-2-ylidene)-2-nitroso-ethanal

Crystal Data

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Appendix 1  Crystal Data

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Appendix 2

Work Carried out between 2 January and 31 March 1995
at Ciba-Geigy (Basel)
A2.1 Introduction

The work on azomethine ylides to date has mainly concentrated on routes to generating the ylides, and their cycloadditions with electron deficient alkenes, rather than discovering conditions under which the ylide undergoes reaction with non-activated alkenes.\(^{129}\) We wished to utilise the cycloaddition of an azomethine ylide, \(262\) and \(Z\)-1-phenyl-2-propenoic acid methyl ester \(263\) to synthesise the kainoid analogue \(265\) by deprotection of the initially formed cycloadduct \(264\) (Scheme A2.1). We therefore needed to determine reaction conditions which would lead to generation of an azomethine ylide, \(262\) without isomerisation of the alkene.

\[
\begin{align*}
R' - N^+ \quad \text{ROTC} & \quad \text{Ph} \\
\text{C} & \text{(Scheme A2.1: The desired reaction sequence)}
\end{align*}
\]

A.2.2 Results and Discussion

A2.2.1 Ylides formed from Methyl \(N\)-(trimethylsilylmethyl)-\(N\)-imino acetate

Our initial attempts were based on the method of Achiwa et al utilising methyl \(N\)-(trimethylsilylmethyl)-\(N\)-imino acetate \(266\) as the azomethine ylide precursor.\(^{130}\) Alkene \(263\) is stable to the described conditions. However, \(266\) which is activated by alkylation, acetylation or treatment with acid did not lead to cycloadduct \(267\) upon attempted reaction with \(263\) under standard conditions (trifluoroacetic acid, in HMPA / ether at 0°C or at 20°C) the alkene being recovered unreacted. Removal of ether leading to a more concentrated solution, prior to the formation of the ylide resulted in no noticable improvement. As a control experiment, the reaction was repeated with methyl cinnamate, forming the cycloaddition product \(268\), as reported by Achiwa et al, in 22% yield.\(^{130}\) Clearly, therefore, the problem was that the alkene, \(263\) is less reactive than the
alkenes reported by Achiwa, which were all activated by at least one conjugated ester group. Such electron deficient alkenes have been shown by quantum mechanical calculations to be the more reactive towards azomethine ylides.

A second route, described by Vedejs, i.e. the desilylation of an iminium salt, was attempted. Imine 266 was methylated with methyl triflate in the presence of caesium fluoride, which desilylates the initially formed iminium salt 269, to afford the azomethine ylide 270. Styrene was then used as a convenient model for the less accessible alkene 263 in the trapping reaction. Instead of the cycloadduct 271, the diamine diester 273 was obtained in low yield (10%) as the only isolable product presumably via the mechanism shown in Scheme A2.3.

\[
\begin{align*}
\text{MeO}_2\text{C}&\text{OH} + \text{SiMe}_3\text{NH}_2 &\rightarrow &\text{MeO}_2\text{C}\text{H} \quad \text{SiMe}_3 \\
\text{MgSO}_4 &\rightarrow &\text{N} &\text{MeO}_2\text{C} \\
\text{TFA} &\rightarrow &\text{H} &\text{N} \quad \text{MeO}_2\text{C} \\
\text{HMPA} &\rightarrow &\text{X} &263 \\
\end{align*}
\]

\[
\begin{align*}
i) &\text{methyl cinnamate} \\
ii) &\text{benzoyle chloride}
\end{align*}
\]

**Scheme A2.2: Reactions of the Azomethine Ylide**

Methylation of 266 was successful as indicated by the presence of N-methyl substituents and the subsequent desilylation of the iminium salt 269 had clearly taken place. However, rather than reacting with styrene, ylide 270 had added to iminium salt 269 to give iminium salt 272 which on work-up was cleaved to secondary amine 273. The methylation of imine 266 with methyl triflate was rapid, and therefore there was a high concentration of 269. However, desilylation to the required azomethine ylide 270 is slow, which was, therefore, generated in the presence of a large excess of iminium salt.

Vedejs et al also reported that activated alkenes reacted well with ylides generated in this manner, but found it difficult to explain why unactivated
alkenes failed to react. It is now clear from our results that the ylide is more likely to attack the parent iminium salt than undergo a dipolar cycloaddition with unactivated alkenes. Slow addition of iminium salt 269 to a solution of caesium fluoride and alkene should disfavour the formation of 273, as the iminium salt would only be present in low concentrations. However, the salt 269 was found to be too unstable (in CDCl₃) to be utilised in this manner.

Scheme A2.3: Postulated mechanism for the formation of 273

A2.2.2 Ylides formed from secondary amines and paraformaldehyde

Our attention then turned to a report by Tsuge et al that azomethine ylides formed by reaction of sarcosine methyl ester and paraformaldehyde in a sealed tube at 180°C reacted with styrene to form the cycloadduct, 271 (Scheme A2.4). However, treatment of alkene 263 under the reported conditions did not lead to the desired cycloadduct, but instead to isomerisation of the alkene. Since the isomerised alkenes did not lead to cycloaddition products it can be
inferred that they are less activated than styrene. This observation is in accordance with DeShong's results which show that in intramolecular reactions unactivated di-substituted alkenes were less reactive than corresponding monosubstituted analogues.133

However, the ethyl ester of N-benzylglycine, which is stable, in contrast to sarcosine ester, was also found to react with paraformaldehyde in the presence of K₂CO₃ and styrene to form the 2,3-disubstituted compound 277 in 16% yield. nOe Experiments have shown this to be the 2,3-cis substituted isomer; irradiation of the proton at the 2-position (ca. 3.6 ppm) on the pyrrolidine ring led to an enhancement of the peak attributed to the proton at the 3-position (ca. 3.4 ppm). This enhancement indicates the close proximity of the two protons and, therefore, the cis nature of C2-C3 bond. We, therefore, used this reaction as the model in our search for conditions under which the ylide 276 could be formed, and reacted with unactivated alkenes, but are sufficiently mild that isomerisation of alkene 263 does not occur.

\[
\begin{align*}
\text{MeO}_2 \text{C} \quad \text{N-Me} + \text{CH}_2 \text{O} & \xrightarrow{180^\circ \text{C}} \quad \text{MeO}_2 \text{C} \quad \text{N-Me} \\
274 & \quad \text{Styrene} \\
274 & \quad \text{N-Me} \quad \text{Ph} \\
270 & \quad \text{MeO}_2 \text{C} \\
271 & \quad \text{MeO}_2 \text{C} \\
263 & \quad \text{Isomerised Alkene}
\end{align*}
\]

**Scheme A2.4: Tsuge's Method of Azomethine Ylide Formation**

\[
\begin{align*}
\text{Ph} \quad \text{N} + \text{CH}_2 \text{O} & \xrightarrow{180^\circ \text{C}} \quad \text{Ph} \quad \text{EtO}_2 \text{C} \\
275 & \quad \text{Styrene} \\
275 & \quad \text{Ph} \quad \text{EtO}_2 \text{C} \\
276 & \quad \text{Ph} \quad \text{EtO}_2 \text{C} \\
277 & \quad \text{2,3 cis isomer}
\end{align*}
\]

**Scheme A2.5: Reaction of Styrene with the Azomethine Ylide Generated from N-Benzylglycine, ethyl ester.**
We envisaged that replacement of K$_2$CO$_3$ with a stronger dehydrating agent may allow the reaction to yield 277 to proceed at a temperature lower than the 180°C reported by Tsuge.\textsuperscript{132} Thus titanium tetrachloride (0.25 equiv) was employed as the dehydrating agent, this ratio is the optimum specified by Carlson and Nilsson for the maximisation of the yield in the formation of imines and enamines using this reagent.\textsuperscript{134}

![Scheme A2.6: Reaction of N-Benzylglycine with Strong Dehydrating Reagents](image)

However, rather than the required cycloadduct, 277, the diamine, 278 was isolated instead, in 23% yield. The potent dehydrating agent triethyl aluminium (1 equiv.) also led to 278 in 24% yield. Two methods of forming the diamine can be envisaged: by reaction of the starting amine with the metal coordinated intermediate 279, or by attack of N-benzyl glycine ester on the iminium salt 280, although, of course, it is also possible that ylide 276 maybe involved.

![Scheme A2.7: Postulated mechanisms for the formation of 278](image)

It is clear that the alkene 263 is not compatible with the high temperature conditions used in Tsuge's sealed tube reaction (Scheme A2.4).\textsuperscript{132} We decided to use an open vessel and investigate the reaction more carefully. Mesitylene
was employed as solvent since it allowed the use of a range of temperatures up to its boiling point of 165°C.

\[
\begin{align*}
278 &+ K_2CO_3 \xrightarrow{\text{Mesitylene} \ 145°C} 275 + \text{Et}_2O \xrightarrow{K_2CO_3} 277 \xrightarrow{\text{Mesitylene} \ 160°C} 281
\end{align*}
\]

**Scheme A2.8:** Reaction of N-Benzylglycine, ethyl ester with paraformaldehyde at temperatures lower than 180°C

At 145°C in mesitylene, a mixture of diamine 278, (17%), and oxazolidine 281 (16%) were formed, 281 being formed by a cycloaddition between the ylide and formaldehyde. Increasing the reaction temperature to 160°C yielded the required cycloadduct 277, (10%) and oxazolidine 281, (37%), demonstrating that the ylide is generated at lower temperatures. As reported by Joucla, this result confirms that at lower temperatures the azomethine ylide 276 reacts preferentially with formaldehyde over styrene, whereas activated alkenes compete successfully. Thus the high reaction temperatures required for reaction with styrene do not reflect a high energy barrier to the cycloaddition, but rather that the reactive and transient ylide finds alternative reaction partners. In the sealed tube reaction no 281 was isolated, suggesting that under these conditions 281 reverts back to the ylide, as reported by Joucla.

**A2.2.3 Ylides formed by the decomposition of 1,1-diamines**

The fact that no cycloadduct 277 was formed at 145°C, but the diamine 278 was obtained, whereas at 160°C the diamine is absent but the cycloadduct 277 was isolated instead, suggests that 278 is a precursor to the ylide 276.

\[
\begin{align*}
278 \xrightarrow{\text{Styrene} \ Sealed \ tube \ 180°C \ or \ Mesitylene \ 160°C} 277
\end{align*}
\]

**Scheme A2.9:** 1,1-Diamines as Azomethine Ylide Precursors
Indeed, we found that heating diamine, 278 in the presence of styrene either in a sealed tube at 180°C, or in mesitylene at 160°C, led to the formation of the required cycloadduct, in 10% and 20% yields respectively, (Scheme A2.10), presumably from reaction of azomethine ylide 276 formed by fragmentation of diamine 278. Intramolecular deprotonation α to an ester group followed by the fragmentation of the resulting zwitterion 282 would form azomethine ylide 276 and the N-benzyl glycine ester 275. Under the conditions described by Tsuge, 275 can be reacted with more paraformaldehyde to form the precursor 278.132

Utilizing 278, we sought to generate the azomethine ylide 276 under lower temperature conditions. We suspected that at lower temperatures methylation of 278 would induce fragmentation to form the tertiary amine 284 and the iminium salt 280. Amine 284 could then deprotonate iminium salt 280 to form the required ylide. However, on methylation of 278, with methyl triflate at -78°C, in the presence of styrene we did not isolate any cycloadduct, but rather the dimethyl triflate salt, 285, indicating that diamine, 278 was decomposing rapidly to form 284, which was then further methylated by methyl triflate, which was reacting preferentially with 284 rather than the diamine 278. Methylation of amine 284 under these conditions would explain the lack of formation of cycloadducts, since 285 cannot deprotonate the iminium salt 280 to form the ylide 276.

Scheme A2.10: Formation of Azomethine Ylides via Fragmentation of 1,1-Diamines
Scheme A2.11: Fragmentation of 1,1-Diamines via Methylation with Methyl Trifluoromethanesulfonate

Less reactive methylating regents were tried: methyl iodide failed to methylate the diamine 278, and although dimethyl sulfate at 50°C methylated the diamine (NMR evidence), subsequent reaction led to an unstable, and uncharacterised compound.

A2.2.4 Conclusions

We were unable to accomplish our aim of producing the kainoid analogue 265 via an azomethine cycloaddition. No conditions were found for the generation of azomethine ylides under which they reacted successfully with non-activated alkenes, except for those which are conditions, *i.e.* the LDA deprotonation of amine N-oxides, and sealed tube reactions at 180°C. This disparity in reactivity has never been fully explained.

Although we did not obtain the target compound we uncovered the new and versatile azomethine ylide precursor 278. It is possible that the designed synthesis of similar, but unsymmetrical 1,1-diamines, *i.e.* 286, may allow the production of azomethine ylides at temperatures lower than the 160 °C currently
required. This could be accomplished by varying the $N$-substituents on one of the nitrogen atoms to increase the basicity of the amine, which should facilitate deprotonation of the site $\alpha$ to the ester moiety and thus induce fragmentation at lower temperatures. The first hint that this is possible was seen in the spontaneous fragmentation of the methylated diamine 278 at 0 $^\circ$C.

![Figure A2.1: Postulated Azomethine Ylide Precursors](image-url)
A2.3 Experimental Details to Appendix 2

**General Details**

Glassware was flame dried and cooled under Argon. Solvents were dried by passing through alumina. N.M.R. Spectra were recorded on a Brucker AC300 spectrometer at 300MHz (1H spectra) or 75.5 Hz (13C spectra) or on a Varian Unity 500 spectrometer at 500MHz (1H spectra). T.L.C. analyses were performed using Merck precoated silica 60F254 plates. Column Chromatography refers to gravity chromatography on Merck silica gel 60 (230-400 Mesh).

**Methyl N-(trimethylsilylmethyl) N-iminoacetate, 266**

This was prepared according to the literature procedure\(^{130}\) in >95% yield and used crude.

**Attempted preparation of N-Benzoyl-3-methoxycarbonylmethyl-4-phenylpyrrolidine-2-carboxylic acid methyl ester, 267**

Method (i)

To a stirring solution of 263 (176 mg, 1 mmol) and trifluoroacetic acid (150 mg, 1.2 mmol) at 0 °C in HMPA (10 ml) was added, dropwise, crude product 266 (1.04 g, 6 mmol) in ethereal solution (10 ml). The solution was stirred at 0 °C for 45 min and at 20 °C for 45 min., diluted with benzene (20 ml) and washed sequentially with brine (40 ml), aqueous NaHCO\(_3\) (40 ml), and brine (40 ml). The organic phase was separated and dried (MgSO\(_4\)) and the solvent was removed *in vacuo*. The crude material was dissolved in pyridine (2 ml) and stirred at 0 °C. To this solution was added, dropwise, benzoyl chloride (930 mg, 6.6 mmol), the reaction was stirred at 0°C for 1.5 h, diluted with dichloromethane and washed with 2 M HCl, aqueous NaHCO\(_3\), and brine. The solvent was removed *in vacuo*. T.L.C. examination of the reaction mixture indicated that the alkene was unreacted and the work up was, therefore, halted.

Method (ii)

To a solution of the imine 266 (1.04 g, 6 mmol) in ether (10ml) was added acetonitrile (1 ml) and 263 (176 mg, 1 mmol). The ether was removed *in vacuo*
Appendix 2  Work carried out at Ciba-Geigy (Basel)

and the resulting solution cooled to 0 °C. To this solution was added, dropwise, trifluoroacetic acid (150 mg, 1.2 mmol) and the reaction was stirred at 0 °C for 1.5 h. The crude product was worked up and treated with benzoyl chloride as described above, and monitored by T.L.C. which showed that neither the alkene 266 or the benzoyl chloride had reacted.

**Attempted preparation of 1-Methyl-3-phenyl-pyrrolidine-2-carboxylic acid methyl ester 271**

To stirring solution of imine 269 (520 mg, 3 mmol) in dry dichloromethane (15ml) at 0 °C, was added methyl triflate (490 mg, 3 mmol) and the reaction allowed to warm to room temperature over 1h. The reaction was then cooled to 0 °C and to it was added styrene (50 mg, 0.5mmol) and anhydrous caesium fluoride (2.10 g, 14 mmol). The reaction was stirred overnight during which time it turned dark brown. The solvent was removed in vacuo and the resulting oil chromatographed with hexane:ethyl acetate (2:1/v) and then hexane:dimethoxyethane (2:1/v) to yield 2-methylamino-3-(methyltrimethylsilyl)methyl-amino)-succinic acid dimethyl ester, 273 as a yellow oil (40 mg 10%) m/z (FD)290 M⁺; δ_H(CDCl₃) 3.74 (s, 3H), 3.71 (s, 3H), 3.56 (d, J=11 Hz, 1H), 3.23 (d, J= 11 Hz, 1H), 2.33 (s, 3H), 2.25 (s, 3H), 1.60 (broad s, 1H) δ_C(CDCl₃) 174.3, 169.7, 72.6, 63.9, 51.7, 51.0, 46.8, 41.8, 35.1, -1.6 and the minor diastereomer δ_C(CDCl₃) 173.0, 170.6, 69.8, 62.4, 52.1, 51.2, 45.3, 42.6, 35.5, 30.3, -1.6

**1-Benzyl-3-phenyl-pyrrolidine-2-carboxylic acid ethyl ester 277**

A mixture of N-benzylglycine ethyl ester (390 mg, 2.0 mmol), formaldehyde (300 mg, 10 mmol), styrene (200 mg, 1 mmol) and K₂CO₃ (500 mg, excess) were placed in a sealed tube and heated at 180 °C for 15 h. After cooling to ambient temperature the reaction products were stirred with ethyl acetate (50 ml) for 2h. The mixture was filtered and the filtrate concentrated in vacuo to yield a brown oil, which was chromatographed using hexane:ethyl acetate (2:1 v/v), then hexane:dimethoxyethane (10:1 v/v) to yield pyrrolidine 277, as a colourless oil (50 mg), 16% yield. m/z (FD)309 (M⁺); δ_H(CDCl₃) 7.45-6.99 (m, 10H), 4.08 (d,
\[ J = 12.5 \text{Hz}, 1\text{H}], 3.6 \text{ (m, 2H), 3.40 (m, 3H), 3.11 (m, 1H), 2.37 (m, 1H), 2.10 (m, 1H)} 1.86 \text{ (m, 1H), 0.59 (t, } J = 8\text{Hz, 3H);} \delta_{\text{C}(\text{CDCl}_3)} 172.0, 140.9, 129.1, 128.5, 128.2, 128.0, 127.1, 126.4, 70.3, 59.8, 58.0, 52.5, 47.7, 30.7, 13.8.

**Attempted preparation of 1-Benzyl-3-phenyl-pyrrolidine-2-carboxylic acid ethyl ester 277**

To a stirring mixture of N-benzylglycine ethyl ester (390 mg, 2 mmol), formaldehyde (300 mg, 10 mmol) and styrene (200 mg, 2 mmol) in dry toluene (50 ml) at 0 °C, was added, dropwise, titanium tetrachloride (90 mg, 0.25 mmol) and the solution stirred at 0°C for 2.5h after which time tlc evidence showed that no reaction had occurred. The reaction was stirred at ambient temperature for 15h, then diluted with toluene and washed with aqueous NaHCO₃ and brine. The organic layer was dried with MgSO₄ and the solvent removed \textit{in vacuo} and the resulting oil chromatographed using hexane:ethyl acetate (5:1 \%) as eluent to yield \{Benzyl-[(benzyl-ethoxycarbonylmethylamino)-methyl]amino\} acetic acid ethyl ester 278, (90mg, 23%) \( m/z \) (FD) 398 (M⁺); \( \delta_{\text{H}} \) (CDCl₃) 7.35-7.15 (m, 10H) 4.22 (q, \( J = 7\text{Hz}, 4\text{H})); \( \delta_{\text{C}} \) (CDCl₃) 171.8, 139.3, 128.9, 128.3, 127.0, 73.2, 60.1, 55.7, 51.8, 14.3

**Attempted preparation 1-Benzyl-3-phenyl-pyrrolidine-2-carboxylic acid ethyl ester 277**

To a stirring solution of N-benzylglycine ethyl ester (390 mg, 2 mmol), paraformaldehyde (300 mg, 10 mmol) and styrene (200 mg, 1 mmol) in dry toluene (25 ml) at 0 °C was added triethyl aluminium (1.0 M in hexanes) (2.0 ml, 2 mmol). The reaction was monitored by tlc and after 3 h another 2 equivalents of triethyl aluminium (4.0 ml, 4 mmol) were added, and after a further 1h a final equivalent of triethyl aluminium (2.0 ml, 2 mmol) was added. After 6h the reaction was washed with 2M NaOH (30 ml), extracted into toluene (20 ml) and washed with brine (40 ml). The organic phase was separated and dried (MgSO₄). The solvent was removed \textit{in vacuo} to afford an oil which was chromatographed with hexane:ethyl acetate (5:1 \%) to yield 278, 95mg, 24%, identical with that obtained above.
1-Benzyl-3-phenyl-pyrrolidine-2-carboxylic acid ethyl ester 277

N-Benzylglycine ethyl ester (390 mg, 2 mmol), paraformaldehyde (300 mg, 10 mmol), styrene (200 mg, 2.0 mmol) and anhydrous K$_2$CO$_3$ (500 mg, excess) were placed in dry mesitylene (9 ml) and heated to ca. 160 °C for 15h. The reaction was cooled to ambient temperature and the solvent removed in vacuo. The resulting oil was chromatographed using hexane:dimethoxyethane (5:1 v/v) as eluent, to yield pyrrolidine 277, (60mg, 10%). The chromatography column was eluted with methanol to collect the more polar material, this residue was chromatographed using hexane:ethyl acetate (5:1 v/v) yielded 3-benzyl-4-oxazolidine-2-carboxylic acid ethyl ester 281 as a colourless oil (174mg, 37%).

$\text{m/z (FAB) 235 (M}^+\text{); found C; 66.4, H; 7.3, N; 5.9%, C}_{13}\text{H}_{17}\text{NO}_3 \text{ requires C; 66.4, H; 7.3, N; 6.0 %; $^1$H (CDCl}_3\text{) 7.40-7.29 (m, 5H) 4.44 (s, 2H) 4.3-4.1 (m, 2H+1H) 3.9-3.8 (m, 3H) 3.66 (dd, J= 8 and 5 Hz, 1H) 1.23 (t, J=7Hz, 3H); $^1$C (CDCl}_3\text{) 171.9, 138.2, 128.8, 128.5, 127.5, 87.1, 67.3, 64.5, 61.1, 58.8, 14.2}$

Attempted preparation of 1-Benzyl-3-phenyl-pyrrolidine-2-carboxylic acid ethyl ester 277

N-Benzylglycine ethyl ester (390 mg, 2 mmol), paraformaldehyde (300 mg, 10 mmol), styrene (200 mg, 2.0 mmol) and anhydrous K$_2$CO$_3$ (500 mg, excess) were placed in dry mesitylene (9 ml) and heated to ca. 145 °C for 2h during which time the N-benzylglycine ethyl ester reacted. Tlc. and N.M.R. showed that the reaction contained the diamine 278, and the oxazolidine, 281 neither of which were isolated.

1-Benzyl-3-phenyl-pyrrolidine-2-carboxylic acid ethyl ester 277

Diamine 278 (400 mg, 1 mmol) and styrene (100 mg, 1 mmol) were placed in a sealed tube and heated at 180 °C for 15h. The reaction was cooled to ambient temperature, stirred with ethyl acetate for 1h, then filtered and the filtrate was concentrated in vacuo to yield a yellow oil. The oil was chromatographed using hexane:dimethoxyethane (10:1 v/v) as eluent to yield a mixture of pyrrolidine 277 (ca. 10% yield) and the starting diamine 278.
1-Benzyl-3-phenyl-pyrrolidine-2-carboxylic acid ethyl ester 277

Diamine 278 (400 mg, 1 mmol) and styrene (100 mg, 1 mmol) were dissolved in dry mesitylene (10 ml) and heated to 160°C for 2h. The solvent was removed in vacuo and the resulting oil chromatographed using hexane:dimethoxyethane (5:1 v/v) as eluent to yield a mixture of pyrrolidine 277 (ca. 21%) and a trace amount of 278.

Attempted preparation of 1-Benzyl-3-phenyl-pyrrolidine-2-carboxylic acid ethyl ester 277

To a stirring solution of 278 (200 mg, 0.5 mmol) and styrene (50 mg, 0.5 mmol) in toluene at 0°C, methyl triflate (60 mg, 0.5 mmol) was added dropwise the reaction was stirred at ambient temperature for 1.5h before the temperature was raised to 70°C for 0.5h. The reaction was washed with aqueous NaHCO₃ (20 ml) and brine (20 ml). The organic phase was dried (MgSO₄) and the solvent removed in vacuo. The oil was stirred with diethyl ether for 0.5h and then left in the fridge overnight to yield a white solid, benzyl-ethoxycarbonylmethyl-dimethyl-ammonium triflate, 285, (30 mg, 27%). m.p. 96-97°C; m/z (FAB) 520 (M⁺+149); δH (CDCl₃) 7.5 (m, 5H) 4.86 (s, 2H), 4.34 (s, 2H), 4.30 (q, J= 7Hz, 2H) 3.35 (s, 6H) 1.31 (t, J= 7Hz, 3H).

Preparation of {Benzyl-[(benzyl-ethoxycarbonylmethylamino)-methyl]amino} acetic acid ethyl ester 278

To a stirring solution of N-benzyl glycine ethyl ester (1.95 g, 10 mmol) and paraformaldehyde (1.50 g, 50 mmol) in toluene (30 ml) at 20°C was added, dropwise, triethyl aluminium (1M in hexanes) (12 ml, 12 mmol) and the reaction stirred for 2h. The reaction was washed with 2M NaOH (40 ml), extracted into toluene (30 ml) and washed with brine (10 ml). The organic phase was dried over MgSO₄ and the solvent removed in vacuo. The resulting oil was stirred with hexane for 0.5h, then left in the fridge for 15h. The resulting white solid removed. The solvent from the filtrate removed in vacuo to yield the required diamine 278, 2.40 g, 60%.
A2.4 References for Appendix 2


Appendix 3

List of Research Colloquia, Lectures and Seminars
### A.3 List of Research Colloquia, Lectures and Seminars

There follows a list of research colloquia, lectures and seminars that have been addressed by external speakers and arranged by the Department of Chemistry during the period of the author's residence as a postgraduate student.

* Denotes attended by the author.

**1992-1993 (August 1 - July 31)**

<table>
<thead>
<tr>
<th>Date</th>
<th>Speaker(s)</th>
<th>Topic</th>
</tr>
</thead>
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<tr>
<td>October 15</td>
<td>Dr. M. Glazier &amp; Dr. S. Tarling, Oxford University &amp; Birbeck College London</td>
<td>It pays to be British!- The chemist's role as an expert witness in patent litigation</td>
</tr>
<tr>
<td>October 20</td>
<td>Dr. H.E. Bryndza, Du pont central Research</td>
<td>Synthesis, reactions and thermochemistry of metal (alkyl) cyanide complexes and their impact on olefin hydrocyanation catalysis*</td>
</tr>
<tr>
<td>October 22</td>
<td>Prof. A. Davies, University College London</td>
<td><em>The Ingold-Albert Lecture</em> The behavior of hydrogen as a pseudo-metal</td>
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<tr>
<td>October 28</td>
<td>Dr. J.K. Cockcroft, University of Durham</td>
<td>Recent developments in powder diffraction</td>
</tr>
<tr>
<td>October 29</td>
<td>Dr. J. Emsley, Imperial College London</td>
<td>The shocking history of phosphorus*</td>
</tr>
<tr>
<td>November 4</td>
<td>Dr. T.P. Kee, University of Leeds</td>
<td>Synthesis and co-ordination chemistry of silylated phosphites</td>
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<tr>
<td>November 5</td>
<td>Dr. C. J. Ludman, University of Durham</td>
<td>Explosions, A demonstration lecture*</td>
</tr>
<tr>
<td>November 11</td>
<td>Dr. D. Robinst, Glasgow University</td>
<td>Pyrrolizidine alkanoids: Biological activity, biosynthesis and benefits*</td>
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<tr>
<td>November 12</td>
<td>Prof. M. R. Truter, University College London</td>
<td>Luck and logic in Host-Guest chemistry</td>
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<tr>
<td>November 18</td>
<td>Dr. R. Nix†, Queen Mary College London</td>
<td>Characterisation of heterogeneous catalysts</td>
</tr>
<tr>
<td>November 25</td>
<td>Prof. Y. Vallee, University of Caen.</td>
<td>Reactive thiocarbonyl compounds*</td>
</tr>
<tr>
<td>November 25</td>
<td>Prof. L. D. Quin†, University of Massachusetts, Amherst</td>
<td>Fragmentation of phosphorus heterocycles as a route to phosphoryl species with uncommon bonding</td>
</tr>
<tr>
<td>November 26</td>
<td>Dr. D. Humber, Glaxo, Greenford</td>
<td>AIDS- The development of novel series of inhibitors of HIV</td>
</tr>
<tr>
<td>December 2</td>
<td>Prof. A. F. Hegarty, University College, Dublin</td>
<td>Highly reactive enols stabilised by steric protection</td>
</tr>
<tr>
<td>December 2</td>
<td>Dr. R. A. Aitken†, University of St. Andrews</td>
<td>The versatile cycloaddition chemistry Bu₃P.CS₂*</td>
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<tr>
<td>December 3</td>
<td>Prof. P. Edwards, Birmingham University</td>
<td><em>The SCI Lecture- What is a metal?</em></td>
</tr>
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December 9  Dr.A.N. Burgess, ICI Runcorn
The structure of perfluorinated ionomer membranes

1993

January 20  Dr.D.C. Clary†, University of Cambridge
Energy flow in chemical reactions

January 21  Prof.L. Hall, Cambridge
NMR-Window to the human body

January 27  Dr.W. Kerr, University of Strathclyde
Development of the Pauson-Khand annulation reaction: organocobalt mediated synthesis of natural and unnatural products*

January 28  Prof.J. Mann, University of Reading
Murder, magic and medicine*

February 3  Prof.S.M. Roberts, University of Exeter
Enzymes in organic synthesis

February 10  Dr.D. Gillies†, University of Surrey
NMR and molecular motion in solution

February 11  Prof.S. Knox, Bristol University
The Tilden Lecture Organic chemistry at polynuclear centres

February 17  Dr.R.W. Kemmitt†, University of Leicester
Oxatrimethylenemethane metal complexes

February 18  Dr.I. Fraser, ICI Wilton
Reactive processing of composite materials

February 22  Prof.D.M. Grant, University of Utah
Single crystals, molecular structure, and the chemical shift anisotropy

February 24  Prof.C.M.J. Stirling†, University of Sheffield
Chemistry on the flat reactivity of ordered systems

March 10  Dr.P.K. Baker, University College of N. Wales, Bangor
Chemistry of highly versatile 7-coordinate complexes

March 11  Dr.R.A.Y. Jones, University of East Anglia
The chemistry of wine making*

March 17  Dr.R.J.K. Taylor†, University of East Anglia
Adventures in natural product chemistry*

March 24  Prof.I.O. Sutherland†, University of Liverpool
Chromogenic reagents for cations*

May 13  Prof.J.A. Pople, Carnegie-Mellon University, Pittsburg, USA
The Boys-Rahman Lecture Applications of molecular orbital theory

May 21  Prof.L. Weber, University of Beilefeld
Metallo-phospha alkenes as synthons in organometallic chemistry

June 1  Prof.J.P. Konopelski, University of California, Santa Cruz
Synthetic adventures with enantiomerically pure acetals

June 2  Prof.F. Ciardelli, University of Pisa
Chiral Discrimination in the stereospecific polymerisation of alpha olefins

June 7  Prof.R.S. Stein, University of Massachusetts
Scattering studies of crystalline and liquid crystalline polymers
Appendix 3  
Research Colloquia, Lectures and Seminars

June 16  
Prof. A.K. Covington, University of Newcastle  
Use of ion selective electrodes as detectors in ion chromatography

June 17  
Prof. O.F. Nielsen, H.C. Ørsted Institute, University of Copenhagen  
Low frequency IR and Raman studies of hydrogen bonded liquids

1993-1994 (August 1 - July 31)

1993

September 13  
Prof. Dr. A.D. Schüter, Freie Universität, Berlin, Germany.  
Synthesis and characterisation of molecular rods and ribbons.

September 13  
Dr. K.J. Wynne, Office of Naval Research, Washington, USA.  
Polymer surface design for minimal adhesion.

September 14  
Prof. J.M. DeSimone, University of North Carolina, Chapel Hill, USA.  
Homogeneous and heterogeneous polymerisations in enviromentially responsible carbon dioxide.

September 28  
Prof. H. Ilia, North Eastern Hill University, India  
Synthetic strategies for cyclopentanoids via dithioacetals.*

October 4  
Prof. F.J. Fehért, University of California, Irvine, USA.  
Bridging the gap between surfaces and solution with sessliquioxanes

October 14  
Dr. P. Hubberstey, University of Nottingham.  
Alkali metals Alchemist’s nightmare, Biochemist’s puzzle, technologist’s dream.

October 20  
Dr. P. Quayle†, University of Manchester.  
Aspects of Aqueous ROMP chemistry

October 21  
Prof. R. Adams†, Universit of South Carolina, USA.  
Chemistry of metal carbonyl cluster complexes: Development of cluster based alkyne hydrogenation catalysts

October 27  
Dr. R.A.L. Jones†, Cavendish Laboratory, Cambridge.  
Perambulating polymers

November 10  
Prof. M.N.R. Ashfold†, University of Bristol.  
High resolution photofragment translational spectroscopy: A new way to watch Photodissociation

November 17  
Dr. A. Parker†, Rutherford Appleton Laboratory, Dicot.  
Applications of time resolved raman spectroscopy to chemical and biochemical problems

November 24  
Dr. P.G. Bruce†, University of St. Andrews.  
Structure and properties of inorganic solids and polymers.

November 25  
Dr. R.P. Wayne, University of Oxford.  
The origin and evolution of the atmosphere.

December 1  
Prof. M.A. McKervey†, Queen’s University, Belfast.  
Synthesis and applications of chemically modified calixarenes.*

December 8  
Prof. O. Meth-Cohn†, University of Sunderland.  
Friedel’s folly revisited - A super way to fused pyrimidines*
December 16  Prof. R.F. Hudson, University of Kent.
Close encounters of the second kind.

1994
January 26  Prof. J. Evans†, University of Southampton.
Shining light on catalysis.
February 2  Dr. A. Masters†, University of Manchester.
Modelling water without using pair potentials
February 9  Prof. D. Young†, University of Sussex.
Chemical and Biological studies on the co-enzyme tetrahydrofolic acid.
February 16 Prof. K.H. Theopold†, University of Delaware, USA.
Paramagnetic chromium alkyls : Synthesis and reactivity.
February 23 Prof. P.M. Maitlis†, University of Sheffield.
Across the border : From homogeneous to heterogeneous catalysis.
March 2  Dr. C. Hunter†, University of Sheffield.
Non-covalent interactions between aromatic molecules. *
March 9  Prof. F. Wilkinson, Loughborough University of Technology.
Nanosecond and picosecond laser flash photolysis
March 10  Prof. S.V. Ley, University of Cambridge.
New methods for organic synthesis
March 25 Dr. J. Dilworth, University of Essex.
Technetium and rhenium compounds with applications as imaging agents.
April 28 Prof. R.J. Gillespie, McMaster University, Canada.
The molecular structure of some metal fluorides and oxofluorides : Apparent exceptions to the VSEPR model
May 12  Prof. D.A. Humphreys, McMaster University, Canada.
Bringing knowledge to life.

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October 5 Prof. N.L. Owen, Brigham Young University, Utah, USA.
Determining molecular structure - the INADEQUATE way.
October 19 Prof. N. Barlett, University of California, USA.
Some aspects of Ag (II) and Ag (III) chemistry *
November 2 Dr. P.G. Edwards, University of Wales, Cardiff.
The manipulation of electronic and structural diversity in metal complexes - New ligands
November 3 Prof. B.F.G. Johnson, Edinburgh University.
Arene-metal clusters. *
November 9 Dr. G. Hogarth, University College, London.
New Vistas in metal-imido chemistry. *
November 10 Dr. M. Block, Zeneca Pharmaceuticals, Macclesfield.
Large-scale manufacture of ZD 1542, a thromboxane antagonist synthase inhibitor.
November 16 Prof. M. Page, University of Huddersfield.
Four-membered rings and β-lactamase.
November 23  Dr. J.M.J. Williams, University of Loughbrough.  
New approaches to asymmetric catalysis.
December 7  Prof. D. Briggs, ICI and University of Durham.  
Surface mass spectrometry

1995
January 11  Prof. P. Parsons, University of Reading.  
Applications of tandem reactions in organic synthesis.
January 18  Dr. G. Rumles, Imperial College, London.  
Real or imaginary third order non-linear optical materials.
January 25  Dr. D.A. Roberts, Zeneca Pharmaceuticals.  
The design and synthesis of inhibitors of the renin-angiotensin system.
February 1  Dr. T. Cosgrove, Bristol University.  
Polymers do it at interfaces.
February 8  Dr. D. O'Hare, Oxford University.  
Synthesis and solid-state properties of poly-, oligo- and multidecker metalocenes.
February 22 Prof. E. Schaumann, University of Clausthal.  
Silicon- and sulfur-mediated ring-opening reactions of epoxide.
March 1  Dr. M Rosseinsky, Oxford University.  
Fullerene intercalation chemistry.
March 22 Dr. M. Taylor, University of Auckland, New Zealand.  
Structural methods in main-group chemistry
April 26  Dr. M. Schroder, University of Edinburgh.  
Redox-active macrocyclic complexes : Rings, Stacks and liquid crystals.*
May 3  Prof. E.W. Randall, Queen Mary and Westfield College.  
New perspectives in NMR imaging.
May 24  Prof. A.J. Kresge, University of Toronto  
The Ingold Lecture, Reactive intermediates : Carboxylic-acid enols and other unstable species.