Nitroso derivatives of l,3-dithiol-2-ylidenes, and related systems

Chalton, Michael Allen

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

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

Department of Chemistry
University of Durham

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

May 1996

Declaration

The work described in this thesis was carried out by the author, in the Department of Chemistry, University of Durham between October 1992 and September 1995. It has not been submitted previously for a degree at this, or any other, University.

Statement of Copyright

Abstract

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

by

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

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

May 1996

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 subtituents 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 positon, 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 accomplised 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."

'The Adventure of the Resident Patient'; Sir Arthur Conan Doyle.

Contents

APPENDIX 2 151

A2.1 INTRODUCTION 152
A.2.2 RESULTS AND DISCUSSION 152
A2.2.1 Ylides formed from Methyl N-(trimethylsilylmethyl)-N-imino acetate 152
A2.2.2 Ylides formed from secondary amines and paraformaldehyde 154
A2.2.3 Ylides formed by the decompostion of 1,1-diamines 157
A2.2.4 Conclusions 159
A2.3 EXPERIMENTAL DETAILS TO APPENDIX 2 161
A2.4 REFERENCES FOR APPENDIX 2 166

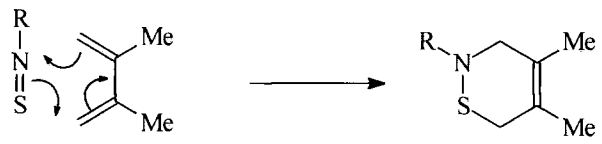
Chapter 1

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.[1] 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).

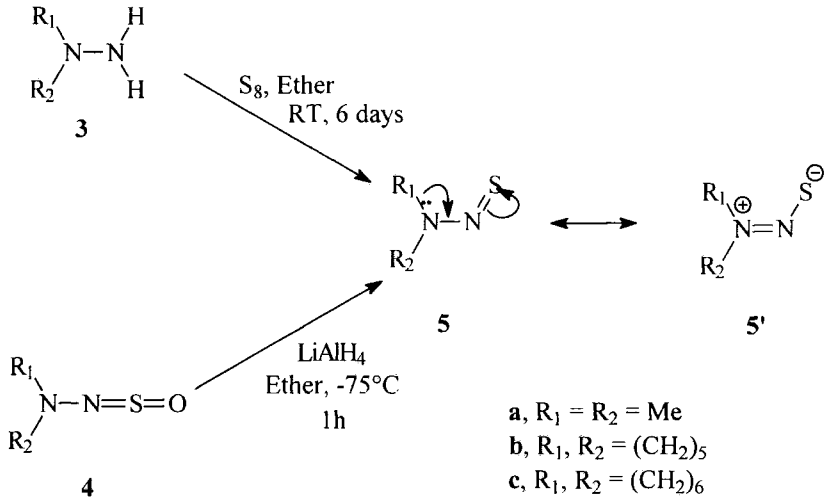


1 **2**

***Scheme 1.1**: Diels-Alder Trapping of a Thionitroso Intermediate*

Since their discovery in 1966,[2] 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* [3] and *N*-thionitrosoamines have been prepared by Middleton.[2b]

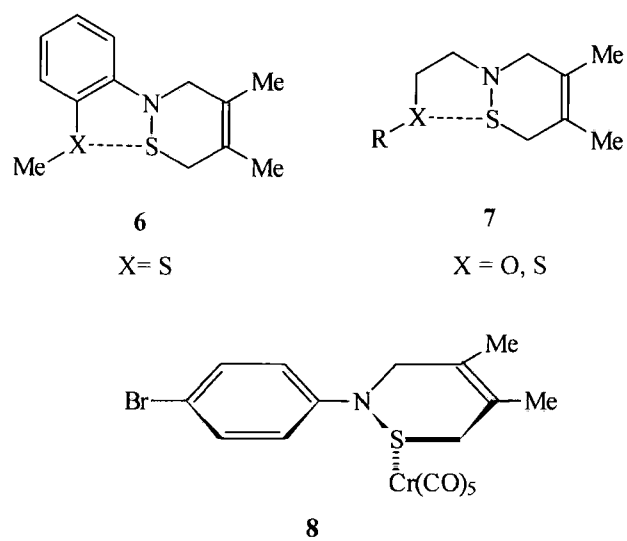
The thionitrosamines **5** were isolated as purple solids in low yields (*ca.* 15-30%) from either the reaction of 1,1-dialkylhydrazines **3** with elemental sulfur, or by the lithium aluminium hydride reduction of thionyldimethylhydrazine **4** (Scheme 1.2). At temperatures above -30°C, the thionitrosamines 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'**.



3 4 5 5'

***Scheme 1.2**: Generation of N-Thionitrosamines*

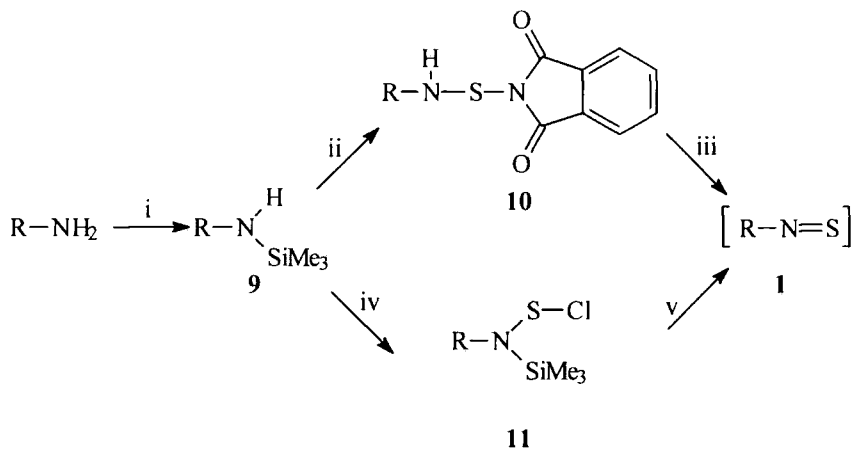
Recently, work has been carried out on *C*-thionitroso compounds and much information about the generation of such thionitroso compounds has been gained.[4] To date, no isolable *C*-thionitroso compound has been prepared, and only recently have shelf-stable Diels-Alder adducts **6-8** been reported [5, 6] 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]



6 X= S **7** X = O, S **8**

***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.[7] Reaction of the silylated amine, **9** with phthalimide sulfenyl chloride led to the formation of phthalimide derivatives, **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 **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*,[8] 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.[5] The reaction of the silylated amine, **9** with sulfur dichloride yielded the unstable *N*-chlorothio-*N*-trimethylsilyl amines **11**. These were immediately reacted with a base to induce a 1,2-elimination reaction which formed the required thionitroso intermediate **1**.



***Scheme 1.3**: Convenient Methods of Generating Thionitroso Intermediates*

Reagents and Conditions i) Et_3N, Me_3SiCl, Ether; ii) Phthalimide sulfenyl chloride, chloroform; iii) Et_3N, Acetone; iv) 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 2.9Å, [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 stablised by both a dipolar form and a non-bonded sulfur-sulfur interaction.

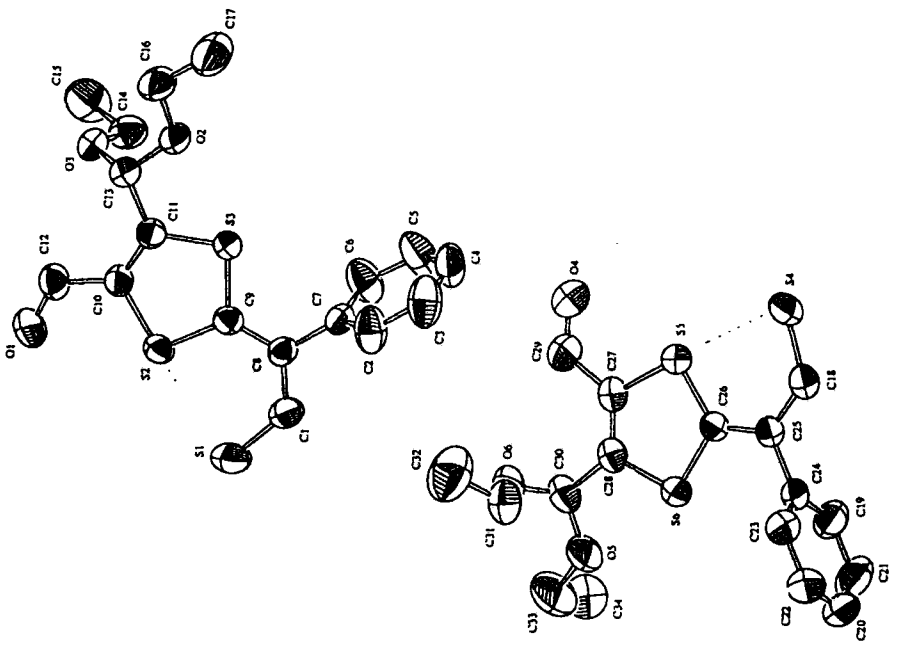
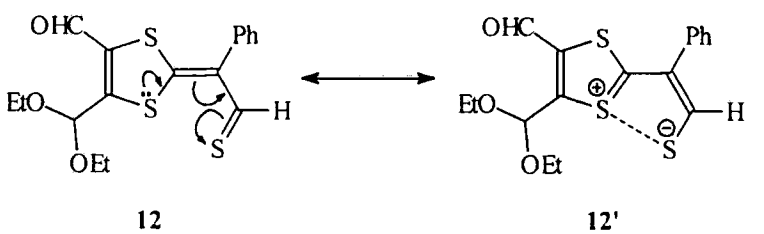


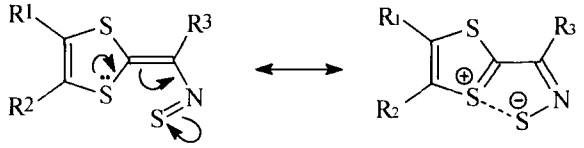
Figure 1.2**: X-Ray Molecular Structure of Thioaldehyde **12



12 **12'**

***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).



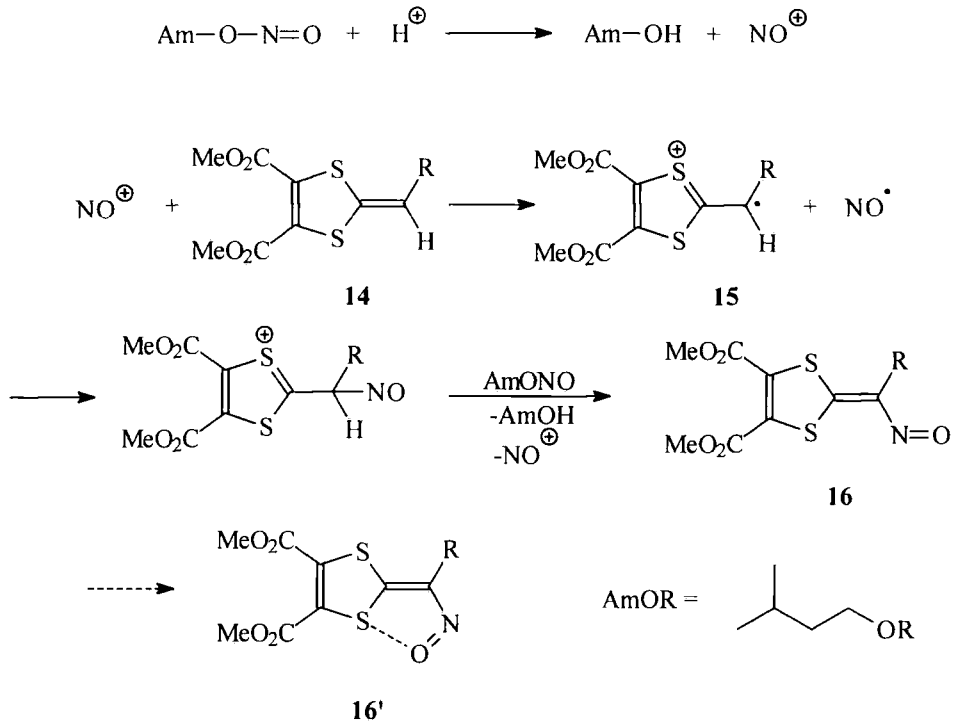
13 **13'**

***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

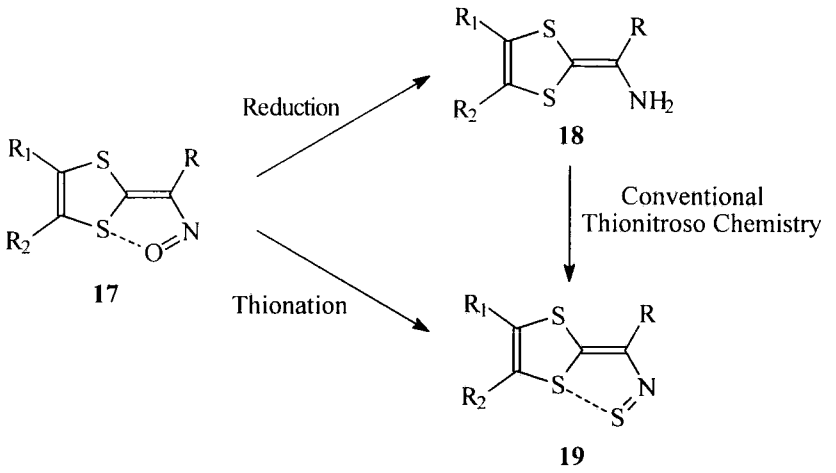
of the chemistry and scope of the nitrosation reaction, coupled with possible X-ray crystallographic studies, should identify whether or not the nitroso-alkene was stabilised by the envisaged intramolecular interaction.



***Scheme 1.4**: Nitrosation Mechanism According to Cava*[12]

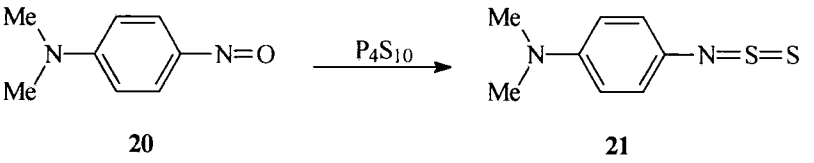
The nitroso species **17** may also be considered as interesting models for their thionitroso counterparts **19** and could be used to determine the most favourable substituents for both the ylidene, and 4- and 5- dithiole substituents. The polarisation of the nitrogen-oxygen double bond in a nitroso-alkene 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.[15]



***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 **20** and found that the reactions yielded dithionitrites **21** (Scheme 1.6) indicating that sulfur-nitrogen double bonds could be formed this way.[16] We hoped that in our system the intramolecular sulfur-sulfur interaction would prevent thionation proceeding beyond the thionitroso stage.



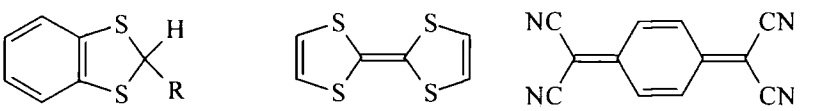
***Scheme 1.6**: Thionation of Aryl-Nitroso Species*

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 **22** reported by Hurtley and Smiles in 1926.[17] 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.[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.[19] The modifications made to the TTF structure include: varying the 4- and 5- substituents, extending the dimensionality present in the structure,[20] and separating the two dithiole rings with conjugated spacer units.[21]



22 **23** **24**

***Figure 1.5**: Important Compounds in the Development of Dithiole Chemistry*

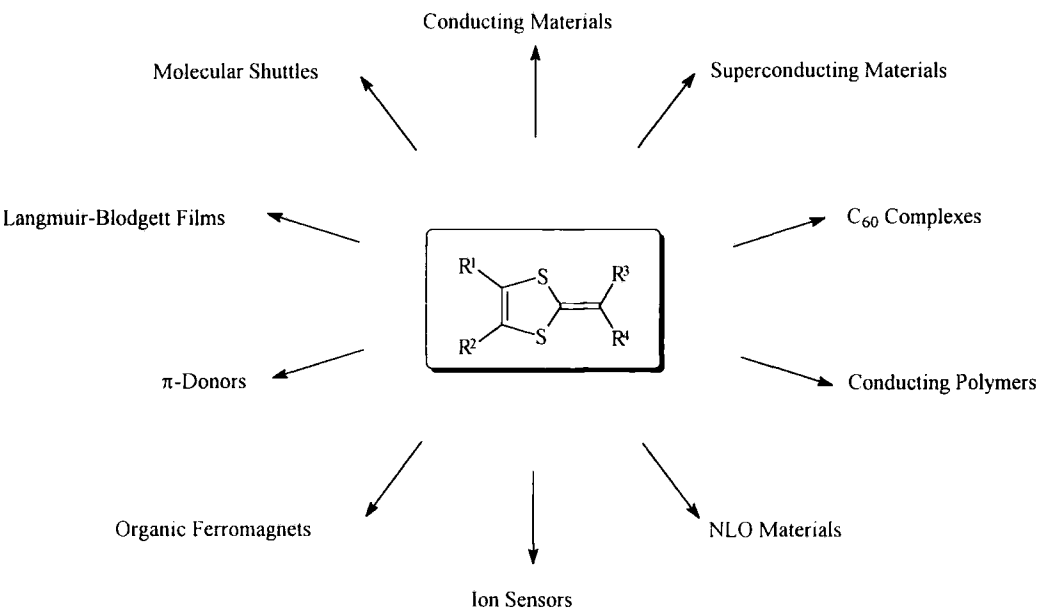
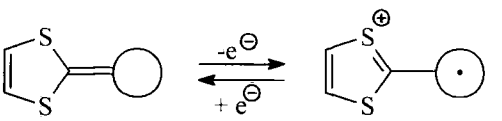


***Figure 1.6**: Applications of the 1,3-Dithiole Unit in a Post-TTF Era*

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).[13]

The applications rely on the electron-donating nature of the 1,3-dithiole ring **25**. This donating ability is due to the system forming a 6π aromatic 1,3-dithiolium cation **26**.(Scheme 1.7)[13]



25 **26**

Neutral Cation-radical

***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

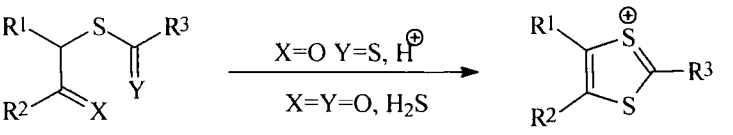
(c) Formation of 2 bonds: [3+2] atom fragments

(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 **27**, are readily prepared by the reaction of carbamic acid salts with β-chloroketones. Reaction with an acid for molecules with at least 1 thione group,[22] or with hydrogen sulfide for molecules with two ketonic groups,[23] leads to the required cyclisation step in high yield to give the 1,3-dithiolium system **28**. (Scheme 1.8)

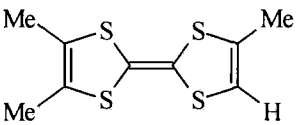


27 **28**

a $R_1 = R_2 = Me$
b $R_1 = R_2 = H$
c $R_1, R_2 = -(CH_2)_3-$

***Scheme 1.8**: Typical Dithiolium Cation Formation by Acid Catalysed Cyclisation*

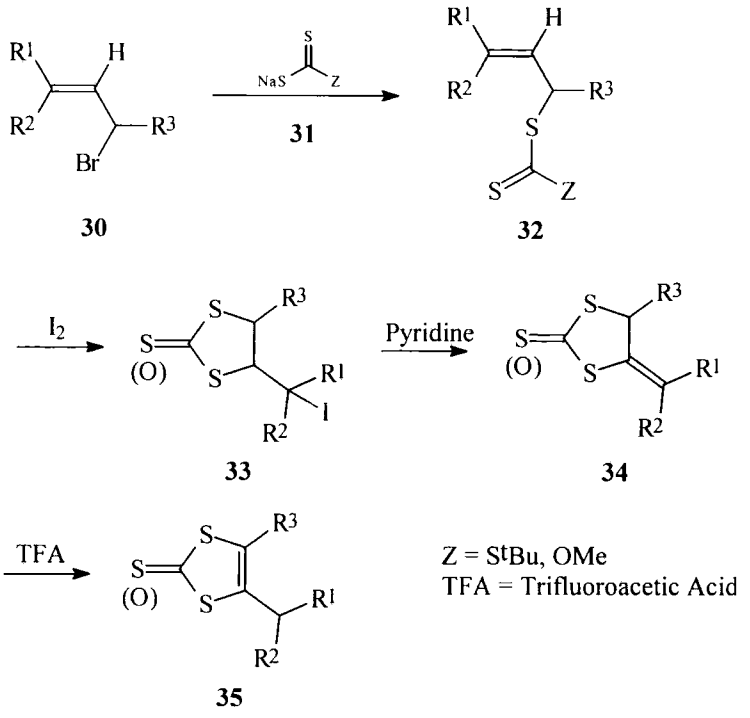
This method of dithiole formation is still widely used for the synthesis of dithiole derivatives witha range of 4- and 5- substituents, including 4,5-dimethyl,[22a] **28a**; 4,5-dihydro,[24] **28b**; and fused ring,[25] **28c** groups. Recently this type of cyclisation has been utilised by Moore and Bryce in the large-scale synthesis of both trimethyltetrathiafulvalene,[26] **29** as well as the parent system, tetrathiafulvalene **23**.[24]



29

***Figure 1.7**: Trimethyltetrathiafulvalene*

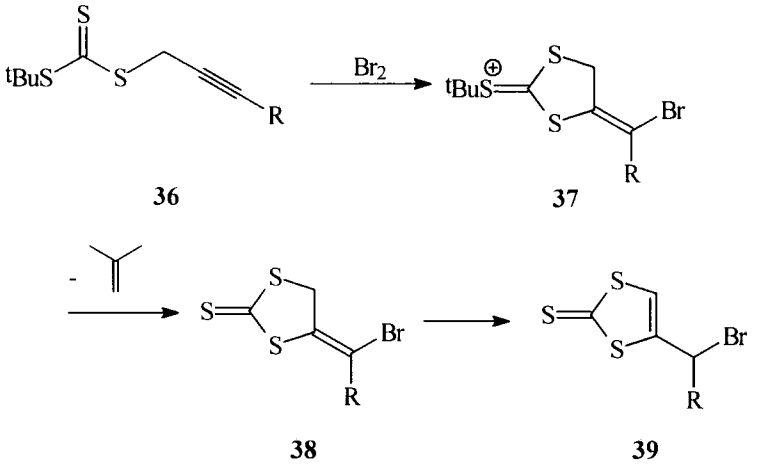
Iodine catalysed cyclisation of trithiocarbonates onto alkynes has also been utilised in the synthesis of dithiole systems. Haley showed that trithiocarbonates, or dithiocarbonates **32** prepared by the action of sodium di- (Z = OMe) or trithiocarbonates (Z = tBuS) **31**, and allyl halides **30** cyclised in the presence of iodine, to form the dithiolanes **33** Sequential treatment of **33** with pyridine and trifluoroacetic acid induced elimination of hydrogen iodide, to produce **34**, followed by isomerisation to afford the desired 1,3-dithiole system **35**.[27] (Scheme 1.9)



***Scheme 1.9**: Iodine Induced Dithiole Formation*

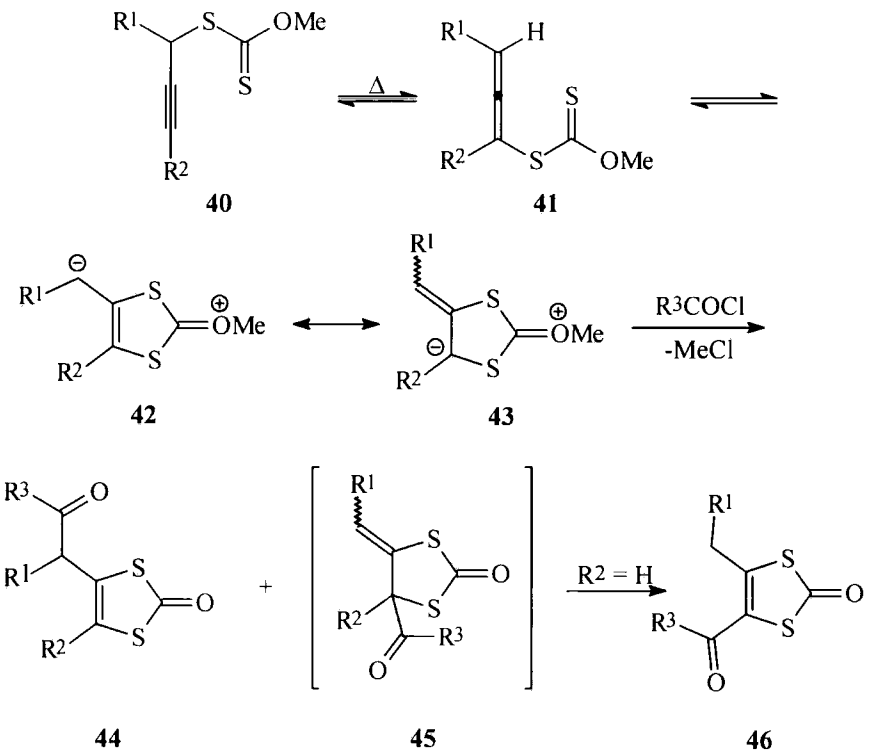
Haley also reported a similar bromine induced cyclisation to yield a 1,3-dithiole system.[28] Reaction of sodium t-butyl-trithiocarbonate with propargyl halides led to the compounds **36**. Reaction of **36** with bromine induced a cyclisation reaction to form a dithiolane structure **37**; elimination of 2-methylpropene, yielding **38** and an isomerisation afforded the required 1,3-dithiole system **39**. (Scheme 1.10)

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



36 **37** **38** **39**

***Scheme 1.10**: Dithiole Systems from Propargyl Halides*

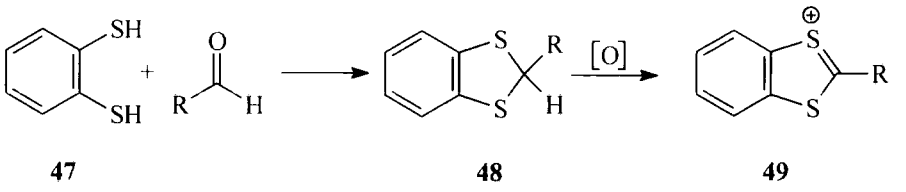


40 **41** **42** **43** **44** **45** **46**

***Scheme 1.11**: Dithiole Systems from Thermal Rearrangements*

(b) Formation of 2 bonds: [4+1] atom fragments

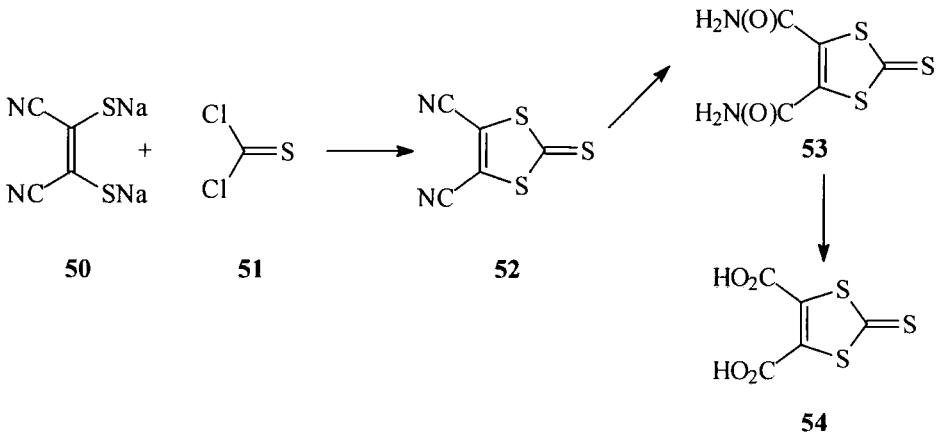
Under this category comes the initial synthesis of a dithiole ring, **48** by Hurtley and Smiles by the reaction of 1,2-dimercaptobenzene **47** with various aldehydes.[17] Oxidation of these systems leads to the formation of the benzo-fused dithiolium salt **49** (Scheme 1.12).



47 **48** **49**

***Scheme 1.12**: The First Dithiole Synthesis Reported by Hurtley and Smiles*

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.[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).

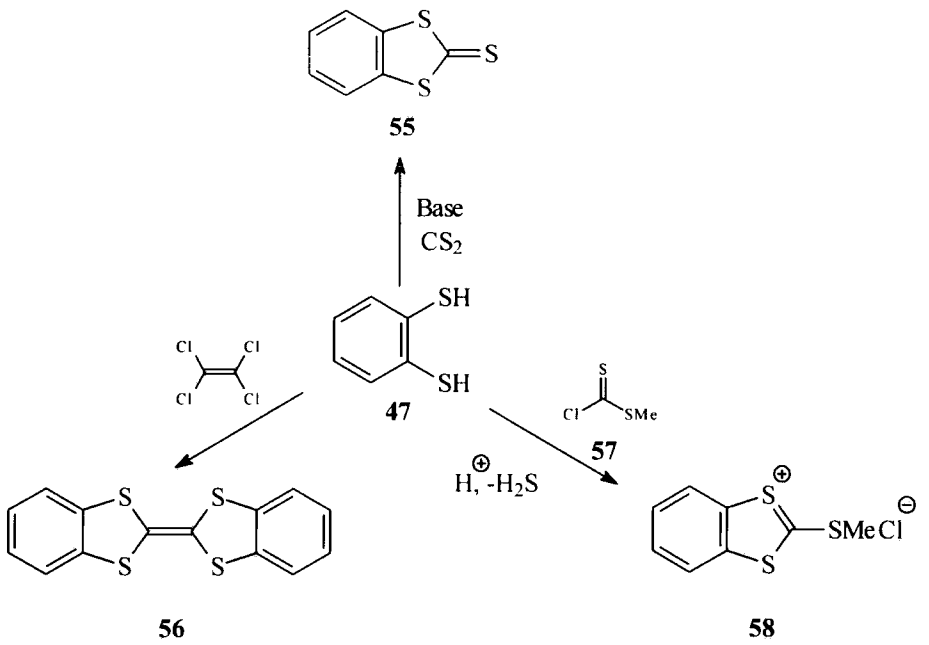


50 **51** **52** **53** **54**

***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

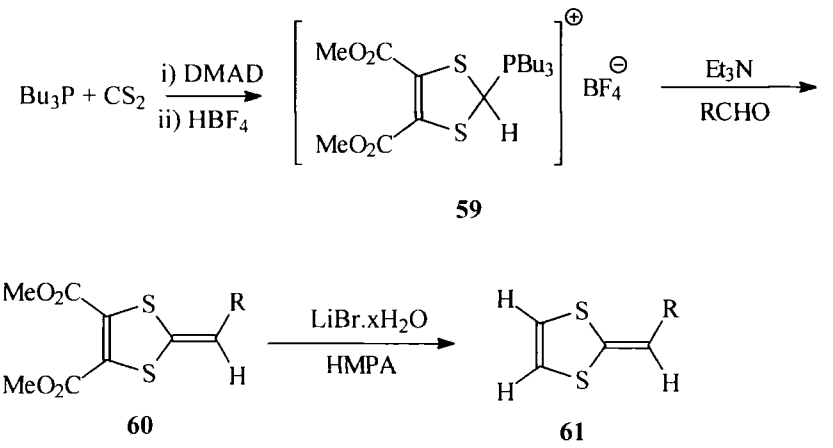
reaction with tetrachloroethene forms the benzofused TTF **56**, albeit in modest yield.[31] Reaction with carbon disulfide under basic conditions affords 1,3-dithiole-2-thione **55**,[32] and reaction with **57** affords the 2-methylthio-1,3-dithiolium salts **58**.[33]



***Scheme 1.14**: Formation of Dithioles from 1,2-Dimercaptobenzene*

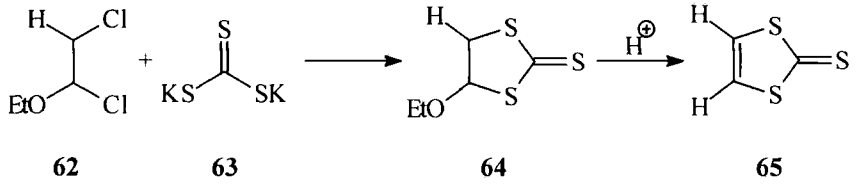
(c) Formation of 2 bonds: [3+2] atom fragments

Under this methodology is, possibly, the simplest route to the dithiole ring system. In 1979 Cava *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).[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.[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.[36]



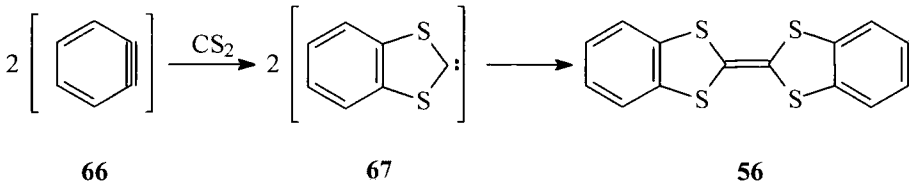
***Scheme 1.15**: Dithiole Synthesis from a Phosphine-Carbon Disulfide Complex*

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.

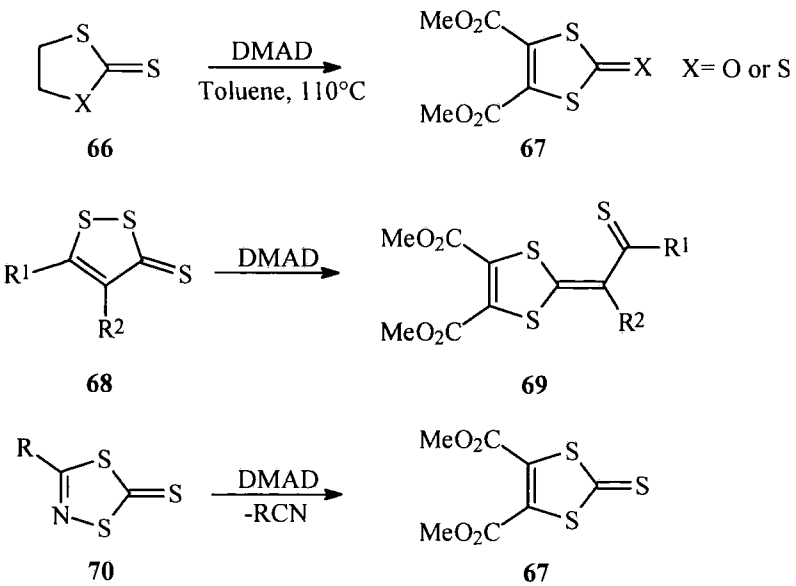


66 **67** **56**

***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 dithole-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.



66 **67**

68 **69**

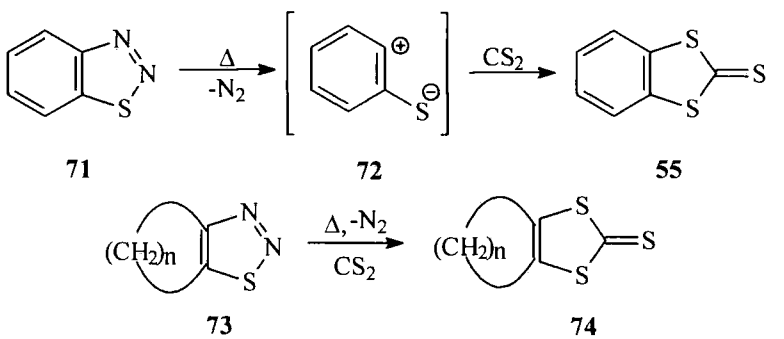
70 **67**

***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.[41] This approach was successfully employed by Bryce and Gorgues in the preparation of the stable thioaldehyde **12**.[9] (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**,[42] and although this reaction was reported as irreproducible by Behringer and Deichmann,[43] the results were confirmed in 1985 by Paton *et al.*[44]

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, **72** which, when intercepted with carbon disulfide formed the benzo-fused 1,3-dithiole-2-thione **55** (Scheme 1.19).[45] 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.[46]

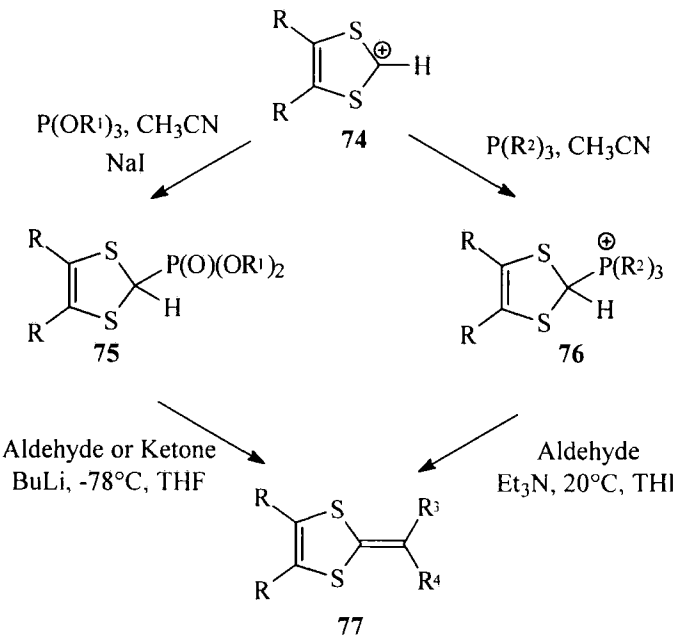


***Scheme 1.19**: Dithiole Synthesis from 1,2,3-Thiadiazoles*

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

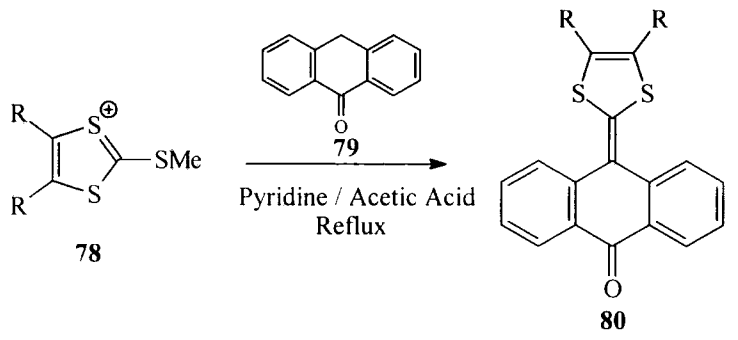
The dithiol-ylidene system **77** is usually formed by either a Wittig[35, 47] or Emmons-Horner reaction[48] (Scheme 1.20). Most of the methods of producing the dithiole ring system yield a product which can be 'slotted' somewhere in the scheme to produce these reagents. Both Wittig and Emmons-Horner reagents are

prepared from 2*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.[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.[22b, 49a, 50]



***Scheme 1.20**: 1,3-Dithiol-2-ylidene Derivatives from Wittig and Emmons-Horner Chemistry*

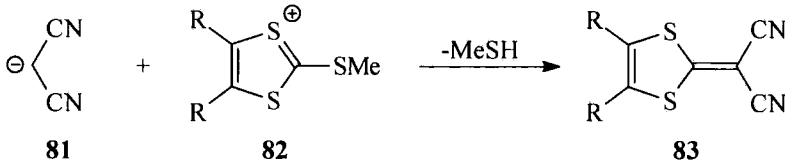
Wittig reagents **76** are produced by the reaction of the dithiolium salt with an alkyl or aryl phosphine,[47] to afford the phosphonium salt in high yield. Emmons-Horner reagents **75** are produced by the reaction of trialkylphosphites with dithiolium salts (if iodide is not the counter ion, then 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[48], rather than aldehydes.[34]



***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,[51] and Bryce and Moore[48] 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).[52]

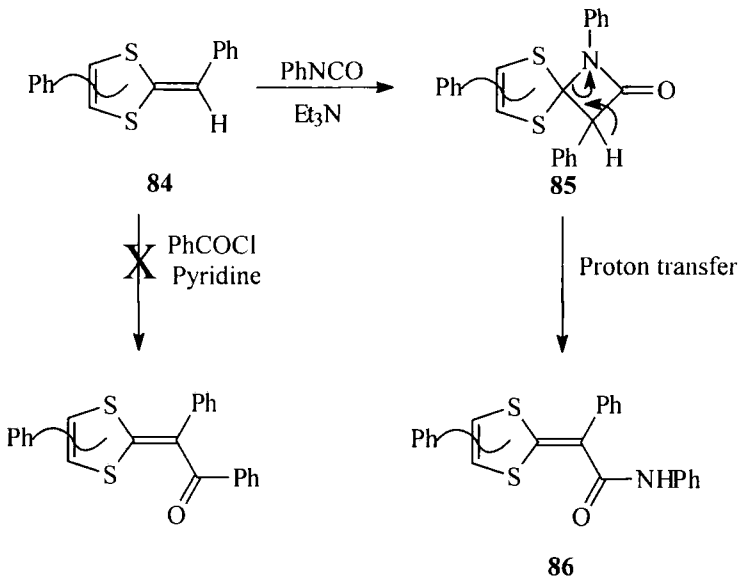


***Scheme 1.22**: 1,3-Dithiol-2-ylidene Species via Knoevenagel Methodology*

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[12] (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 benzoylation 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,[53] a nucleophilic reaction, but rather a cycloaddition involving the ylidene bond and

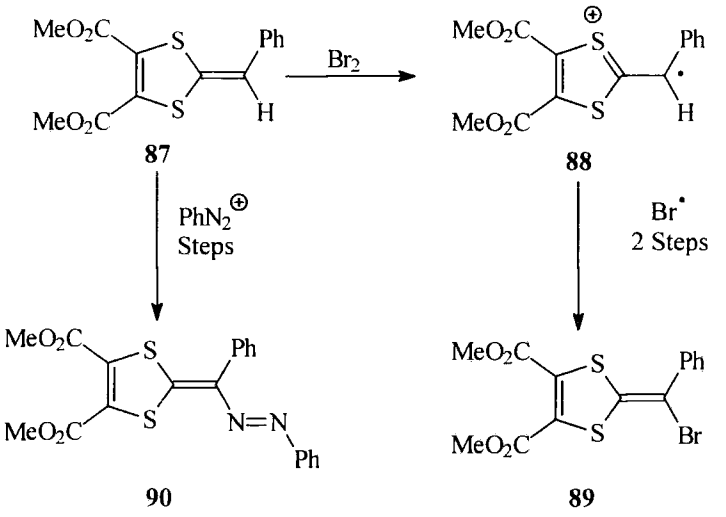
the nitrogen-carbon double bond of the isocyanate to afford **85**, followed by fragmentation of the lactam ring to yield the amide **86**.



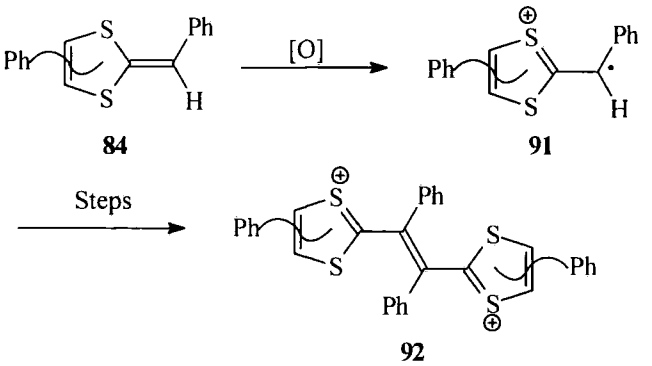
***Scheme 1.23**: Reactions of the 1,3-Dithiol-2-ylidene System*

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.[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).[55]

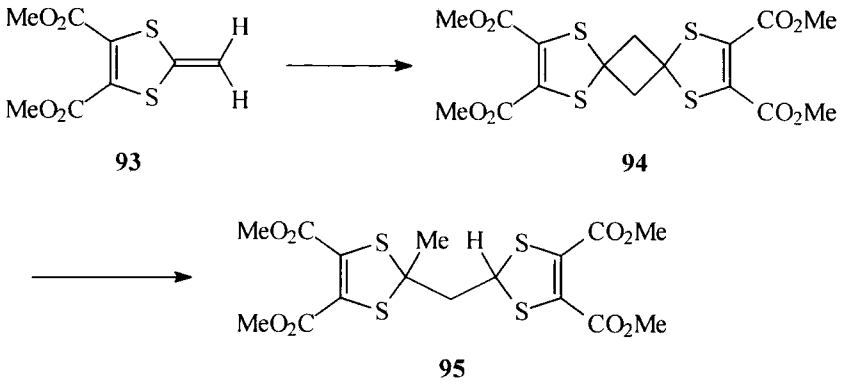


***Scheme 1.24**: Radical Bromination of a 1,3-Dithiol-2-ylidene and Reaction of a 1,3-Dithiol-2-ylidene with a Diazonium Salt*



***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**.

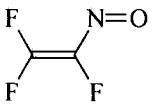


***Scheme 1.26**: An Unexpected Reaction of a 1,3-Dithiol-2-ylidene System*

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.[57] Three further examples of conjugated nitroso species were reported in the late 1970's *viz.* nitroso-carbonyls,[58] nitrosyl cyanide[58] and *C*-nitroso imines.[59] All of these were shown to act as dienophiles; nitroso-alkenes are a further example of conjugated nitroso species.[60]



96

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

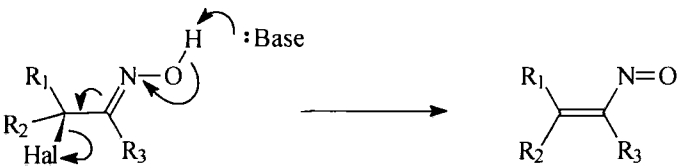
The first example of an isolable nitroso-alkene, **96** was reported by Griffin and Haszeldine in 1960.[61] Many further examples of nitroso-alkenes with various β-substituents including alkyl,[62] aryl,[63] dialkylamino[64] or halogen[65] substituents have been reported, but these usually exist in solution as transient intermediates, their presence determined, either spectroscopically, or more convniently, by the appearance of a characteristic blue colour in solution. The lifetime of nitroso-alkene species varies from short periods at low temperature[65] (*ca.* -50 °C) to

several weeks at room temperature.[62] Further examples of nitroso-alkenes, including all examples of terminal alkenes [*i.e.* containing the unit CH_2=C(R)NO] can only be inferred by the presence of trapped products.[66]

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.

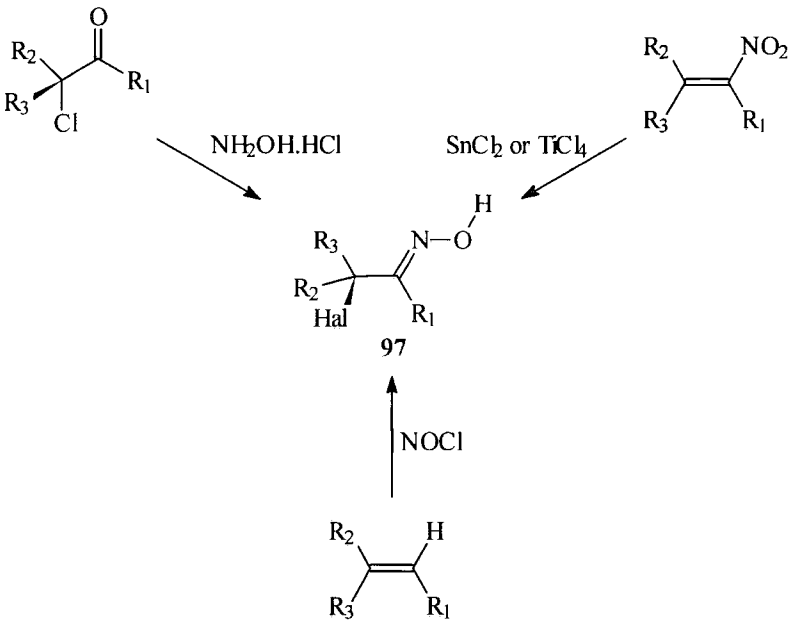
Elimination reactions provide the most important method of accessing nitroso-alkenes **98**, *viz.* the reaction between α-halo-oximes **97** and non-nucleophilic bases (Scheme 1.28).



97 **98**

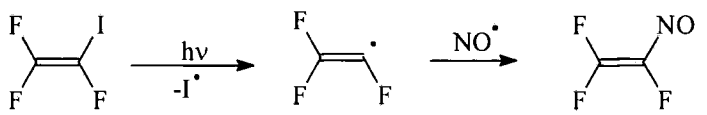
***Scheme 1.28**: Nitroso-alkenes from α-Halo oximes*

The susceptibility of nitroso-alkenes to nucleophilic attack at the β-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,[67] 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.[63, 66, 68] The preparation of α-halo oximes **97** is documented in the literature[69] and three methods are detailed in Scheme 1.29.



***Scheme 1.29**: Routes to α-Halo Oximes*

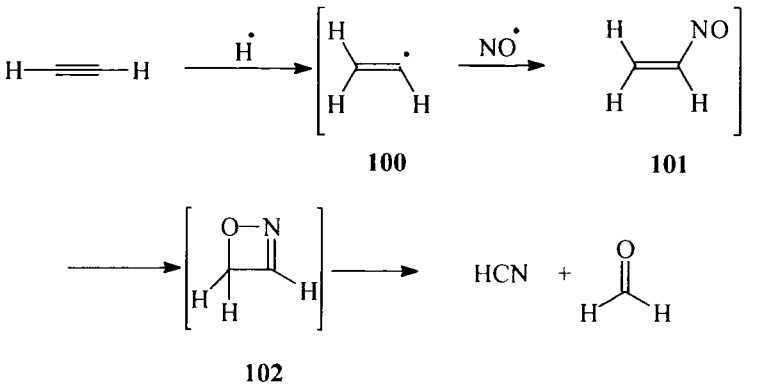
A second method of forming nitroso-alkenes (and the more relevant in terms of the present study) is the addition of nitric oxide to radical species. This was the postulated process in the formation of the nitroso-alkene **96**, by the irradiation of iodo-trifluoroethene **98** in the presence of nitric oxide (Scheme 1.30).[61] Irradiation of **98** formed the trifluoroethene radical **99** which combined with the radical nitric oxide to afford **96**.



98 **99** **96**

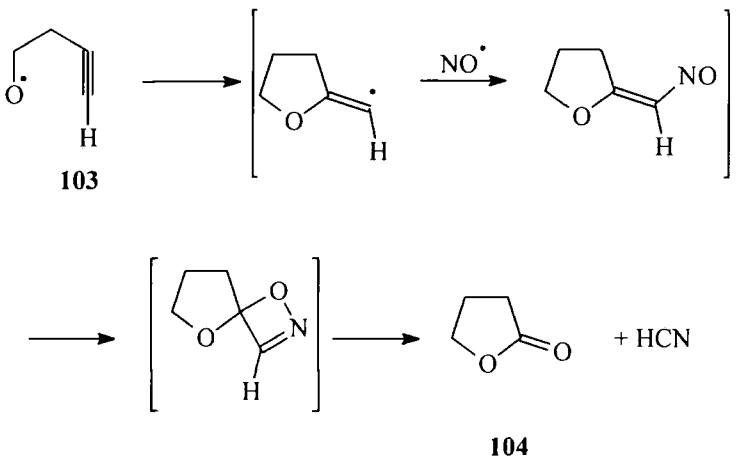
***Scheme 1.30**: Formation of 1,1,2-Trifluoro-2-nitroso Ethene*

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).[70]



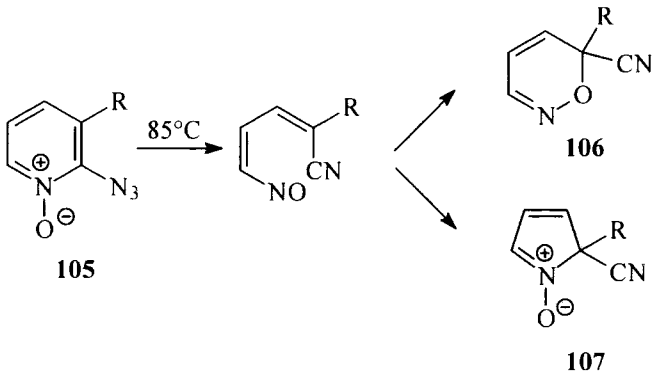
***Scheme 1.31**: Postulated Nitroso-Alkene Intermediate for the Reaction of Ethyne with Atomic Hydrogen and Nitric Oxide*

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 nitroso-alkenes **16** by the reaction of isoamylnitrite 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]

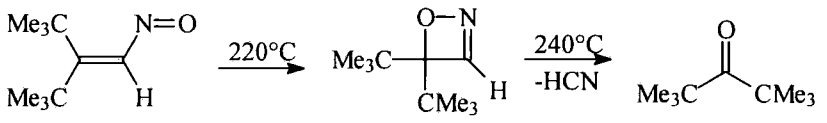


***Scheme 1.33**: Thermolysis of 2-Azidopyridine-1-oxides*

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**.[72]

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.



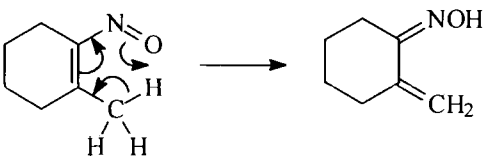
108 **109** **110**

***Scheme 1.34**: Thermally Controlled Decomposition of a Nitroso-Alkene*

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).

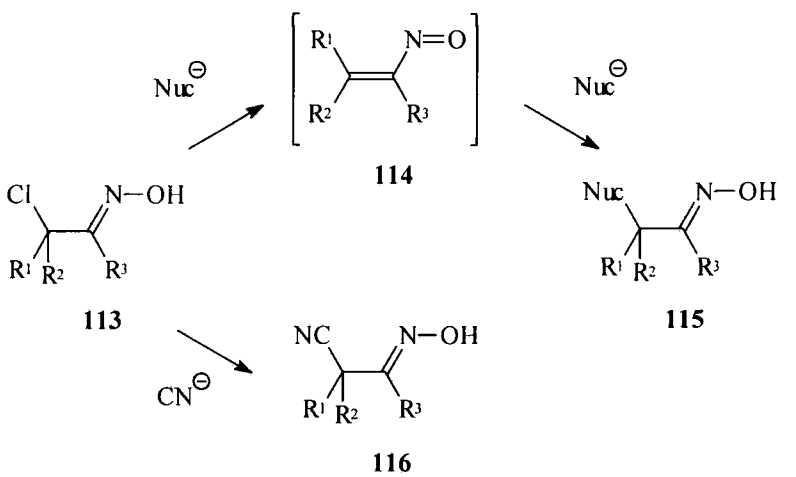
Compounds such as **111**, with a β-methyl group, have shown that nitroso-alkenes are also able to undergo a [1,5]-hydrogen shift reaction to form β-unsaturated oximes, **112** *e.g.* Scheme 1.35.[73]



111 **112**

Scheme 1.35: *1,5 Hydrogen Shift in a β-methyl Substituted Nitroso-Alkene*

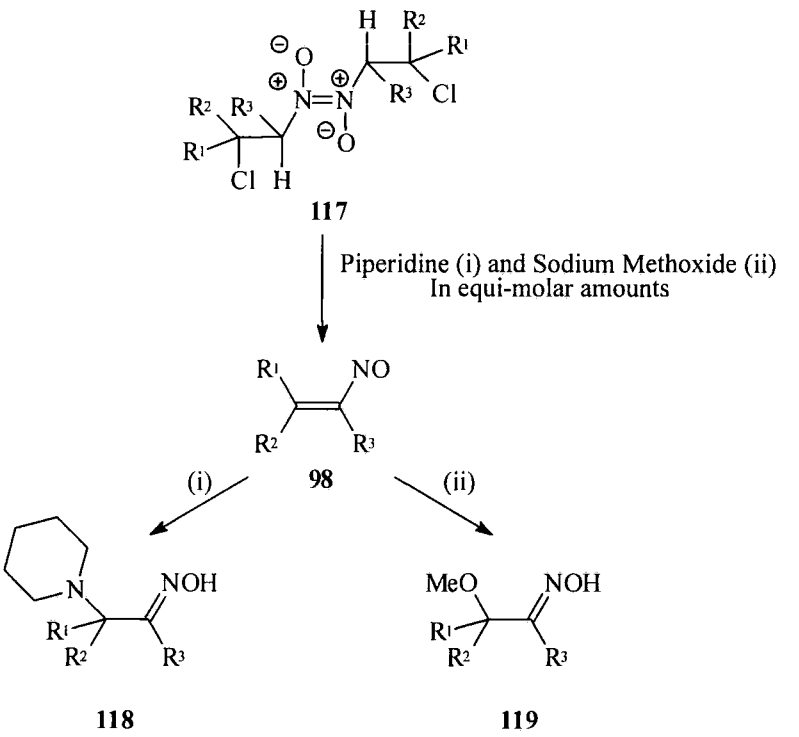
Nitroso-alkenes are highly susceptible to nucleophilic attack at the β-carbon in a Michael-addition fashion (Scheme 1.36). Thus the reaction of β-chloro-oximes **113**, as nitroso-alkene precursors, in the presence of a strong nucleophile leads to an overall substitution reaction *via* **114** whereby 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 α-Chloro-oximes*

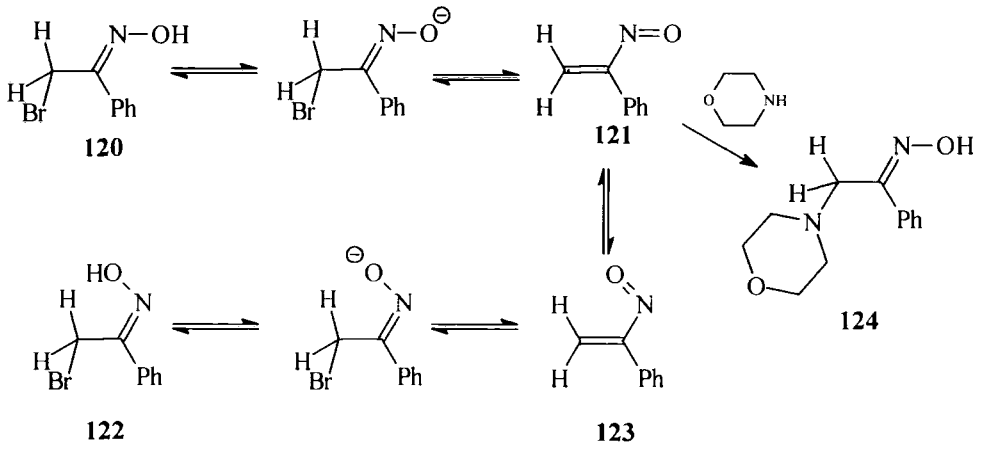
Investigation of reactions of nitroso-alkene dimers **117** in the presence of both sodium methoxide and piperidine has determined that the major product is

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**.



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

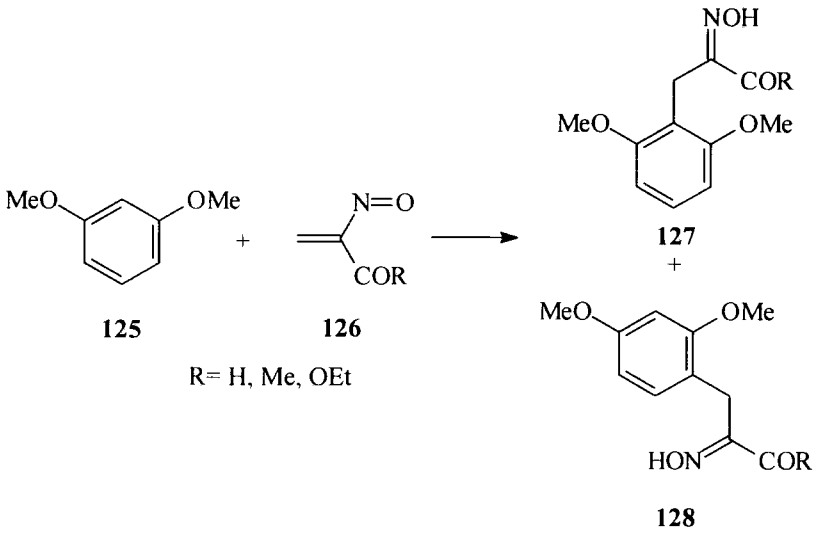
Reaction of both *anti-* **120** and *syn* - **122** α-bromo-acetophenone oximes with morpholine, led to the formation of *anti-* α-morpholino-acetophenone oxime **124**.[74] This provides evidence of nitroso-alkene intermediacy in the reaction, deprotonation of both *syn-* and *anti-* compounds leading 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).



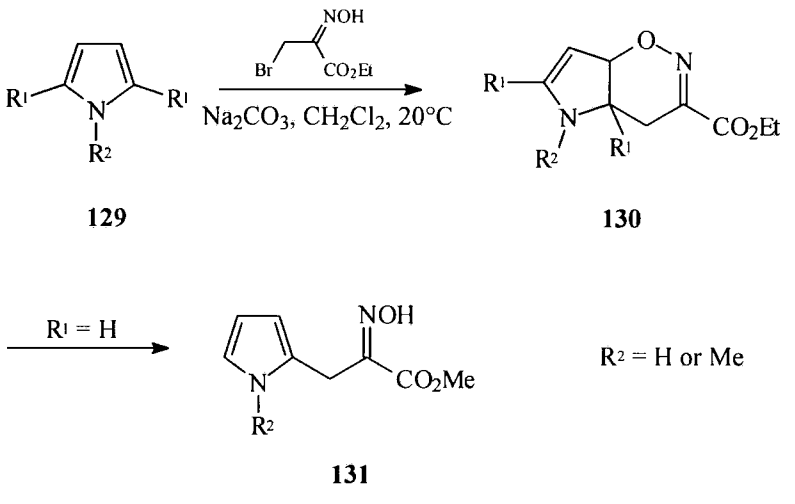
Scheme 1.38: *Preferential Nucleophilic Attack upon the Anti- Configuration of Nitroso-Alkenes*

Nitroso-alkenes react with a variety of nucleophiles *e.g.* primary and secondary amines,[77] alcohols[76] and thiols[77], in either reactions to give only the Michael-type addition products, or in other cases further reactions may occur.[78] The reaction of nitroso-alkenes with carbon nucleophiles has found use in the alkylation of nucleophilic carbon centres under mild conditions.[79] The reaction of an α-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 nuclophile 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.* **125** to afford **127** and **128** and heteroaromatic systems and the most electrophilic of nitroso-alkenes *e.g.* **126**, the reaction with heteroaromatics being the more successful of the two (Scheme 1.39).[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).[81] Reaction of pyrrole **129** with a nitroso-alkene resulted in the [4+2] cycloaddition product **130** which, when R^1 was a proton, underwent a proton shift to afford the oxime **131**.

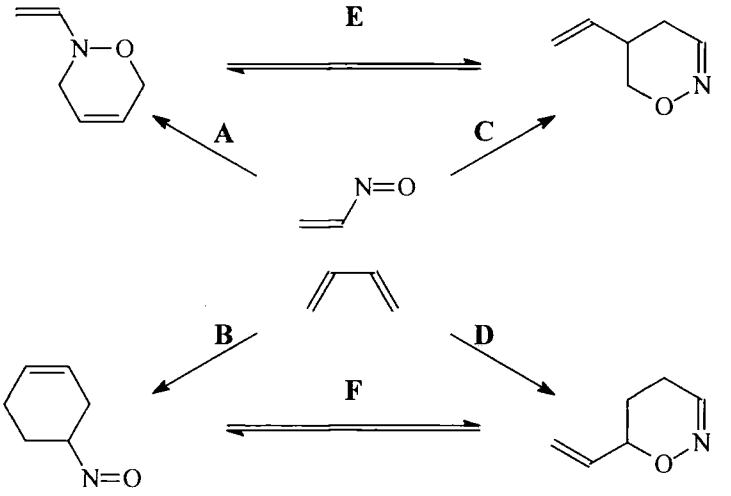


Scheme 1.39: *Alkylation of Aromatic Rings via Nitroso-alkenes*



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.[65, 66, 80] 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.[82]

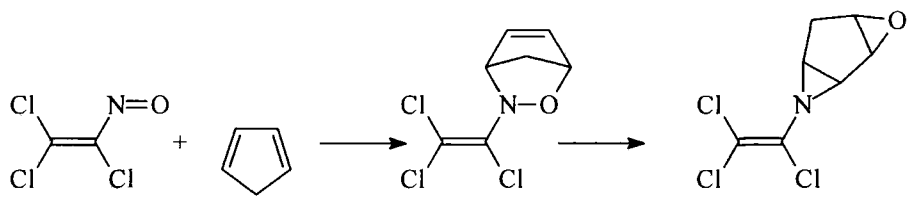


A, **B**, **C**, **D**: Thermally allowed Cycloadditions
E, **F**: Thermally allowed Interconversions

***Scheme 1.41**: Cycloaddition Pathways for Nitroso-alkenes and Dienes*

Reactions where the nitroso group acts as a 2π unit, although common in other nitroso containing functionalities, are more unusual in nitroso-alkenes.[65] They are usually only encountered with halogenated nitroso-alkenes, or in the case of [2+2] cycloadditions, if the second 2π 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).[65]

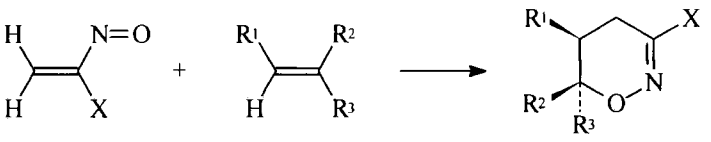


132 **133** **134**

***Scheme 1.42:** [4+2] Cycloaddition of a Nitroso-Alkene with a Cyclic Diene*

A more important cycloaddition reaction of nitroso-alkenes is their participation as a 4π system to react with alkenes to produce 1,2-oxazines **137** (paths C and D), although there is no unequivocal evidence for the existence of path C in any reactions. This reaction was first noticed by Gilchrist and

Faragher[66] in the cycloaddition between α-nitrososty rene 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.[80, 83] 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:[84] there is no evidence for the existence of long-lived dipolar intermediates.[60] 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).[80]



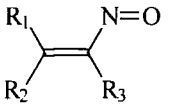
135 **136** **137**

***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,[61] 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.[65, 67] The presence of these groups stablises the nitroso-alkene moiety by hindering the decomposition pathways.

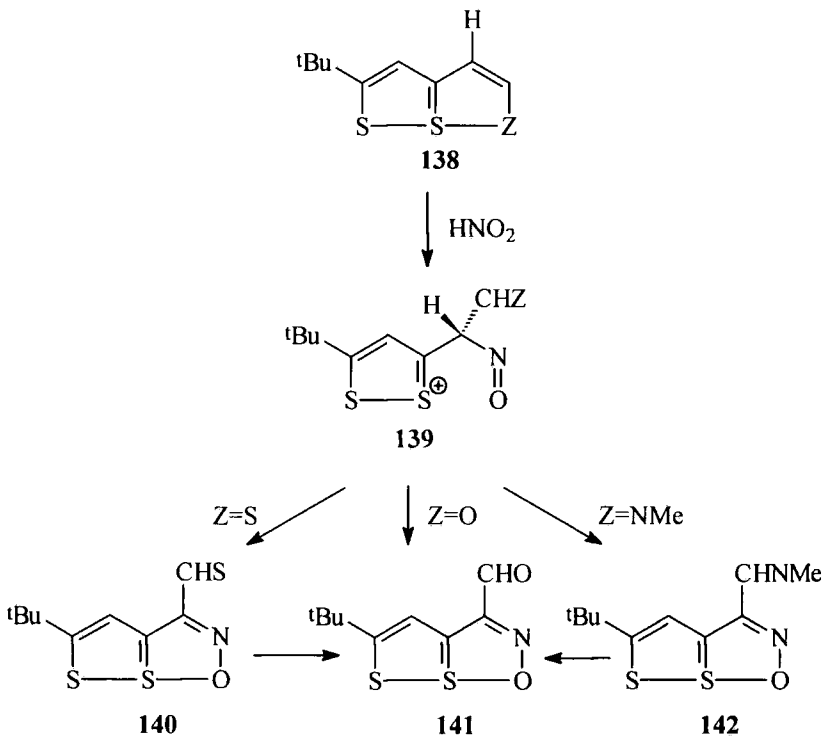


98

R_1	R_2	R_3
H	2,4,6-$C_6H_2Me_3$	H
Cl	Cl	Me

Figure 1.8 *Representative Stable Nitroso-alkenes*

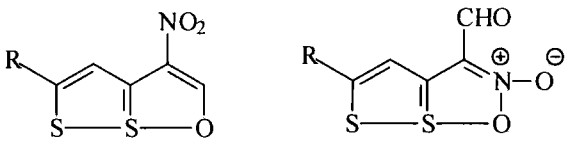
There have been several reports of heteropentalene structures[85, 86] *e.g.* **140-142** which can formally be considered as nitroso-alkenes. Reaction of 6a-thiathiophthens **138** (Z= S) or oxadithiapentalenes **138**, (Z=O) with nitrous acid, affects a nitrosation reaction, followed by a rearrangement 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.[86] 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**.[86] 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.[86] 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**.



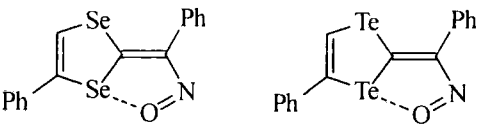
143 **144**

Scheme 1.45: *Possible Structures for a Nitro-substituted Heteropentalene*

In these heteropentalene structures the nitroso-alkene moiety is stabilised by the formation of a hypervalent system **141**. The X-ray crystal structure[87] 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.[88]

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*

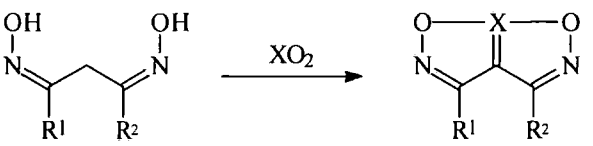
have reported the selenium analogues of their heteropentalene systems,[89] and Cava has reported similar systems where the nitroso-alkene is stabilised by a non-bonded interaction with a chalcogen atom of a 1,3-diselenole, **145**[90, 14] or 1,3-ditellurole ring, **146** [91]. In neither of these papers 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.



145 **146**

Figure 1.9: *Nitroso-alkenes Stabilised by Intramolecular Interactions to Selenium or Tellurium Atoms*

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



147 **148**

a X = S
b X = Se
c X = Te

Scheme 1.46: *Synthesis of a Heteropentalene Containing Two Nitroso Groups*

Chapter 2

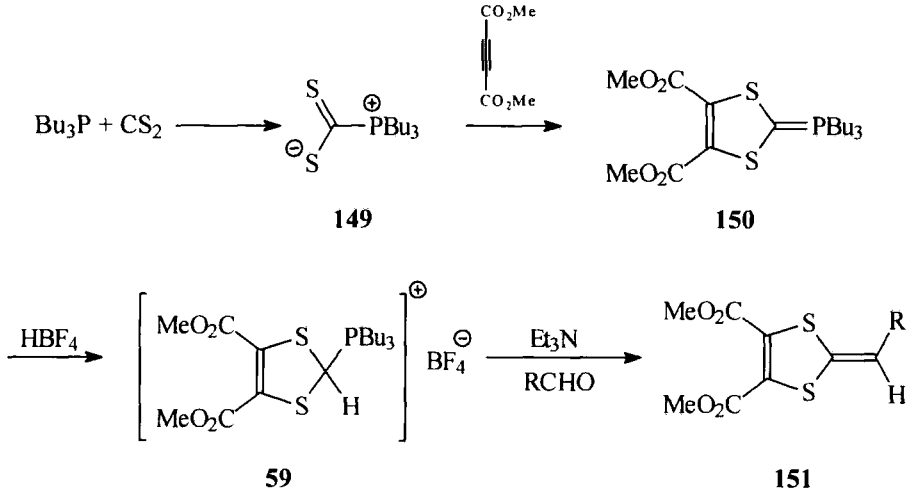
1-(1,3-Dithiol-2-ylidene) methane systems

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 subsitituents with differing electronic characteristics and by determining whether or not the nitroso-alkene was isolable, we could discover the optimum substituents for nitroso-alkene stablity 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



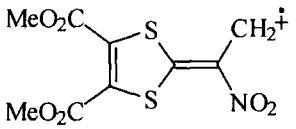
***Scheme 2.1**: Preparation of 1-(4,5-Dicarbomethoxy-1,3-dithiol-2-ylidene) Methane Derivatives*

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.[47]

2.2.2 Hydrocarbon ylidene substituents

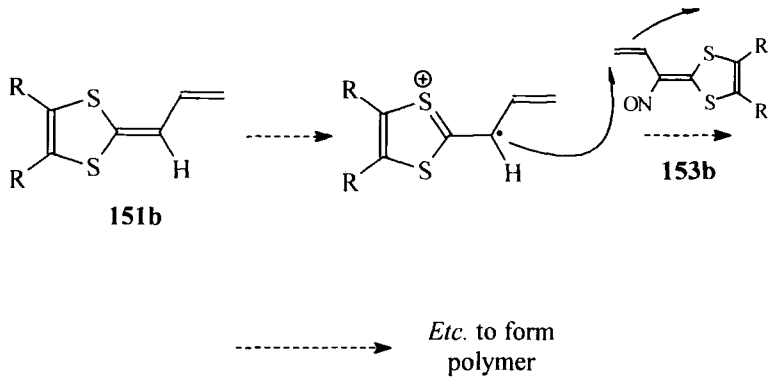
Cava's initial paper on nitroso-alkenes [12] mentioned only one ylidene substituent, namely a phenyl group: we therefore, investigated whether a simple alkyl chain would similarly produce a stable nitroso-alkene. The Wittig reaction of **150** with butanal proceeded cleanly to afford compound **151a** in 80% yield as a viscous orange oil. It was, however, impossible to isolate the corresponding nitroso-alkene **153a**. The nitrosation reaction, as described by Cava[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 (CI) 291, fragment **152** (M^++1)]. It was concluded, therefore that saturated ylidene substituents disfavour the stability of the nitroso-alkenes.



152

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

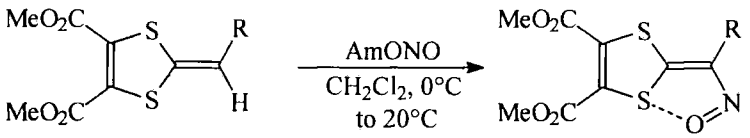
In order to determine the degree of unsaturation necessary in the ylidene substituent, compound **151b** was prepared and isolated as an orange solid in 61% yield. Nitrosation of **151b** yielded a green solid *ca.* 50% yield The product was highly insoluble and could not be characterised. A proton spectrum 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 **153b** 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*



151 **153**

R	Non-nitrosated			Nitrosated		
	Compound	Nature	Yield / %	Compound	Nature	Yield / %
C_3H_7	**151a**	Orange oil	80	**153a**	Unstable	n.a.
$CH=CH_2$	**151b**	Orange solid	61	**153b**	Green Solid	*ca.* 50
$Ph(OMe)_2$	**151c**	Impure	n.a.	**153c**	Unstable	n.a.
$Ph\text{-}NO_2$	**151d**	Yellow Crystals	82	**153d**	Green oil	n.a.
$Ph\text{-}(NO_2)_2$	**151e**	Orange crystals	80	**153e**	Green crystals	48
$Ph\text{-}CF_3$	**151f**	Yellow Crystals	64	**153f**	Green oil	n.a.
$Ph(Cl)_2$	**151g**	Yellow oil	90	**153g**	Green Crystals	27

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 ($J_{H\text{-}F}$ = 4Hz) (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.

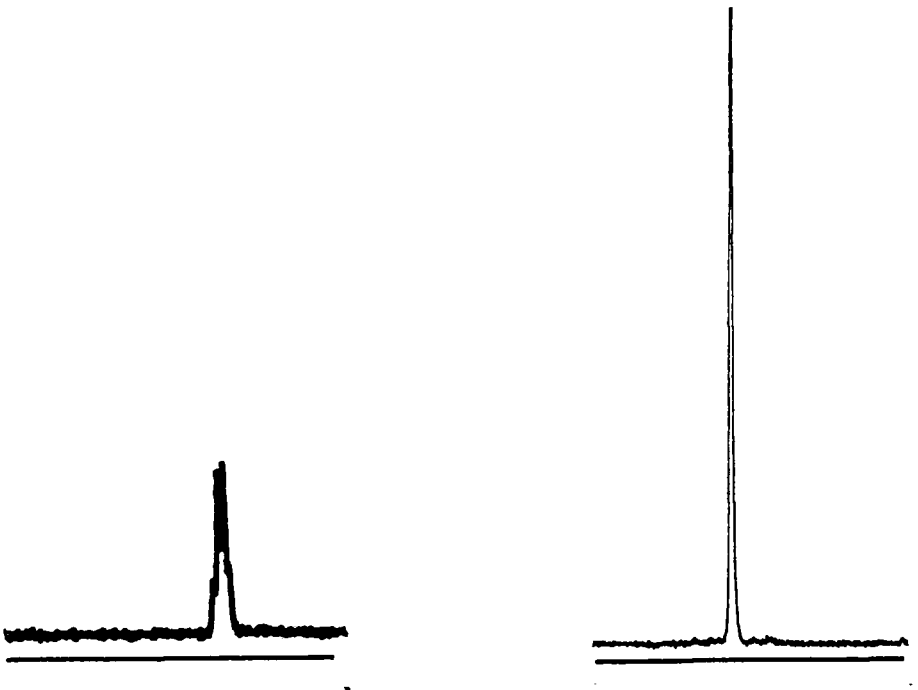


Figure 2.2**: Comparison of the Vinyl Peaks in the ^1H NMR spectra of Compounds **151f** and **151g

Attempted nitrosation of compound **14**[34] 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.

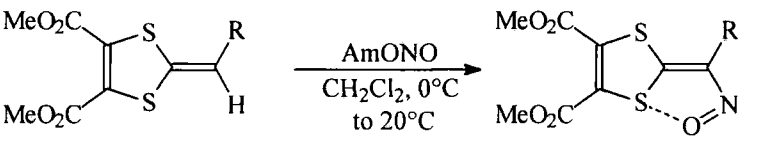
This failure of nitrosonium tetrafluoroborate to effect a clean nitrosation is possibly due to there being too high a concentration of nitrosonium ions. This

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.

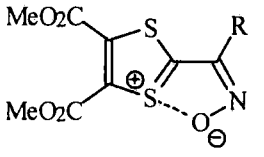
***Table 2.2**: Summary of compounds for section 2.2.4*



151 **153**

R	Non-nitrosated			Nitrosated		
	Compound	Nature	Yield / %	Compound	Nature	Yield / %
2-Thienyl	**151h**	Brown Solid	n.a.	**153h**	Unstable	n.a.
5-Nitro-2-thienyl	**151j**	Orange Crystals	87	**153j**	Unstable	n.a.
5-Nitro-2-furyl	**151k**	Dark red crystals	90	**153k**	Unstable	n.a.
2-Pyridyl	**151l**	Orange Crystals	89	**153l**	Green Crystals	50

The X-ray structure was solved[93,94] 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).[10]



153'

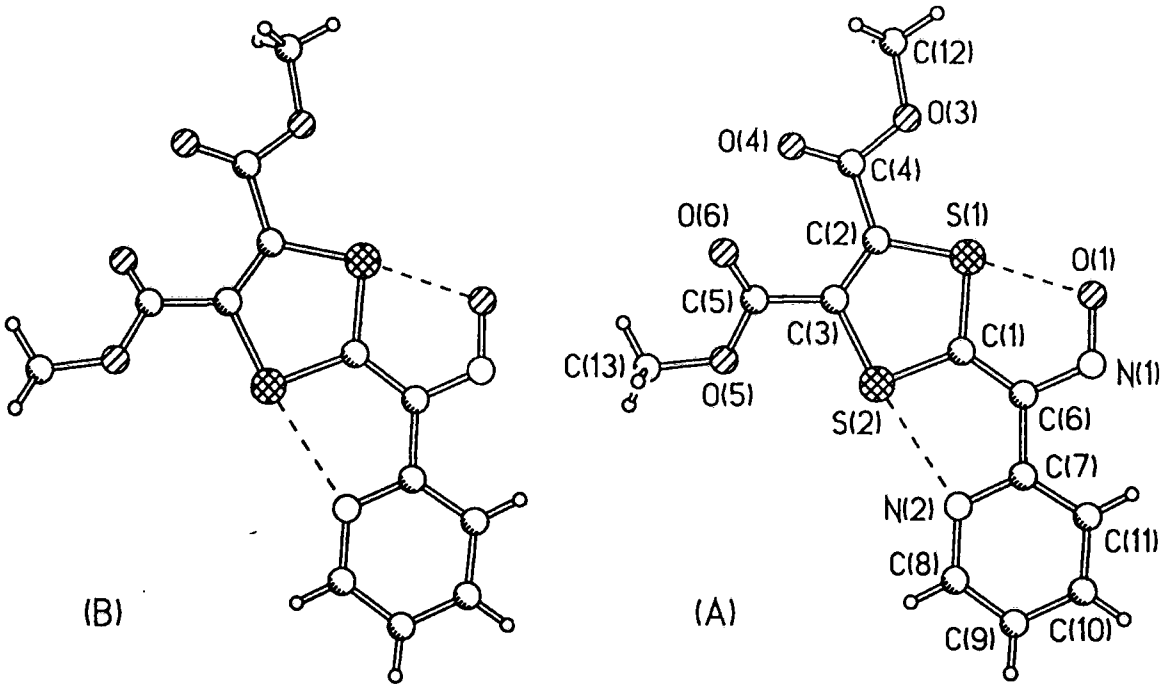
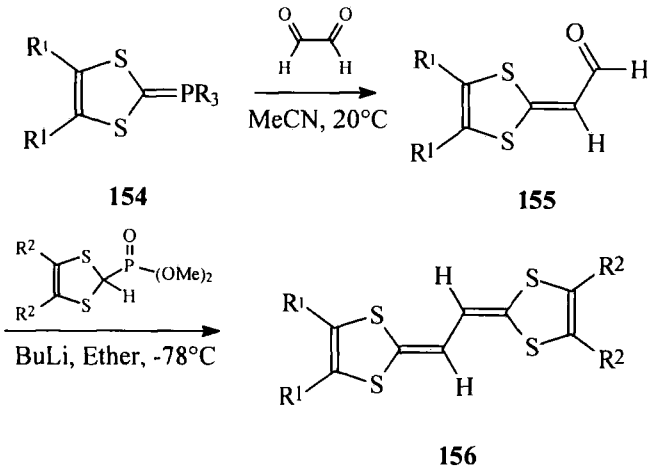


Figure 2.3**: X-Ray Molecular Structure of Nitroso-alkene **153'

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).[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.

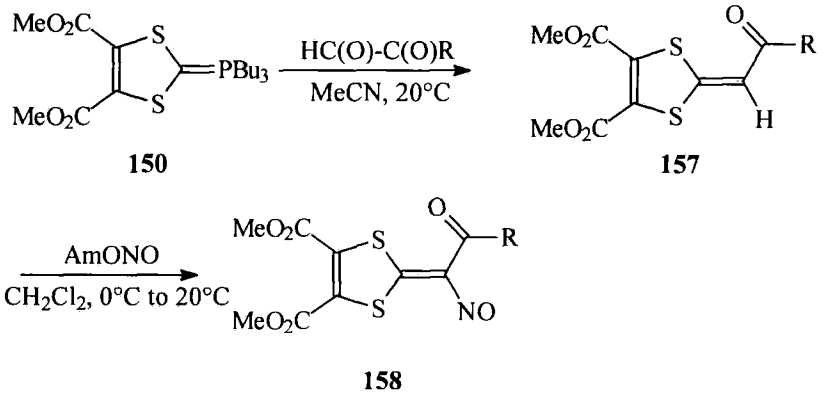


154 **155** **156**

***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.[47b] Both the reactions led only to the mono-reacted product, and with methylglyoxal it is notable that reaction occured 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 **157a** and **157b** proceeded to give the expected green coloured solution from which nitroso-alkenes **158a** and **158b** were isolated as green solids in 45% and 70% yield respectively. At this point during our study, Cava reported the preparation of compound **158b** in good yield, although the melting point he reported is markedly different from that we obtained (Mp 127-128°C, lit. 116°C). All other data indicate the two compounds are identical.[14]



150 **157**

158

***Scheme 2.4**: Preparation of Dithiole Systems with Ylidene Carbonyl Groups*

***Table 2.3**: Summary of Compounds for Section 2.2.5*

R	Non-nitrosated			Nitrosated		
	Compound	Nature	Yield / %	Compound	Nature	Yield / %
Me	**157a**	Yellow solid	70	**158a**	Green Crystals	45
H	**157b**[47b]	Yellow solid	89	**158b**[14]	Green Crystals	70

Recrystallisation of compound **158a** from dichloromethane/hexane 1:10 $^{v}/_{v}$ 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, **153l**. 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).[86] As found with the pyridyl derivative **153l** the presence of the ester groups prevented efficient stacking of the molecules.

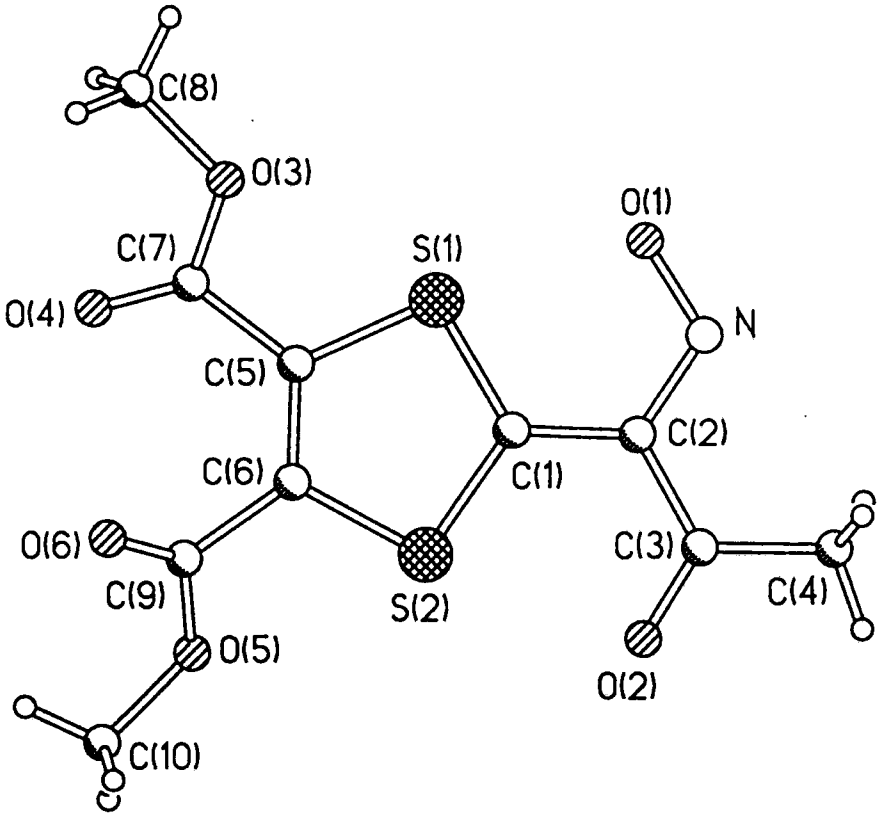
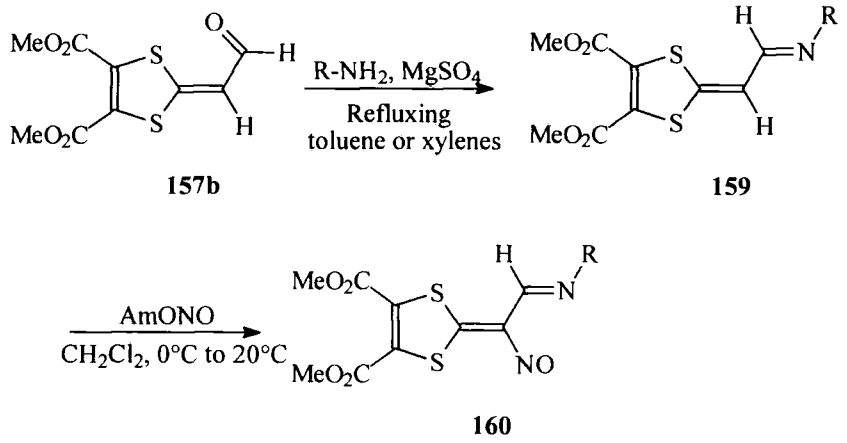


Figure 2.4**: X-ray Crystal Structure of Nitroso-alkene **158a

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).[95]

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.



157b **159** **160**

***Scheme 2.5**: Generation of Dithiol-Ylidene Systems with Conjugated Imino Substituents*

***Table 2.4**: Summary of Imine Derivatives*

R	Non-nitrosated			Nitrosated		
	Compound	Nature	Yield / %	Compound	Nature	Yield / %
4-Tolyl	**159a**	Orange solid	40	**160a**	Buff powder	23
2-Thiazolyl	**159b**	Orange solid	59	**160b**	Dark red oil	n.a.

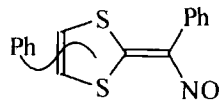
Nitrosation of compound **159a**, under standard conditions afforded the required nitroso substituted imine in 23% yield as a buff coloured powder, although in dichloromethane or chloroform solution this acquired the expected green colouration. Attempted nitrosation of imine **159b**, led to production 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 stablising the nitroso-alkenes. The

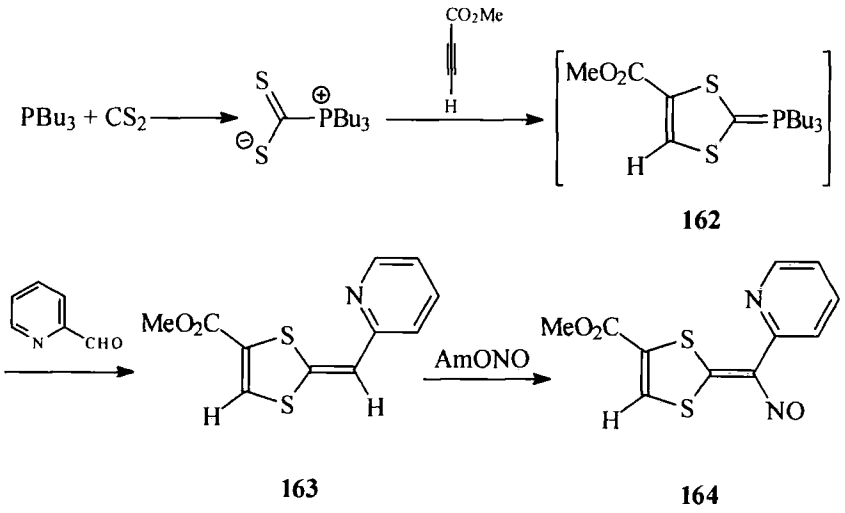
only other 4- or 5- dithiole substituent previously prepared was a 4-phenyl devivative **161** reported by Cava.[12]



161

***Figure 2.6**: 4-Phenyl Dithiole Derivative Described by Cava*

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



162

163 **164**

***Scheme 2.6**: Preparation of 1-(4-Carbomethoxy)-1,3-ditihol-2-ylidene)-1-(2-pyridyl) nitroso methane*

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).

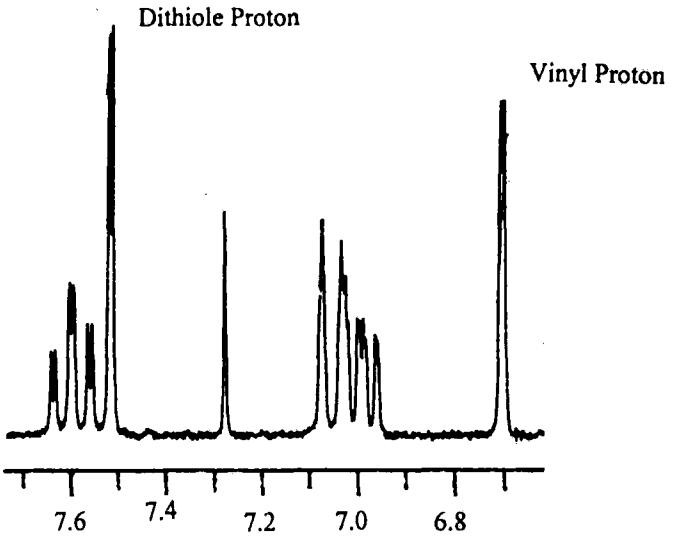
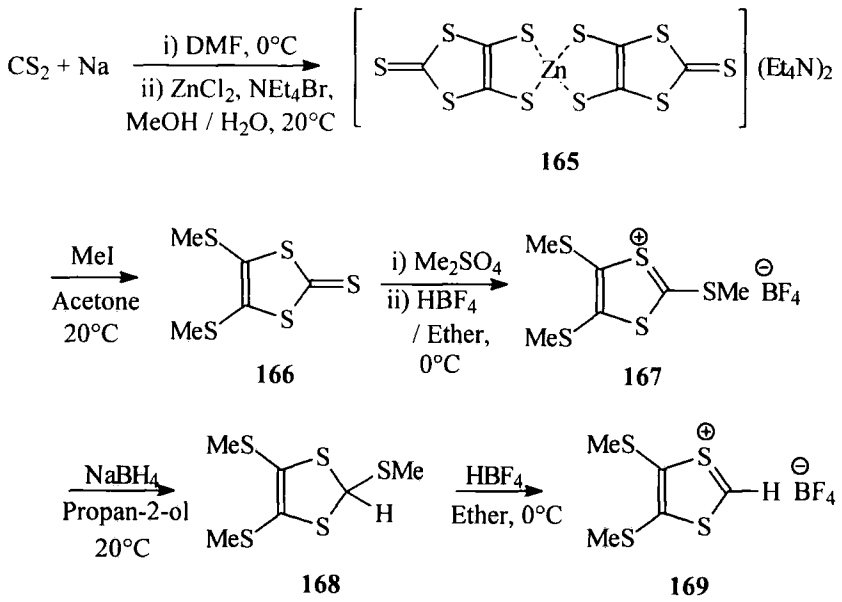


***Figure 2.7**: Section of the Proton NMR Spectrum of **163** Showing the Two Peaks Due to the Mixture of s-cis and s-trans isomers*

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 versitile 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**.

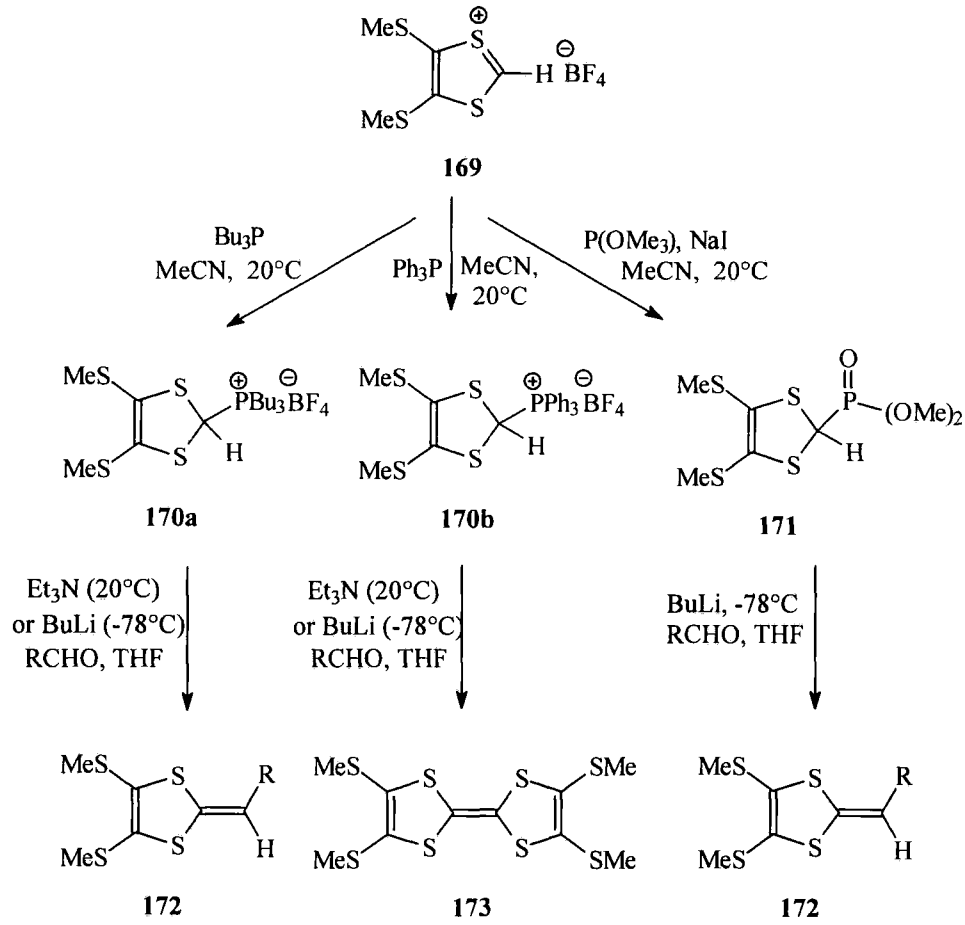


***Scheme 2.7**: Preparation of 4,5-Dimethylthio-1,3-ditholium Tetrafluoroborate*

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[101] **171**, or b) the preparation of a Wittig salt **170a** or **170b**[101] (scheme 2.8).

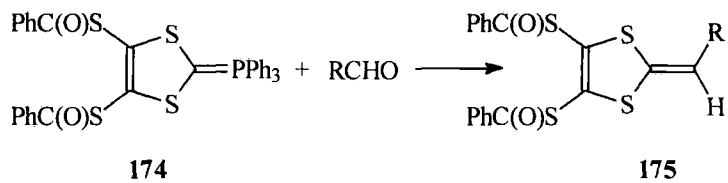
The Wadsworth-Emmons reagents are easily prepared following the procedure outlined by Moore and Bryce.[101] Thus, reaction of **169** with trimethyl phosphite in the presence of sodium iodide, led to the Wadsworth-Emmons reagents in high yields as dark red, unstable oils, reaction of **171** with a base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

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



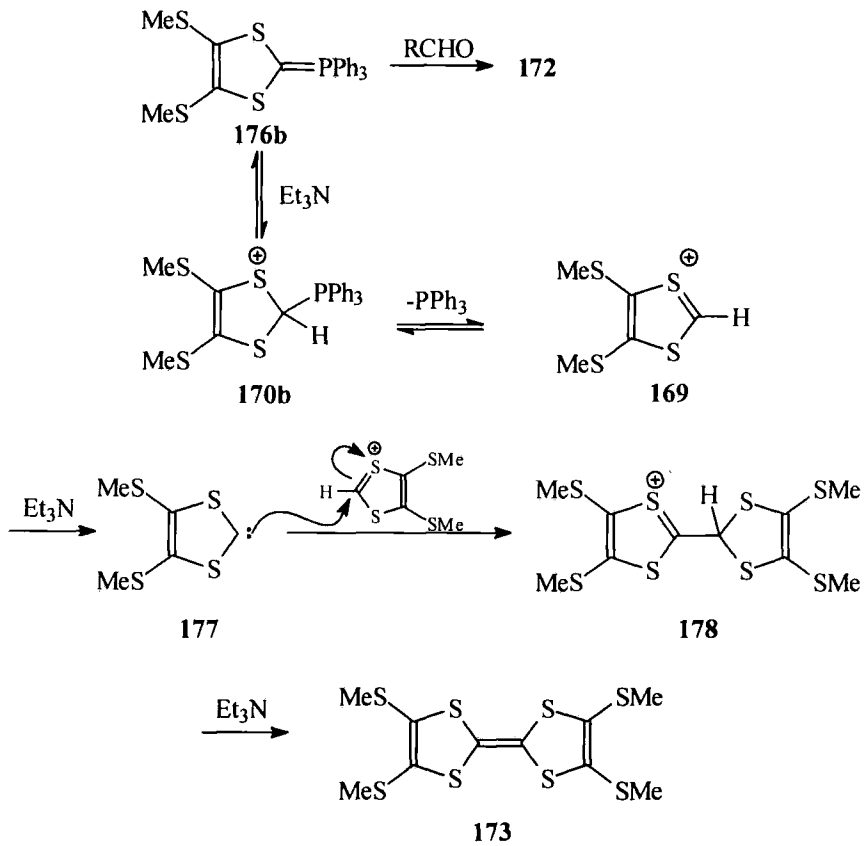
***Scheme 2.8**: Routes to 4,5-Di(methylthio)-1,3-dithiol-2-ylidene Systems*

However, reaction with the triphenylphosphine Wittig reagent **170b** led to the formation of the tetra(methylthio)tetrathiafulvalene **173**.[103] This is in contrast to the results of the reaction with glyoxal as reported by Moore and Bryce whereby the 1,3-dithiol-2-ylidene is formed in good yield[101] 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).[47a]



***Scheme 2.9**: Use of a Triphenyl Wittig Reagent in Forming 1,3-Dithiol-2-ylidene Systems*

The dimerisation reaction of **169** to **173** is well known in the literature, and extensively utilised in the preparation of tetrathiafulvalene derivatives.[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**.

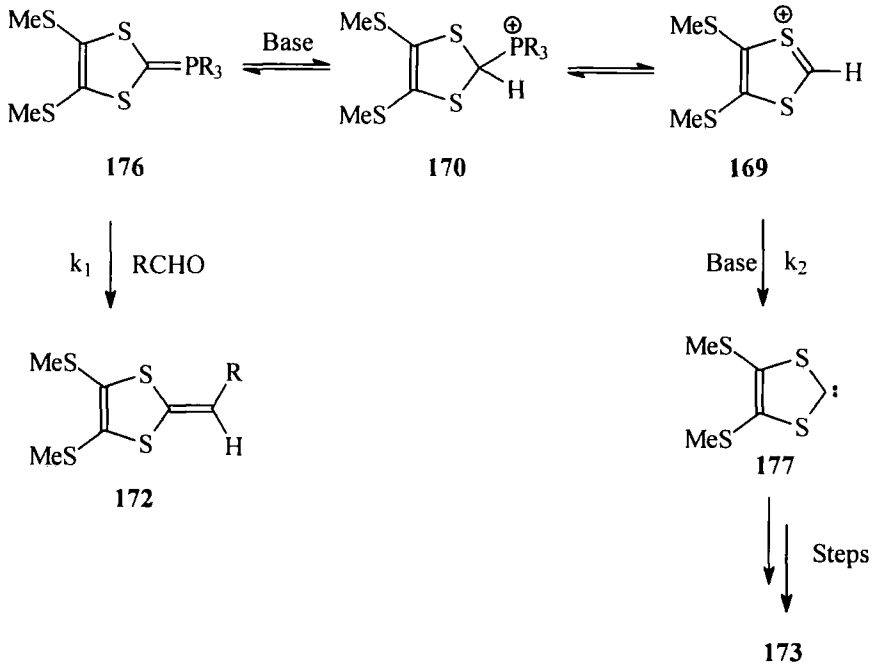


***Scheme 2.10**: Formation of Tetra(methylthio)tetrathiafulvalene*

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.



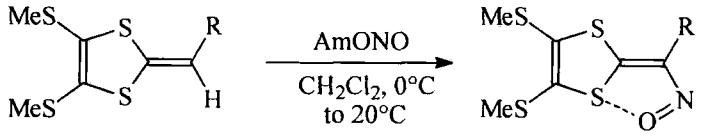
Scheme 2.11**: Possible Reaction Pathways for the Phosphonium Salts **170a** & **170b

(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*



172 **179**

R	Non-nitrosated			Nitrosated		
	Compound	Nature	Yield / %	Compound	Nature	Yield / %
Phenyl	**172a**	Yellow Oil	55	**179a**	Brown Solid	82
Pyridyl	**172b**	Yellow Oil	60	**179a**	Brown Solid	35
2,4-$(NO_2)_2$ Phenyl	**172c**	Black Solid	82	**179a**	Red brown Oil	n.a.

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 absorbtions 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 **153l** and methylthio **179a** nitroso species show the characteristic weak nitroso-alkene absorption[60] at about 650 nm.

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

Compound	Colour	Absorbance 1 (MeCN)		Absorbance 2 (MeCN)	
		λ / nm	ε / l mol^{-1} cm^{-1}	λ / nm	ε / l mol^{-1} cm^{-1}
151l	Green	302	1.60 x 10^4	443	1.44 x 10^4
164	Green	304	1.53 x 10^4	441	1.72 x 10^4
179b	Brown	313	4.45 x 10^3	466	4.76 x 10^3

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 figuere 2.13.[93] As was found for **151l** 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.

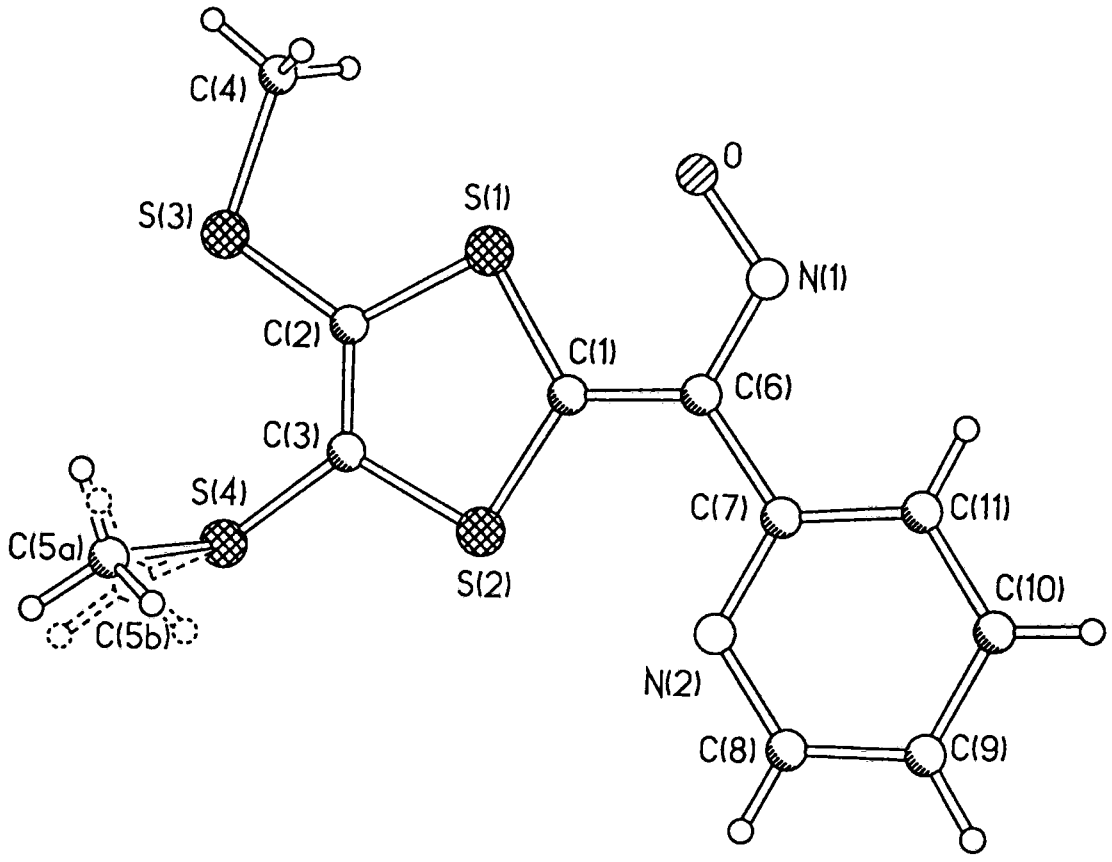


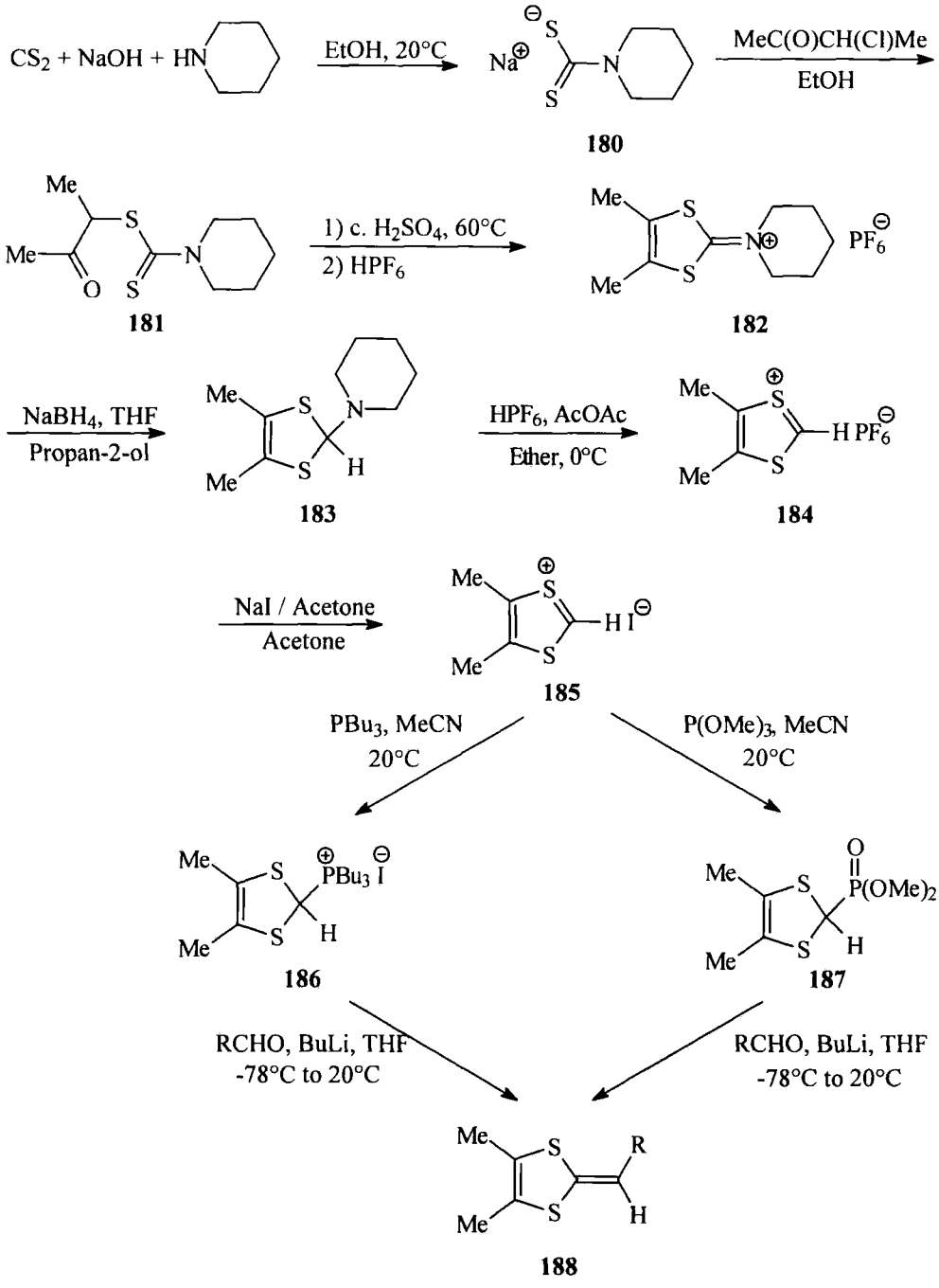
Figure 2.8**: X-ray Molecular Structure of Nitroso-alkene **179b

2.3.4 Preparation of 4,5-dimethyl derivatives

Having determined that the nitroso-alkenes could be stabilised by a intra-molecular interaction with a dithiole ring substituted with electron withrawing 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

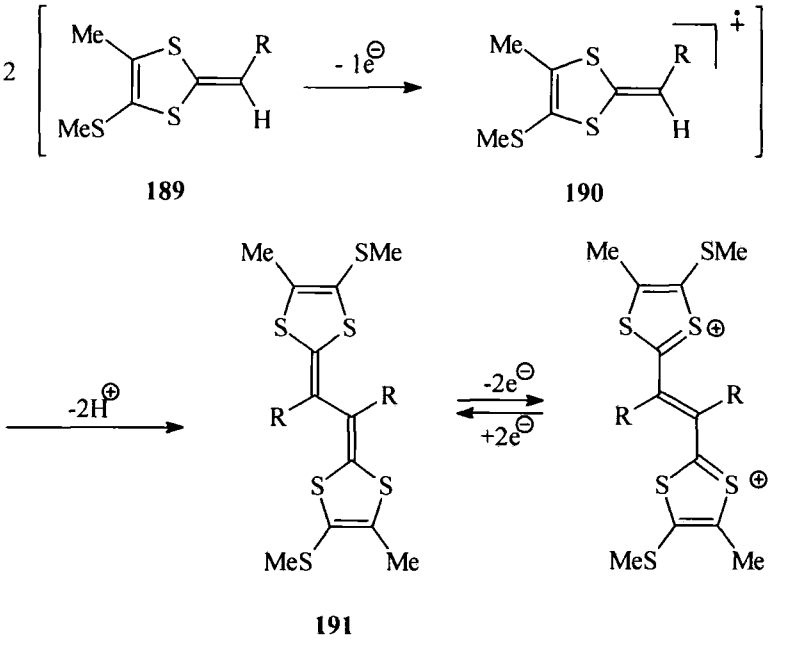
which an excess of sodium iodide in acetone was added to precipitate **185** as a bright yellow solid. [26]



***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 substiuent

was prepared in 50% yield in both the Wadsworth-Emmons and Wittig proceedures. 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]



***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.

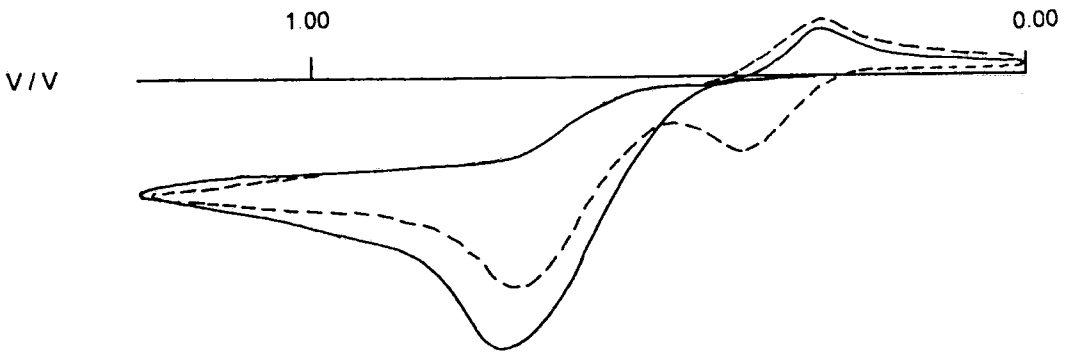
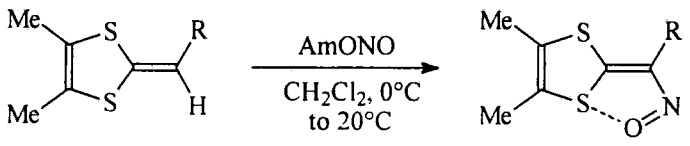


***Figure 2.9**: Cyclic Voltamogram for compound **188a** in Acetonitrile at 20°C with Tetrabutylammonium Hexafluorophosphate as Electrolyte.*

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



188 **192**

R	Non-nitrosated			Nitrosated		
	Compound	Nature	Yield / %	Compound	Nature	Yield / %
Phenyl	**188a**	Off-white solid	50	**192a**	Unstable	n.a.
2,4-$(NO_2)_2$ phenyl	**188b**	Dark purple solid	87	**192b**	Green Crystals	85

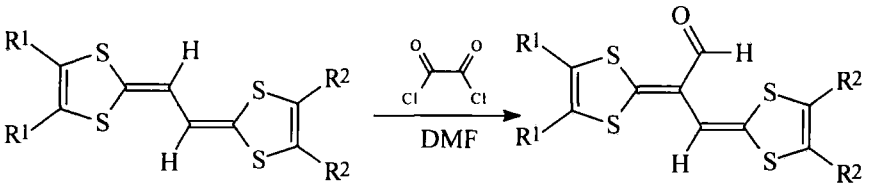
To investigate further whether the ylidene substituent, or the 4- and 5-dithiole substituents played the dominant role in stabilising the nitroso-alkene species, compound **188b** was prepared in 87% yield as a purple-black solid. The darker colour possibly being due to intramolecular charge transfer.[105] 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.



156 **193**

***Scheme 2.14**: Vilsmeier Reaction of 1,2-bis-(1,3-dithiol-2-ylidene) Ethane Systems*

One reaction of these systems is a Vilsmeier formylation with a dimethyl formamide / oxalyl chloride complex to form **193** (scheme 2.14). Only monoformylation occured according to Yoshida,[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.[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:[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 occured, 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.

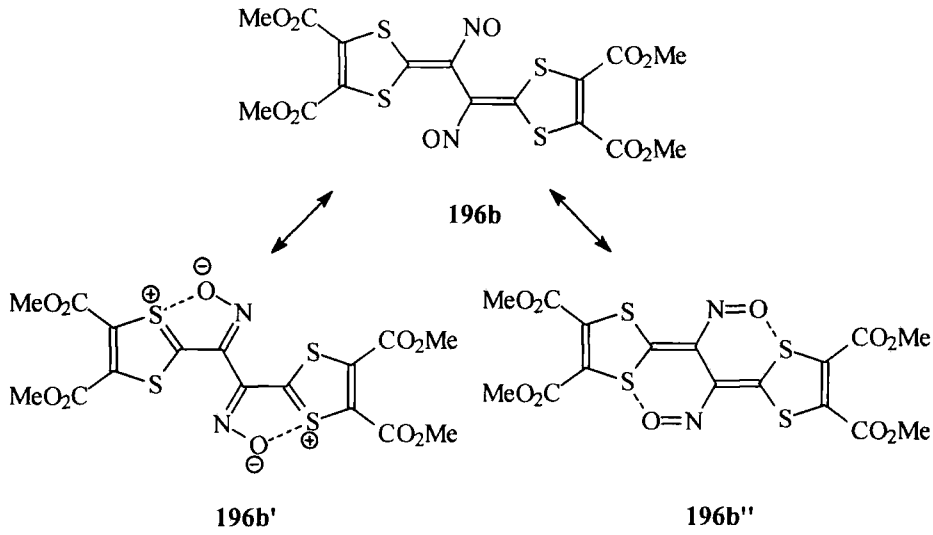
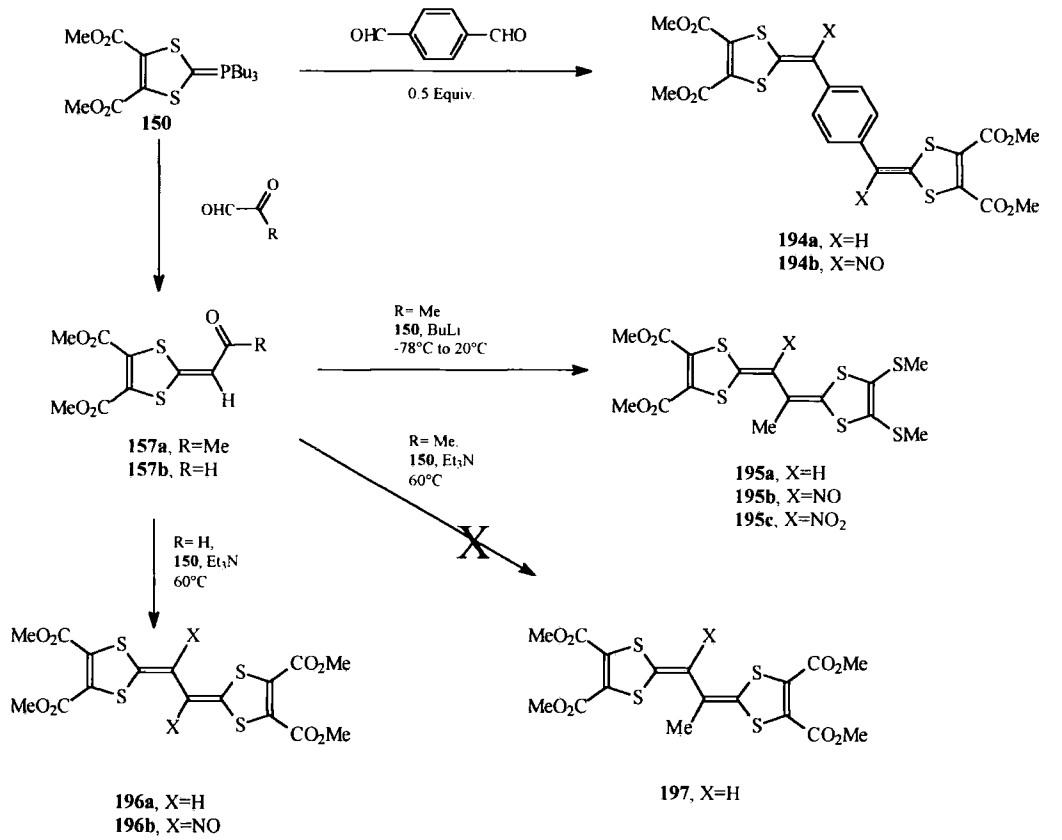


Figure 2.10**: Possible Explanations for the Unexpected Stability of **196b

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 possibilty 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

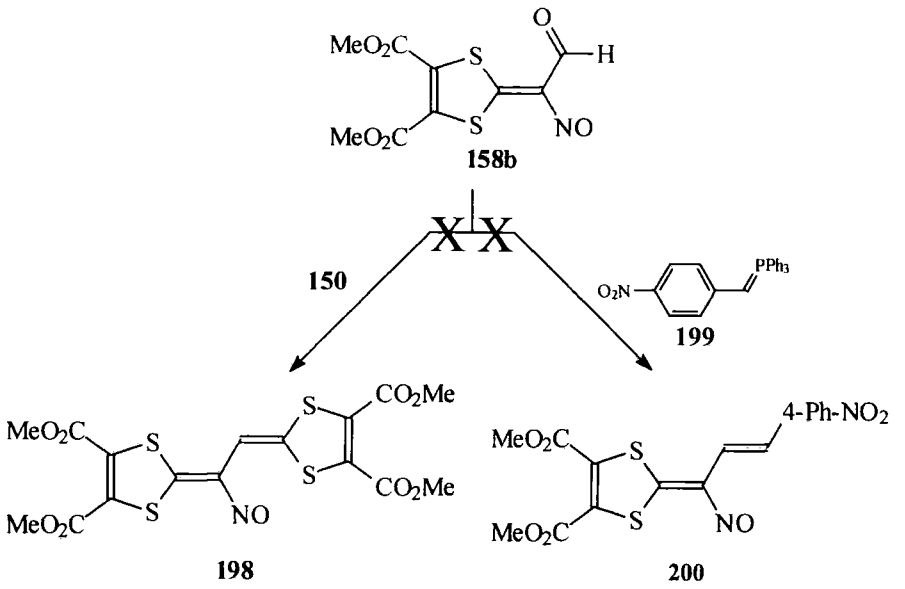
To explore further if the unexpected stability of 1,2-dinitroso-1,2-bis-(4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-ethane we prepared the phenyl spaced analogue, **194a**, by the Wittig reaction of **150** with terephthalaldehyde proceeded which proceeded twice in 50% yield without need to isolate the mono Wittig product.[35] Nitrosation of **194a** proceeded smoothly and *bis*-nitroso-alkene **194b** could be isolated as a green solid in 36% yield.



***Scheme 2.15**: Routes to Compounds for Section 2.4*

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 betweeen 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 decompostion of starting materials. It became apparent that this route would be unsuccessful and that a fresh approach was necessary.



Scheme 2.16**: Attempted Wittig Reactions of Compound **158b

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[108] 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.[101] 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 destablise the one nitroso-alkenes as it is 'tied up' in stabilising the other with an S---O interaction.

2.5 Conclusions

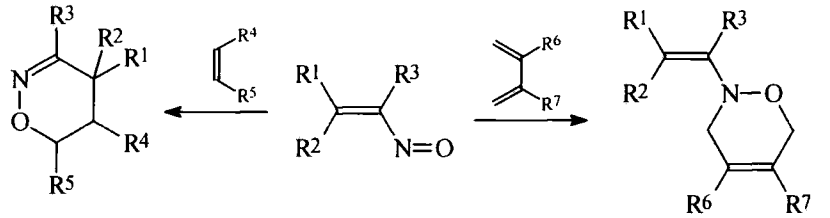
We have investigated the effect of the ylidene and 4- and 5- substituents in stabilising the nitroso-alkene moiety, and shown that the stability is enhanced by the use of electron-withdrawing substituents. It has been shown that the effect of the exo-cyclic substituent has the greater bearing on the 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.[109] 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).[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**.



201 **114** **202**

***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_2O & CH_2N 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 and 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 indictes that these highly stable nitroso-alkenes are also unreactive as heterodienes.

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).

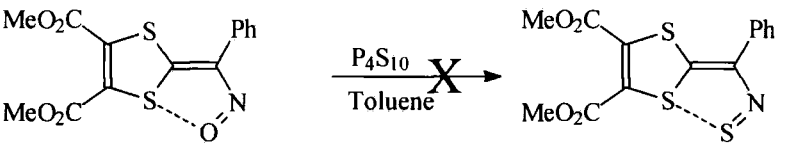
2.7 Attempted Generation of Thionitroso Species

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 transfomation 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]



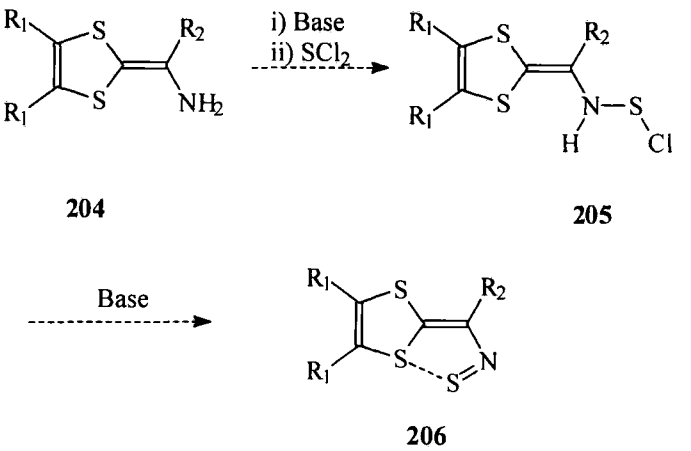
14 **203**

***Scheme 2.18**: Attempted Thionation with Phosphorus Pentasulfide*

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 occured (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 neccessary 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**.



204 **205**

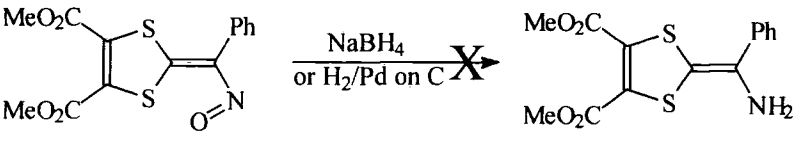
206

***Scheme 2.19**: Postulated Route to Thionitroso Systems*

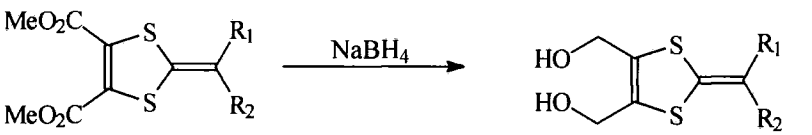
2.7.3.1 Preparation of Amines by Reduction of Nitroso Species

It is known that nitroso compounds are intermediates in the reduction of nitro species to amines,[110] 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 occured (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.[111] 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%).

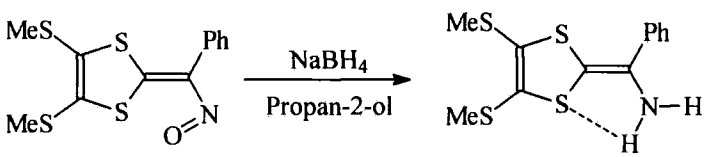


14



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

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.



179a **207**

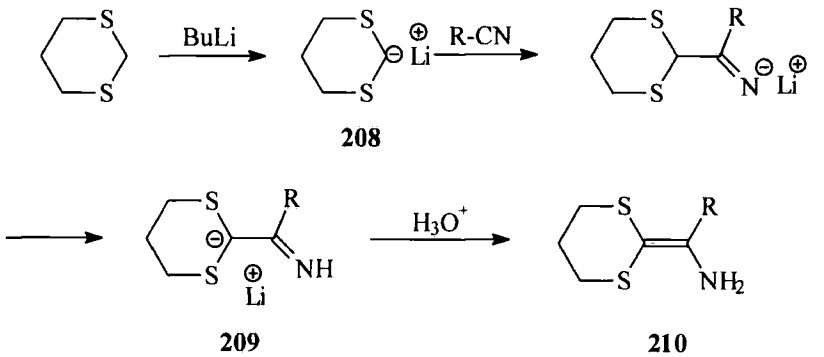
Scheme 2.21**: Borohydride Reduction of Compound **179a

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_2N & CH_2S peaks [typically δ_H 4.0 ppm, (broad s, 2H) and 3.0 ppm, (broad s, 2H) respectively[7]] in the proton NMR spectrum.

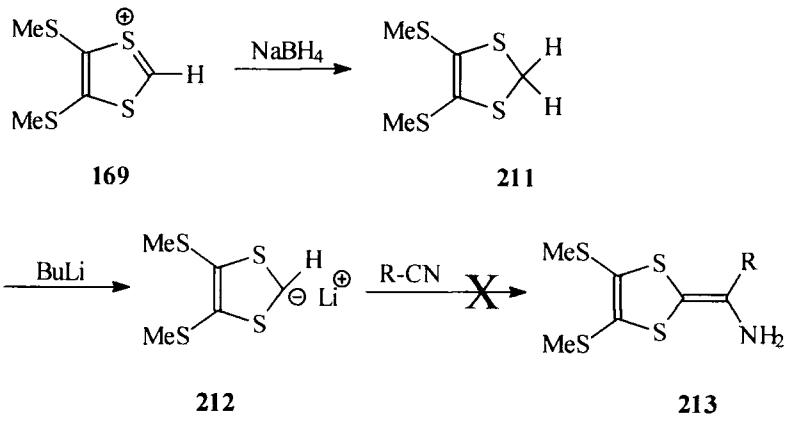
2.7.3.2 Preparation of Amines from Dithiole anions

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.



***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.



***Scheme 2.23**: Attempted Generation of a Dithiole Ene-amine*

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-cinnimaldehyde. Upon nitrosation (Scheme 3.1), rather than obtaining the expected green solution, the reaction mixture merely darkened and a dark orange solid was isolated.

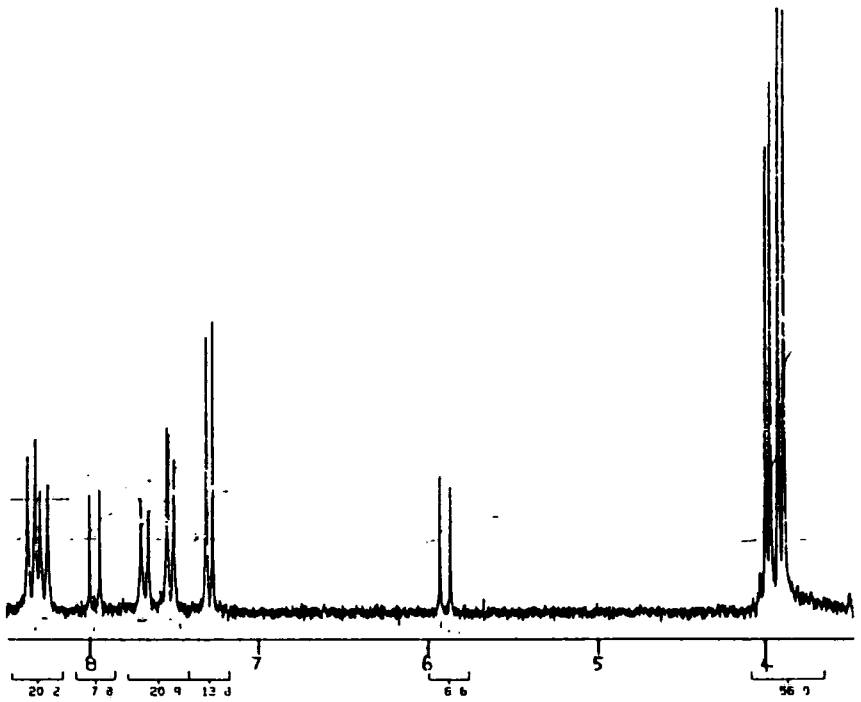
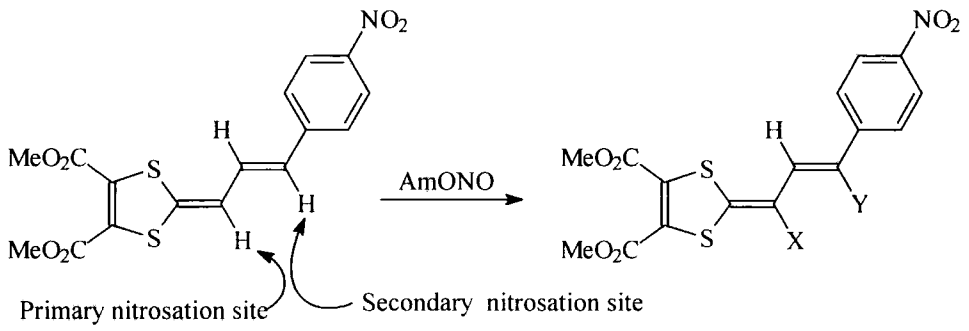


Figure 3.1**: Proton NMR Spectrum of Compound **215

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 δ_H 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.



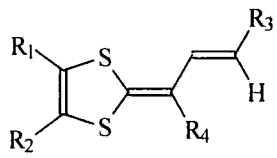
214 **215**, X,Y= NO or NO_2

***Scheme 3.1**: Possible Dinitrosation of an Extended Dithiol-2-Ylidene System*

3.2 Reaction of Wittig reagent 150 with Simple ketones

3.2.1 Introduction

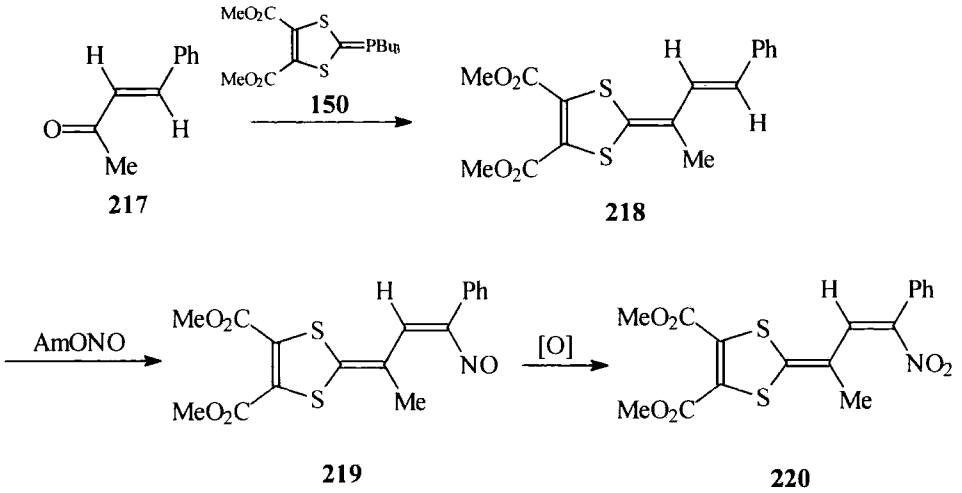
The most convenient way to block the primary reaction site would be to react the Wittig reagent with α,β-unsaturated ketones, leading to molecules such as **216**. The Wittig reagent **150**, is known to react with ketones as described by Cava[34] in the initial paper on the generation and reactivity of this reagent, and also with α,β-unsaturated aldehydes.[34] However, there has been no report of the Wittig reagent reacting with α,β-unsaturated ketones. Therefore, it was neccesary 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.



216

***Figure 3.2**: General Form of the Extended Systems*

3.2.2 Use of Methyl and Phenyl substituents as 'blocking groups'

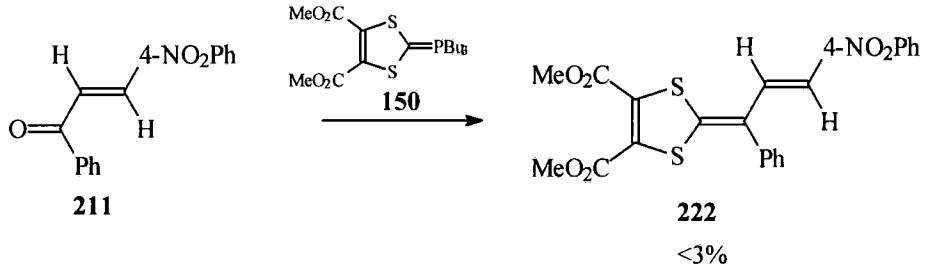


***Scheme 3.2**: The use of a Methyl Functionality as a 'Blocking Group'*

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 occured. 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 apperance 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 occuping 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*

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 hinderance. [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.

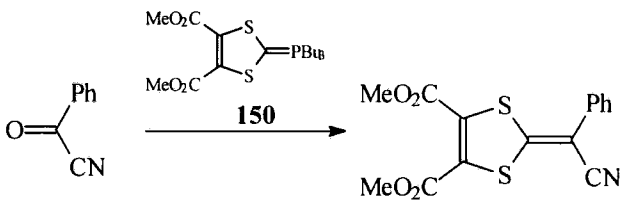
3.3 Highly electron deficient 'blocking groups' for the vinyl site

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.



223 **224**

***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]

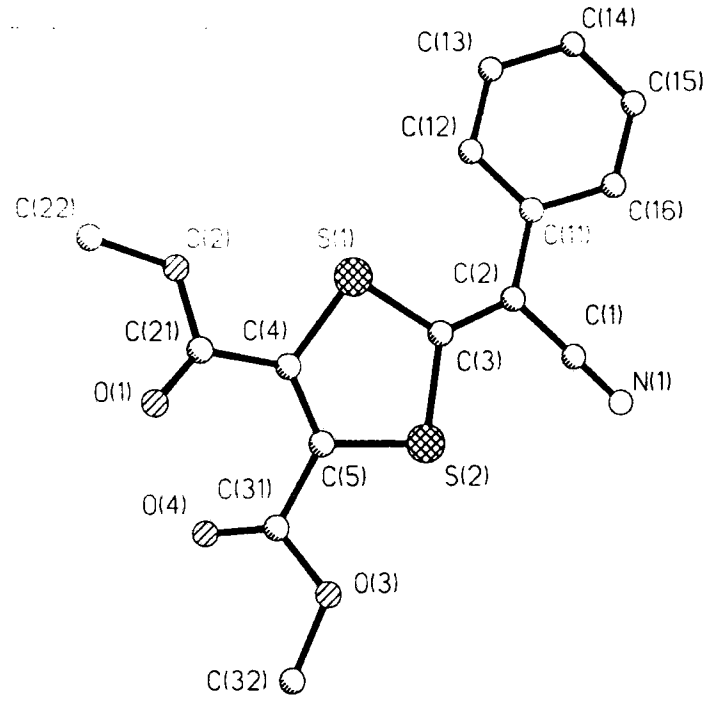
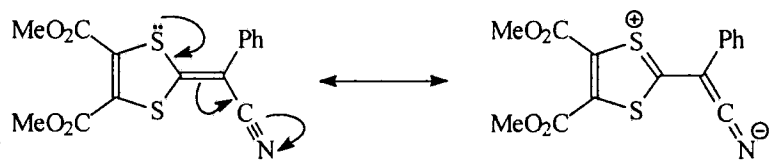


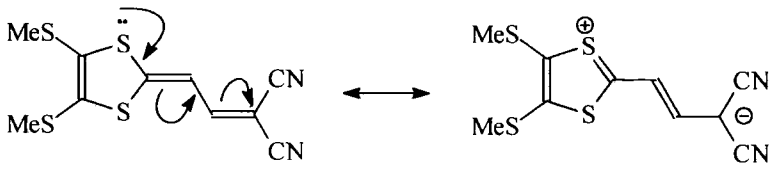
Figure 3.3**: X-ray Molecular Structure of Compound **224

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 (*ie.* it exsists in the form **225'**).[114] 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.[115]

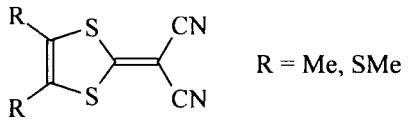


224 **224'**

***Figure 3.4**: Possible Donor-Acceptor Nature of the 1-(Dithiol-2-ylidene)-1-cyano methane Systems*



225 225'

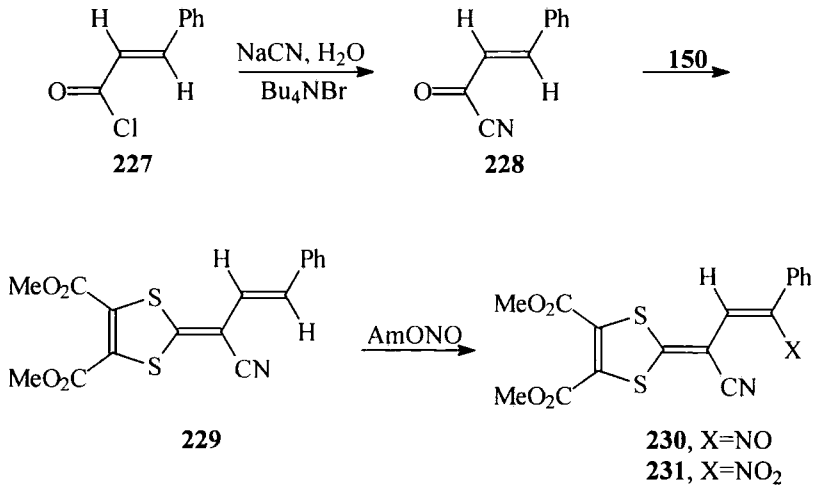


226

***Figure 3.5**: 1,3-Dithiol-2-ylidene Dicyanomethylene 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,[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 occured. 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 (CI) 405 (M^++1)] and nitroso [m/z (CI) 389 (M^++1)] groups and a parent-daughter scan showed that the two molecules **230** and **231** existed independently of each other.



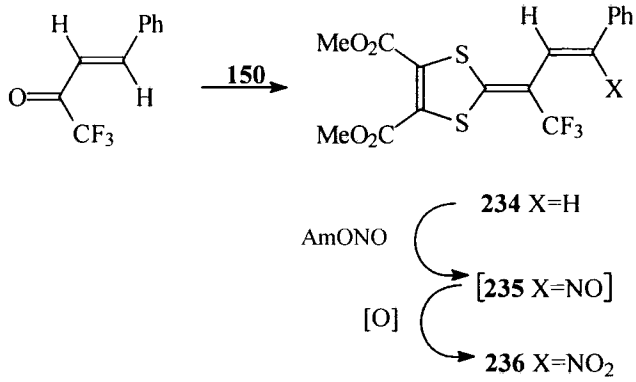
***Scheme 3.5**: The use of a Nitrile Functionality as a 'Blocking Group'*

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 ^{1}H 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 $J_{H\text{-}F}$ values, the vinyl protons can be assigned, since $^3J_{H\text{-}F}$ will be greater than $^4J_{H\text{-}F}$. In this case, the $J_{H\text{-}F}$ values are 1.62 and 0.92 Hz, thus the proton with the $J_{H\text{-}F}$ value of 1.62 Hz is that lying closest to the trifluoromethyl group, in this case the peak at δ 6.77 ppm. The proton decoupled fluorine spectrum showed as expected, a singlet due to the three equivalent fluorine nuclei.

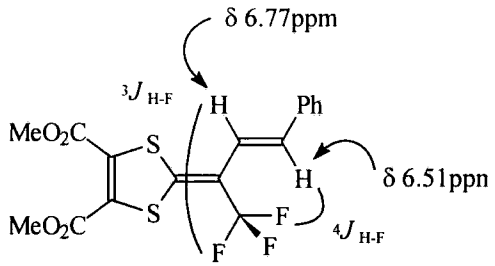


Figure 3.6**: H---F Coupling Interactions in Compound **234

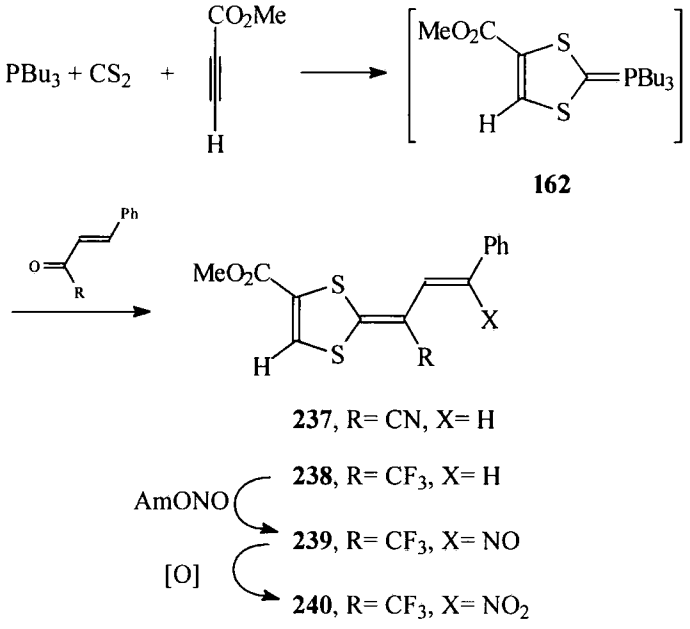
Nitrosation of compound **234** was attempted utilising the standard procedure and led to a yellow product in 52% yield. This was shown to be solely the nitro derivative **236** [m/z (CI) 448 (M^++1)], both before and after chromatographic purification.

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 occured. This effect is attributed to the reduced reactivity of the α,β-unsaturated derivatives in these Wittig reactions.



***Scheme 3.7**: Mono-Ester Extended Systems*

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 *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-*cis* isomer and the other for the s-*trans* isomer.

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 stablising 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

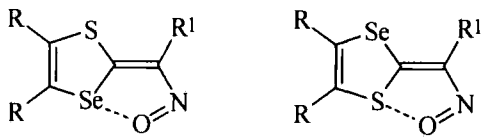
1-(1,3-Diselenol-2-ylidene) methane Systems

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[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.[117] However this system would be expected to lead to inseparable cis and trans isomers **241a** and **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.



241a **241b**

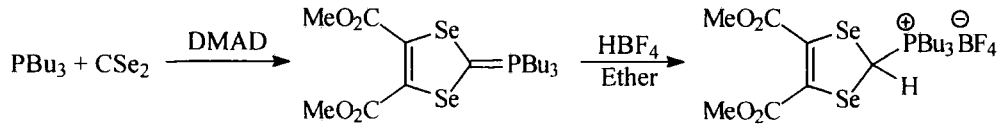
***Figure 4.1**: Isomers of 1,3-Selenathiol-2-ylidene Systems*

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.[117] Established routes to the systems, involved the use of the noxious, fetid and commercially unavailable reagent, carbon diselenide.[47b, 118]

Synthesis of the systems **242** and **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).[47a] 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.



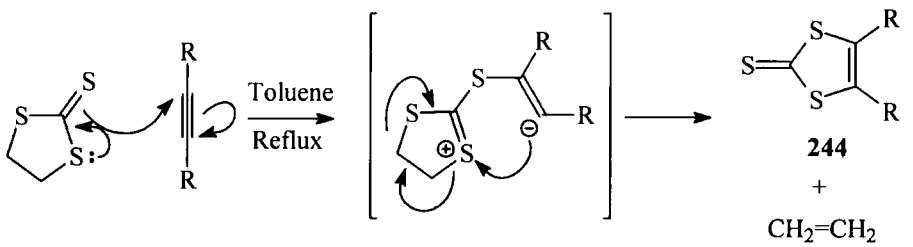
242 **243**

***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).[39]

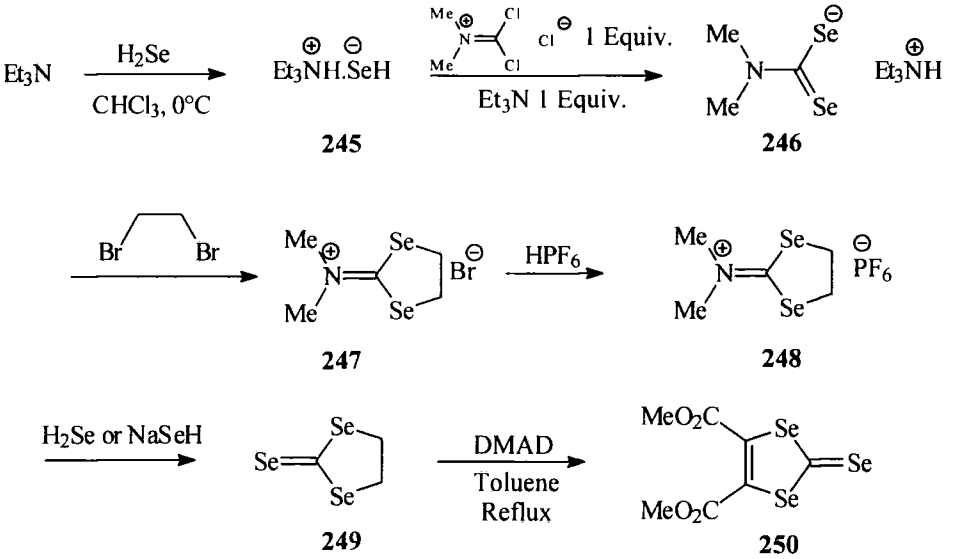


66

***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[119] and Wudl[120]; its reaction with alkynes, including dimethyl acetylenedicarboxylate has also been investigated.[121]

4.2.2 Synthesis of 4,5-dicarbomethoxy-1,3-diselenole-2-selone



***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.[119] 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 hexafluorophsophoric 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[121] 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

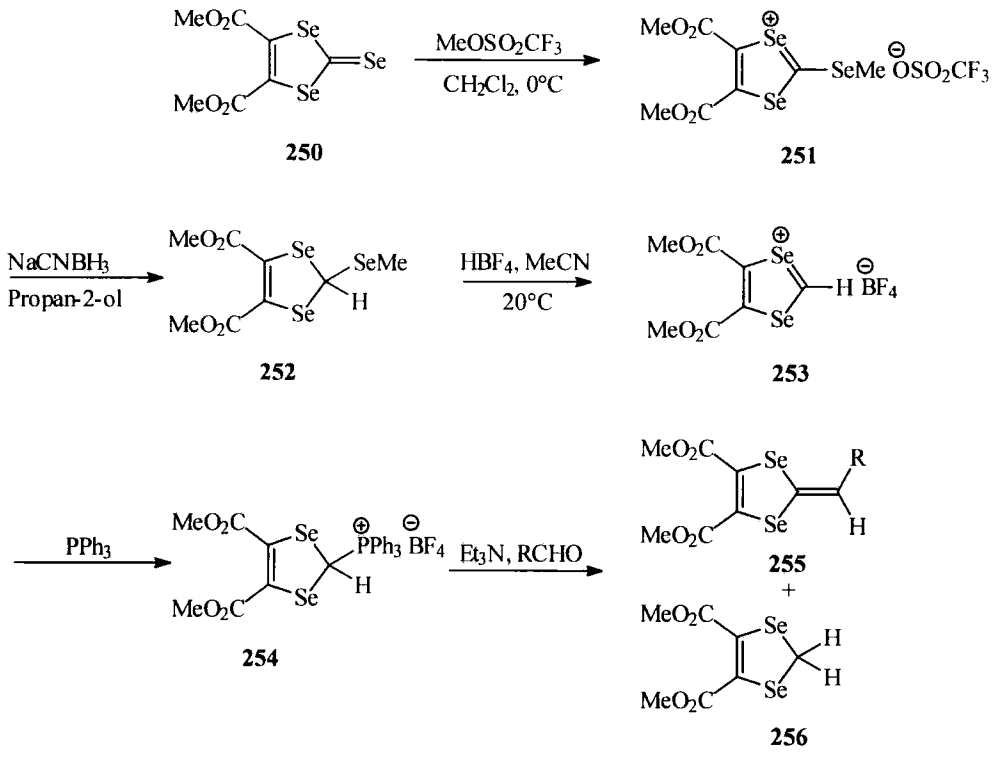
The use of thiones as starting materials for the preparation of 1,3-dithiol-2-ylidene systems is well documented for systems incorporating a range of substituents, including di(methylthio) and ethanedithio at the 4- and 5- positions on the dithiole ring.[100, 101] This route has not been extended to 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.



***Scheme 4.4**: Preparation of 1,3-Diselenol-2-ylidene Systems*

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[47b] when it was prepared by the sequence outlined in Scheme 4.2, however, substitution of

tributylphosphine for triphenylphospine 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 tetrafluorborate salt **254**. The resultant ylide was trapped with an appropriate aldehyde to afford **255a-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.[123] 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*

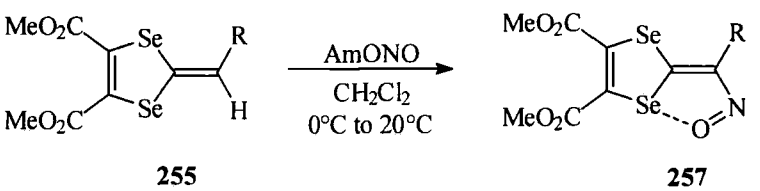
R	Yield of **255** [a]	Yield of **256** [a]
2-CF_3-C_6H_4 (**a**)	31	24
2-Pyridyl (**b**)	21	42[b]
2,4-Di-NO_2-C_6H_3 (**c**)	30	20
C(O)Me (**d**)	34	16
CHO (**e**)[47b]	36	32[b]

[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, succesfully 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.



255 **257**

***Scheme 4.5**: Nitrosation of 1,3-diselenol-2-ylidene*

***Table 4.2**: Nitroso Derivatives of 1,3-Diselenol-2-ylidenes*

R	Compound	Nature	Yield / %
2-CF_3-C_6H_4	**257a**	Green Solid	37
C(O)Me	**257d**	Green Crystals	55
CHO	**257e**	Green Crystals	34

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

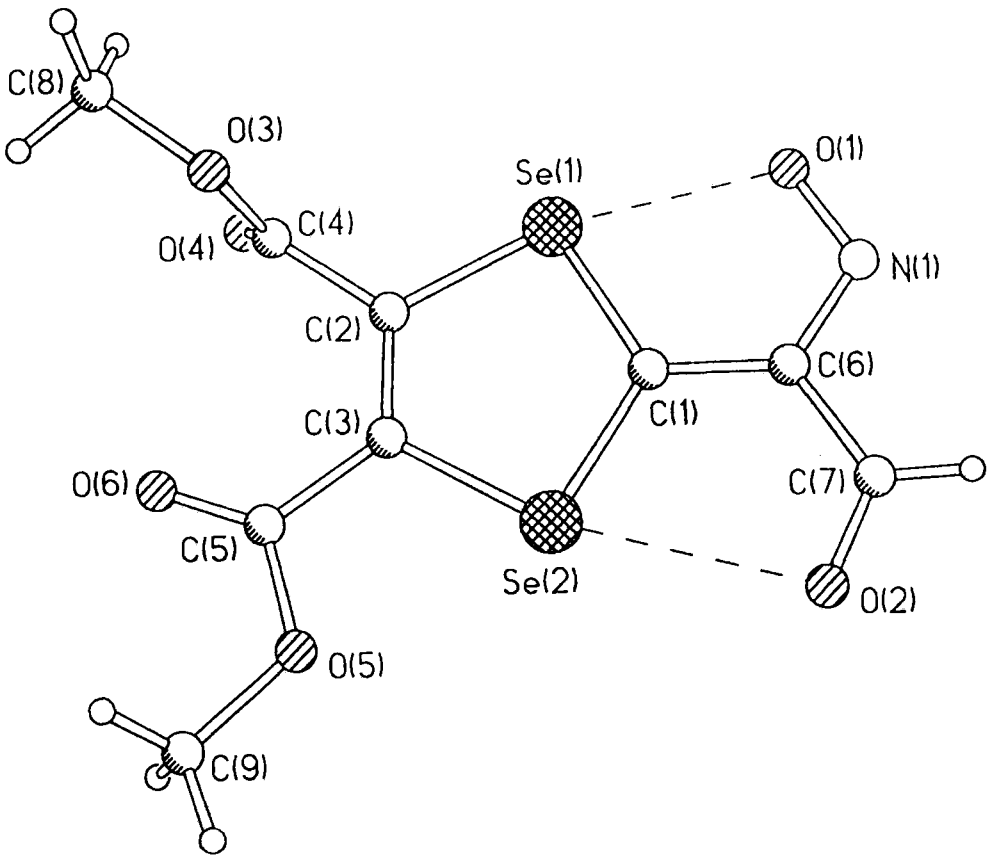


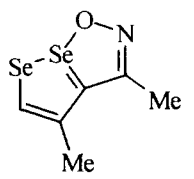
Figure 4.1**: X-ray Molecular Structure of Nitroso-alkene **257e

The X-ray molecular structure (Figure 4.1) was solved[93] 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 inclinded 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

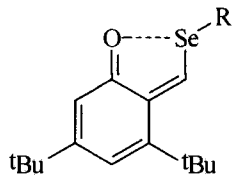
exhibit a close Se---O interaction with a selenium atom in the diselenole ring. In accordance with earlier results (see section 2.2) and those found by Reid *et al*[86] the nitroso oxygen atom is more closely bound (Se---O 2.51Å) than the carbonyl (Se---O 2.73Å). Interestingly, the interatomic distances 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 diselenole 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[124] of 2.04Å being significantly closer to the Se-O covalent bond length of 1.91Å than the 1,3-diselenole system studied. Structures **259**[125] and **260**[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).[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,[14] although no crystallographic evidence for the *cisoid* nature of the nitroso-alkenes was presented.

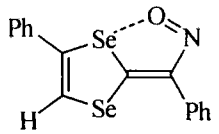


258



259, R = Cl
260, R = Ph

***Figure 4.2**: Systems with Selenium-Oxygen Close Contacts.*



261

***Figure 4.3**: The Nitroso-alkene reported by Cava*

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 embeded 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 impingent 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.* 1×10^{-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.

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[34] subsequentaly modified by Hansen.[127] 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.[34]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[34], from benzaldehyde.

Red Solid (68%). m.p. 89-90 °C (lit. [34] 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; $C_{11}H_{14}O_4S_2$ requires 274.0334; ν_{max}(neat) 2958, 2936, 2876, 1744, 1716 and 1270 cm^{-1}; δ_H ($CDCl_3$) 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* (CI) 259(M^++1); HRMS Found 258.9871; $C_{10}H_{11}O_4S_2$ requires 259.0098; ν_{max}(KBr) 3026, 2962, 1762, 1724, 1609, 1579, 1424 and 1230 cm^{-1}; δ_H($CDCl_3$) 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-dithiol-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; $C_{14}H_{11}NO_6S_2$ 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($CDCl_3$) 7.37 (m, 4H), 6.94 (s, 1H), 3.87 (s, 3H) and 3.83 (s, 3H).

1-(4,5-Dicarbomethoxy-1,3-dithiol-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; $C_{14}H_{10}N_2O_8S_2$ 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($CDCl_3$) 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$^v/_v$). 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-dithiol-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* (CI) 285 [expected *m/z* (EI) 287] ν_{max}(KBr) 2955, 1635, 1588, 1435, 1256.

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

Green crystals (48% yield) m.p. 156-157°C [Found: C, 39.0; H, 2.0, N, 9.6; $C_{14}H_9N_3O_9S_2$ requires C, 39.3; H, 2.1; N, 9.8%] *m/z* (EI) 428(M^+); ν_{max}(KBr) 1749, 1734, 1538, 1349 and 1264 cm^{-1}; δ_H($CDCl_3$) 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-dithiol-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; $C_{14}H_9Cl_2NO_5S_2$ requires C, 41.4; H, 2.2; N, 3.5%] *m/z* (EI) 407(M^+); ν_{max}(neat)1749, 1734, 1608, 1538 and 1193 cm^{-1}; δ_H($CDCl_3$) 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-dithiol-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) methane, 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^+); ν_{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^+); ν_{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^+); ν_{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).

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; $C_{13}H_{10}N_2O_5S_2$ requires C, 46.2; H, 3.0; N, 8.3%] *m/z* (EI) 338(M^+); ν_{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); λ_{max}(MeCN)(ε/ mol l^{-1} cm^{-1}) 302 ($1.60x10^4$), 443 ($1.44x10^4$),642 (117).

X-ray quality crystals were grown from dichloromethane/methanol ($1:10^{v}/_{v}$).

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[47b], Yellow solid (yield 70%) m.p. 110-111 °C (lit [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; $C_{10}H_{10}O_5S_2$ requires C, 43.8; H, 3.7%] *m/z* (EI) 274(M^+); ν_{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[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* (CI) 350(M^++1); ν_{max}(KBr) 2949, 1720, 1579, 1476, 1432 and 1259 cm^{-1}; δ_H($CDCl_3$) 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: $C_{12}H_{10}N_2O_4S_3$ requires C, 42.1; H, 2.9; N, 8.2%] *m/z* (CI) 343(M^++1); ν_{max}(KBr) 3853, 1726, 1587, 1486 and 1261 cm^{-1}; δ_H($CDCl_3$) 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; $C_9H_7NO_6S_2$ requires C, 37.4; H, 2.4; N, 4.9%] *m/z* (EI) 289(M^+); ν_{max} (KBr) 1744, 1735, 1651, 1400, 1268, and 1221 cm^{-1}; δ_H($CDCl_3$) 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; $C_{10}H_9NO_6S_2$ requires C, 39.6; H, 3.0; N, 4.6%] *m/z* (EI) 303(M^+), ν_{max} (KBr) 1752, 1734, 1718, 1700, 1653 , 1541 , 1534 and 1261 cm^{-1}; $\delta_H(CDCl_3)$ 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); ν_{max}(KBr) 2960, 1734, 1728, 1619, 1507, 1430, 1260 and 1224 cm^{-1}; $\delta_H(CDCl_3)$ 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: $C_{11}H_9NO_2S_2$ requires C, 52.6; H, 3.6; N, 5.6%] *m/z* (EI) 251(M^+); ν_{max}(KBr)

3047, 2946, 1702, 1583 and 1283 cm^{-1}; $\delta_H(CDCl_3)$ † 8.63 (m, 2H), 7.60(td, *J*= 7.5, 1.5 Hz, 2H), 7.51* (s, 1H,) 7.50* (s, 1H), 7.06-6.86 (m, 4H), 6.69‡(s, 1H), 6.68‡ (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: $C_{11}H_8N_2O_3S_2$ requires C, 47.1; H, 2.9; N, 10.0%] *m/z* (EI) 280(M^+); ν_{max}(KBr) 3094, 3051, 1727, 1587, 1554 , 1449 and 1244 cm^{-1}; $\delta_H(CDCl_3)$ 8.70-8.85 (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); λ_{max}(MeCN)(ε/mol l^{-1} cm^{-1}) 304 (1.53x 10^4), 441 (1.72x10^4).

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[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[98] from the zincate salt **165**. (95%). m.p. 99-100°C (lit.[98] 100-101°C).

---

† The appearence of 2 peaks for the vinyl‡ and 5-substituent on the dithiole ring* 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%).[100]

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

To a stirring solution of 4,5-di(methylthio)-1,3-dithiolium tetrafluoroborate (3.38g, 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 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 proceedure 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 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 then dried ($MgSO_4$). 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 $C_{12}H_{12}S_4$; requires 283.9822; ν_{max}(neat) 2916, 2848, 1595, 1578, 1496, 1441 and 1427 cm^{-1}; δ_H($CDCl_3$) 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; ν_{max}(neat) 2917, 1582, 1532, 1494, 1465, 1421, 1314, 1216 and 1147 cm^{-1}; δ_H($CDCl_3$) 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$^v/_v$) 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* (CI) 375(M^++1) ν_{max}(KBr) 1600, 1581, 1533, 1507, 1482 and 1332 cm^{-1}; δ_H($CDCl_3$) 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 methodolgy (*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 ($MgSO_4$). 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 $C_{12}H_{12}S_2$ requires C, 65.4; H, 5.5%] *m/z* (EI) 220(M^+); ν_{max}(KBr) 2913, 2850, 1596,1576, 1551 and 1440 cm^{-1}; δ_H ($CDCl_3$) 7.2 (m, 5H) 6.46 (s, 1H) 1.99 (s, 3H) 1.98 (s, 3H); E_{ox}(1st cycle) = 0.74, E_{red} (1st Cycle) = 0.24, E_{ox} (2nd and 3rd cycles) = 0.39 ,0.72 E_{red} (2nd and 3rd cycles) = 0.28 V.

1-(4,5-Dimethyl-1,3-dithiol-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); ν_{max}(KBr) 1597, 1576, 1500, 1453, 1320, 1300 and 1259 cm^{-1}; δ_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 analoguosly to diethyl-4,5-diethyl-1,3-dithiole-2-ylphosphonate described by Moore and Bryce[48] to yield **187** as an unstable dark red hygroscopic oil (90% yield); δ_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[101]. Off-white solid 0.62g, (52% yield), identical to the sample prepared by Wittig methodolgy.

1-(4,5-Dimethyl-1,3-dithiol-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; $C_{12}H_9N_3O_5S_2$ requires 338.9984; ν_{max} (KBr) 3111, 1602, 1540, 1530, 1355 and 1190 cm^{-1}; δ_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; ν_{max}(KBr) 2955, 1754, 1740 1722, 1577, 1501 and 1257 cm^{-1}; $\delta_H(CDCl_3)$ 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; ν_{max}(KBr) 2955, 1745, 1569, 1435, 1268 and 1178 cm^{-1}; $\delta_H(CDCl_3)$ 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 ($MgSO_4$). 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; $C_{15}H_{16}O_4S_6$ requires C, 39.8; H, 3.6%] *m/z* (D.C.I.) 452(M^++1), ν_{max}(KBr) 2948, 1731, 1712, 1578, 1436, 1291, 1263 and 1035 cm^{-1}; δ_H($CDCl_3$) 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.

Attempeted Cycloaddition reaction between 4,5-dicarbomethoxy-1,3-ditihole-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 cycloaddtion 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, 153l 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 occured.

Attempted Cycloaddition reaction between 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso-methane, 153l 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 occured.

Attempted Cycloaddition reaction between 4,5-dicarbomethoxy-1,3-dithiol-2-ylidene)-1-(2-pyridyl)-1-nitroso-methane, 153l 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 2*H*-dihydropyran (0.1 ml, 1.1 mmol, excess) and the solution heated to reflux for 3 days during which no reaction occured. 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, 67μmol). The reaction temperature was increased stepwise to 70°C when a reaction started to occur. The reaction was stirred for 3h 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 16h, during which time the solution turned orange. The reaction was poured into water (100 ml) and extracted wth dichloromethane (3x30 ml), the combined organic phases were washed with water and dried ($MgSO_4$). 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 16h with 1atm.

of hydrogen at *ca* 0 °C, after which time the catalyst was filtered off. The solvent was removed *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* (CI) 300(M^++1); ν_{max}(KBr) 3256, 2988, 2962, 2920, 1497, 1417 ,1302 and 1261 cm^{-1}; δ_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[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 [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; $C_{16}H_{13}NO_6S_2$ requires C, 50.6; H, 3.5; N, 3.4%] *m/z* (EI) 379(M^+), ν_{max}(KBr) 1735, 1711, 1577, 1508, 1335 and 1287 cm^{-1}; δ_H($CDCl_3$) 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: δ_H($CDCl_3$) 8.33 (d, *J*= 6.8Hz, 2H), 7.96 (d, *J*= 12.5Hz, 1H), 7.51 (d, *J*= 6.8Hz, 2H), 5.89 (d, *J*= 12.5Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H)

Di-substituted: δ_H($CDCl_3$) 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; $C_{17}H_{16}O_4S_2$ requires C, 58.6; H, 4.6; %] *m/z* (CI) 349(M^++1); ν_{max}(KBr) 3054, 2986, 1736 and 1235 cm^{-1};

$\delta_H(CDCl_3)$ 7.3 (m, 5H), 6.71(d, *J*= 15.0Hz, 1H), 6.42 (d, *J*= 15.5Hz, 1H), 3.85(s, 6H), and 1.90 (s, 3H)

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 (50ml) was added, dropwise, *n*-butyl lithium (1.6M 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* (CI) 456 (M^++1); $\delta_H(CDCl_3)$ 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 1h. 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: $C_{15}H_{11}NO_4S_2$ requires C, 54.0; H, 3.3; N, 4.2%] *m/z* (EI) 333(M^+); ν_{max}(KBr) 2187, 1755, 1728, 1582, 1508 , 1430 and 1240 cm^{-1}; $\delta_H(CDCl_3)$ 7.6-7.3 (m, 5H), 3.91(s, 3H) and 3.87 (s, 3H); $\delta_C(CDCl_3)$ 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 ($MgSO_4$). 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: $C_{17}H_{13}NO_4S_2$ requires C, 56.8; H, 3.6; N, 3.9%] *m/z* (CI) 360(M^++1); ν_{max}(KBr) 3054, 2986, 2211, 1738 and 1265 cm^{-1}; δ_H($CDCl_3$) 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: $C_{17}H_{13}F_3O_4S_2$ requires C, 50.8; H, 3.2%] *m/z* (CI) 403(M^++1); δ_H($CDCl_3$) 7.38 (m, 5H), 6.77(dq, J_{HH}= 16Hz, $^3J_{HF}$= 1.6Hz, 1H), 6.51 (dq, J_{HH}= 16.5Hz, $^4J_{HF}$= 0.9Hz, 1H) and 3.87 (s, 6H), δ_F($CDCl_3$) -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 18h. 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; $C_{15}H_{11}F_3O_2S_2$ requires 344.01523; ν_{max}(KBr) 3155, 1720 and 1257 cm^{-1}; $\delta_H(CDCl_3)$[†] 7.35 (m, 10H+2H), 6.8-6.45(m, 4H), 3.84(s, 3H) and 3.83(s, 3H) $\delta_F(CDCl_3)$ -58.3 (s, 3F), -58.7 (s, 3F)

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

To a stiring solution of the required 1,3-dithiole derivative (*ca* 0.1mmol) in dry dichloromethane (5ml) at 0°C was added isoamyl nitrite (0.5ml, excess). The solution was stirred at this temperature for 15min then allowed to warm to ambient temperature and stirred for a further 15min. 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 appearence 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

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]; $\delta_H(CDCl_3)$ 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; $\delta_H(CDCl_3)$ 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: 447.00888; $C_{17}H_{12}F_3NO_6S_2$ requires 447.00581; ν_{max}(KBr) 3155, 1735, 1561 and 1383 cm^{-1}; $\delta_H(CDCl_3)$ 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; $C_{15}H_{10}F_3NO_4S_2$ requires 388.98033; ν_{max}(neat) 3155, 1712, 1573 and 1366 cm^{-1}; $\delta_H(CDCl_3)$ 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 triselenocarbonate[119] (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 recrystalised 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; $\delta_H(CDCl_3)$ 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 ($MgSO_4$), removal of the solvent *in vacuo* yielded the selenoether **252**, as an unstable orange oil (235 mg, 91% yield), [$\delta_H(CDCl_3)$ 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; $C_{15}H_{11}F_3O_4Se_2$ requires C, 38.3; H, 2.36 %]; *m/z* (CI,^{80}Se) 473(M^++1); ν_{max}(KBr) 1727, 1584, 1433, 1310, 1244, 1168 and 1120 cm^{-1}; $\delta_H(CDCl_3)$ 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; $C_{13}H_{11}NO_4Se_2$ requires C, 38.7; H, 2.8; N, 3.5%]; *m/z* (CI, ^{80}Se) 406 (M^++1); δ_H($CDCl_3$) 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; $C_{14}H_{10}N_2O_8Se_2$ requires C, 34.2; H, 2.1; N, 5.7%]; *m/z* (CI , ^{80}Se) 494(M^++1); ν_{max}(KBr) 1740, 1718, 1624, 1533, 1434 and 1245 cm^{-1}; δ_H ($CDCl_3$) 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* (CI, ^{80}Se) 371(M^++1); ν_{max}(KBr) 1734, 1701, 1625, 1577, 1475, 1434 and 1231 cm^{-1}; δ_H (d_6-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[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 *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.[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* (CI, ^{80}Se) 317(M^++1); HRMS Found 315.8757 $C_7H_8O_4Se_2$ requires 315.8753; ν_{max}(neat) 1716, 1567, 1431 and 1239 cm^{-1}; δ_H ($CDCl_3$) 4.52 (s, 2H), 3.80 (s, 6H). δ_C ($CDCl_3$) 163.66, 134.55, 53.61, 14.02.

Preparation of the nitrosated derivitives 257, General Procedure:

To a stirring solution of the appropriate 1,3-diselenol-2-ylidene derivative **255** (*ca.* 50 mg) in dichloromethane at 0°C was added isoamylnitrite (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 *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* (CI, ^{80}Se) 502 (M^++1); HRMS Found 500.8840 $C_{15}H_{10}F_3NO_5Se_2$ requires 500.8841; δ_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); δ_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; $C_{10}H_9NO_6Se_2$ requires C, 30.2; H, 2.3; N, 3.5 %]; *m/z* (CI, ^{80}Se) 400 (M^++1); ν_{max} (KBr) 1741, 1703, 1641, 1400, 1283 and 1223; δ_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; $C_9H_7NO_6Se_2$ requires C, 28.2; H, 1.8; N, 3.7 %]; *m/z* (CI, ^{80}Se) 386 (M^++1); ν_{max}(KBr) 1734, 1653, 1396, 1281, 1247 and 1211cm^{-1}; δ_H($CDCl_3$) 11.12 (s,1H), 3.99 (s, 3H), 3.90 (s,3H).

References

1. M. R. Bryce, J. Becher, B. Fält-Hansen, *Adv. Heterocyl. Chem.*, 1992, **55**, 19.
2. a) P. Tavs, *Angew. Chem. Int. Ed. Eng.*, 1966, **5**, 1048; b) W.J. Middleton, *J. Am. Chem. Soc.*, 1966, **88**, 3842.
3. M. Takahashi, R. Okazaki, N. Inamoto, T. Sugawara, H. Iwamura, *J. Am. Chem. Soc.*, 1992, **114**, 1830.
4. Y. G. Shermolovich, A. V. Solov'ev, A. V. Borodin, V. V. Pen'kovskii, V. V. Trachevskii, L. N. Markovskii, *Zh. Org. Chim.* 1991, 27, 1637. *Engl Trans.*, 1991, **27**, 1433.
5. M. R. Bryce, A. Chesney, J. N. Heaton, G. N. McKelvey, M Anderson, *Tetrahedron Lett.*, 1994, **35**, 5275.
6. M. R. Bryce, A. Chesney, G. N. McKelvey, A. S. Batsanov, J. A. K. Howard, M. Anderson, *J. Chem. Soc., Perkin Trans. 1*, 1996 In press.
7. M. R. Bryce, P. C. Taylor, *J. Chem. Soc., Chem. Commun.*, 1988, 950; M. R. Bryce, P. C. Taylor, *J. Chem. Soc. Perkin. Trans. 1*, 1990, 3225.
8. L. N. Markovskii, A. V. Borodin, A. V. Solov'ev, N. R. Kolesnik, Yu. G. Shermolovich, *Zh. Org. Chim.*, 1990, **26**, 2083. *Engl. Trans*: 1990, **26**, 1779.
9. P. Frère, A. Belysamine, Y. Gouriou, M. Jubalt, A. Gorgues, G. Duguay, S. Wood, C. D. Reynolds, M. R. Bryce, *Bull. Chim. Soc. Fr.*, 1995, **132**, 975.
10. A. Bondi, *J. Phys. Chem.*, 1964, **68**, 441.
11. N. Svenstrup, J. Becher, *Synthesis*, 1995, 215.
12. M. P. Cava, M. V. Lakshmikantham, *J. Org. Chem.*, 1981, **46**, 3246.
13. T. K. Hansen, J. Becher, *Adv. Mater.*, 1993, **5**, 288.
14. B. G. Gowenlock, K. G. Orrell, V. Sik, G. Vasapallo, M. V. Lakshmikantham, M. P. Cava, *Polyhedron*, 1994, **13**, 675.
15. W. M. McGregor, D. C. Sherrington, *Chem. Soc. Rev.*, 1993, **22**, 199; J. W. Greidanus, *Can. J. Chem.*, 1970, **48**, 3530; K. F. Wai, M. P. Sammes, *J. Chem. Soc., Perkin Trans. 1*, 1991, 183; P. Beslin, D. Lagain, J. Vialle, *Tetrahedron*, 1981, **37**, 3839; G. W. Kirby, W. M. McGregor, *J. Chem. Soc., Perkin Trans. 1*, 1990, 3175.
16. D. H. R. Barton, M. J. Robson, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1246.

17. W. R. H. Hurtley, S. Smiles, *J. Chem. Soc.*, 1926, 1821.

18. J. P. Ferraris, D. O. Cowan, V. Walatka, J Perlstein, *J. Am. Chem. Soc.*, 1973, **95**, 948; L. B. Coleman, W. Cohen, D. J. Sandman, F. G. Yamagishi, A. F. Garito, A. J. Heeger, *Solid State Commun.*, 1973, **12**, 1125.

19. G. Schukat, A. M. Richter, E. Fanghänel, *Sulfur Reports*, 1987, **7**, 155.

20. M. R. Bryce, W. Devonport, A. J. Moore, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1761.

21. A. S. Benahmed-Gasmi, P. Frère, A. Belyasmine, K. M. A. Malik, M. B. Hursthouse, A. J. Moore, M. R. Bryce, M. Jubault, A. Gorgues, *Tetrahedron Lett.*, 1993, **34**, 2131 and references therein.

22. a) E. Campaigne, N. W. Jacobsen, *J. Org. Chem.*, 1964, **29**, 1703; b) A. Mas, J. M. Fabre, E. Torreilles, L. Giral, G. Brun, *Tetrahedron Lett.*, 1977, 2579.

23. D. Leaver, W. A. H. Robertson, D, McKinnon, *Proc. Chem. Soc.*, 1960, 252

24. A. J. Moore, M. R. Bryce, *Manuscript in Preparation.*

25. E. Fanhangel, *J. Prakt. Chem.*, 1975, **317**, 123.

26. A. J. Moore, M. R. Bryce, A. S. Batsanov, J. C. Cole, J. A. K. Howard, *Synthesis*, 1995, 675.

27. N. F. Haley, M. W. Fichtner, *J. Org. Chem.*, 1980, **45**, 2959.

28. N. F. Haley, M. W. Fichtner, *J. Org. Chem.*, 1980, **45**, 175.

29. M. A. Poelert, S. Z. Zard, *Synlett.*, 1995, 325.

30. L. R. Melby, H. D. Hartzler, W. A. Sheppard, *J. Org. Chem*, 1974, **39**, 2456

31. G. S. Bajwa, K. D. Berlin, H. A. Pohl, *J. Org. Chem.*, 1976, **41**, 145.

32. E. Klinsberg, *Synthesis*, 1972, 29.

33. E. Campaigne, R. D. Hamilton, N. W. Jacobson, *J. Org. Chem.*, 64, **29**, 2877.

34. M. Sato, N. C. Gonnella, M. P. Cava, *J. Org. Chem.*, 1979, **44**, 930.

35. M. Sallé, A. Belyasmine, A. Gorgues, M Jubault, N. Soyer, *Tetrahedron Lett.*, 1991, **32**, 2897.

36. M. V. Lakshmikantham, M. P. Cava, *J. Org. Chem.*, 1976, **41**, 882.

37. C. H. Chen, *J. Chem. Soc., Chem. Commun.*, 1976, 920.

38. I. Degani, R. Fochi, *Synthesis*, 1976, 471.

39. D. B. J. Easton, D. Leaver, *Chem. Commun.*, 1965, 585.
40. B. R. O'Connor, F. N. Jones, *J. Org. Chem.*, 1970, **35**, 2002.
41. a) H. Behringer, R. Wiedenmann, *Tetrahedron Lett.*, 1965, 3705; b) D. B. J. Easton, D. Leaver, T. J. Rawlings, *J. Chem. Soc., Perkin Trans. 1*, 1972, 41.
42. D. Noel, J. Vialle, *Bull. Chem. Soc. Fr.*, 1967, 2239.
43. H. Behringer, D. Deichmann, *Tetrahedron Lett.*, 1967, 1013.
44. D. J. Greig, M. McPherson, R. M. Paton, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1205.
45. R. Huisgen, V. Webendörfer, *Experimentia*, 1961, **17**, 566.
46. H. K. Spenser, M. P. Cava, *J. Org. Chem.*, 1976, **41**, 730.
47. a) T. K. Hansen, M. R. Bryce, J. A. K. Howard, D. S. Yufit, *J. Org. Chem.*, 1994, **59**, 5324; b) T. Sugimoto, H. Awaji, I. Sugimoto, T. Kawase, S. Yoneda, Z. Yoshida, T. Kobayashi, H. Anzai, *Chem. Mater.*, 1989, **1**, 535.
48. A. J. Moore, M. R. Bryce, *J. Chem. Soc., Perkin Trans. 1*, 1991, 157.
49. a) F. Wudl, M. L. Kaplan, E. J. Hufnagel, E. W. Southwick, *J. Org. Chem.*, 1974, **39**, 3608. b) J. P. Ferraris, T. O. Poehler, A. N. Bloch, D. O. Cowan, *Tetrahedron Lett.*, 1973, **27**, 2553.
50. a) A. Takamizawa, K. Hirai, *Chem. Pharm. Bull.*, 1969, **17**, 1924.
51. R. Gompper, E. Kutter, *Chem. Ber.*, 1965, **98**, 2825.
52. a) H. Berger, *Diplomaarbeit*, Freiburg-im-Breisgau; b) H. Behringer, R. Wiedenmann, *Tetrahedron Lett.*, 1965, **41**, 3705. c) M. R. Bryce, A. Green, *Unpublished results.*
53. H. Spies, K. Gewald, R. Mayer, *J. Prakt. Chem.*, 1974, **316**, 907.
54. W. Kirmse, L. Horner, *Justus Leibigs Ann. Chem.*, 1958, **614**, 4.
55. D. Lorcy, R. Carlier, A. Robert, A Tallec, P. Le Maguerès, L. Ouahab, *J. Org. Chem.*, 1995, **60**, 2443.
56. T. K. Hansen, M. R. Bryce, *Unpublished Results.*
57. For a review J. H. Boyer in 'The Chemistry of the Nitro and Nitroso Groups', *Ed.* S. Patai, Wiley, London, 1969, Chapter 5, pp 215.
58. G. W. Kirkby, *Chem. Soc. Rev.*, 1977, **6**, 1.

59. T. L. Gilchrist, C. J. Harris, F. D. King, M. E. Peek, C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1976, 2161.

60. For a review: T. L. Gilchrist, *Chem. Soc. Rev.*, 1983, **12**, 53.

61. C. E. Griffin, R. N. Hazeldine, *J .Chem. Soc.*, 1960, 1398.

62. K. Wieser, A. Berndt, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 70.

63. A. Dornow, H. D. Jordan, *Chem. Ber.*, 1961, **94**, 76.

64. P. Bravo, C. Ticozzi, *Gazz. Chim. Ital.*, 1975, **105**, 91.

65. E. Francotte, R. Merènyi, V. Vandenbulcke-Coyette, H. G. Viehe, *Helv. Chim. Acta*, 1981, **64**, 1208.

66. R. Faragher, T. L. Gilchrist, *J. Chem. Soc., Perkin Trans. 1*, 1979, 249.

67. W. Höbold, U. Prietz, W. Pritzkow, *J. Prakt. Chem.*, 1969, **311**, 260.

68. P. Ciattoni, L. Rivolta, *Chim. Ind. (Milan)*, 1967, **49**, 1186.

69. a) P. Blumbergs, C. B. Thanawalla, A. B. Ash, C. N. Lieske, G. M. Steinberg, *J. Org. Chem.*, 1971, **36**, 2023; b) A. Dornow, H. D. Jordan, A. Müller, *Chem. Ber.*, 1961, **94**, 67; c) L. J. Beckham, W. A.. Fessler, M. A. Kise, *Chem. Rev.*, 1951, **48**, 319.

70. A. G. Sherwood, H. E. Guning, *J. Am. Chem. Soc.*, 1963, **85**, 3506.

71. J.-M.. Surzur, C. Dupuy, M. P. Bertrand, R. Nouguier, *J. Org. Chem.*, 1972, **37**, 2782.

72. R. A. Abromovitch, B. W. Cue, *J. Am. Chem. Soc.*, 1976, **98**, 1478.

73. W. Kisan, W. Pritzkow, *J. Prakt. Chem.*, 1978, **320**, 59.

74. J. H.. Smith, J. H. Heidema, E. T. Kaiser, *J. Am. Chem. Soc.*, 1972, **94**, 9276.

75. M. Ohno, N. Naruse, *Bull. Chem. Soc. Jpn.*, 1966, **39**, 1125.

76. W. Pritzkow, H. Schaefer, P. Pabst, A. Ebenroth, J. Beger, *J. Prakt. Chem.*, 1965, **29**, 123.

77. R. U. Lemieux, T. L.. Nagabhushan, I. K. O'Neill, *Tetrahedron Lett.*, 1964, 1909.

78. H. Lerche, J. Treiber, T. Severin, *Chem. Ber.*, 1980, **113**, 2796.

79. E. J. Corey, L. S. Melvin, M. F. Haslanger, *Tetrahedron Lett.*, 1975, 3117.

80. T. L. Gilchrist, T. G. Roberts, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1283.

81. T. L. Gilchrist, A. Lemos, *J. Chem. Soc., Perkin Trans. 1*, 1993, 1391.

82. E. C. K. Lai, D. Mackay, N. J. Taylor, K. N. Watson, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1497.

83. a) R. Farahger, T. L. Gilchrist, *J. Chem. Soc., Chem. Commun.*, 1978, 847; b) R. Faragher, T. L. Gilchrist, *J. Chem. Soc., Perkin Trans. 1*, 1979, 249; c) D. E. Davies, T. L. Gilchrist, T. G. Roberts, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1275; d) T. L. Gilchrist, D. A. Lingham, T. G.. Roberts, *J. Chem. Soc., Chem. Commun.*, 1979, 1079; e) G. M. Iskanda, V. S. Gulta, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1891.

84. H. U. Reissig, C. Hippeli, T. Arnold, *Chem. Ber.*, 1990, **123**, 2403.

85. a) R. J. S. Beer, D. Cartwright, R. J. Gait, R. A. W. Johnstone, *Chem. Commun.*, 1968, 688.

86. R. M. Christie, A. S. Ingram, D. H. Reid, R. G. Webster, *J. Chem. Soc., Perkin Trans. 1*, 1974, 722.

87. P. L. Johnson, I. C. Paul, *J. Am. Chem. Soc.*, 1969, **91**, 781.

88. K. I. G.. Reid, I. C. Paul, *J. Chem. Soc. (B)*, 1971, 952.

89. J. D. Dingwall, A. R. Dunn, D. H. Reid, K. O. Wade, *J. Chem. Soc., Perkin Trans. 1*, 1972, 1360.

90. M. V. Lakshmikantham, Y. A. Jackson, M. P. Cava, *J. Org. Chem.*, 1988, **53**, 3529.

91. M. V. Lakshmikantham, M. P. Cava, M. Albeck, L. Engman, F. Wudl, E. Aharon-Shalom, *J. Chem. Soc., Chem Commun.*, 1981, 828.

92. M. Perrier, J. Vialle, *Bull. Soc. Chim. Fr.*, 1979, 199.

93. G.M. Sheldrick, *Acta Crystallogr., Sect. A*, 1990, **46**, 467.

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

95. D. L. Boger, W. L. Corbett, T. T. Curran, A. M. Kasper, *J. Am. Chem. Soc.*, 1991, **113**, 1713.

96. H. D. Hartzler, *J. Am. Chem. Soc.*, 1971, **93**, 4961.

97. D. L. Lichtenberger, R. L. Johnston, K. Hinkelmann, J. Suzuki, F. Wudl, *J. Am. Chem. Soc.*, 1990, **112**, 3302.

98. S. Wawzonek, S. M. Heilmann, *J. Org. Chem.*, 1974, **39**, 511.

99. B. Fetkenheuer, H. Fetkenheuer, *Ber.*, 1927, **60B**, 2528.

100. a) G. Steimecke, R. Kirmse, E. Hoyer, *Z. Chem.*, 1975, **15**, 28; b) G. Steimecke, H.-J. Sieler, R. Kirmse, E. Hoyer, *Phosphorus Sulpur*, 1979, **7**, 49.

101. A. J. Moore, M. R. Bryce, *Tetrahedron Lett.*, 1992, **33**, 1373.

102. A. J. Moore, M. R. Bryce, *Unpublished Results.*

103. P. R. Moses, J. Q. Chambers, *J. Am. Chem. Soc*, 1974, **96**, 945.

104. H. Gotthardt in *Comprehensive Heterocyclic Chemistry*, Ed. H. R. Kratritzky, C. W. Rees; Volume 6, Pergamon Press, London, 1984, 813.

105. For an example of 1,3-dithioles in donor-acceptor molecules see: A. K-Y. Jen, V. P. Rao, K. J. Drost, K. Y. Wong, M. P. Cava, *J. Chem. Soc., Chem. Commun.*, 1994, 2057.

106. Y. Misaki, Y. Matsumura, Y. Sugimoto, Z. Yoshida, *Tetrahedron Lett.*, 1989, **30**, 5289.

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

108. K. Ishikawa, K. Akiba, N. Inamoto, *Tetrahedron Lett.*, 1976, **41**, 3695; K. Akiba, K. Ishikawa, N. Inamoto, *Bull. Chem. Soc. Jpn.*, 1978, **51**, 2674

109. G. Schukat, E. Fanghänel, *J. Prakt. Chem.*, 1985, **327**, 767.

110. P. A. S. Smith, *Open Chain Nitrogen Compounds*, W. A. Benjamin, Inc., 1966, p 422.

111. A. Gorgues, *Personal Communication.*

112. C. B. Page, M. B. van Niel, D. Westwood, *J. Chem. Soc., Perkin Trans 1*, 1988, 269.

113. S. Ncube, A. Pelter, K. Smith, P. Blatcher, S. Warren, *Tetrahedron Lett.*, 1978, 2345.

114. M. R Bryce, A. J. Moore, A. S. Batsanov, J. A .K. Howard, *Unpublished results.*

115. M. R Bryce, A. J. Moore, A. Green, *Unpublished results.*

116. K. E. Koenig, W. P. Weber, *Tetrahedron Lett.*,1974, 2275.

117. M. Narita, C. U. Pittman, *Synthesis*, 1976, 489.

118. a) L. S.. Hendriksen, E. S. S. Kristiansen, *Int. J. Sulfur Chem.*, 1972, **2**, 133; b) W-H. Pan, J. P. Fackler, H-W. Chen, *Inorg. Chem.*, 1981, **20**, 856; c) L. Hendricksen, *Acta Chem. Scand.*, 1967, **21**, 1981.

119. S. Chakroune, *Ph. D. Thesis*, Université Montpellier II, 1993.

120. F. Wudl, E. Aharon-Shalom, S. H. Bertz, *J. Org. Chem.*, 1981, **46**, 4612.

121. M. V. Lakshmikantham, M. P. Cava, *J. Org. Chem.*, 1976, **41**, 883.

122. T. K. Hansen, M. V. Lakshimantham, M. P. Cava, R. M. Metzger, J. Becher, *J. Org. Chem.*, 1991, **56**, 2720.

123. J. Nakayama, K. Fujiwara, K. Hoshino, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 3567.

124. C. Allen, J. C. A. Boeyens, A. G. Briggs, L. Denner, A. J. Markwell, D. H. Reid, B. G. Rose, *J. Chem. Soc., Chem. Commun.*, 1987, 967.

125. H. W. Roesky, K. L. Weber, U. Seseke, W. Pinkert, M. Noltenmeyer, W. Clegg, G. M. Sheldrick, *J. Chem. Soc., Dalton Trans.*, 1985, 565.

126. D. H. R. Barton, M. B. Hall, Z. Lin, S. I. Parekh, J. Reibenspies, *J. Am. Chem. Soc.*, 1993, **115**, 5056.

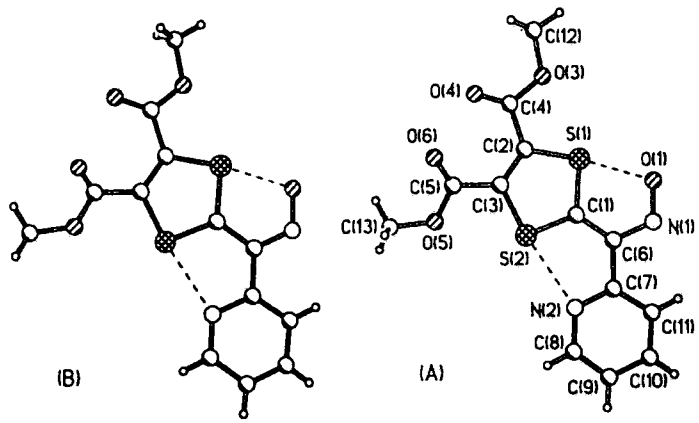
127. T. K. Hansen, Ph.D. Thesis, *University of Odense*, Denmark, 1992.

128. A. J. Moore, M.R. Bryce, *Unpublished results.*

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	$C_{13}H_{10}N_2O_5S_2$	
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) Å	$\alpha = 90°$
	b = 9.512 (4) Å	$\beta = 107.53\ (1)°$
	c = 13.669 (6) Å	$\gamma = 90°$
Space group	P2 (1)/c (No. 14)	
Z value	8	
Density (calculated)	1.565 Mgm^{-3}	
F_{000}	1392	
μ / cm^{-1}	4.1	

Intensity Measurements

Radiation	Mo-K_α
Temperature	20°C
$2\theta_{max}$	46.5°
No. of reflections measured	Total: 10766
	Independent: 3983

Structure Solution and Refinement

Structure solution	Direct methods
Refinement	Full-matrix least-squares
Goodness of Fit Indicator	1.064

Bond lengths / Å

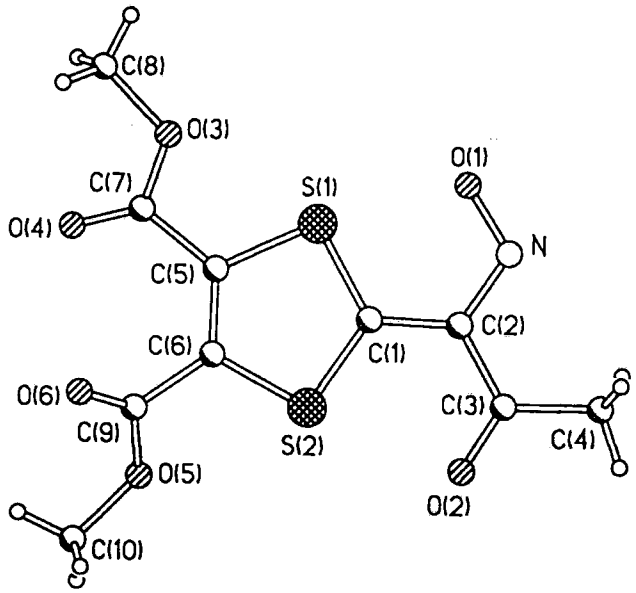
S(1A)-C(1A)	1.732(4)	S(1A)-C(2A)	1.755(4)
S(1A)-O(1A)	2.359(3)	S(2A)-C(1A)	1.712(4)
S(2A)-C(3A)	1.732(4)	S(2A)-N(2A)	2.698(3)
O(1A)-N(1A)	1.266(4)	O(3A)-C(4A)	1.323(5)
O(3A)-C(12A)	1.442(5)	O(4A)-C(4A)	1.190(5)
O(5A)-C(5A)	1.331(5)	O(5A)-C(13A)	1.456(5)
O(6A)-C(5A)	1.180(5)	N(1A)-C(6A)	1.345(5)
N(2A)-C(7A)	1.329(5)	N(2A)-C(8A)	1.353(5)
C(1A)-C(6A)	1.385(5)	C(2A)-C(3A)	1.343(5)
C(2A)-C(4A)	1.489(5)	C(3A)-C(5A)	1.505(5)
C(6A)-C(7A)	1.492(5)	C(7A)-C(11A)	1.399(5)
C(8A)-C(9A)	1.359(6)	C(9A)-C(10A)	1.382(6)
C(10A)-C(11A)	1.377(5)	S(1B)-C(1B)	1.720(4)
S(1B)-C(2B)	1.745(4)	S(1B)-O(1B)	2.353(3)
S(2B)-C(1B)	1.720(4)	S(2B)-C(3B)	1.729(4)
S(2B)-N(2B)	2.682(3)	O(1B)-N(1B)	1.288(4)
O(3B)-C(4B)	1.314(5)	O(3B)-C(12B)	1.444(5)
O(4B)-C(4B)	1.197(5)	O(5B)-C(5B)	1.324(5)
O(5B)-C(13B)	1.452(5)	O(6B)-C(5B)	1.195(5)
N(1B)-C(6B)	1.336(5)	N(2B)-C(7B)	1.336(5)
N(2B)-C(8B)	1.339(5)	C(1B)-C(6B)	1.409(5)
C(2B)-C(3B)	1.347(5)	C(2B)-C(4B)	1.491(5)
C(3B)-C(5B)	1.504(6)	C(6B)-C(7B)	1.475(5)
C(7B)-C(11B)	1.409(5)	C(8B)-C(9B)	1.380(6)
C(9B)-C(10B)	1.358(6)	C(10B)-C(11B)	1.380(5)

Bond angles / °

C(1A)-S(1A)-C(2A)	94.9(2)	C(1A)-S(1A)-O(1A)	77.5(1)
C(2A)-S(1A)-O(1A)	171.4(2)	C(1A)-S(2A)-C(3A)	95.9(2)
C(1A)-S(2A)-N(2A)	76.6(2)	C(3A)-S(2A)-N(2A)	172.4(2)
N(1A)-O(1A)-S(1A)	106.0(2)	C(4A)-O(3A)-C(12A)	117.0(3)
C(5A)-O(5A)-C(13A)	115.6(3)	O(1A)-N(1A)-C(6A)	115.3(3)
C(7A)-N(2A)-C(8A)	117.9(3)	C(7A)-N(2A)-S(2A)	99.3(2)
C(8A)-N(2A)-S(2A)	142.9(3)	C(6A)-C(1A)-S(2A)	124.6(3)
C(6A)-C(1A)-S(1A)	119.8(3)	S(2A)-C(1A)-S(1A)	115.6(2)
C(3A)-C(2A)-C(4A)	127.0(3)	C(3A)-C(2A)-S(1A)	116.4(3)
C(4A)-C(2A)-S(1A)	116.4(3)	C(2A)-C(3A)-C(5A)	126.3(4)
C(2A)-C(3A)-S(2A)	117.1(3)	C(5A)-C(3A)-S(2A)	116.3(3)
O(4A)-C(4A)-O(3A)	124.8(4)	O(4A)-C(4A)-C(2A)	125.1(4)
O(3A)-C(4A)-C(2A)	110.1(3)	O(6A)-C(5A)-O(5A)	125.0(4)
O(6A)-C(5A)-C(3A)	125.2(4)	O(5A)-C(5A)-C(3A)	109.7(3)
N(1A)-C(6A)-C(1A)	121.3(3)	N(1A)-C(6A)-C(7A)	114.7(3)
C(1A)-C(6A)-C(7A)	123.9(3)	N(2A)-C(7A)-C(11A)	122.6(3)
N(2A)-C(7A)-C(6A)	115.7(3)	C(11A)-C(7A)-C(6A)	121.8(3)
N(2A)-C(8A)-C(9A)	122.8(4)	C(8A)-C(9A)-C(10A)	119.3(4)
C(11A)-C(10A)-C(9A)	118.9(4)	C(10A)-C(11A)-C(7A)	118.4(4)
C(1B)-S(1B)-C(2B)	95.2(2)	C(1B)-S(1B)-O(1B)	77.4(2)
C(2B)-S(1B)-O(1B)	172.1(2)	C(1B)-S(2B)-C(3B)	95.2(2)
C(1B)-S(2B)-N(2B)	77.6(2)	C(3B)-S(2B)-N(2B)	172.8(2)
N(1B)-O(1B)-S(1B)	106.2(2)	C(4B)-O(3B)-C(12B)	117.1(3)
C(5B)-O(5B)-C(13B)	116.0(3)	O(1B)-N(1B)-C(6B)	115.4(3)
C(7B)-N(2B)-C(8B)	118.2(3)	C(7B)-N(2B)-S(2B)	98.7(2)
C(8B)-N(2B)-S(2B)	143.0(3)	C(6B)-C(1B)-S(2B)	123.1(3)
C(6B)-C(1B)-S(1B)	121.0(3)	S(2B)-C(1B)-S(1B)	115.9(2)
C(3B)-C(2B)-C(4B)	127.0(3)	C(3B)-C(2B)-S(1B)	116.1(3)
C(4B)-C(2B)-S(1B)	116.8(3)	C(2B)-C(3B)-C(5B)	127.0(4)
C(2B)-C(3B)-S(2B)	117.5(3)	C(5B)-C(3B)-S(2B)	115.3(3)
O(4B)-C(4B)-O(3B)	125.2(4)	O(4B)-C(4B)-C(2B)	124.3(4)
O(3B)-C(4B)-C(2B)	110.4(3)	O(6B)-C(5B)-O(5B)	125.4(4)
O(6B)-C(5B)-C(3B)	124.3(4)	O(5B)-C(5B)-C(3B)	110.2(3)
N(1B)-C(6B)-C(1B)	119.9(3)	N(1B)-C(6B)-C(7B)	116.4(3)
C(1B)-C(6B)-C(7B)	123.7(3)	N(2B)-C(7B)-C(11B)	122.4(3)
N(2B)-C(7B)-C(6B)	116.9(3)	C(11B)-C(7B)-C(6B)	120.7(3)

N(2B)-C(8B)-C(9B)	122.9(4)	C(10B)-C(9B)-C(8B)	118.5(4)
C(9B)-C(10B)-C(11A)	120.8(4)	C(10B)-C(11B)-C(7B)	117.1(4)

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



Crystal Data

Empirical Formula	$C_{10}H_9NO_6S_2$	
Formula Weight	303.30	
Crystal Colour, habit	Emerald, pinakoidal	
Crystal dimensions/ mm	0.44 x 0.24 x 0.20	
Crystal system	Monoclinic	
Unit cell parameters	a = 7.4523(15)	$\alpha = 90°$
	b = 15.911(3)	$\beta = 107.749(14)°$
	c = 11.30(2)	$\gamma = 90°$
Space group	P2(1)/c (No. 14)	
Z value	4	
Density (calculated)	1.575 Mgm^{-3}	
F_{000}	624	
μ / cm^{-1}	4.4	

Intensity Measurements

Radiation	Mo-K_α
Temperature	20 °C
$2\theta_{max}$	50°
No. of reflections measured	Total: 3019
	Independent: 2249

Structure Solution and Refinement

Structure solution	Direct methods
Refinement	Full-matrix least-squares
Goodness of Fit Indicator	1.060

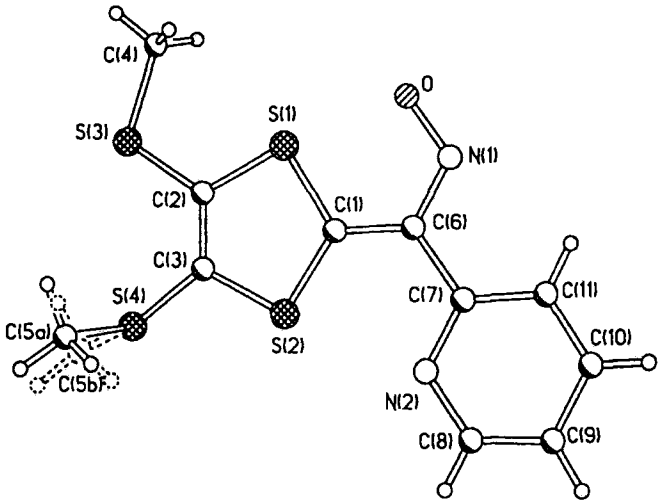
Bond lengths / Å

S(1)-C(1)	1.707 (2)	O(5)-C(10)	1.463 (2)
S(1)-C(5)	1.746 (2)	O(6)-C(9)	1.195 (2)
S(2)-C(1)	1.705 (2)	N-C(2)	1.357 (3)
S(2)-C(6)	1.723 (2)	C(1)-C(2)	1.409 (3)
O(1)-N	1.264 (3)	C(2)-C(3)	1.465 (3)
O(2)-C(3)	1.214 (3)	C(3)-C(4)	1.498 (3)
O(3)-C(7)	1.313 (3)	C(5)-C(6)	1.348 (3)
O(3)-C(8)	1.453 (3)	C(5)-C(7)	1.492 (3)
O(4)-C(7)	1.181 (3)	C(6)-C(9)	1.498 (3)
O(5)-C(9)	1.319 (3)		

Bond angles

C(1)-S(1)-C(5)	95.13 (9)	C(2)-C(3)-C(4)	119.4 (2)
C(1)-S(2)-C(6)	95.62 (10)	C(6)-C(5)-C(7)	126.5 (2)
C(7)-O(3)-C(8)	117.0 (2)	C(6)-C(5)-S(1)	116.1 (2)
C(9)-O(5)-C(10)	116.5 (2)	C(7)-C(5)-S(1)	117.4 (2)
O(1)-N-C(2)	114.7 (2)	C(5)-C(6)-C(9)	127.0 (2)
C(2)-C(1)-S(2)	121.9 (2)	C(5)-C(6)-S(2)	116.9 (2)
C(2)-C(1)-S(1)	121.9 (2)	C(9)-C(6)-S(2)	116.0 (1)
S(2)-C(1)-S(1)	116.19 (12)	O(4)-C(7)-O(3)	125.6 (2)
N-C(2)-C(1)	121.3 (2)	O(4)-C(7)-C(5)	124.9 (2)
N-C(2)-C(3)	117.6 (2)	O(3)-C(7)-C(5)	109.5 (2)
C(1)-C(2)-C(3)	121.1 (2)	O(6)-C(9)-O(5)	126.0 (2)
O(2)-C(3)-C(2)	119.2 (2)	O(6)-C(9)-C(6)	124.2 (2)
O(2)-C(3)-C(4)	121.5 (2)	O(5)-C(9)-C(6)	109.8 (2)

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	$C_{11}H_{10}N_2OS_4$	
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	α = 103.641 (5)°
	b = 8.6368 (5) Å	β = 92.427 (6)°
	c = 10.5357 (6) Å	γ = 98.716 (6)°
Space group	P-1	
Z value	2	
Density (calculated)	1.559 g cm^{-3}	
F_{000}	324	
μ / cm^{-1}	7.0	

Intensity Measurements

Radiation	Mo-K_α
Temperature	20°C
$2\theta_{max}$	50
No. of reflections measured	Total: 2894
	Independent: 2334

Structure Solution and Refinement

Structure solution	Direct methods
Refinement	Full-matrix least-squares
Goodness of Fit Indicator	1.017

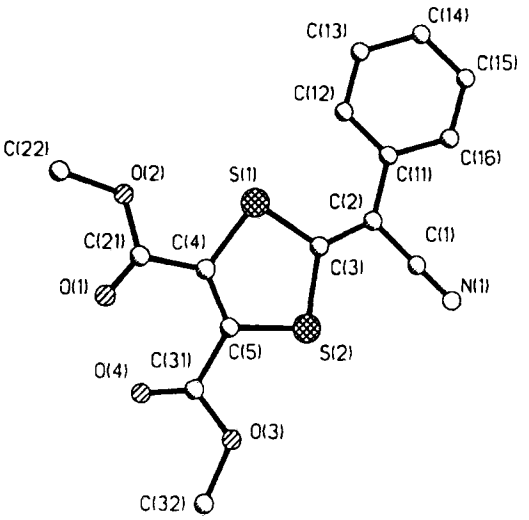
Bond lengths / Å

S(1)-C(1)	1.730(2)	S(1)-C(2)	1.758(2)
S(1)-O	2.359(1)	S(2)-C(1)	1.703(2)
S(2)-C(3)	1.736(2)	S(2)-N(2)	2.734(2)
S(3)-C(2)	1.739(2)	S(3)-C(4)	1.788(2)
S(4)-C(5B)	1.65(2)	S(4)-C(3)	1.755(2)
S(4)-C(5A)	1.845(12)	O-N(1)	1.276(2)
N(1)-C(6)	1.345(2)	N(2)-C(7)	1.333(2)
N(2)-C(8)	1.341(2)	C(1)-C(6)	1.417(2)
C(2)-C(3)	1.347(3)	C(6)-C(7)	1.468(2)
C(7)-C(11)	1.398(2)	C(8)-C(9)	1.372(3)
C(9)-C(10)	1.378(3)	C(10)-C(11)	1.361(3)

Bond angles /°

C(1)-S(1)-C(2)	95.06(8)	C(1)-S(1)-O	77.60(7)
C(2)-S(1)-O	172.58(7)	C(1)-S(2)-C(3)	96.46(8)
C(1)-S(2)-N(2)	76.60(7)	C(3)-S(2)-N(2)	172.98(7)
C(2)-S(3)-C(4)	103.87(9)	C(5B)-S(4)-C(3)	101.4(6)
C(3)-S(4)-C(5A)	99.8(4)	N(1)-O-S(1)	106.4(1)
O-N(1)-C(6)	115.7(2)	C(7)-N(2)-C(8)	117.7(2)
C(7)-N(2)-S(2)	97.8(1)	C(8)-N(2)-S(2)	144.1(1)
C(6)-C(1)-S(2)	124.2(1)	C(6)-C(1)-S(1)	120.3(1)
S(2)-C(1)-S(1)	115.5(1)	C(3)-C(2)-S(3)	122.5(1)
C(3)-C(2)-S(1)	116.5(1)	S(3)-C(2)-S(1)	121.0(1)
C(2)-C(3)-S(2)	116.4(1)	C(2)-C(3)-S(4)	126.0(1)
S(2)-C(3)-S(4)	117.6(1)	N(1)-C(6)-C(1)	120.0(2)
N(1)-C(6)-C(7)	116.0(2)	C(1)-C(6)-C(7)	124.0(2)
N(2)-C(7)-C(11)	121.9(2)	N(2)-C(7)-C(6)	116.9(2)
C(11)-C(7)-C(6)	121.2(2)	N(2)-C(8)-C(9)	123.8(2)
C(8)-C(9)-C(10)	118.0(2)	C(11)-C(10)-C(9)	119.5(2)
C(10)-C(11)-C(7)	119.2(2)		

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



Crystal Data

Empirical Formula	$C_{15}H_{11}NO_4S_2$	
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) Å	α = 90°
	b = 7.391(3) Å	β = 103.07(3)°
	c = 16.178 (8) Å	γ = 90°
Space group	P2(1) / n	
Z value	4	
Density (calculated) / Mgm^{-3}	1.469	
F_{000}	688	

Intensity Measurements

Radiation	Mo-K_α
Temperature	293(2)
$2\theta_{max}$	50.04
No. of reflections measured	Total: 3535
	Independent: 2655

Structure Solution and Refinement

Structure solution	Direct methods
Refinement	Full-matrix least-squares
Goodness of Fit Indicator	0.798

Bond lengths / Å

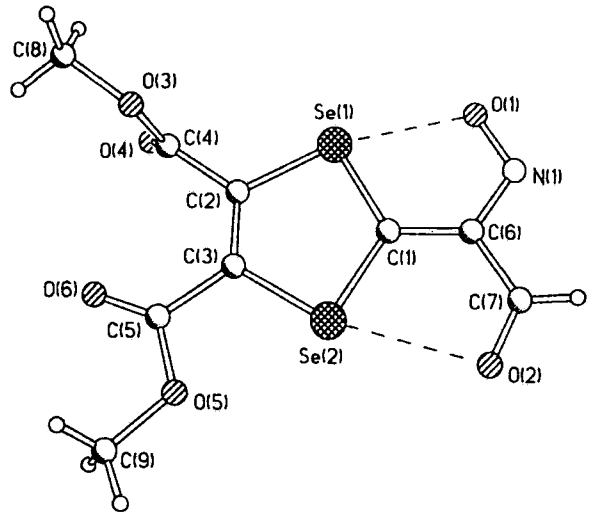
S(1)-C(3)	1.743(3)	C(11)-C(12)	1.391(4)
S(1)-C(4)	1.746(3)	C(11)-C(16)	1.392(4)
S(2)-C(5)	1.739(3)	C(12)-C(13)	1.379(5)
S(2)-C(3)	1.756(3)	C(12)-H(12)	0.94(4)
O(1)-C(21)	1.199(3)	C(13)-C(14)	1.373(6)
O(2)-C(21)	1.330(3)	C(13)-H(13)	0.95(4)
O(2)-C(22)	1.454(4)	C(14)-C(15)	1.378(6)
O(3)-C(31)	1.322(4)	C(14)-H(14)	0.93(4)
O(3)-C(32)	1.463(4)	C(15)-C(16)	1.374(5)
O(4)-C(31)	1.188(4)	C(15)-H(15)	0.98(5)
N(1)-C(1)	1.148(4)	C(16)-H(16)	0.90(3)
C(1)-C(2)	1.428(4)	C(22)-H(22a)	1.05(6)
C(2)-C(3)	1.371(4)	C(22)-H(22b)	0.85(5)
C(2)-C(11)	1.477(4)	C(22)-H(22c)	1.05(6)
C(4)-C(5)	1.351(4)	C(32)-H(32a)	1.00(6)
C(4)-C(21)	1.486(4)	C(32)-H(32b)	0.91(5)
C(5)-C(31)	1.496(4)	C(32)-H(32c)	0.96(5)

Bond angles / °

C(3)-S(1)-C(4)	96.37(13)	C(13)-C(14)-H(14)	119(2)
C(5)-S(2)-C(3)	96.39(13)	C(15)-C(14)-H(15)	121(2)
C(21)-O(2)-C(22)	116.2(3)	C(16)-C(15)-C(14)	120.1(4)
C(31)-O(3)-C(32)	116.2(3)	C(16)-C(15)-H(15)	117(3)
N(1)-C(2)-C(2)	179.0(3)	C(14)-C(15)-H(15)	123(3)
C(3)-C(2)-C(1)	115.5(3)	C(16)-C(15)-C(11)	121.7(3)
C(3)-C(2)-C(11)	127.4(3)	C(15)-C(16)-H(16)	120(2)
C(1)-C(2)-C(11)	117.0()	C(11)-C(16)-H(16)	119(2)
C(2)-C(3)-S(1)	125.7(2)	O(1)-C(21)-O(2)	125.0(3)
C(2)-C(3)-S(2)	120.9(2)	O(1)-C(21)-C(4)	125.2(3)

S(1)-C(3)-S(2)	113.4(2)	O(2)-C(21)-C(4)	109.8(2)
C(5)-C(4)-C(21)	126.7(2)	O(2)-C(22)-H(22a)	105(3)
C(5)-C(4)-S(1)	116.9(2)	O(2)-C(22)-H(22b)	113(3)
C(21)-C(4)-S(1)	116.3(2)	H(22a)-C(22)-H(22b)	108(5)
C(4)-C(5)-C(31)	126.6(3)	O(2)-C(22)-H(22c)	99(3)
C(4)-C(5)-S(2)	116.7(2)	H(22a)-C(22)-H(22c)	117(4)
C(31)-C(5)-S(2)	116.4(2)	H(22b)-C(22)-H(22c)	115(4)
C(12)-C(11)-C(16)	117.2(3)	O(4)-C(31)-O(3)	125.4(3)
C(12)-C(11)-C(2)	123.0(3)	O(4)-C(31)-C(5)	124.3(3)
C(16)-C(11)-C(2)	119.6(3)	O(3)-C(31)-C(5)	110.2(2)
C(13)-C(12)-C(11)	121.0(4)	O(3)-C(32)-H(32a)	100(3)
C(12)-C(12)-H(12)	121(2)	O(3)-C(32)-H(32b)	108(3)
C(11)-C(12)-H(12)	118(2)	H(32a)-C(32)-H(32b)	115(5)
C(14)-C(13)-C(12)	120.7(4)	O(3)-C(32)-H(32c)	107(3)
C(14)-C(13)-H(13)	126(3)	H(32a)-C(32)-H(32c)	108(4)
C(12)-C(13)-H(13)	114(3)	H(32b)-C(32)-H(32c)	117(4)
C(13)-C(14)-C(15)	119.3(3)		

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



Crystal Data

Empirical Formula	$C_9H_7NO_6Se_2$	
Formula Weight	383.08	
Crystal Colour	Green	
Crystal dimensions/ mm	0.40 x 0.20 x 0.18	
Crystal system	orthorhombic	
Unit cell parameters	a = 9.270(1)Å	$\alpha = 90°$
	b = 24.337(3)Å	$\beta = 90°$
	c = 5.3406 (6)Å	$\gamma = 90°$
Space group	Pna2(1)	
Z value	4	
Density (calculated)	$2.112 Mgm^{-3}$	
F_{000}	736	

Intensity Measurements

Radiation	Mo-K_α
Temperature	20°C
$2\theta_{max}$	51.5
No. of reflections measured	Total: 4896
	Independent: 1667

Structure Solution and Refinement

Structure solution	Direct methods
Refinement	Full-matrix least-squares
Goodness of Fit Indicator	1.104

Bond lengths / Å

Se(1)-C(1)	1.857(10)	Se(1)-C(2)	1.886(10)
Se(1)-O(1)	2.513(8)	Se(2)-C(1)	1.852(10)
Se(2)-C(3)	1.887(10)	Se(2)-O(2)	2.733(8)
O(1)-N(1)	1.244(13)	O(2)-C(7)	1.21(2)
O(3)-C(4)	1.334(13)	O(3)-C(8)	1.441(13)
O(4)-C(4)	1.171(14)	O(5)-C(5)	1.322(14)
O(5)-C(9)	1.439(12)	O(6)-C(5)	1.207(12)
N(1)-C(6)	1.368(14)	C(1)-C(6)	1.393(14)
C(2)-C(3)	1.33(2)	C(2)-C(4)	1.502(15)
C(3)-C(5)	1.492(14)	C(6)-C(7)	1.44(2)

Bond angles / °

C(1)-S(1)-C(2)	92.5(5)	C(1)-S(1)-O(1)	73.5(4)
C(2)-S(1)-O(1)	165.7(4)	C(1)-S(2)-C(3)	92.3(4)
C(1)-S(1)-O(2)	73.6(4)	C(3)-S(2)-O(2)	165.9(4)
N(1)-O(1)-S(1)	107.2(6)	C(7)-O(2)-S(2)	99.0(7)
C(4)-O(3)-C(8)	117.1(10)	C(5)-O(5)-C(9)	117.2(9)
O(1)-N(1)-C(6)	115.7(9)	C(6)-C(1)-S(2)	122.3(8)
C(6)-C(1)-S(1)	120.6(8)	S(2)-C(1)-S(1)	117.1(5)
C(3)-C(2)-C(4)	124.1(9)	C(3)-C(2)-S(1)	118.7(8)
C(4)-C(2)-S(1)	117.2(8)	C(2)-C(3)-C(5)	125.9(10)
C(2)-C(3)-S(2)	119.4(8)	C(5)-C(3)-S(2)	114.7(8)
O(4)-C(4)-O(3)	124.1(10)	O(4)-C(4)-C(2)	126.0(10)
O(3)-C(4)-C(2)	109.8(9)	O(6)-C(5)-O(5)	125.8(10)
O(6)-C(5)-C(3)	123.9(11)	O(5)-C(5)-C(3)	110.1(9)
N(1)-C(6)-C(1)	123.0(11)	N(1)-C(6)-C(7)	115.3(10)
C(1)-C(6)-C(7)	121.7(9)	O(2)-C(7)-C(6)	123.2(9)

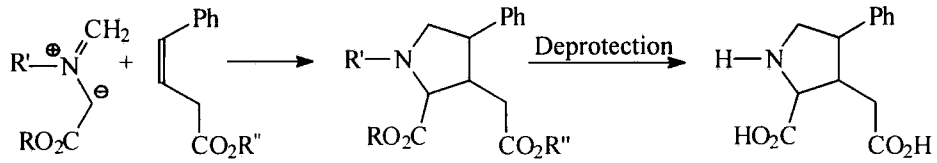
Appendix 2

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 cycloaddtions 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.



262 **263** **264** **265**

***Scheme A2.1**: The desired reaction sequence*

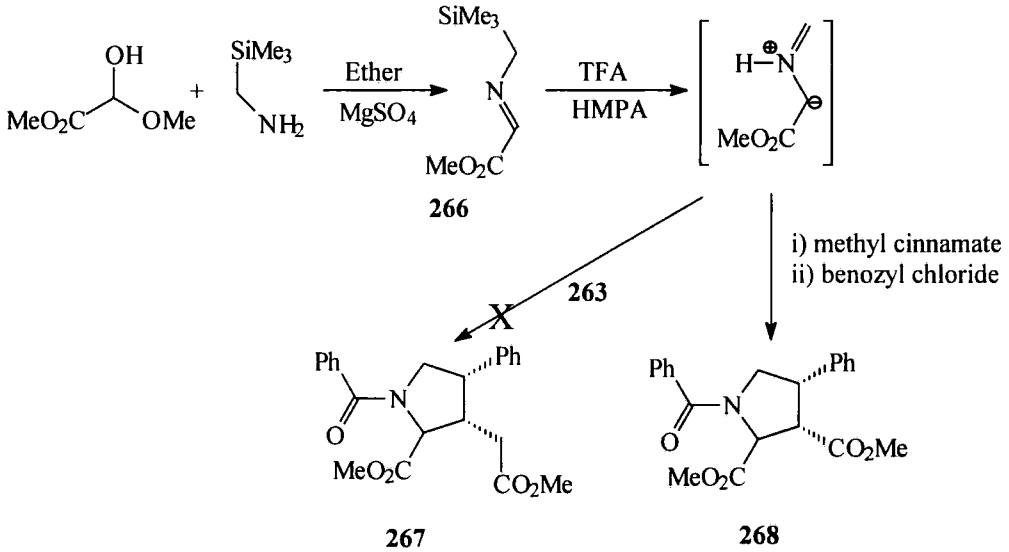
A.2.2 Results and Discussion

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.[131] 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.

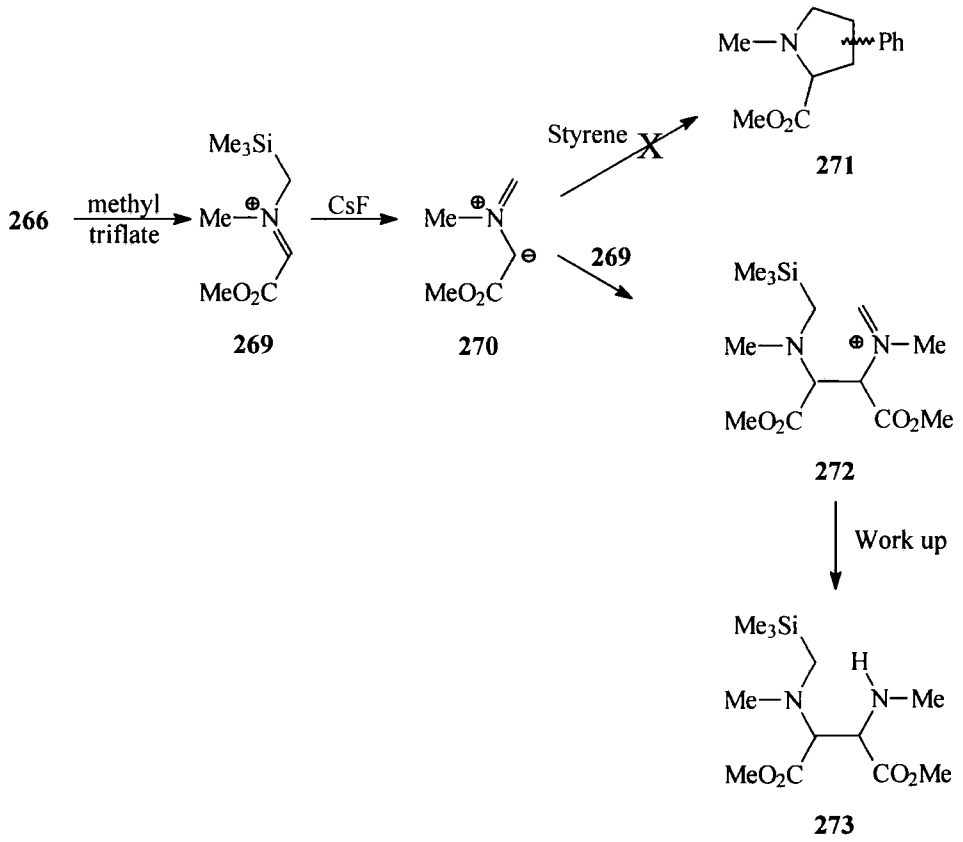


***Scheme A2.2**: Reactions of the Azomethine Ylide*

Methylation of **266** was successful as indicated by the presence of *N*-methyl substituents and the subsquent 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 prescence 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 $CDCl_3$) to be utilised in this manner.



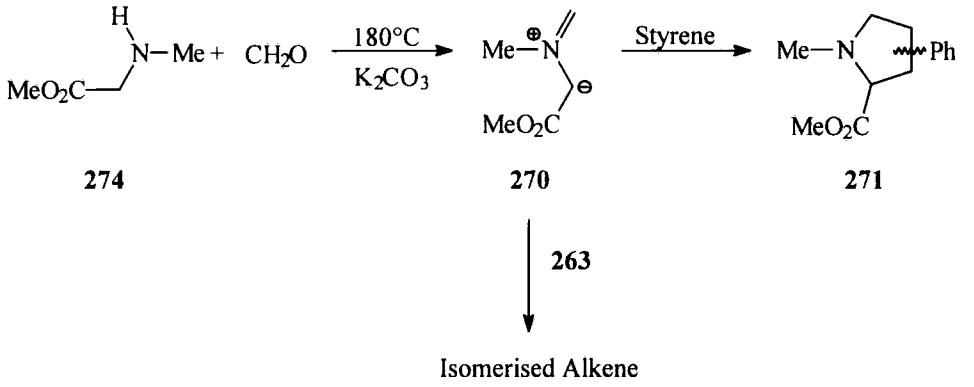
***Scheme A2.3**: Postulated mechanism for the formation of 273*

A2.2.2 Ylides formed from secondary amines and paraformaldehyde

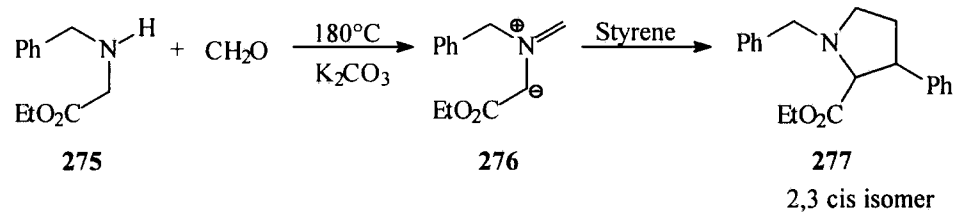
Our attention then turned to a report by Tsuge *et al* that azomethine ylides formed by reaction of sarcosine methyl ester and paraformaldehyde in a sealed tube at 180°C reacted with styrene to form the cycloadduct, **271** (Scheme A2.4).[132] However, treatment of alkene **263** under the reported conditions 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 K_2CO_3 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.

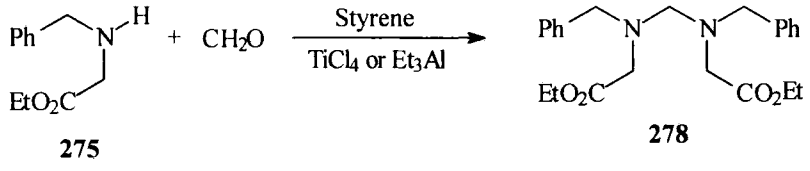


***Scheme A2.4**: Tsuge's Method of Azomethine Ylide Formation*



***Scheme A2.5**: Reaction of Styrene with the Azomethine Ylide Generated from N-Benzylglycine, ethyl ester.*

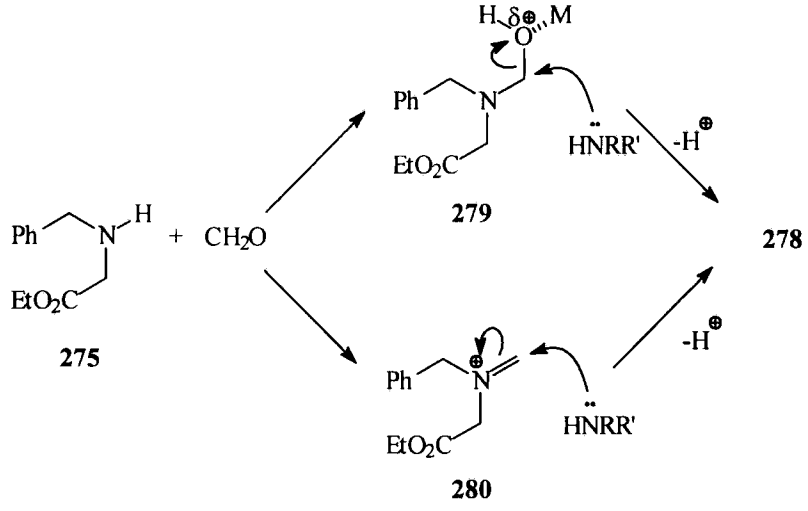
We envisaged that replacement of K_2CO_3 with a stronger dehydrating agent may allow the reaction to yield **277** to proceed at a temperature lower than the 180°C reported by Tsuge.[132] Thus titanium tetrachloride (0.25 equiv) was employed as the dehydrating agent, this ratio is the optimum specified by Carlson and Nilsson for the maximisation of the yield in the formation of imines and enamines using this reagent.[134]



275 **278**

***Scheme A2.6**: Reaction of N-Benzylglycine with Strong Dehydrating Reagents*

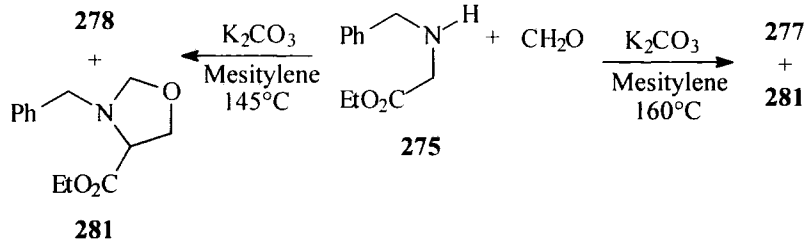
However, rather than the required cycloadduct, **277**, the diamine, **278** was isolated instead, in 23% yield. The potent dehydrating agent triethyl aluminium (1 equiv.) also led to **278** in 24% yield. Two methods of forming the diamine can be envisaged: by reaction of the starting amine with the 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*

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).[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.

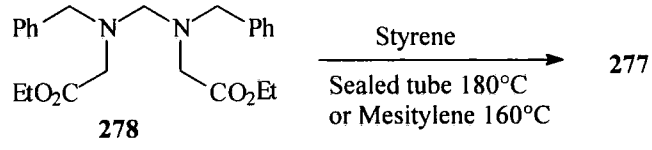


***Scheme A2.8**: Reaction of N-Benzylglycine, ethyl ester with paraformaldehyde at temperatures lower than 180°C*

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 confims that at lower temperatures the azomethine ylide **276** reacts preferentially with formaldehyde over styrene, whereas activated alkenes compete successfully.[135] 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 decompostion of 1,1-diamines

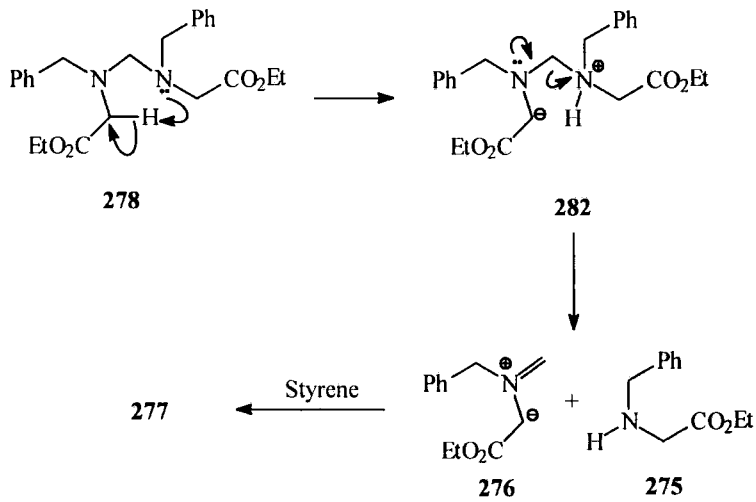
The fact that no cycloadduct **277** was formed at 145°C, but the diamine **278** was obtained, whereas at 160°C the diamine is absent but the cycloadduct **277** was isolated instead, suggests that **278** is a precursor to the ylide **276**.



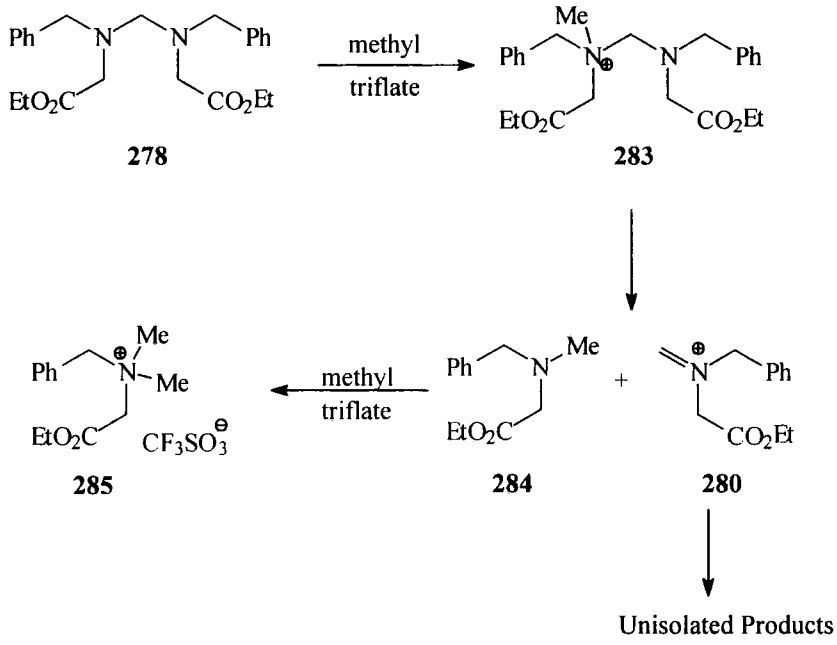
***Scheme A2.9**: 1,1-Diamines as Azomethine Ylide Precursors*

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*

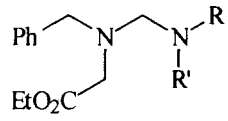
Less reactive methylating regents were tried: methyl iodide failed to methylate the diamine **278**, and although dimethyl sulfate at 50°C methylated the diamine (NMR evidence), subsequent reaction led to an unstable, and uncharacterised compound.

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, *ie* 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, *ie* **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 α 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 °C.



286

***Figure A2.1**: Postulated Azomethine Ylide Precursors*

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-phenyl-pyrrolidine-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*

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 ($2:1^{v}/_{v}$) and then hexane:dimethoxyethane ($2:1^{v}/_{v}$) to yield 2-methylamino-3-(methyl-trimethylsilanylmethyl-amino)-succinic acid dimethyl ester, **273** as a yellow oil (40 mg 10%) *m/z* (FD)290 M^{+}; $\delta_H(CDCl_3)$ 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) $\delta_C(CDCl_3)$ 174.3, 169.7, 72.6, 63.9, 51.7, 51.0, 46.8, 41.8, 35.1, -1.6 and the minor diastereomer $\delta_C(CDCl_3)$ 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 K_2CO_3 (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^{+}); $\delta_H(CDCl_3)$ 7.45-6.99 (m, 10H), 4.08 (d,

J= 12.5Hz, 1H), 3.6 (m, 2H), 3.40 (m, 3H), 3.11 (m, 1H), 2.37 (m, 1H), 2.10 (m, 1H) 1.86 (m, 1H), 0.59 (t, *J*= 8Hz, 3H); $\delta_C(CDCl_3)$ 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 occured. The reaction was stirred at ambient temperature for 15h, then diluted with toluene and washed with aqueous $NaHCO_3$ and brine. The organic layer was dried with $MgSO_4$ and the solvent removed *in vacuo* and the resulting oil chromatographed using hexane:ethyl acetate (5:1 $^v/_v$) as eluent to yield {Benzyl-[(benzyl-ethoxycarbonylmethylamino)-methyl]amino} acetic acid ethyl ester **278**, (90mg, 23%) *m/z* (FD) 398 (M^+); δ_H ($CDCl_3$) 7.35-7.15 (m, 10H) 4.22 (q, *J*=7Hz, 4H) 3.86 (s, 4H) 3.63 (s, 2H) 3.43 (s, 4H) 1.23 (t, *J*=7Hz, 6H); δ_C ($CDCl_3$) 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 ($MgSO_4$). The solvent was removed *in vacuo* to afford an oil which was chromatographed with hexane:ethyl acetate (5:1 $^v/_v$) 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_2CO_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-oxazolidine-4-carboxylic acid ethyl ester **281** as a colourless oil (174mg, 37%). *m/z* (FAB) 235 (M^+); found C; 66.4, H; 7.3, N; 5.9%, $C_{13}H_{17}NO_3$ requires C; 66.4, H; 7.3, N; 6.0 %; δ_H ($CDCl_3$) 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); δ_C ($CDCl_3$) 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, 10mmol), styrene (200 mg, 2.0 mmol) and anhydrous K_2CO_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 strirred at ambient temperature for 1.5h before the temperature was raised to 70°C for 0.5h. The reaction was washed with aqueous $NaHCO_3$ (20 ml) and brine (20ml). The organic phase was dried ($MgSO_4$) 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**, (30mg, 27%). m.p. 96-97°C; m/z (FAB) 520 (M^++149); δ_H ($CDCl_3$) 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 $MgSO_4$ 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**, 2.40g, 60%.

A2.4 References for Appendix 2

129. For a review of Azomethine Chemisty see: O. Tsuge, S. Kanemasa, *Adv. Heterocycl. Chem.*, 1989, **45**, 231.

130. N. Imai, Y. Terao, K. Achiwa, *Chem. Pharm. Bull.*, 1987, **35**, 2085.

131. E. Vedejs, G. R. Martinez, *J. Am. Chem. Soc.*, 1979, **101**,6452.

132. O. Tsuge, S. Kanemasa, M. Ohe, K. Yorozu, S. Takenaka, K. Ueno, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 4067.

133. P. DeShong, D. A. Kell, D. R. Sidler, *J. Org. Chem.*, 1985, **50**, 230.

134. R. Carlson, Å. Nilsson, M. Strömqvist, *Acta Chem. Scand. B*, 1983, **37**, 7.

135. R. Bureau, J. Mortier, M. Joucla, *Bull. Soc. Chim. Fr.*, 1993, **130**, 584.

Appendix 3

List of Research Colloqiua, Lectures and Seminars

A.3 List of Research Colloqiua, Lectures and Seminars

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

* Denotes attended by the author.

1992-1993 (August 1 - July 31)

1992

October 15	Dr.M. Glazier & Dr. S. Tarling, Oxford University & Birbeck College London. It pays to be British!- The chemists role as an expert witness in patent litigation
October 20	Dr.H.E. Bryndza, Du pont central Research Synthesis, reactions and thermochemistry of metal (alkyl) cyanide complexes and their impact on olefin hydrocyanation catalysis*
October 22	Prof.A. Davies, University College London *The Ingold-Albert Lecture* The behavior of hydrogen as a pseudo-metal
October 28	Dr.J.K. Cockcroft, University of Durham Recent developments in powder diffraction
October 29	Dr.J. Emsley, Imperial College London The shocking history of phosphorus*
November 4	Dr.T.P. Kee, University of Leeds Synthesis and co-ordination chemistry of silylated phosphites
November 5	Dr.C.J. Ludman, University of Durham Explosions, A demonstration lecture*
November 11	Dr.D. Robins†, Glasgow University Pyrrolizidine alkanloids: Biological activity, biosynthesis and benefits*
November 12	Prof.M.R. Truter, University College London Luck and logic in Host-Guest chemsitry
November 18	Dr.R. Nix†, Queen Mary College London Characterisation of heterogeneous catalysts
November 25	Prof. Y. Vallee, University of Caen. Reactive thiocarbonyl compounds*
November 25	Prof.L.D. Quin†, University of Massachusetts, Amherst Fragmentation of phosphorus heterocycles as a route to phosphoryl species with uncommon bonding
November 26	Dr.D. Humber, Glaxo, Greenford AIDS- The development of a novelseries of inhibitors of HIV
December 2	Prof.A.F. Hegarty, University College, Dublin Highly reactive enols stabilised by steric protection
December 2	Dr.R.A. Aitken†, University of St. Andrews The versatile cycloaddition chemistry $Bu_3P.CS_2$*
December 3	Prof.P. Edwards, Birmingham University *The SCI Lecture*- What is a metal?

December 9 Dr.A.N. Burgess, ICI Runcorn
The structure of perfluorinated ionomer membranes

1993

January 20 Dr.D.C. Clary†, Univeristy 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
Chemsitry on the flat reactivity of ordered systems

March 10 Dr.P.K. Baker, University College of N. Wales, Bangor
Chemistry of highly versitile 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

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 frequencey 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 enviromentally responsible carbon dioxide.

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

October 4 Prof. F.J. Feher†, University of California, Irivine, 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 caarbonyl 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 Appelton 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 apllications 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 potenials

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.

1994-1995 (August 1 - July 31)

1994

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.