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**SYNTHESIS AND REACTIONS OF DITHIAZINES
AND RELATED HETEROCYCLES**

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(Graduate Society)

Department of Chemistry
University of Durham

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

September 1993.



14 JAN 1994

DECLARATION

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Dedicated to the Memory of

George Robert Davison

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LIST OF ABBREVIATIONS

CI	chemical ionisation
<i>m</i> CPBA	<i>meta</i> -chloroperoxybenzoic acid
CV	cyclic voltammetry
DCI	desorptive chemical ionisation
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEI	desorptive electron (impact) ionisation
DMAD	dimethyl acetylenedicarboxylate
DMF	<i>N,N</i> -dimethylformamide
DMS	dimethyl sulphate
DMSO	dimethyl sulphoxide
EI	electron (impact) ionisation
ESR	electron spin resonance
FAB	fast atom bombardment
IR	infrared
ISC	inter-system conversion
LAH	lithium aluminium hydride
MMPP	magnesium monoperoxyphthalic acid
MS	mass spectrometry
NMR	nuclear magnetic resonance
TCNQ	7,7,8,8-tetracyano- <i>p</i> -quinodimethane
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	tetramethylsilane
UV	ultraviolet
UV-VIS	ultraviolet-visible
VT	variable temperature

ABSTRACT

Synthesis and Reactions of Dithiazines and Related Heterocycles

by

Gordon R. Davison B.Sc. (Hons.)

A thesis submitted for the degree of Doctor of Philosophy
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September 1993

The chemistry of heterocyclothiazenes is surveyed, with particular emphasis being placed on the dithiazine heterocyclic class. The known synthetic routes to dithiazines are discussed and the chemical, physical and spectroscopic properties of these heterocycles are reviewed.

A wide range of novel 1,4,2-dithiazine derivatives have been efficiently synthesised, the key synthetic step being nitrogen ring expansion of 1,3-dithiolium cation salts by iodine-ammonia methodology. The utility and scope of this methodology have been developed. A variety of analytical techniques have been used to characterise the 1,4,2-dithiazines. Notably, the first X-ray crystal structures of the heterocycle are presented. Mechanisms for the ring expansion reaction are discussed.

Reactions of 1,4,2-dithiazines have been extensively studied; the compounds act as precursors to a variety of other heterocyclic systems (isothiazoles, dithiins and thiophenes), and provide access to useful synthetic intermediates (mono-protected 1,2-dithiols).

The iodine-ammonia approach has also been used to synthesise derivatives of the rare 1,2,3-dithiazine system, representing the first chemical route to this heterocycle. In related studies, the X-ray crystal structure of a 1,2-dithiole-3-thione is described; the molecule is characterised by a three-dimensional array of non-bonded intermolecular close sulphur-sulphur contacts.

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CHAPTER 1

INTRODUCTION



1.1 General Introduction.

The study of heterocyclic chemistry continues to be of considerable interest to both the academic and commercial sectors. It has been estimated that approximately fifty percent of the ten million compounds recorded in Chemical Abstracts are heterocyclic.^{1a} A significant proportion of biologically active natural products and the majority of synthetically derived pharmaceutical and agrochemical products are based on heterocyclic systems. However, so much research has now been carried out in this area, that it is no longer a simple matter to find new structural classes of heterocyclic compound.

There is continued significant interest in the study of organic heterocyclic systems containing multiple sulphur and nitrogen atoms, the heterocyclothiazenes.^{1a-1c} These heterocycles exhibit a fascinating array of physical and chemical properties. The compounds are, therefore, finding applications in fields as diverse as agrochemicals, pharmaceuticals and food additives. There are also initiatives to use cyclothiazene systems as components in organic metals. Heterocyclothiazene systems fall on the border between organic and inorganic chemistry. They contain two of the three most widespread heteroatoms in organic chemistry. The ring systems are usually electron rich and inherently reactive. These attributes make new heterocyclothiazenes worthwhile and challenging synthetic targets.

Oakley has produced a detailed review on binary sulphur-nitrogen compounds, *i.e.* those containing only sulphur and nitrogen, and heterocyclothiazenes, *i.e.* compounds containing sulphur, nitrogen and carbon.^{1b} A useful distinction is made between the various classes of heterocyclothiazene by consideration of their ring size and π -electron count. Representative examples of systems which have been obtained are included in Figure 1; not all isomeric possibilities are shown. Single canonical forms, rather than delocalised π -electron systems, are depicted to clarify the origins of π -electrons. The use of π -electron counting to subdivide the structural classes is of value, but this approach has some limitations. By definition, in-plane non-bonding electrons, *i.e.* lone pairs on sulphur and nitrogen atoms, are ignored in this treatment.

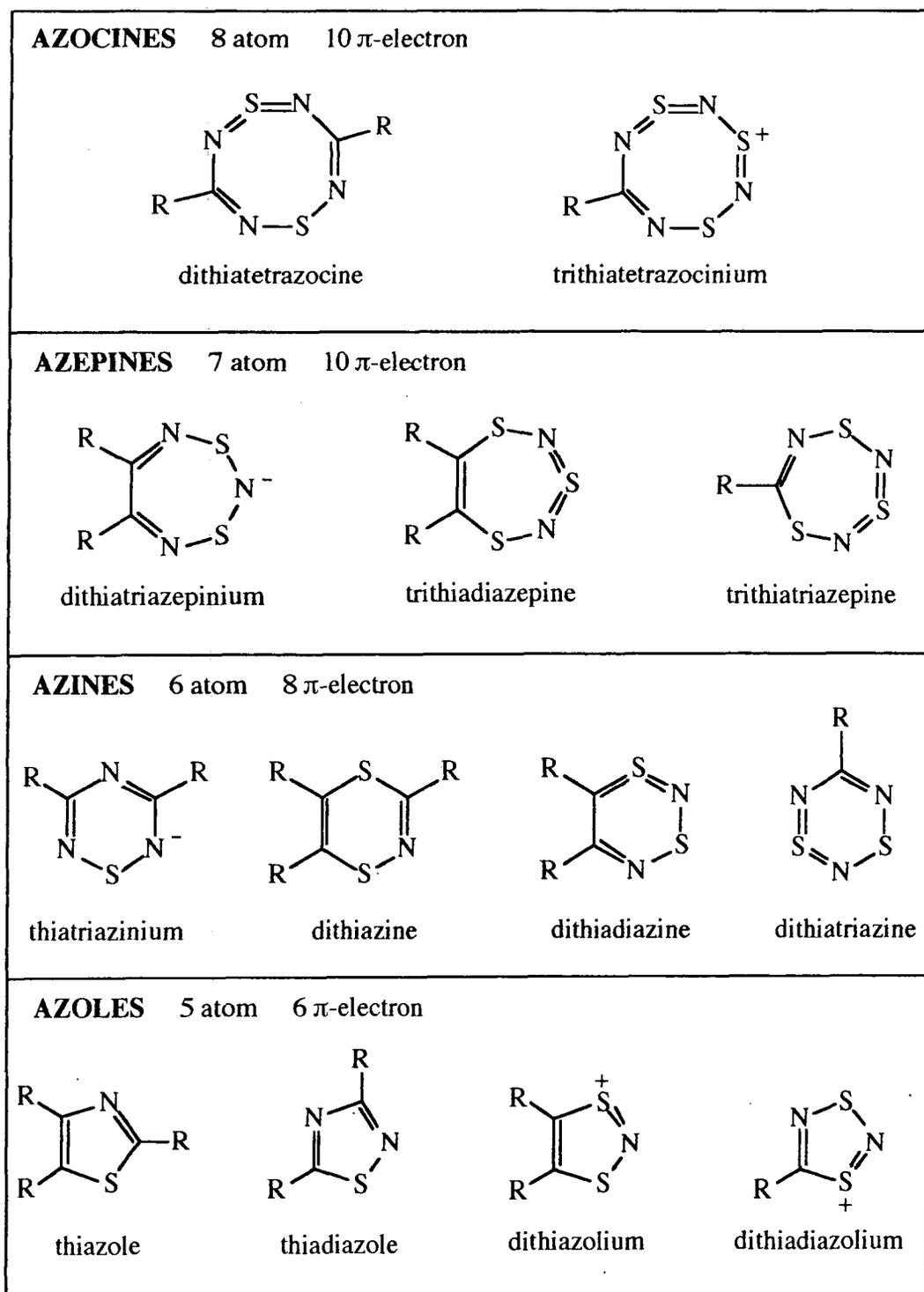


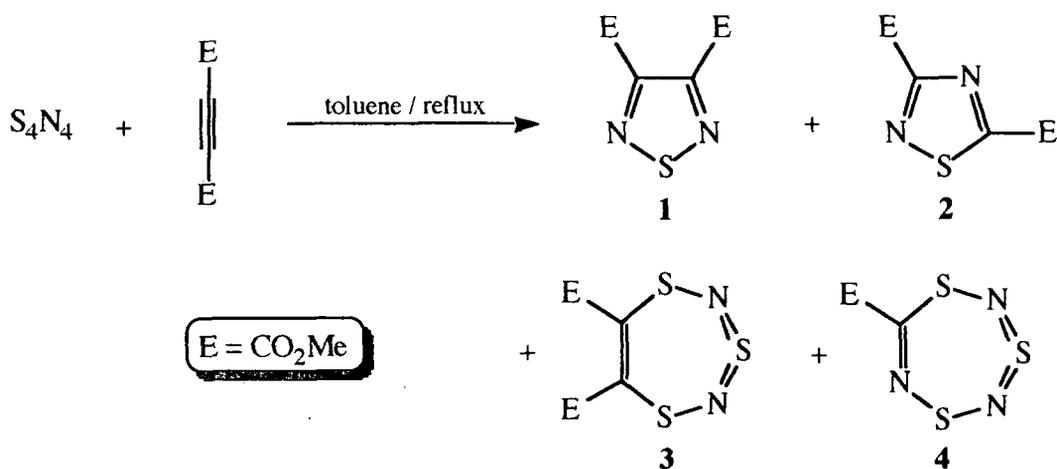
Figure 1

In reality, the structures and properties of these heteroatom-rich systems are determined as much by lone-pair repulsions as by the nature of the π -electron framework. It is, however, interesting to note that many of the conceptual models of organic

chemistry have relevance to these systems of more inorganic nature. Thus, frontier orbital, aromaticity and delocalisation concepts can often be invoked to explain the physical, chemical and structural features of the heterocyclothiazenes.

The synthesis and characterisation of these mixed organic-inorganic systems has undergone a period of rapid growth over the last decade. Synthetic approaches employed vary considerably; some follow clear mechanistic principles, whilst others clearly involve a measure of serendipity. Several examples of representative heterocyclothiazene syntheses are now described.

In recent years, heterocyclothiazenes have been the subject of a fascinating study by Rees and co-workers.^{1a, 2} In early reactions, they refluxed tetrasulphurtetranitride, S_4N_4 , with dimethyl acetylenedicarboxylate (DMAD) in toluene (Scheme 1).

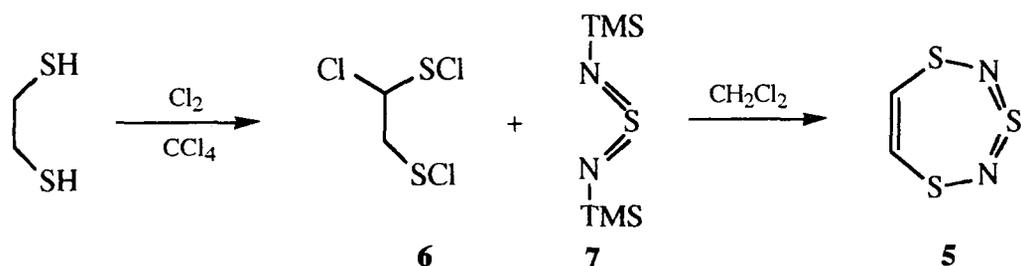


Scheme 1

The major product was 1,2,5-thiadiazole diester **1**, formed in 60% yield. This compound was largely expected and postulated to have arisen by cycloaddition between DMAD and a sulphur diimide unit of sulphur nitride. However, the three minor products **2**, **3** and **4** were unexpected. 1,2,4-Thiadiazole diester **2** (8%) resulted from cleavage of the acetylene triple bond. Most interesting of all were the minor products **3** and **4**, in which five and six heteroatoms, respectively, of the original S_4N_4 had been retained in

the product. The structures of the previously unreported heterocyclic systems, trithiadiazepine **3** and trithiatriazepine **4**, were confirmed by X-ray crystallography. Both compounds are formally ten π -electron ring systems and were, therefore, predicted to exhibit aromatic character. This was reflected in the planar rings of both species, as well as their surprisingly high stability.

Attempts to prepare the parent trithiadiazepine **5** (Scheme 2) by hydrolysis and decarboxylation of diester **3** failed.^{1a} However, **5** was obtained in 30% yield by an alternative route³ employing condensation of an ethanedithiol derivative **6** with bis-(trimethylsilyl)sulphurdiimide **7**, a common building block in heterocyclothiazene chemistry.

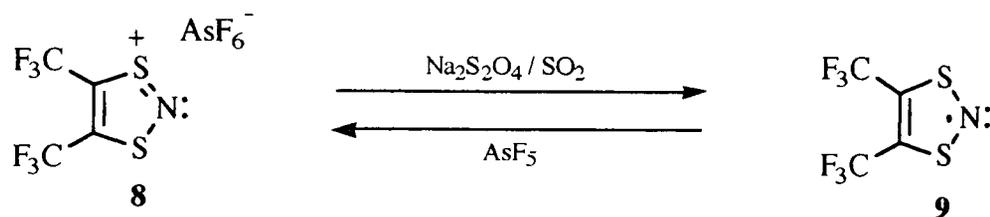


Scheme 2

X-Ray crystallography of trithiadiazepine **5** showed it to be planar, with delocalised ring character. The protons of **5** resonate at 7.76 ppm and it is thermally stable up to 180°C. It was also found to be stable towards aqueous acids, Lewis acids and bases such as triethylamine. Resistance to cycloaddition and methylation reactions was also observed. However, compound **5** was found to undergo a range of electrophilic substitution reactions including acylation, nitration and bromination. These physical and chemical properties are all consistent with true aromatic behaviour, as predicted by the ten π -electrons of this ring system.

The heterocyclothiazenes considered so far have been neutral species or ionic

salts. A further important class is based on radical systems. The synthesis of a representative heterocyclothiazanyl radical is shown in Scheme 3.⁴



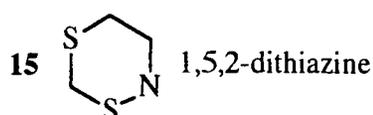
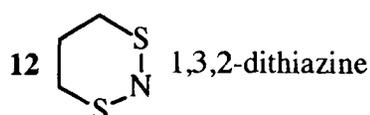
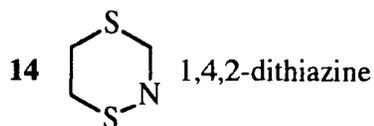
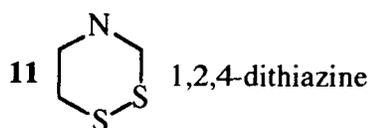
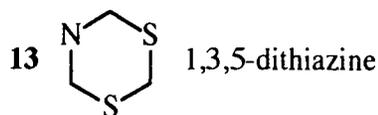
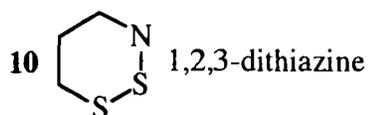
Scheme 3

1,3,2-Dithiazolium salt **8** is a six π -electron species. Reduction of this salt with sodium dithionite in liquid sulphur dioxide at room temperature led to 4,5-bis-(trifluoromethyl)-1,3,2-dithiazolyl **9** in 88% yield. This radical system contains seven π -electrons and was found to be an air and light sensitive black-green liquid. Electron diffraction studies showed that **9** had a planar ring structure in the gas phase. Magnetic susceptibility and ESR spectroscopic studies showed that at 20°C the compound exists as an equilibrium mixture of 65% paramagnetic free radical and 35% diamagnetic dimer. Interestingly, it was found that **9** could be quantitatively oxidised back to the original cationic species **8** by a variety of oxidants, *e.g.* AsF₅, Cl₂, Br₂.

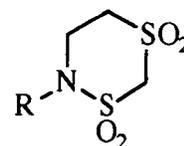
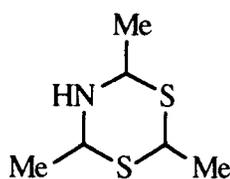
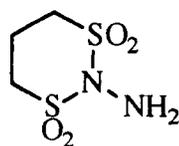
A diverse range of heterocyclothiazene systems have been synthesised and characterised. Variation in ring size of between five and eight atoms, with π -system counts of six, seven, eight and ten electrons have been described for neutral, cationic, anionic and radical systems. Of these systems, the eight π -electron heterocyclothiazenes are probably the least studied. Due to the potential anti-aromatic nature of these species, they are often more synthetically challenging and tend to decompose prior to characterisation. Their chemistry is also less well explored. We recognised, therefore, that eight π -electron heterocyclic systems offered considerable opportunities for further studies into their synthesis, chemical and physical properties. The remainder of Chapter 1 will consider eight π -electron heterocyclothiazenes, specifically dithiazines.

1.2 The Dithiazines.

All six possible isomers **10** - **15** of the dithiazine system are to some extent described in the literature.^{1c}



1,2,3-Dithiazines **10** are rare species. They are discussed further in Section 1.3. The 1,2,4-dithiazine system **11** also has few literature reports. Some 5,6-dihydro derivatives of **11** have been described.⁵ The 1,3,2-dithiazine system **12** has been described only as the reduced 1,1,3,3-tetraoxide derivative **16**.⁶

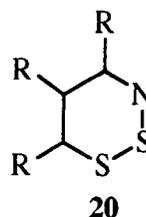
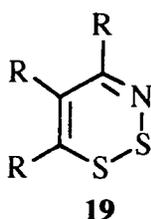


X-Ray crystallography showed that the ring system of **16** is non-planar. Conversely, the

1,3,5-dithiazine system **13** is more widespread and, therefore, more thoroughly investigated. 1,3,5-Dithiazine derivative **17**, thialdine, has been identified as a flavouring component in meat.^{1c} Other 1,3,5-dithiazines have subsequently been postulated as flavour enhancement agents. The 1,4,2-dithiazine system **14** is reasonably well known, primarily as the 1,1-dioxide. This system is discussed further in Section 1.4. Finally, the 1,5,2-dithiazine isomer **15** is another rare heterocyclic system. The only recorded examples are 1,1,5,5-tetraoxides of the type **18**.⁷

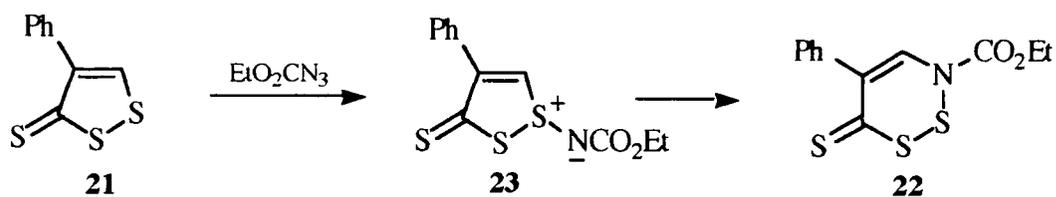
1.3 The 1,2,3-Dithiazine System.

The arrangement of atoms found in the 1,2,3-dithiazine ring system has very few literature reports as either the eight π -electron system **19** or as reduced derivatives of type **20**.



This is perhaps not surprising, bearing in mind the three contiguous heteroatoms, incorporating the labile disulphide functionality. In the case of the eight π -electron system **19**, where two π -electrons are derived from each sulphur atom, this situation is aggravated by the destabilising effects of potential anti-aromaticity.

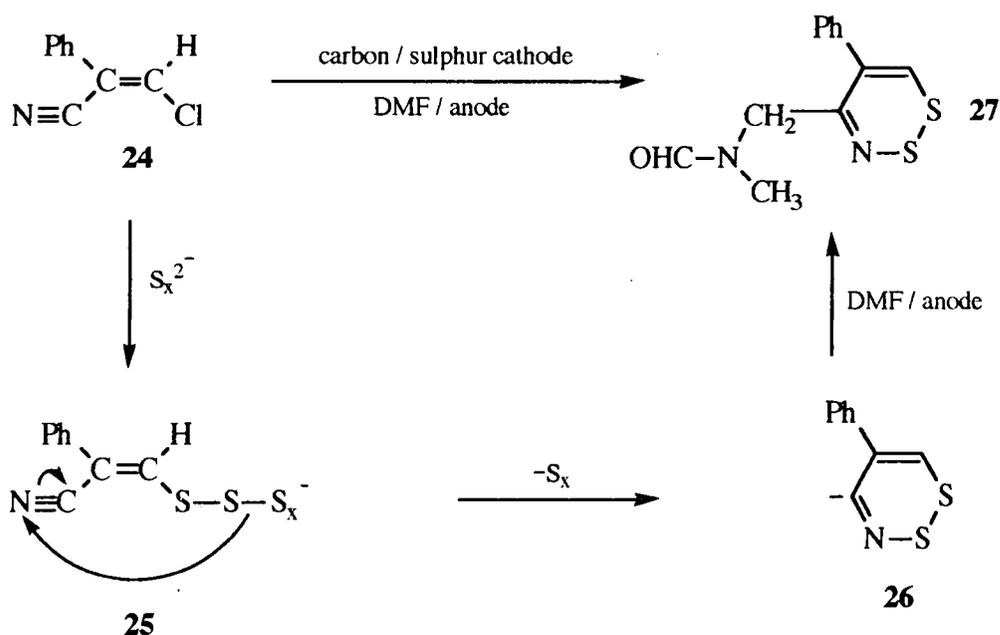
The first recorded literature example of a 1,2,3-dithiazine derivative came as late as 1976.⁸ Thermal decomposition of ethyl azidoformate (Scheme 4), in the presence of 1,2-dithiole-3-thione derivative **21** led to 1,2,3-dithiazine **22**, in 57% yield.



Scheme 4

The reaction was postulated to occur *via* initial attack of a nitrene on the sterically favoured S-1 position of **21**. The resulting ylide **23** then underwent a 1,2-rearrangement of C-5, with nitrogen ring-expansion, to furnish dithiazine **22**. Whilst this is an interesting result in that it confirms the stability of the amino-disulphide group in a six-membered ring, product **22** contains only six π -electrons in its ring, in a non-delocalised configuration.

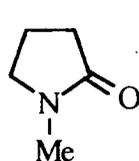
The first report of a formal eight π -electron, delocalised 1,2,3-dithiazine came over a decade later.⁹ An electrochemical method was employed, using a carbon-sulphur cathode. In a typical experiment, propionitrile derivative **24** was dissolved in dimethylformamide (DMF) and the solution subjected to electrolysis (Scheme 5).



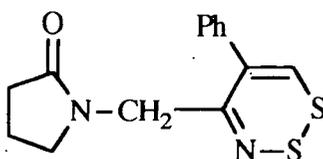
Scheme 5

The carbon-sulphur cathode was proposed to act as a source of polysulphide dianions. Nucleophilic substitution of a suitable leaving group, such as chloride or tosyl, by this dianion gave the polysulphide intermediate **25**. Ring closure with concomitant loss of a neutral polysulphur fragment was then thought to lead to carbanionic systems such as **26**. This carbanion is trapped by an oxidised DMF fragment, resulting from anodic oxidation, to give the observed 1,2,3-dithiazine product **27**, in 20% yield. The isolation of dithiazine **27** was highly significant as, at the time of publication, 1989, it was the first example of an eight π -electron 1,2,3-dithiazine.

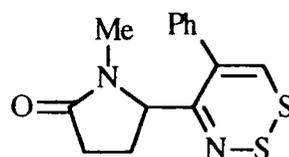
During these studies, the authors varied the reaction solvent. By replacing DMF with *N*-methylpyrrolidin-2-one **28**, two analogous 1,2,3-dithiazine isomers **29** and **30** were isolated, as a mixture, in overall yield of 10%. It was not subsequently possible to separate this isomeric mixture.



28

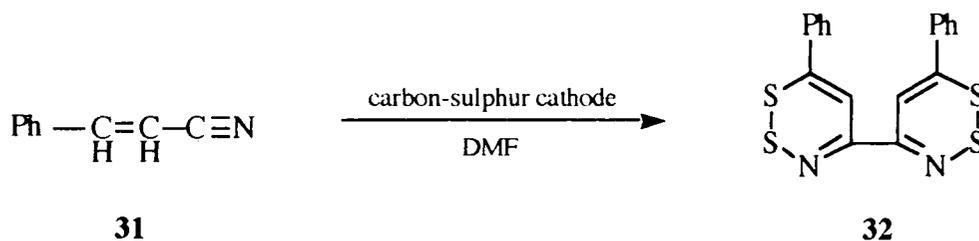


29



30

Characterisation of these 1,2,3-dithiazines included NMR, IR and MS data. Unfortunately, no further indications were given as to the physical or chemical properties of these novel compounds. A later report by the same workers extended the scope of this electrochemical route, to include activated alkenes which did not contain facile leaving groups, for example cinnamitrile **31** (Scheme 6).¹⁰ The bis-(1,2,3-dithiazine) **32** was obtained in 75% yield, as a solid. No mechanism was offered for the formation of this compound. However, it seems plausible that the sigma bond connecting the rings may be derived from the coupling of electrochemically-generated radical intermediates. Other activated alkene precursors gave a range of species including thiophenes, dithiins and thiones.



Scheme 6

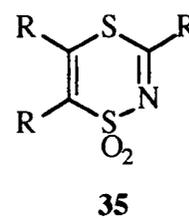
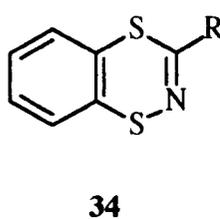
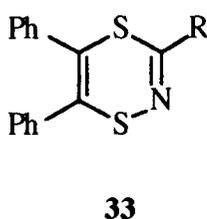
It was noted that this method, although it led to the synthesis of some novel heterocyclic species, had significant limitations. The reactions were described as very complex, with competing ionic and radical pathways likely. In many cases, this led to a multiplicity of products and the reaction appeared difficult to control. Variations in applied current, support electrolyte and solvent were all found to have a bearing on the identities of products isolated, as well as their relative distribution.

At the time of writing, the chemistry of 1,2,3-dithiazines remains totally unexplored.

1.4 The 1,4,2-Dithiazine System.

1.4.1 Overview.

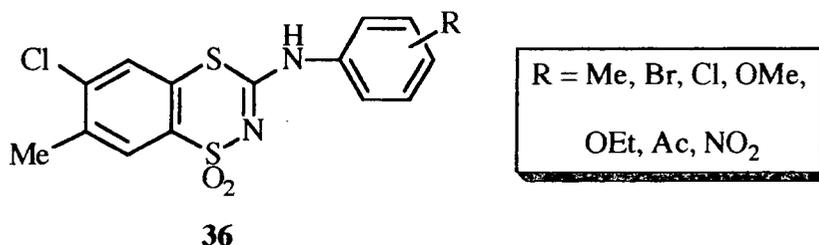
This heterocyclic system is more widely established.^{1c} Most examples have multiple phenyl substituents *e.g.* **33**, benzo-fused substituents **34**, or are 1,1-dioxide derivatives **35**. The 1,4,2-dithiazine system, as represented by structure **33**, is formally eight π -electron.



The 1,4,2-dithiazine system is, therefore, theoretically capable of displaying anti-aromaticity, with implications for the thermodynamic stability of the species. The multiple phenyl groups and benzo-fused system of structures **33** and **34**, respectively, may play a role in stabilising the heterocyclic core, by mesomeric release or withdrawal of electron density from it, thereby negating the effects of anti-aromaticity to some extent.

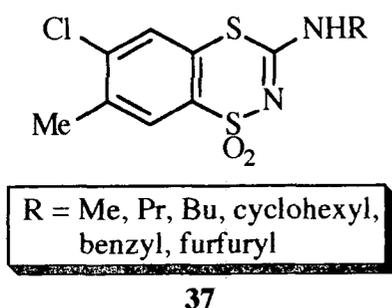
It is not surprising, therefore, that a large proportion of the isolated 1,4,2-dithiazines reported carry these substituents; the systems thereby have higher inherent thermodynamic stability. The final reasonably common derivative, 1,1-dioxides of the type **35**, are stabilised by a different effect. Because both lone pairs of the S-1 atom are involved in bonding to oxygen atoms, they can take no part in contributing to the π -system. Consequently, 1,1-dioxide derivatives of **35** are six π -electron, non-delocalised systems. As such, they may be expected to enjoy significantly enhanced thermodynamic stability, again explaining their relative ubiquity. At the outset of the present work, 1,4,2-dithiazine derivatives which did not bear the characteristics of structures **33-35** were considerably less common.

Much study of the biological properties of the 1,4,2-dithiazine system has been undertaken. The 1,1-dioxide analogue in particular has received attention. Derivatives of **36** were found to have diuretic and electrolyte-elimination properties, the magnitudes of which were found to be correlated to the nature of the substituent, R.¹¹

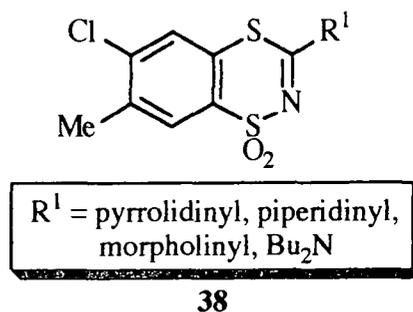


Similarly, derivatives of **37** and **38** have shown some diuretic, anti-arrhythmic and anti-hypertensive activity.¹² Related analogues have been evaluated for herbicidal

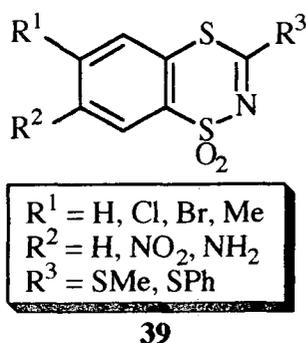
and fungicidal activity.¹³ A range of derivatives of **39** were found to be useful as selective herbicides and fungicides in agrochemical applications. Derivative **40** showed significant herbicidal activity against *Monochoria vaginalis*.



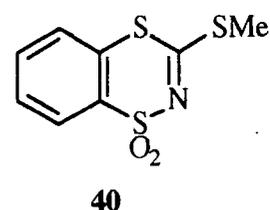
R = Me, Pr, Bu, cyclohexyl,
benzyl, furfuryl



R¹ = pyrrolidinyl, piperidinyl,
morpholinyl, Bu₂N



R¹ = H, Cl, Br, Me
R² = H, NO₂, NH₂
R³ = SMe, SPh



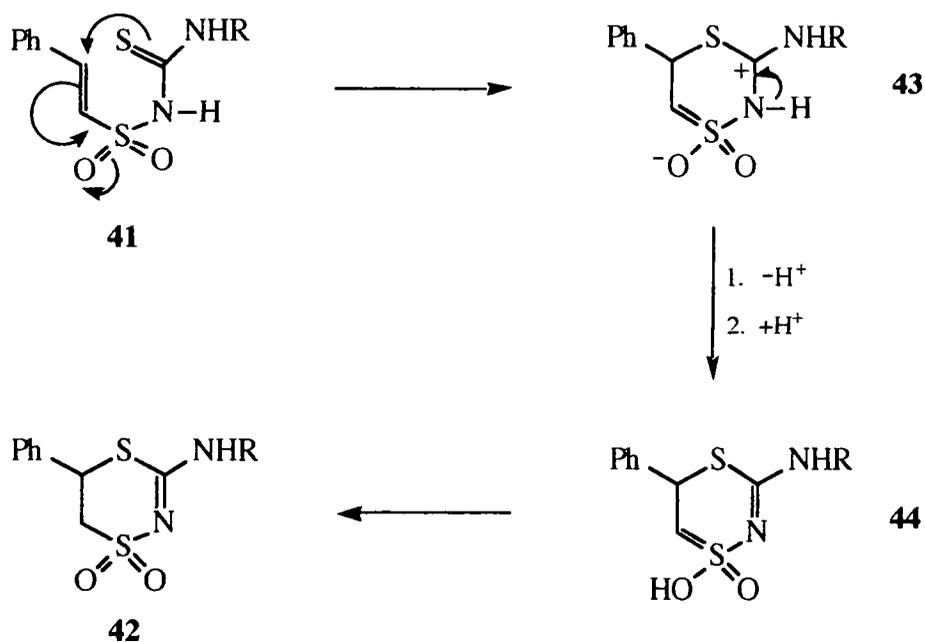
The remainder of this section on 1,4,2-dithiazines will describe the methods of synthesis available and explore known chemical, physical and spectroscopic properties.

1.4.2 Synthetic Approaches to 1,4,2-Dithiazines.

1.4.2.1 α,β -Unsaturated Sulphone Route.

This route is dealt with first as it has two anomalies compared with the other approaches to be described. First, it does not lead to the formation of eight π -electron 1,4,2-dithiazines but, rather, to sulphone derivatives. Secondly, it involves a ring-closure reaction, whereas the remaining strategies involve ring-expansion reactions. α,β -Unsaturated sulphones of the type **41** (Scheme 7) undergo intramolecular conjugate

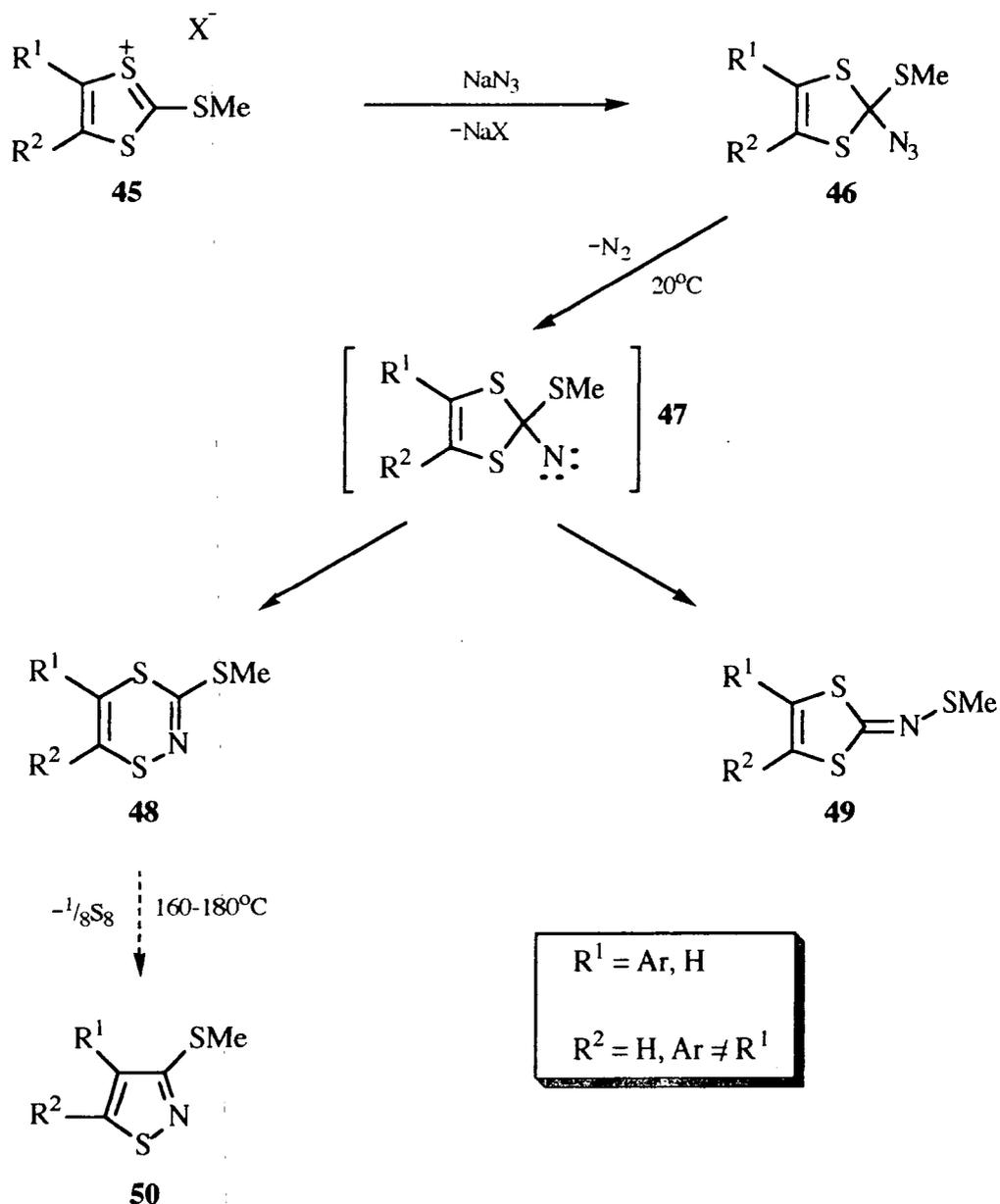
addition to furnish 1,4,2-dithiazine-1,1-dioxides **42**.¹⁴ The mechanism is believed to involve initial nucleophilic attack at the β -position of the α,β -unsaturated sulphone **41** to give zwitterionic intermediate **43**. This intermediate undergoes a proton rearrangement to give enol **44**, which tautomerises to give 1,4,2-dithiazine **42**. Clearly, this route is of no synthetic utility with respect to formation of the more challenging eight π -electron 1,4,2-dithiazine system.



Scheme 7

1.4.2.2 Azide Route.

The first synthesis of an eight π -electron 1,4,2-dithiazine was described by Fanghänel, in 1965.¹⁵ The methodology involved initial reaction of six π -electron 1,3-dithiolium cation salts **45** with an inorganic azide (Scheme 8). The exclusive reaction of nucleophiles at C-2 of 1,3-dithiolium cation salts has been well documented.¹⁶ The resultant organoazide species **46** were found to be thermally unstable, spontaneously eliminating nitrogen at room temperature, to give nitrene intermediates **47**. These nitrenes were found to participate in two competing pathways.

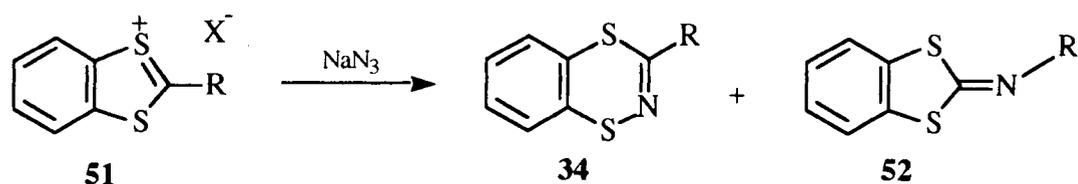


Scheme 8

Insertion of the nitrene into a ring carbon-sulphur bond led to ring-expansion and isolation of the eight π -electron 1,4,2-dithiazines **48** in yields of *ca.* 40%. Conversely, nitrogen insertion into the exocyclic carbon-sulphur bond gave the isomeric imines **49** as the major products (*ca.* 60%). For the unsymmetrical dithiolium salts **45**, the two possible regioisomers of dithiazine **48** were isolated, in approximately 1:1 ratio. Fanghanel also found that the dithiazines **48** were unstable at temperatures of 160–180°C.¹⁵ Desulfurisation occurred to yield isothiazoles **50** in yields of 40–60%.

It has been suggested that the mechanism of ring-expansion may not involve a discrete nitrene intermediate of the type **47**.^{1c} A [1,2] shift of sulphur, with concerted loss of nitrogen, has been alternatively proposed. The use of azides to effect ring-expansion is a well established procedure in heterocyclic synthesis.¹⁷

Nakayama and co-workers subsequently applied azide methodology to the synthesis of a range of 1,4,2-benzodithiazines **34** (Scheme 9).¹⁸



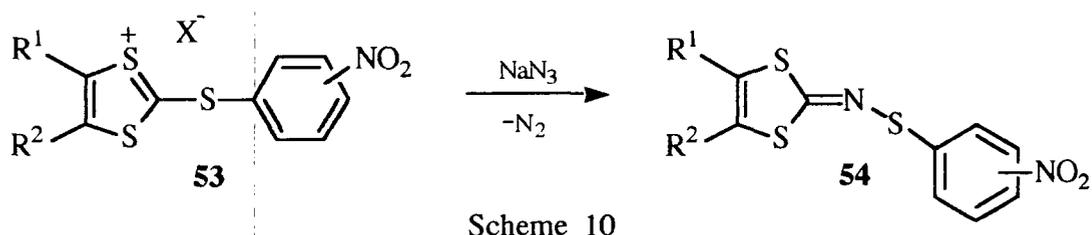
R	34	Yields (%)	52
SMe	37		48
H	90		0
Ph	93		0
morpholino	19		0

Scheme 9

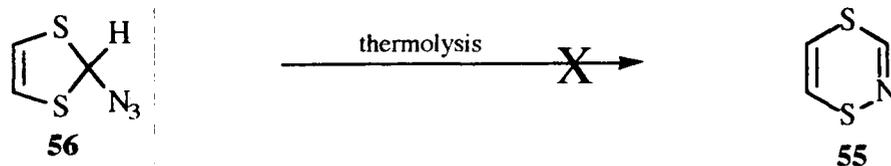
Reaction of 1,3-benzodithiolium cation salts **51** with sodium azide again gave organoazides. Contrary to the findings of Fanghänel,¹⁵ it was necessary to heat these species above ambient temperature to effect nitrene generation. The organoazides were, therefore, refluxed in a range of solvents including benzene, acetonitrile, toluene and xylene. In the case of 3-methylthio-substituted salt **51**, ($\text{R} = \text{SMe}$), competing pathways were again observed, in accord with the original findings by Fanghänel.¹⁵ This gave rise to the 1,4,2-benzodithiazine isomer **34** ($\text{R} = \text{SMe}$) in 37% yield and the corresponding imine isomer **52** ($\text{R} = \text{SMe}$) in 48% yield.

However, for a range of other benzodithiolium cation derivatives **51**, ($\text{R} = \text{H}$, Ph, morpholino), exclusive formation of 1,4,2-benzodithiazine products **34** was noted.

These results indicate a preference for nitrene insertion into C-S bonds over C-H, C-C or C-N bonds. Hence, the observation of competing exocyclic nitrene insertion with the 2-methylthio derivative of salt **51**, where exocyclic or endocyclic reactions both lead to favoured nitrene insertion into a C-S bond. This favourability was subsequently confirmed for a range of 2-(nitroarylthio)-1,3-dithiolium cation salts **53** (Scheme 10).¹⁹ Reaction of these salts with azide ion, followed by nitrogen loss, gave good yields of N-nitroarylthio-2-imino-1,3-dithiole derivatives **54**, with no observation of corresponding 1,4,2-dithiazine derivatives.



Attempts to prepare the parent unsubstituted 1,4,2-dithiazine **55** by azide methodology have also been made (Scheme 11).^{18,20} Thermolysis of 1,3-dithiol-2-yl azide **56** was unsuccessful. The reaction gave only intractable tars.



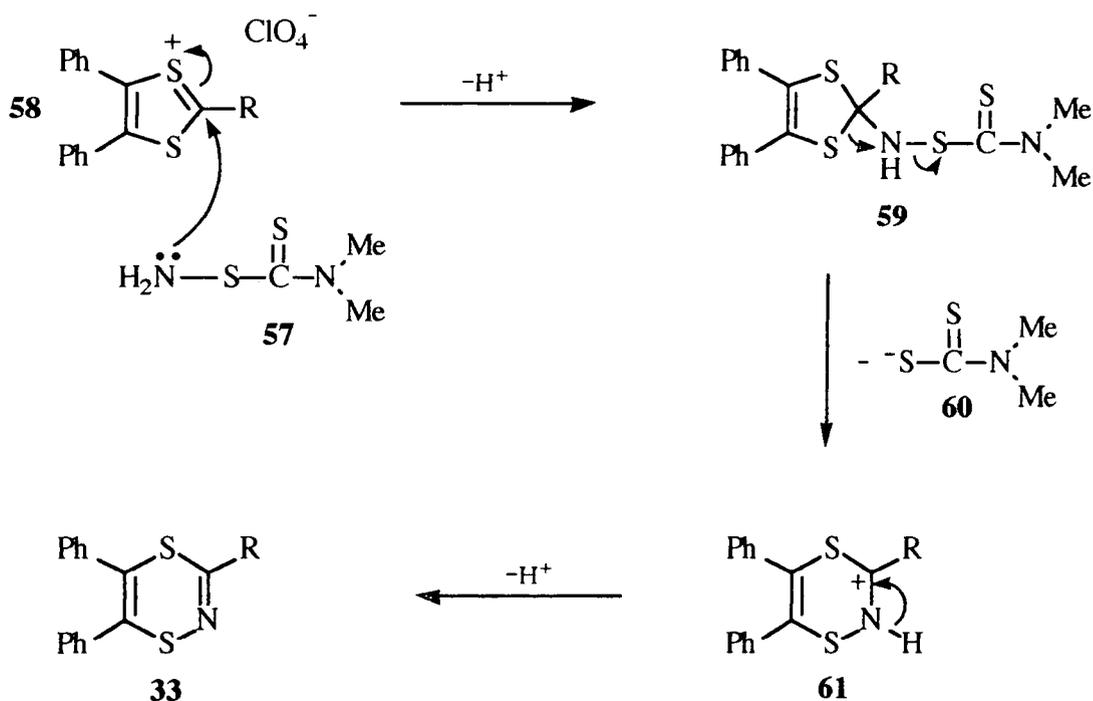
In summary, the azide route enabled the isolation of the first examples of eight π -electron 1,4,2-dithiazines. However, the methodology suffers from some significant limitations. Yields of dithiazines are often unsatisfactory. In the case of 2-thioalkyl or 2-thioaryl substituted 1,3-dithiolium cation salts, *e.g.* **53**, competition of reaction pathways

exists and imine isomer yields often predominated over those of the dithiazines. Whilst intermediate organoazides **46** derived from 2-methylthio-1,3-dithiolium cation salts **45** were reported to spontaneously lose nitrogen at room temperature,¹⁵ the remainder required thermolysis to effect nitrene generation. Typically, this involved refluxing in toluene. As discussed in Section 1.4.3.1, refluxing 1,4,2-dithiazines in toluene brings about efficient desulphurisation, to afford isothiazoles. Thus, the reaction conditions required to generate the nitrene intermediate are also responsible for decomposition of the product. A further drawback of these harsh reaction conditions is that access to less stable 1,4,2-dithiazine derivatives is likely to be precluded. Thus, the synthesis of 1,4,2-dithiazines which do not carry stabilising benzo or phenyl substituents would be difficult to accomplish by the azide route.

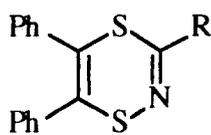
This proposal is borne out by a recent review which described known 1,4,2-dithiazine derivatives, obtained by the azide route, up to 1987.²¹ Of the twenty-three examples noted, seventeen contained either one or more phenyl substituents, or a benzo-fused substituent. Of the remaining six derivatives, five were obtained from 2-methylthio-1,3-dithiolium cations of type **45**, allowing room-temperature formation of the 1,4,2-dithiazine products. The unsuccessful attempt at formation of parent 1,4,2-dithiazine **55**, by thermolysis of precursor azide **56**, further illustrated these limitations. The complex, intractable tar which resulted may have been decomposition products of dithiazine **55**, destroyed under the reaction conditions necessary for nitrene generation.

1.4.2.3 Sulphenamide Route.

Yonemoto *et al*, in 1988, described a new route to 1,4,2-dithiazines.²² An alternative nitrogen source was employed, namely sulphenamide **57** (Scheme 12). The proposed mechanism involved nucleophilic attack by the sulphenamide **57** on 1,3-dithiolium cation salts of type **58**, to furnish the dithiole derivative **59**. Ring-expansion, with loss of the dithiocarbamate anion **60**, gave the protonated cationic species **61**. Deprotonation of **61** afforded the 1,4,2-dithiazine product **33**.



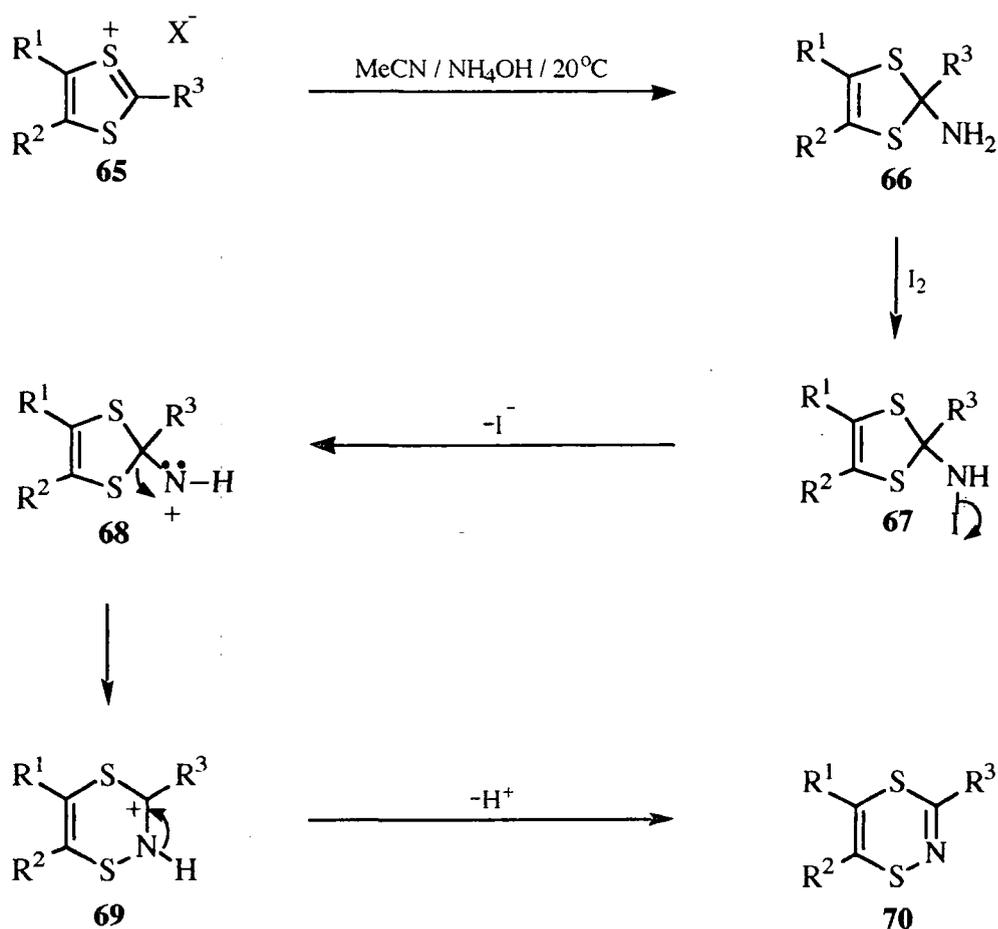
Yields of **33** were generally good (*ca.* 80%) and, importantly, the reaction conditions employed were considerably milder than had been the case with previous approaches to 1,4,2-dithiazines. Reactions were carried out at ambient temperature, albeit for several days. This opened up the possibility of working with derivatives containing less stabilising substituents. Desulphurisation of dithiazine products to isothiazoles should also be eliminated at these lower reaction temperatures. No mention of imine by-products was made. Despite the apparent potential of this new route, the publication described only three 1,4,2-dithiazine derivatives **62-64**, all of which were highly substituted by stabilising groups. The opportunity was not taken to explore the scope of this reaction to access less substituted analogues.



62	R = NMe ₂
63	R = NEt ₂
64	R = Ph

1.4.2.4 Iodine - Ammonia Route.

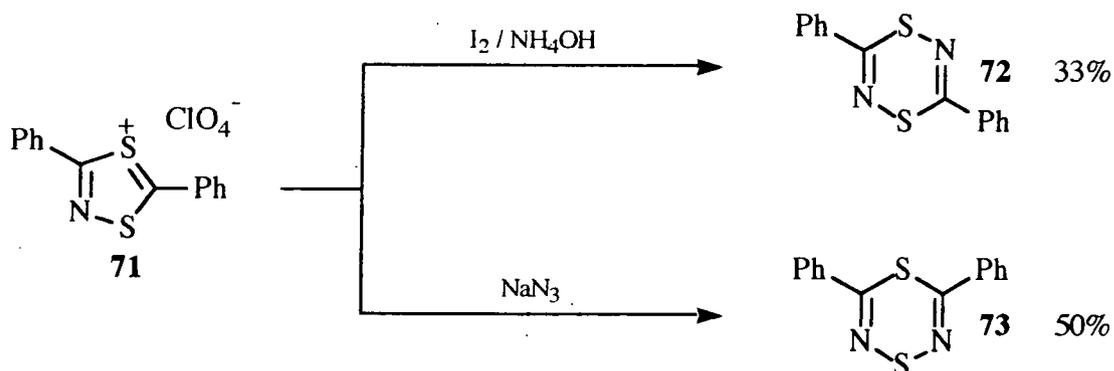
An interesting advance in the synthesis of the 1,4,2-dithiazine system was made in 1989, by Yonemoto and Shibuya. Building on the concept of their earlier work with sulphenamides (Section 1.4.2.3), they published a 1,4,2-dithiazine synthesis based on ammonia as the nitrogen source.²³ The reaction was carried out in acetonitrile at room temperature. Dithiolium cation salt **65** was dissolved in the solvent prior to addition of an equimolar amount of iodine. A large excess, typically ten molar equivalents, of aqueous ammonia solution was next added to the homogeneous solution and the reaction was stirred for *ca.* two hours. Their proposed mechanism is shown in Scheme 13.



Scheme 13

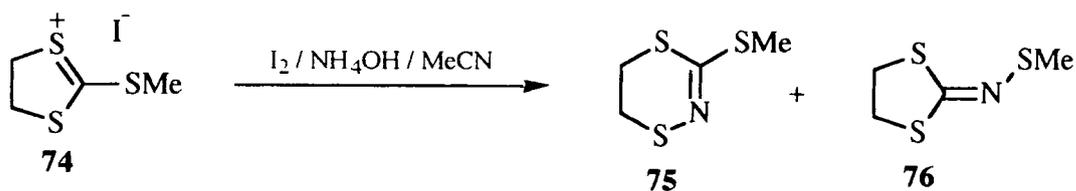
Nucleophilic attack by ammonia on C-2 of 1,3-dithiolium cation salts **65** gave the 2-amino-1,3-dithiole **66**. Oxidative iodination of **66** led to the formation of species **67**. Loss of iodide anion was proposed to occur next, to give a nitrenium ion intermediate **68**. Ring-expansion then occurred, to give the protonated intermediate **69**, deprotonation of which led to the formation of the 1,4,2-dithiazine product **70**.

The evidence offered for nitrenium ion intermediate **68** arose from ring-expansion of a non-symmetrical dithiazolium salt **71** (Scheme 14). Ring-expansion of this salt by iodine-ammonia methodology resulted in the formation of 3,6-diphenyl-1,4,2,5-dithiadiazine **72**. Conversely, ring-expansion of salt **71** by the previously described azide route (Section 1.4.2.2) gave rise to the exclusive formation of isomeric 3,5-diphenyl-1,4,2,6-dithiadiazine **73**. This difference in reactivity was attributed to the contribution of different types of intermediate. Since nitrenes are established intermediates of azide fragmentation,¹⁷ a nitrenium ion intermediate was tentatively suggested for the iodine-ammonia reaction.



Scheme 14

One example of imine isomer formation under iodine-ammonia conditions was noted.²³ This occurred on ring expansion of the non-aromatic substrate **74** (Scheme 15). The major product was the 5,6-dihydro-1,4,2-dithiazine **75** (41% yield), along with a small amount of the 2-imino-1,3-dithiole isomer **76** (7% yield).

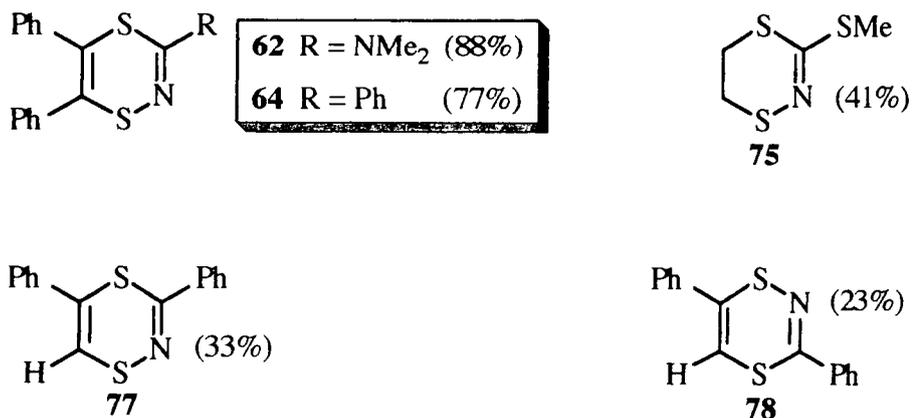


Scheme 15

No other imines were found during similar ring-expansions of other systems. A further point of interest is that the reaction depicted in Scheme 15 showed that non-aromatic substrates would undergo ring-expansion by means of the iodine-ammonia approach, albeit in low yield.

In summary, the iodine-ammonia route appeared to offer some considerable advantages over all previous synthetic approaches to 1,4,2-dithiazines, with generally good product yields (41-88%). Of fundamental importance, the reaction was carried out at ambient temperature. This should enable the ring-expansion of less highly substituted dithiolium salts to be undertaken. Additionally, desulphurisation of the product dithiazines to isothiazoles should not occur to any appreciable extent under these mild reaction conditions. Since only one imine by-product had been obtained, it was further hoped that imine formation would not be a significant side-reaction. The practicalities of the reaction were also advantageous. Reagents were inexpensive and readily available; reaction times were short and work-up procedures straightforward.

1,4,2-Dithiazines **62**, **64**, **75**, **77** and **78** were initially obtained by the iodine-ammonia route.²³ Dithiazine regioisomers **77** and **78** were obtained as products of the same ring-expansion reaction, the overall reaction yield therefore being 56%. This indicates that little or no regiochemical specificity operates in the reaction. The dithiazine derivative **75** is a six π -electron, non-delocalised system and as such may be expected to exhibit greater thermodynamic stability than the remaining eight π -electron systems.

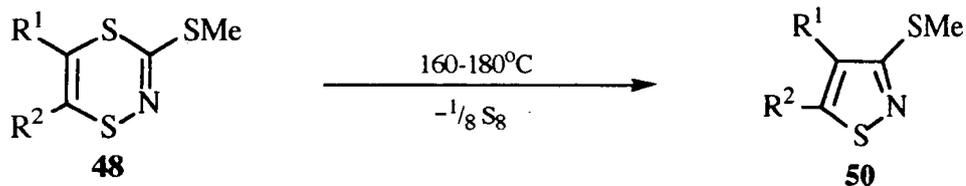


All eight π -electron systems described in the publication by Yonemoto and Shibuya²³ carried at least two stabilising phenyl substituents. The scope of the iodine-ammonia route, with its associated mild reaction conditions, to synthesise less substituted and, therefore, less stabilised eight π -electron 1,4,2-dithiazines, had not been explored during these initial studies.

1.4.3 Chemical, Physical and Spectroscopic Properties of 1,4,2-Dithiazines.

1.4.3.1 Thermolysis of 1,4,2-Dithiazines.

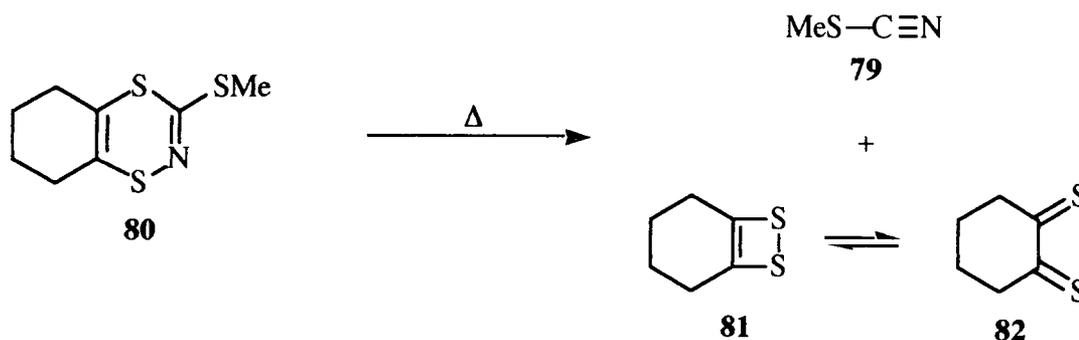
The thermal conversion of 1,4,2-dithiazines to isothiazoles was noted in the publication describing the first synthesis of 1,4,2-dithiazines.¹⁵ By heating the dithiazines **48** (Scheme 16) to 160-180°C, in the absence of solvent, isothiazoles **50** were obtained in yields of 40-60%. Thiazole isomers were not observed.



Scheme 16

No mechanism was proposed for this transformation, but free-radical desulphurisation appears to be a plausible route. Grigg has also suggested a route *via* dipolar intermediates.²⁴ The favourability of the reaction is probably due to the conversion of an eight π -electron system into a six π -electron aromatic one. This reaction is of some synthetic value for the synthesis of specifically functionalised isothiazoles, routes to which are uncommon.^{1a} In subsequent reports, the thermolysis was carried out in solvent, typically toluene.²⁰

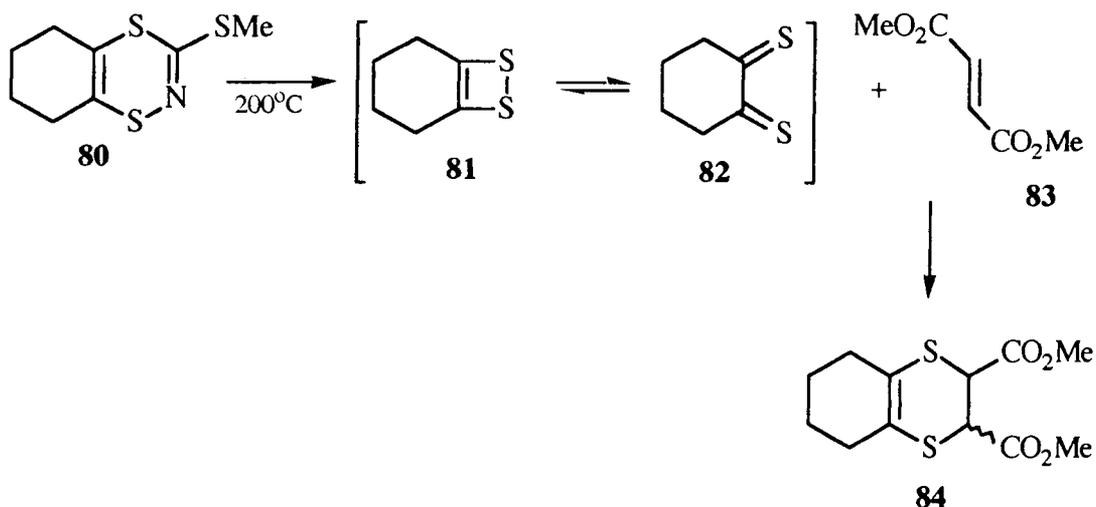
It was later ascertained that a side-reaction to desulphurisation could occur on heating 1,4,2-dithiazines.²⁵ Loss of nitrile fragment **79** (Scheme 17) was reported on heating dithiazine **80**. The other fragment was proposed as the dithiete **81**, possibly in equilibrium with the 1,2-dithiocarbonyl species **82**.



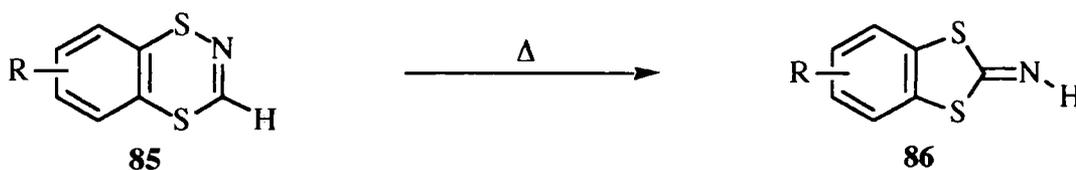
Scheme 17

Supporting evidence for this proposal was obtained by trapping the intermediate **81** or **82** with dimethyl fumarate **83** (Scheme 18), in a Diels-Alder reaction, to give the 1,4-dithiin derivative **84**, in 19% yield.²⁵

The possibility for thermal fragmentation of 1,4,2-dithiazines to give 1,2-dithiocarbonyl intermediates has also been suggested as a minor reaction pathway by other workers.²⁰

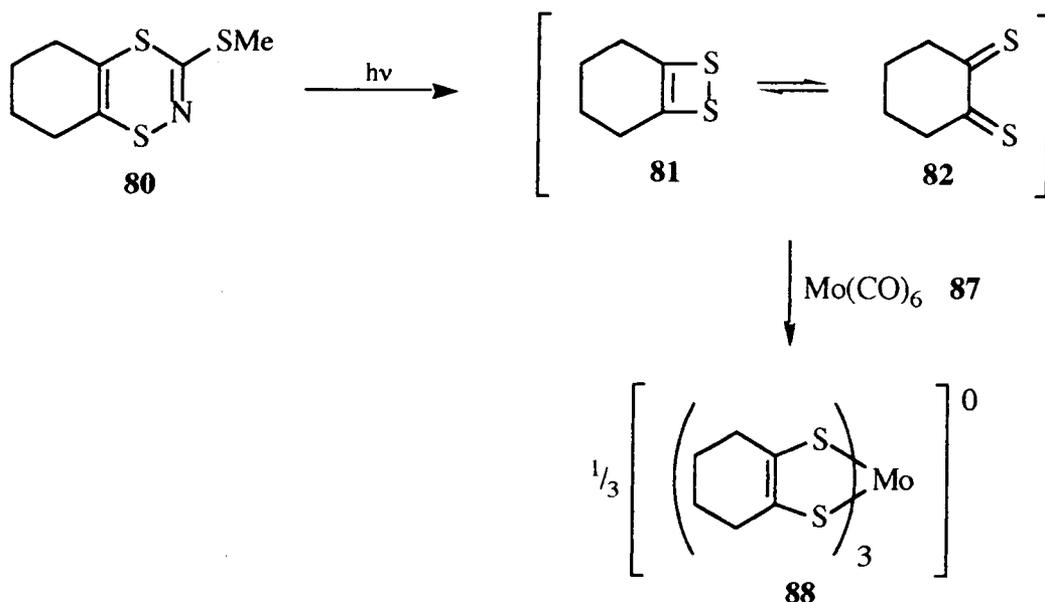


1,4,2-Benzodithiazines **85** (Scheme 19) have been found to undergo isomerisation to corresponding imines **86** on heating.²⁰



1.4.3.2 Photolysis of 1,4,2-Dithiazines.

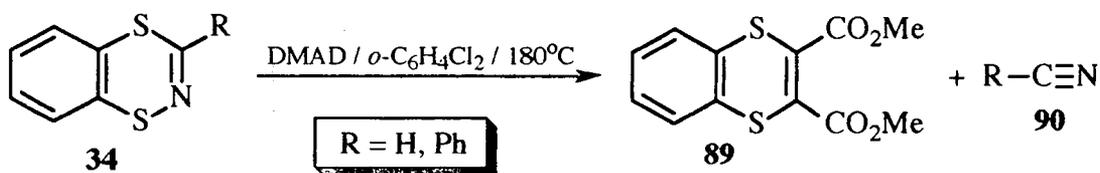
Contrary to the primary thermolysis route of 1,4,2-dithiazines to yield isothiazoles (Section 1.4.3.1), photolysis of dithiazines, *e.g.* **80** (Scheme 20), has been found to give a predominance of the dithiete / dithiocarbonyl intermediate **81** / **82**.²⁶ This intermediate has been trapped with molybdenum hexacarbonyl **87** to give a dithiolene complex **88** (47%). In later studies, it was shown that iron, nickel and tungsten carbonyls would all act as trapping agents for the dithiete / dithiocarbonyl species **81** / **82**, in preparative scale.²⁷ Isothiazoles have not been reported to arise from photochemical fragmentation of 1,4,2-dithiazines.



Scheme 20

1.4.3.3 Cycloaddition Reactions of 1,4,2-Dithiazines.

The Diels-Alder trapping of dithiete-type intermediates arising from thermolysis of 1,4,2-dithiazines has already been described (Section 1.4.3.1, Scheme 18). Nakayama *et al* refluxed 1,4,2-benzodithiazines **34** (Scheme 21) in *o*-dichlorobenzene, with DMAD, to obtain 1,4-benzodithiin **89** in good yields (75-80%), with evolution of nitrile by-products **90**.²⁸

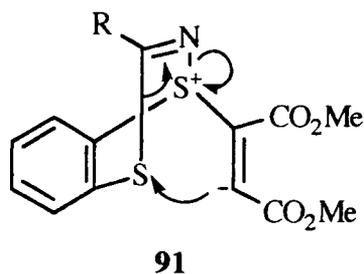


Scheme 21

Similar results could be achieved in the absence of solvent by heating the benzodithiazines **34** to 195°C in the presence of three mole equivalents of DMAD. Ethyl propiolate and benzyne, when used as dienophiles, gave considerably lower yields of

Diels-Alder adducts. Dimethyl fumarate and diethyl azodicarboxylate, however, completely failed to react; starting materials were recovered unchanged.

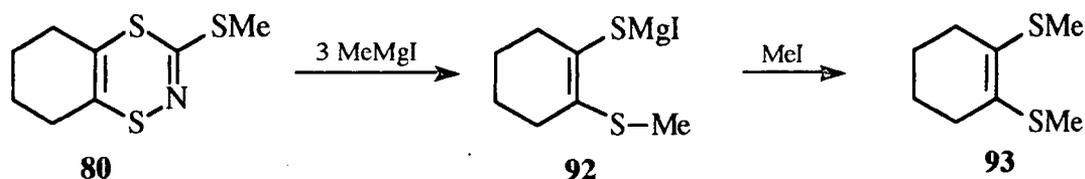
The mechanism postulated for the formation of 1,4-benzodithiin **89** from 1,4,2-benzodithiazines **34** and DMAD involved a stepwise bimolecular pathway, with initial attack by S-1 of the dithiazine on DMAD, to form a zwitterionic intermediate **91**.²⁸



The same workers attempted to extend the dithiin-forming reaction, shown in Scheme 21, by reaction of non-benzo-fused 1,4,2-dithiazines with DMAD, during reflux in toluene.²⁰ No cycloaddition products were obtained.

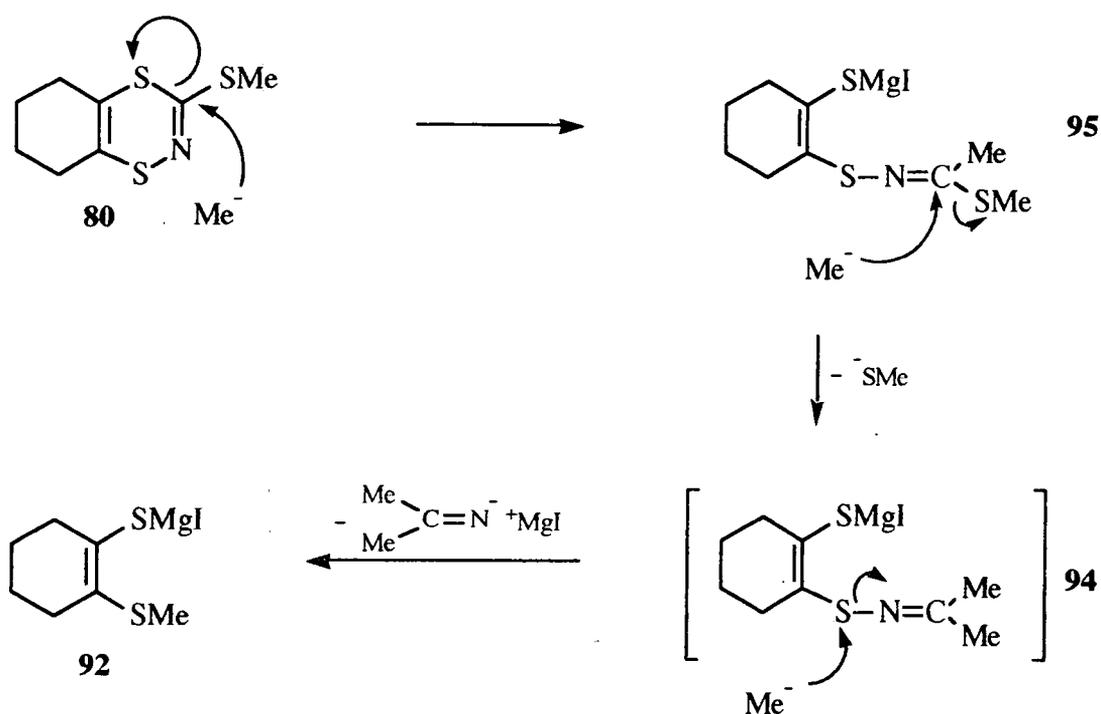
1.4.3.4 Reaction of 1,4,2-Dithiazines with Nucleophiles.

Nucleophiles have been reported to effect ring cleavage of 1,4,2-dithiazines.²⁵ Thus, reaction of dithiazine **80** (Scheme 22) with methyl magnesium iodide gave thiolate salt **92**, in 64% yield. This was subsequently methylated with iodomethane, to furnish 1,2-dimethylthio-cyclohex-1-ene **93**, in 81% yield.



Scheme 22

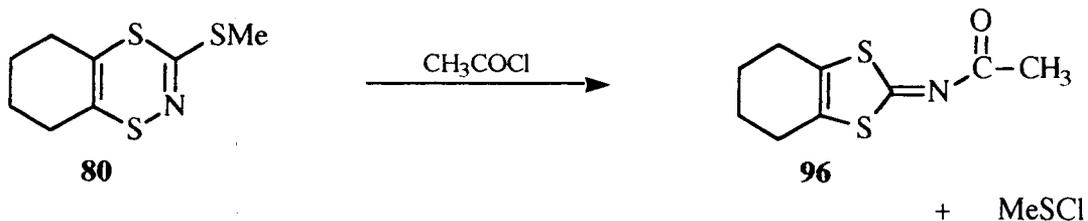
The reaction was described as progressing through intermediate **94**, suggesting the mechanism outlined in Scheme 23. Initial attack of the Grignard reagent on imine carbon C-3 of **80** leads to ring cleavage, giving species **95**. Attack of a second mole of Grignard reagent on **95** brings about nucleophilic substitution, to give described intermediate **94**. Reaction of **94** with a third mole of the nucleophile forms the thiolate salt **92**. Therefore, three mole-equivalents of Grignard reagent were postulated to be required for ring cleavage *via* this mechanism. No further reports or examples of the interaction of nucleophiles with 1,4,2-dithiazines were contained in the literature.



Scheme 23

1.4.3.5 Reaction of 1,4,2-Dithiazines with Electrophiles.

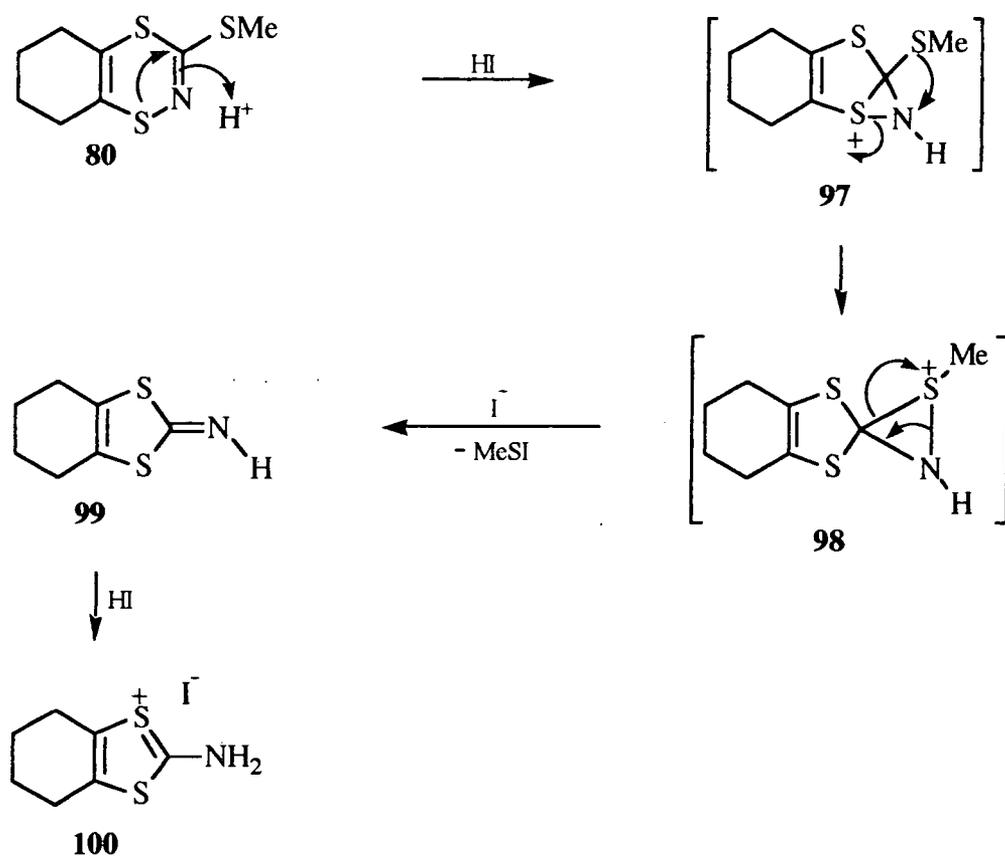
1,4,2-Dithiazines have been found to undergo ring contraction reactions with strong electrophilic reagents.²⁵ Thus, dithiazine **80**, on reaction with acetyl chloride, gave the N-acetyl-2-imino-1,3-dithiole **96**, in 85% yield (Scheme 24).



Scheme 24

Use of strong mineral acids as electrophilic reagents gave analogous products.²⁵

Thus, hydroiodic acid reacted with 1,4,2-dithiazine **80** as shown in Scheme 25.



Scheme 25

The proposed mechanism involved initial protonation of the imine function of **80**, with formation of a thiaziridine ring, to give intermediate **97**, rearrangement of which gave the spiro-intermediate **98**. Loss of a methylthiolium fragment from **98** led to the 2-

imino-1,3-dithiole **99** which, under the acidic reaction conditions, protonated to form the pseudo-dithiolium cation salt **100**. The reaction was carried out in ethanol at 40°C. Free base **99** was liberated and isolated in 93% yield.

1.4.3.6 Oxidation and Reduction of 1,4,2-Dithiazines.

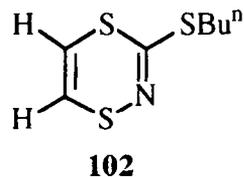
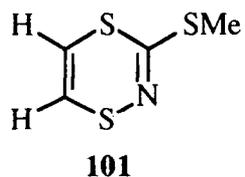
The S^{II} atoms of the 1,4,2-dithiazine ring should be receptive to oxidation by reagents such as *m*-chloroperoxybenzoic acid (*m*CPBA) or hydrogen peroxide.^{1c} Despite this potential, no syntheses of S-oxides or S,S-dioxides (sulphones) from the parent heterocyclic derivatives could be found in the literature. 1,4,2-Dithiazine-1,1-dioxides have been prepared directly, by ring closure reactions (*e.g.* compound **42**, Section 1.4.2.1).

The literature was found to contain no reports concerning the reduction of 1,4,2-dithiazines, by either hydride reagents such as lithium aluminium hydride (LAH), or by means of catalytic hydrogenation.

Studies on the oxidation and reduction properties of the 1,4,2-dithiazine system under electrochemical conditions were also absent from the literature.

1.4.3.7 Spectroscopic Studies on 1,4,2-Dithiazines.

Detailed nuclear magnetic resonance (NMR) studies on 1,4,2-dithiazine derivatives **101** and **102** have been carried out.²⁹ Some proton and carbon chemical shift data are presented in Table 1.



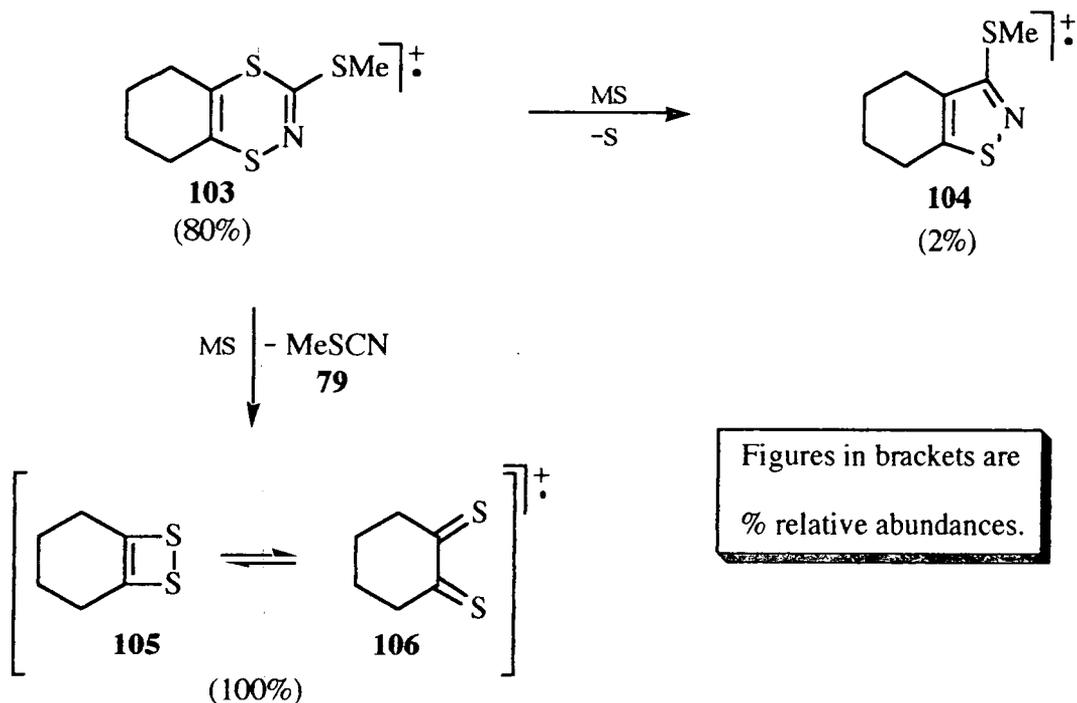
	C-3	C-5	C-6	5-H	6-H
101 δ_H				6.27	6.86
101 δ_C	159.5	117.5	128.6		
102 δ_C	158.7	117.5	128.2		

Table 1. Proton and Carbon Chemical Shifts of Dithiazines **101** and **102** (ppm).

An important finding of these studies was that the carbon and hydrogen atoms at position-6 were more deshielded and appeared downfield relative to the position-5 atoms. As can be seen from Table 1, these results are consistent for derivatives **101** and **102**. Molecular modelling studies (Section 1.4.3.8, Table 3) have suggested that there is little difference between π -electron densities at C-5 and C-6 of 1,4,2-dithiazines, indicating little scope for mesomeric contributions to explain the observed shielding at C-5 and deshielding at C-6. It, therefore, seems reasonable to assume that the deshielding experienced by position-6 and observed by NMR is a consequence of inductive electron withdrawal by N-2, through S-1.

Not surprisingly, C-3 was found to be the most deshielded position in the molecule, experiencing significant electron withdrawal from the adjacent nitrogen at position-2; C-3 may be thought of as having the character of a masked carboxylic acid. The C-3 resonances in molecules **101** and **102** of *ca.* 159 ppm compare well to values of *ca.* 165 ppm for non-conjugated alkyl carboxylic acids.^{30a}

The mass-spectroscopic (MS) fragmentation behaviour of 1,4,2-dithiazines has received some attention.^{26,27} A typically-observed MS fragmentation pattern is shown in Scheme 26, with relative abundance of fragments given.²⁶



Scheme 26

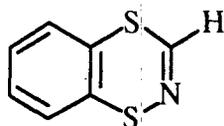
The parent radical ion **103** is clearly seen, in 80% abundance. Desulphurisation of **103**, to give isothiazole radical ion **104**, is limited, the isothiazole species being observed in only 2% abundance. Far more significant is loss of methyl thiocyanate **79** from **103**, to give the dithiete fragment **105**, possibly in equilibrium with dithiocarbonyl radical ion **106**. These fragmentation products are observed in 100% relative abundance.

Attempts have been made to correlate mass spectroscopic, photolytic and thermal breakdown characteristics of 1,4,2-dithiazines.²⁷ From the fragmentation behaviour shown in Scheme 26, the route to dithiete-type species seems to predominate under mass spectroscopic conditions. This parallels results described for photolytic cleavage of 1,4,2-dithiazines (Section 1.4.3.2). However, under thermal fragmentation conditions, desulphurisation to isothiazoles has been found to be the most important pathway (Section 1.4.3.1). Dithiete formation from thermally-induced 1,4,2-dithiazine fragmentation has been noted, but yields of trapped products indicated this to be a minor pathway.

A related finding concerned the fragmentation behaviour exhibited by 1,4-dithiins. Under mass spectroscopic, thermal and photochemical conditions, 1,4-dithiins desulphurise to afford corresponding thiophenes.²⁷

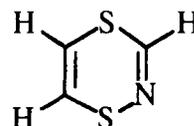
1.4.3.8 Molecular Modelling Studies on 1,4,2-Dithiazines.

Molecular modelling studies have been carried out on known and theoretical 1,4,2-dithiazine derivatives,²¹ using the CNDO/2 method.³¹ This treatment has given insight into the reactivity displayed by 1,4,2-dithiazines and predicted the likely structure of the heterocycle, since, prior to our work reported in this thesis, no X-ray crystallographic data had been published for the system. Derivatives **107** and **55** have been used in these studies. 1,4,2-Benzodithiazine **107** is a known compound.¹⁸ The parent 1,4,2-dithiazine **55**, however, had not been isolated and is, therefore, a model compound.



known compound

107



model compound

55

CNDO/2 predictions for the ring geometries of 1,4,2-dithiazines **107** and **55** are presented in Table 2.²¹ Bond lengths are quoted in Angstroms (Å). The angle, θ , refers to the fold angle of the ring, about an imaginary S1---S4 axis, quoted in degrees (°). Bond lengths of the heterocyclic cores of derivatives **107** and **55** are remarkably similar. The C5-C6 bond length is increased somewhat in compound **107**, probably as a result of dimensional requirements imposed by the benzo-fused substituent.

	S1-N2	N2-C3	C3-S4	S4-C5	C5-C6	C6-S1	S1-S4	θ (°)
107	1.72	1.29	1.73	1.76	1.40	1.75	3.37	14°
55	1.72	1.29	1.74	1.75	1.33	1.74	3.41	11°

Table 2. CNDO/2 Bond Lengths (Å) and Planarity Deviation Angles (°) for **107** and **55**.

The accepted sum of Van der Waals radii for two sulphur atoms is 3.7-3.8 Å.³² Interestingly, the S1-S4 distances calculated for both dithiazines are significantly shorter than this, indicating the possibility for intramolecular overlap of sulphur orbitals to occur. Both heterocyclic cores were calculated as having deviation away from a planar structure. Considering the eight π -electron nature of these heterocycles, this is a predictable result. By bending away from a planar structure, the efficiency of the π -orbital overlap in the ring would be reduced. This would act to partially negate the effects of anti-aromaticity and thus stabilise the heterocycle.

Table 3 contains CNDO/2 predictions for the charge distribution at each atom of the heterocyclic core for compounds **107** and **55**.²¹

	S1	N2	C3	S4	C5	C6
107	0.04	-0.15	0.13	-0.01	0.04	0.03
55	0.05	-0.15	0.12	0.00	0.00	-0.01

Table 3. CNDO/2 Charge at Ring Positions for **107** and **55**.

The values are directly proportional to charge density, *i.e.* negative values indicate high electron density, or nucleophilic character, whereas positive values represent areas of lower electron density, or electrophilic character. Significant polarisation of the imine functionality of the heterocycle is indicated. High electron density is predicted at N-2, whereas C-3 should have significant electrophilic character.

Importantly, S-4 is predicted to be more nucleophilic in character than S-1. On

this basis, the workers who carried out these calculations²¹ disputed the reaction intermediate **91** (Section 1.4.3.3) proposed by Nakayama *et al*²⁸ for reaction between 1,4,2-benzodithiazines **34** and DMAD (Scheme 21). Intermediate **91** would arise by initial nucleophilic attack of benzodithiazine S-1 on DMAD. The CNDO/2 calculations, however, indicate that S-4 is more nucleophilic in character and would, therefore, be more likely to initiate this type of reaction.

The CNDO/2 calculations also enabled some rationalisations to be made concerning observed reactivity patterns of the 1,4,2-dithiazine system.²¹ Energy terms were determined which relate to the favourability or unfavourability of a given reaction. Some values for theoretical dithiazine model **55** are given in Table 4.

1,4,2-Dithiazine Reaction	Energy Term (eV)
Desulphurisation at position S-1 to give thiazole	+7.34
Desulphurisation at position S-4 to give isothiazole	+8.12
Nitrile extrusion to give dithiete	+8.34
Isomerisation to give 2-imino-1,3-dithiolenes	-0.85

Table 4. CNDO/2 Energy Terms for Dithiazine Model **55**.

Higher energy terms are consistent with more favourable reactions. Thus, it can be seen that desulphurisation was predicted to occur slightly more readily at the S-4 position than at S-1. This supports the experimental observation of isothiazole formation, in preference to the thiazole isomer, for thermolysis of 1,4,2-dithiazines (Section 1.4.3.1). Nitrile extrusion to give a dithiete species was predicted to be an even more likely occurrence than desulphurisation. Whilst this explained the observed competition between sulphur and nitrile extrusion reactions during thermolysis of dithiazines (Section 1.4.3.1), in practice the isothiazole-forming reaction was found to predominate. This illustrates some limitations of these quantum chemical calculations. Finally, the isomerisation of dithiazines to corresponding 2-imino-1,3-dithiolene species (Section 1.4.3.1, Scheme 19) was predicted to be an unlikely reaction pathway. This rearrangement has only been observed for 1,4,2-benzodithiazines.²⁰ Since the model

compound **55** is not a benzo-substituted dithiazine, there is not necessarily a disparity between theoretical prediction and experimental observation for this reaction.

1.5 Conclusions.

The diverse and growing family of heteroclothiazenes represent an area of significant opportunity for further exploration. A large number of ring systems belonging to this family have already been isolated and characterised. Particular advances have been made in the last ten to fifteen years. Reaction methodology developments coupled with improving analytical instrumentation continue to extend the boundaries of the subject.

Within the dithiazine heterocyclic class, new analogues continue to be discovered with an intriguing range of chemical, physical and structural properties, as well as interesting commercialisation prospects. Dithiazine chemistry has recently been much advanced by new developments in synthetic methodology. The resultant access to new derivatives has enabled some detailed studies on the physicochemical nature of dithiazines to be undertaken. In the case of the 1,4,2-dithiazines, a comprehensive picture of reactivity patterns continues to emerge.

A considerable challenge still remains, however, to access less stable dithiazine derivatives and to explore their reactions and properties. In the case of the parent 1,4,2-dithiazine, molecular modelling has thus far afforded the only information on the likely nature of this species. Recent synthetic developments should facilitate the isolation of derivatives which are less stabilised by large substituent groups. This research appears attractive from a number of viewpoints. The compounds have considerable potential for medical and agrochemical applications. Creation and optimisation of new methodology in the area of dithiazine synthesis may also find application in other sectors of organic chemistry, in addition to contributing to the fundamental understanding of organic sulphur-nitrogen heterocycles.

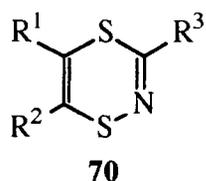
CHAPTER 2

SYNTHESIS AND CHARACTERISATION OF

1,4,2-DITHIAZINE DERIVATIVES

2.1 Introduction.

The 1,4,2-dithiazine ring system, **70**, offered an attractive initial synthetic target as the system may be expected to show a range of interesting chemical, physical and structural properties, arising from the π -electron structure it possesses and the presence of three heteroatoms in the ring.



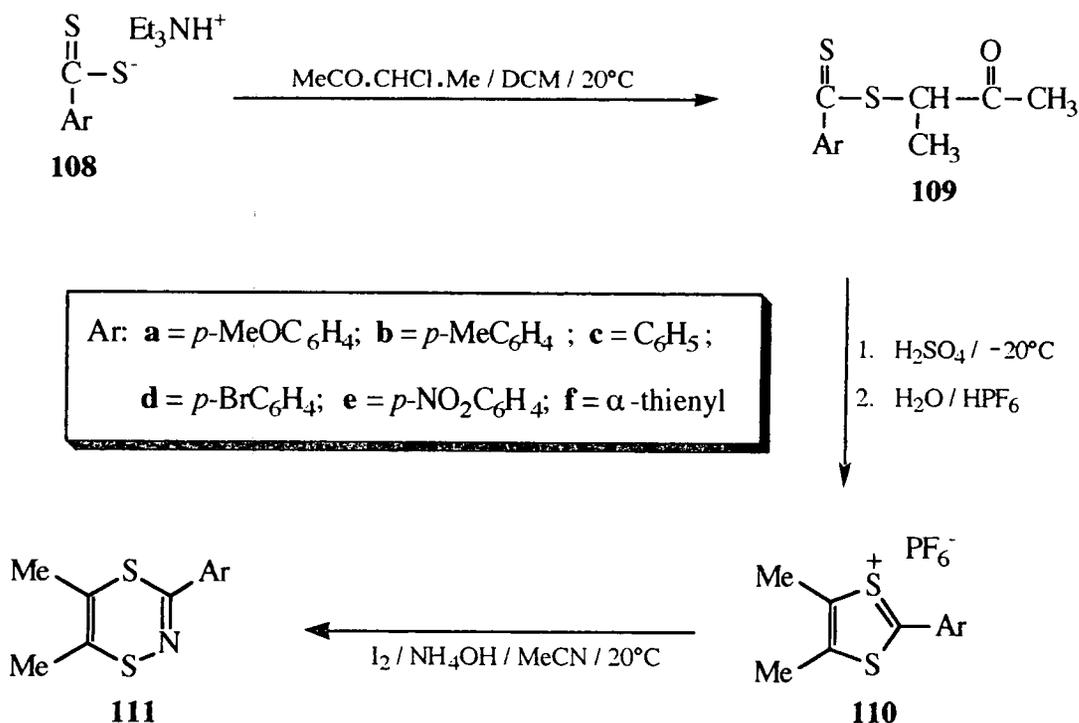
As described in Chapter 1, derivatives of 1,4,2-dithiazines which bear multiple-phenyl or benzo-fused substituents are electronically stabilised. These derivatives are, therefore, quite well represented in the literature.²¹ A significant objective of the current study was to synthesise less substituted 1,4,2-dithiazines, and to explore their reactivity.

The mildest reported conditions for 1,4,2-dithiazine formation involve the iodine-ammonia route (Section 1.4.2.4)²³ and evaluation of this reaction for the synthesis of novel, less substituted 1,4,2-dithiazines was the starting point of our studies.

2.2 Synthesis of 3-Aryl-1,4,2-dithiazines.

2.2.1 Synthetic Details.

Mono-aryl 1,4,2-dithiazines **111** were our initial targets as these derivatives began to develop the theme of eliminating aryl substituents from the dithiazine ring. The synthetic route used is shown in Scheme 27.



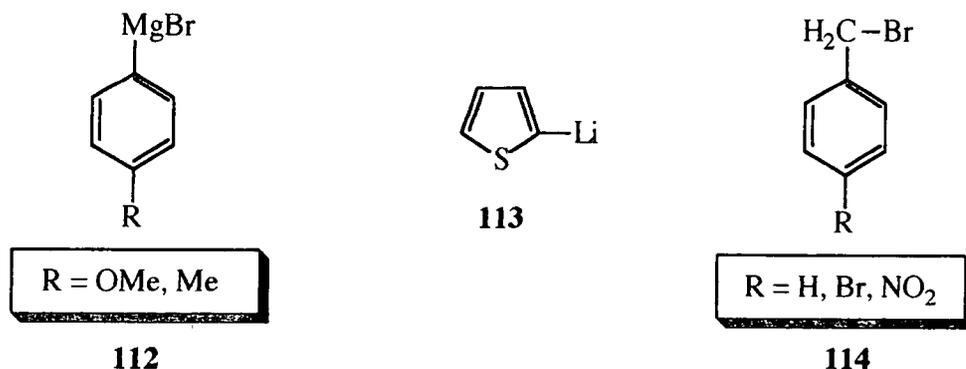
Scheme 27

The range of substituents was chosen with a view to relating observed physicochemical characteristics of the heterocycles to substituent electronic effects. The methodology for synthesis of 1,3-dithiolium cation salts **110** had been previously established and used to good effect at Durham;³³ however, compounds **109a-109f** and **110a-110f** are all new.

2.2.1.1 Synthesis of Dithiobenzoic Acids.

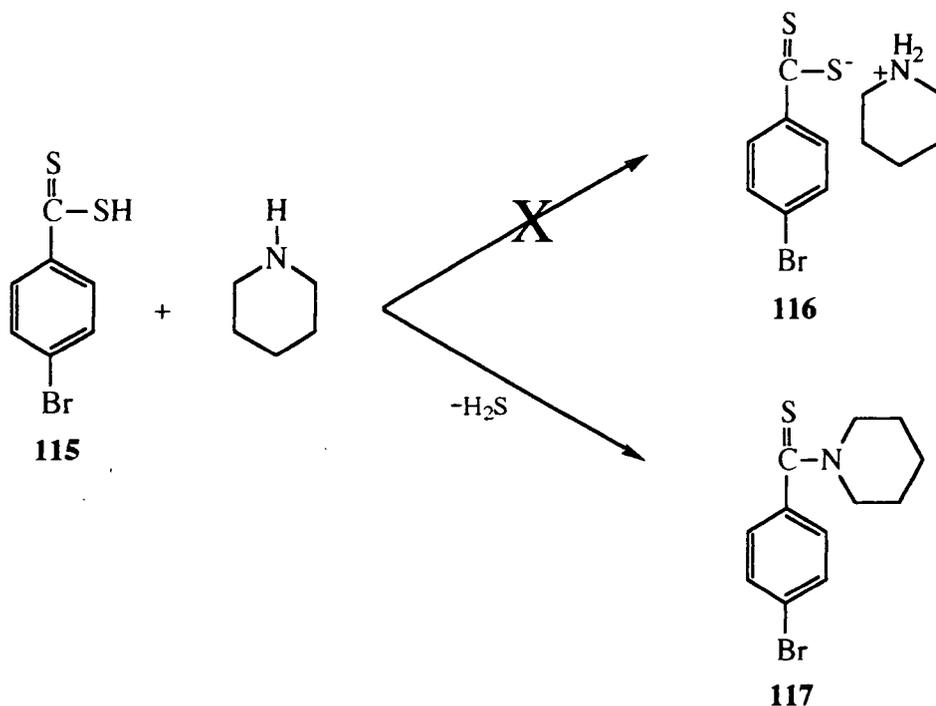
Dithiobenzoic acid salts **108a-108f** (Scheme 27) were synthesised by two different routes. Methoxy, methyl and thienyl salts **108a**, **108b** and **108f** were obtained *via* reaction of appropriate organometallic reagents **112** and **113**³⁴ with carbon disulphide, using a modified literature procedure.³⁵ Conversely, salts **108c-108e** were obtained by reaction of appropriate benzyl bromides **114** with elemental sulphur and sodium methoxide in refluxing methanol, following the patent literature.³⁶ The route *via*

benzyl bromides was found to be inapplicable to the synthesis of salt **108a**, since *p*-methoxybenzyl bromide is known to be thermally unstable;³⁷ following its synthesis by a literature procedure,³⁸ it was found to decompose under the conditions of the above elemental sulphur reaction. Dithiobenzoic acid salts **108a-108f** were isolated in yields of 14-49%.



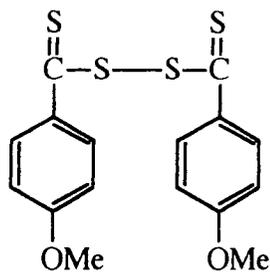
It is noteworthy that *p*-nitrophenyl salt **108e** is described in only one literature report,³⁹ as the morpholino salt. Underlying this fact, salt **108e** was found to be most troublesome to synthesis by the elemental sulphur-sodium methoxide route. After many attempts, the optimum conditions (27% yield) were found to be: very slow addition of *p*-nitrobenzyl bromide to the refluxing sulphur-sodium methoxide mixture, two-fold excess of sodium methoxide and exclusion of oxygen during product work-up.

The literature procedure³³ for isolation of dithiobenzoic acid salts **108** involved liberation of the free acid by hydrochloric acid, followed by isolation as piperidinium salts. This approach was found to suffer from a number of disadvantages. The piperidinium dithioacid salts **108** were frequently contaminated with large quantities of piperidinium hydrochloride by-product. When attempts were made to isolate dithiobenzoic acid **115** as the piperidinium salt **116**, the only product was thioamide **117**,⁴⁰ obtained in 48% yield (Scheme 28).



Reaction of dithioacids with secondary amines, such as piperidine, has been described as a preparative route to thioamides.⁴¹ In the case of dithioacid **115**, the carboxylic carbon is presumably activated to nucleophilic attack as a result of electron withdrawal by the *p*-bromo substituent. These difficulties were overcome by the use of sulphuric acid to liberate the free dithiocarboxylic acid, followed by salt formation with triethylamine. This resulted in much improved purity of the dithioacid salts **108**. Additionally, thioamide formation is precluded by the use of tertiary amines.

An interesting by-product obtained during synthesis of salt **108a** was disulphide **118**, isolated in *ca.* 2% yield. Compound **118** had been previously synthesised,⁴² by oxidation of the sodium salt of the corresponding dithiobenzoic acid with iodine, in potassium iodide solution. It would appear that atmospheric exposure during work-up may have effected the oxidation, to form **118**, in our case.



118

2.2.1.2 Synthesis of Dithiobenzoate Esters.

Dithiobenzoate esters **109a-109f** were synthesised by alkylation of dithiobenzoic acid salts **108a-108f** with 3-chlorobutan-2-one, at room temperature, in dichloromethane (Scheme 27).³³ Column chromatography afforded the dithioesters **109a-109f** as red oils, in yields of 39-91%.

2.2.1.3 Synthesis of 1,3-Dithiolium Cation Salts.

Salts **110a-110f** were synthesised by cyclisation of dithioesters **109a-109f**, during slow addition to concentrated sulphuric acid, with strict control of temperature at -20°C (Scheme 27).³³ The dithiolium cations were isolated as hexafluorophosphate salts **110a-110f**, in yields of 49-90%. These salts are crystalline powders and were found to be shelf stable over a period of many months. Derivatives **110a** and **110f** are highly fluorescent under ultraviolet light. This property is presumably the result of donor-acceptor character arising from conjugation between the electron-releasing aryl substituents and cationic dithiolium rings.

The cyclisation reaction presented some practical difficulties resulting from the high viscosity of the dithioesters **109**. Addition of these compounds to concentrated sulphuric acid, itself viscous at -20°C , often resulted in unreacted "lozenges" of dithioester floating in the acid, which could be prevented by pre-dissolution of the dithioester in an equal volume of dichloromethane or chloroform.

2.2.1.4 Synthesis of 3-Aryl-5,6-dimethyl-1,4,2-dithiazines.

1,4,2-Dithiazines **111a-111f** were synthesised by ring expansion of 1,3-dithiolium cation salts **110a-110f**, initially under conditions described by Yonemoto and Shibuya (Scheme 27).²³ This involved dissolving the salts in acetonitrile and adding one molar equivalent (with respect to the salt) of iodine. The mixture was then stirred at room temperature until homogeneous, after which a large excess (typically, ten molar equivalents) of concentrated aqueous ammonia solution was added dropwise. Immediate darkening of the reaction mixture was usually observed, with formation of a dark precipitate. The reaction was stirred at room temperature for several hours, during which time the solution typically became paler, with a small amount of cream precipitate formed. Aqueous work-up conditions were then employed, with extraction of the product into dichloromethane. The novel 1,4,2-dithiazines **111a-111f** were purified by column chromatography and isolated as yellow crystalline solids, with the exception of derivatives **111c** and **111f**, which were oils, in yields of 33-52%.^{43,44} The characterisation of these materials, particularly their confirmation as dithiazines and not the imine isomers, is described later in this Chapter (Sections 2.4 and 2.5).

2.2.2 Discussion of Results.

All derivatives of **111** are stable under ambient conditions, no significant decomposition being observed after many months storage on the laboratory shelf (NMR evidence).

The advantages of the iodine-ammonia methodology were realised in the series of reactions carried out. Work-up was straightforward and despite attempts to observe imine isomer by-products, none was found during these reactions. As predicted, conducting the reaction at room temperature prevented desulphurisation of the dithiazine products to isothiazoles, which were not observed. In later experiments, the reaction sequence detailed in Scheme 27 was scaled up to yield *ca.* 2 g batches of dithiazines **111**, without serious practical difficulties being encountered.

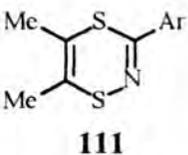
In summary, all stages of Scheme 27 worked satisfactorily, leading to the isolation of six novel 3-aryl-5,6-dimethyl-1,4,2-dithiazines **111a-111f**. The only limitation of the ring expansion reaction was the modest dithiazine yields, 33-52%, obtained under the published reaction conditions.²³ Optimisation of this reaction was clearly, therefore, desirable.

2.2.3 Optimisation of the Iodine-Ammonia Reaction.

Our initial studies had confirmed the suitability of the iodine-ammonia methodology to afford dithiazines, albeit in unsatisfactory yields, using one molar equivalent of iodine and ten molar equivalents of ammonia solution, with respect to the dithiolium cation salts.

We did not want to increase the reaction temperature, in view of our longer-term objective of isolating less stable 1,4,2-dithiazine derivatives. The appearance of the reaction mixture on addition of ammonia solution, combined with thin-layer chromatography (TLC) studies, suggested that the reaction occurred rapidly, and, indeed, it was found to be essentially complete in the first thirty minutes. Increasing the stoichiometry of ammonia solution, to fifteen molar equivalents, or more, had no significant effect on the yield of product isolated.

Conversely, increasing the iodine stoichiometry notably increased dithiazine yields. The optimum stoichiometry was found to be three to five molar equivalents with respect to dithiolium salts **110**. The initial and optimised yields are presented in Table 5. This reaction modification extends the overall utility of the reaction; high purity of the dithiazines was retained, with much improved yields.^{43,44}

 111	<u>Initial Yields (%)^a</u>	<u>Optimised Yields (%)^a</u>
	1 molar equiv. iodine (Yonemoto & Shibuya's conditions) ²³	5 molar equiv. iodine
a (Ar = <i>p</i> -MeOC ₆ H ₄)	33	87
b (Ar = <i>p</i> -MeC ₆ H ₄)	N.A.	83
c (Ar = C ₆ H ₅)	48	87
d (Ar = <i>p</i> -BrC ₆ H ₄)	40	94
e (Ar = <i>p</i> -NO ₂ C ₆ H ₄)	52	61
f (Ar = α -thienyl)	N.A.	86 ^b

^aAcetonitrile, 20°C, 10 molar equiv. ammonia, *ca.* 2 h. ^b3 equivalents iodine.

Table 5. Initial and Optimised Yields of Dithiazines **111**.

2.2.4 Further Studies on the Iodine-Ammonia Reaction.

2.2.4.1 Modification of Reaction Procedure.

Several modifications to the reaction were examined, in the hope of providing evidence for the mechanism of the ring-expansion. The usual order of addition of reagents to the solvent was: dithiolium salt **110**, iodine, then ammonia solution. Addition of ammonia solution first caused decolouration of the yellow salt solution to pale yellow, in approximately two minutes. Iodine was next added, the reaction time and work-up conditions being identical to a control experiment. The yield of isolated dithiazine **111a** was found to be unaffected by varying the order of reagent addition. This result supports the first step of the reaction mechanism outlined by Yonemoto and Shibuya (Scheme 13).²³ Formation of the intermediate amine adduct **66** is suggested, regardless of the reagent addition sequence.

Ring expansion of dithiolium salt **110a** by the iodine-ammonia system was also carried out in *N,N*-dimethylformamide (DMF) rather than acetonitrile as solvent. Both are dipolar, aprotic solvents and the yield of dithiazine **111a** was only marginally higher

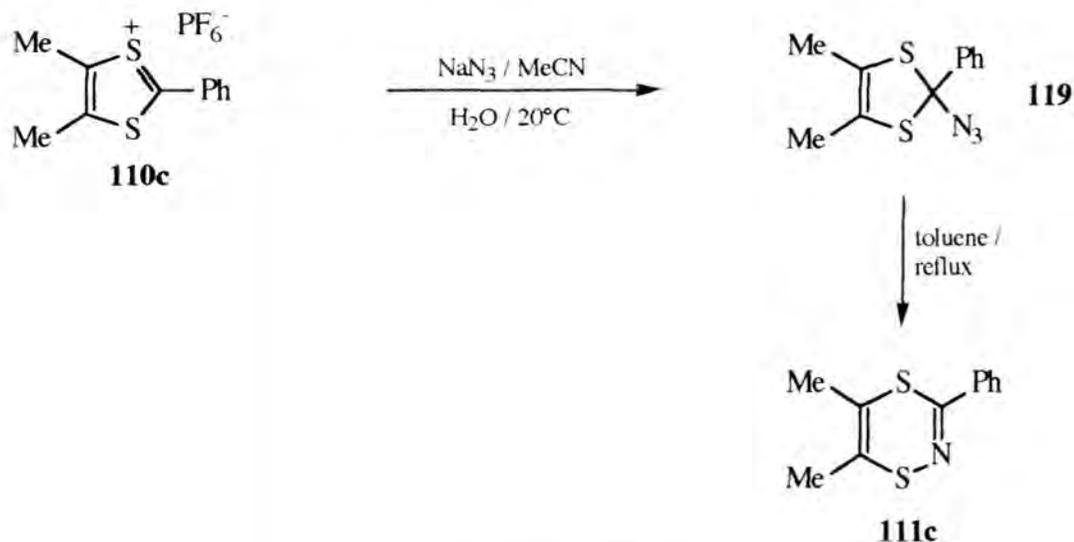
with DMF as solvent, *i.e.* 63% in DMF and 56% in an acetonitrile control. A disadvantage of DMF was the need to remove it by multiple water washes during work-up. Use of DMF may, however, be warranted if the dithiolium salt is insoluble in acetonitrile.

An unsuccessful attempt was made to ring expand salt **110a** in the presence of bromine (five molar equivalents), as a replacement for iodine. No identifiable reaction products were isolated. Destruction of the salt, or dithiazine product, was indicated (NMR and MS evidence), possibly due to oxidation by bromine.

Variation of ammonia stoichiometry was also examined. Reaction of salt **110a** with iodine (five molar equivalents) and ammonia solution (two molar equivalents, *cf.* the usual ten molar equivalents) led to significant reduction in the yield of dithiazine **111a** (*ca.* 4%, *cf.* 56% for control experiment using normal ammonia concentration). It is postulated that much of the ammonia is made unavailable for reaction by adduct formation with iodine, to give $\text{NI}_3 \cdot \text{NH}_3$, a known product of these reagents.⁴⁵ As described in Section 2.2.3, increasing the ammonia stoichiometry above ten molar equivalents had no appreciable effect on dithiazine yields.

2.2.4.2 Comparison of Iodine-Ammonia and Azide Routes.

The azide route to dithiazines was described in Chapter 1 (Section 1.4.2.2). We wished to compare the product types and yields obtained by this reaction with those of the iodine-ammonia route. Azide reactions were carried out on dithiolium salt **110c** (Scheme 29), under conditions approximating to those described by Nakayama *et al.*¹⁸ The impure intermediate azide **119** was isolated and its identity confirmed by NMR. Thermolysis of **119** gave 1,4,2-dithiazine **111c**, in an estimated yield of only *ca.* 4%, in a complex product mixture (NMR evidence). This is in contrast to ring expansion of salt **110c** under optimised iodine-ammonia conditions; dithiazine **111c** was obtained in a yield of 87%. Whilst no attempt was made to optimise the azide route, these initial results clearly showed the far greater synthetic utility of the iodine-ammonia approach.



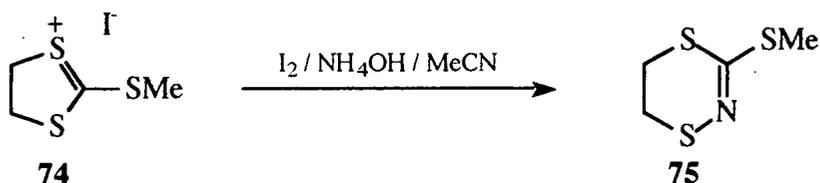
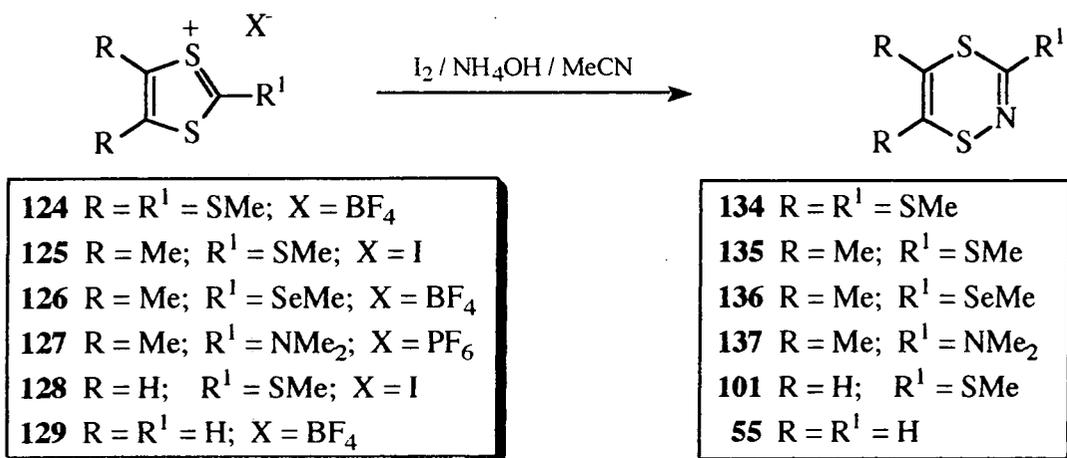
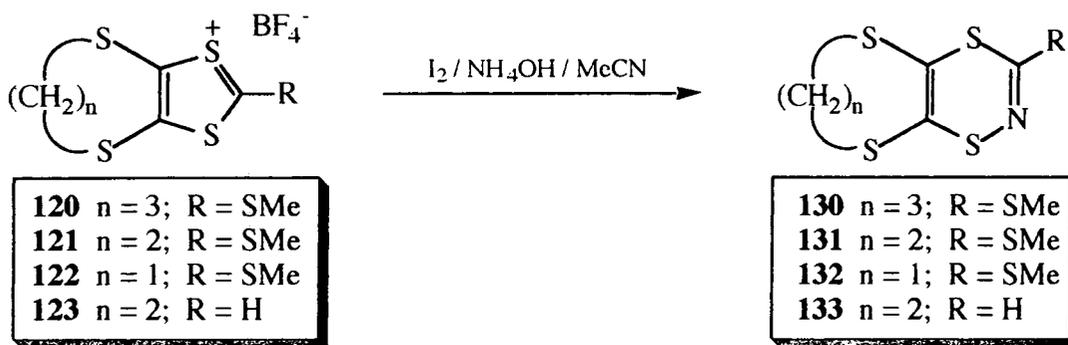
Scheme 29

2.3 Synthesis of Further 1,4,2-Dithiazine Derivatives.

Having thoroughly evaluated the iodine-ammonia route to synthesise a range of 3-aryl-5,6-dimethyl-1,4,2-dithiazines, we next aimed at less substituted 1,4,2-dithiazines, including the first isolation of the parent unsubstituted 1,4,2-dithiazine **55**.

2.3.1 Synthetic Details.

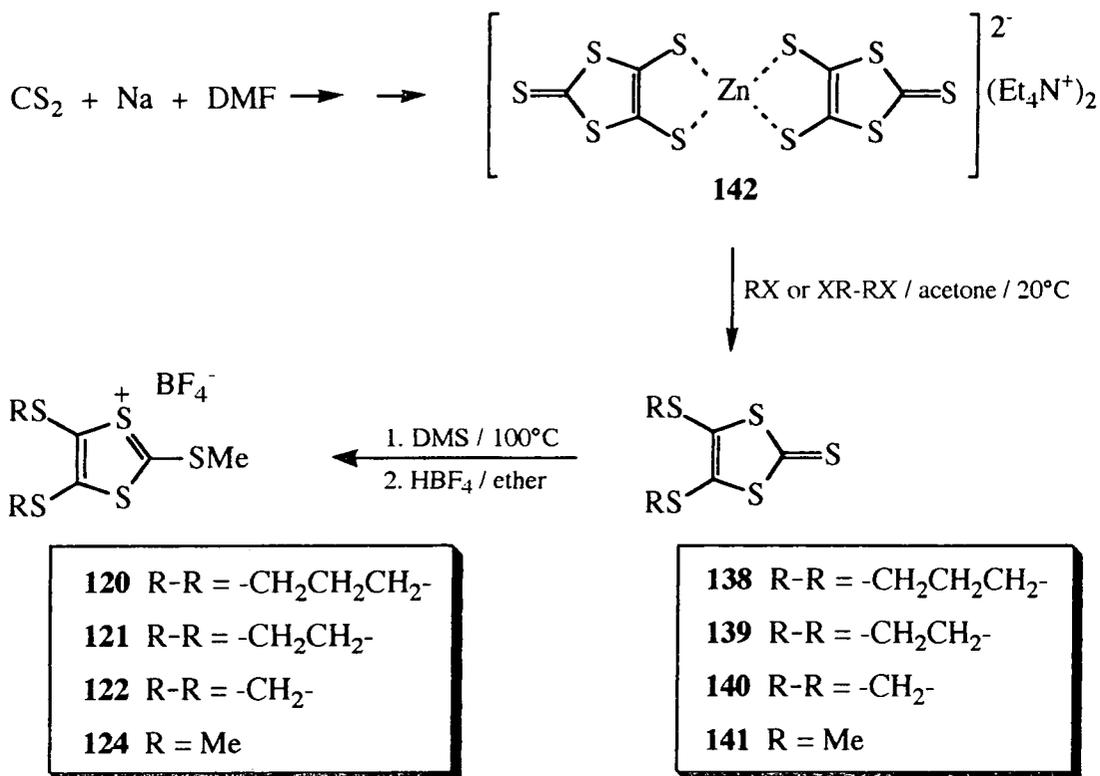
Our target 1,3-dithiolium salts were **120-129**, in order to access 1,4,2-dithiazine derivatives **130-137**, **101** and **55**, respectively (Scheme 30). The series of 1,3-dithiolium cation salts **120-129**, enabled us to define the capabilities and limitations of the iodine-ammonia reaction, to afford 1,4,2-dithiazine derivatives lacking any phenyl substituents. We also planned to examine ring expansion of partially saturated salt **74**, in order to compare our findings with those already published.²³



Scheme 30

2.3.1.1 Synthesis of 1,3-Dithiolium Cation Salts.

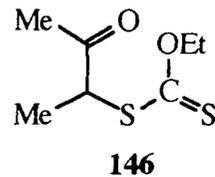
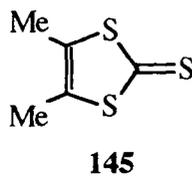
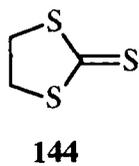
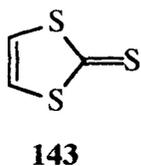
Compounds **120-122** and **124** were synthesised by dimethyl sulphate (DMS) methylation of corresponding precursor thiones **138-141**, derived from alkylation of zincate salt **142** with appropriate alkyl halides (Scheme 31). Zincate **142** was obtained by the reaction of carbon disulphide and sodium, in the presence of DMF, as described by Steimecke *et al.*⁴⁶



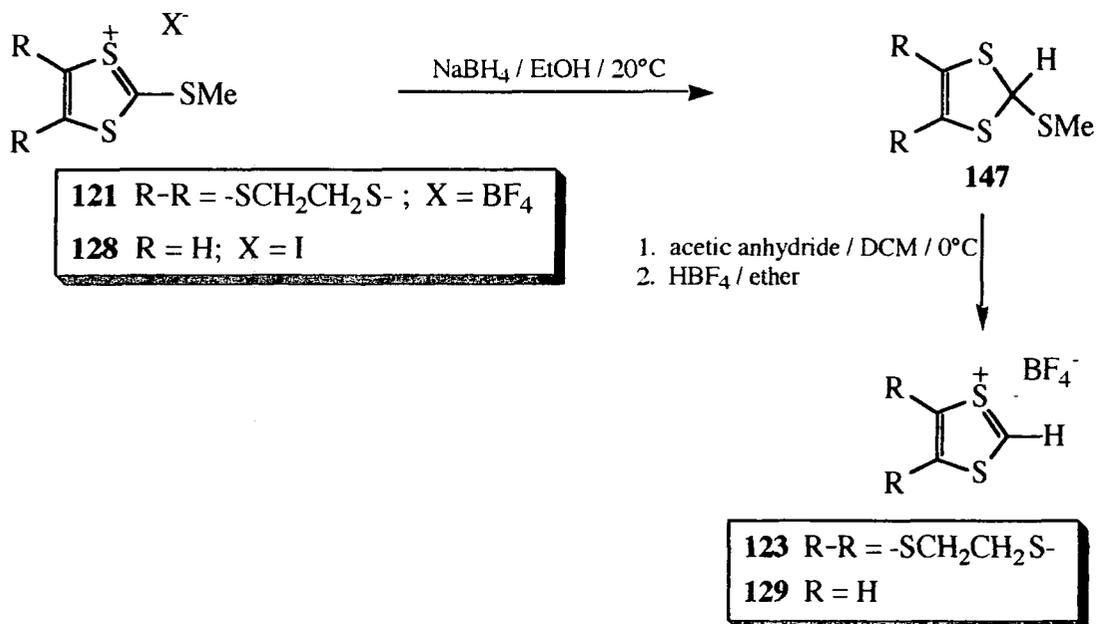
Scheme 31

1,3-Dithiolium salts **120**,⁴⁷ **121**⁴⁸ and **124**⁴⁹ were previously recorded in the literature and obtained in good yields. Salt **122**,⁴⁹ however, proved more difficult to synthesise. Yields of the precursor thione **140** and salt **122** were very low, with much polymeric material in evidence. Attempts to synthesise salt **122**, and, therefore, dithiazine **132**, were subsequently discontinued.

Dithiolium salts **74**²³ and **128**⁵⁰ were synthesised from commercially available thiones **144** and **143**, respectively, by methylation with iodomethane, using a modified literature procedure.⁵⁰ Salt **125**⁵¹ was obtained by iodomethane methylation of thione **145**, itself obtained from xanthate precursor **146**, by a literature procedure.⁵² Salts **126**⁵³ and **127**⁵⁴ were also obtained by modified literature methods.



The remaining 1,3-dithiolium cation salts **123**⁴⁸ and **129**⁵⁵ were obtained *via* salts **121** and **128** respectively, by the literature method⁴⁸ outlined in Scheme 32. Salts **121** and **128** were reduced with sodium borohydride in ethanol to give intermediate dithioles **147**. Acetylation of the methylthio group of **147** was achieved by reaction with acetic anhydride at 0°C. The dithiolium cations were isolated as tetrafluoroborate salts **123** and **129** by the addition of fluoroboric acid.



Scheme 32

The majority of the 1,3-dithiolium cation salts, **120-129** and **74**, were obtained in good yields and found to be reasonably stable under ambient storage conditions. The less substituted species, however, and particularly salts **123** and **129**, decomposed quite rapidly, even at *ca.* 5°C in the dark; these salts were, therefore, reacted immediately.

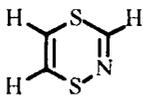
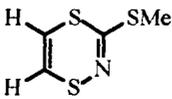
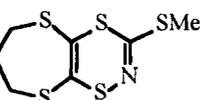
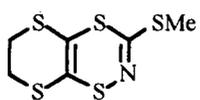
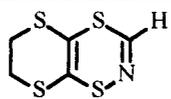
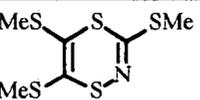
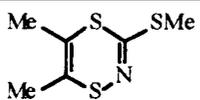
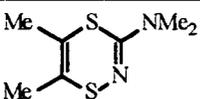
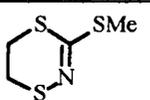
2.3.1.2 Synthesis of 1,4,2-Dithiazine Derivatives.

The 1,3-dithiolium salts **120-129** and **74** were ring expanded using the optimised iodine-ammonia methodology described in Section 2.2.3. Results are given in Table 6.

As for the 3-aryl-1,4,2-dithiazines (Section 2.2.3), five equivalents of iodine (with respect to dithiolium cations) gave higher yields for dithiazine products **130**, **131**, **134** and **135**.⁴⁴ However, the best yield of dithiazine **133** was obtained with only one molar equivalent of iodine, and derivative **137** was obtained in reasonable yield with two equivalents of iodine. Numerous attempts were made to increase the yield of compound **101**. Reaction with five molar equivalents of iodine gave only a 6% yield of **101**. Two molar equivalents of iodine gave **101** in yields of 14% and 26%, for room temperature reactions of sixty and fifteen minutes duration, respectively. Despite several attempts to ring expand 2-methylseleno salt **126** (2-3 equivalents of iodine), dithiazine **136** was not obtained; several reaction products were noted (TLC evidence) and work-up led to the isolation of an intractable oil which did not contain compound **136** (NMR and MS evidence).

Attempts were made to prepare the parent, unsubstituted 1,4,2-dithiazine **55** from 1,3-dithiolium tetrafluoroborate, 0.9 equivalents of iodine and an excess of ammonia, at both 0°C and 20°C. A complex product mixture, which resisted purification, resulted under both sets of reaction conditions. Nonetheless, evidence for the formation, in very low yield, of parent dithiazine **55** came from ¹H NMR and MS analyses (high resolution mass and characteristic fragmentation pattern) of the product mixture resulting from reaction at 20°C.

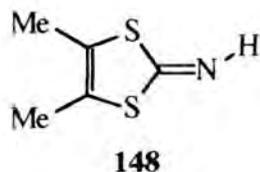
Ring expansion of 1,3-dithiolium salt **74** resulted in the exclusive formation of the 5,6-dihydro-1,4,2-dithiazine derivative **75**, in 42% yield. A previous study of this reaction under comparable conditions,²³ gave a virtually identical yield of dithiazine **75**. However, the previous study also reported isolation of the corresponding imine isomer **76**, in 7% yield (Section 1.4.2.4, Scheme 15). Despite exhaustive attempts to observe this imine in our own reactions, no evidence for its existence was found.

1,4,2-Dithiazine Derivative.	Yield (%).	Optimum Conditions ^a
55 	ca. 1	0.9 eq. I ₂ , 20°C, 30 m
101 	26	2 eq. I ₂ , 20°C, 15 m
130 	12	5 eq. I ₂ , 20°C, 1 h
131 	54	5 eq. I ₂ , 20°C, 2 h
133 	25	1 eq. I ₂ , 20°C, 40 m
134 	38	5 eq. I ₂ , 20°C, 2.5 h
135 	38	5 eq. I ₂ , 20°C, 4 h
137 	65	2 eq. I ₂ , 20°C, 23 h
75 	42	5 eq. I ₂ , 20°C, 2 h

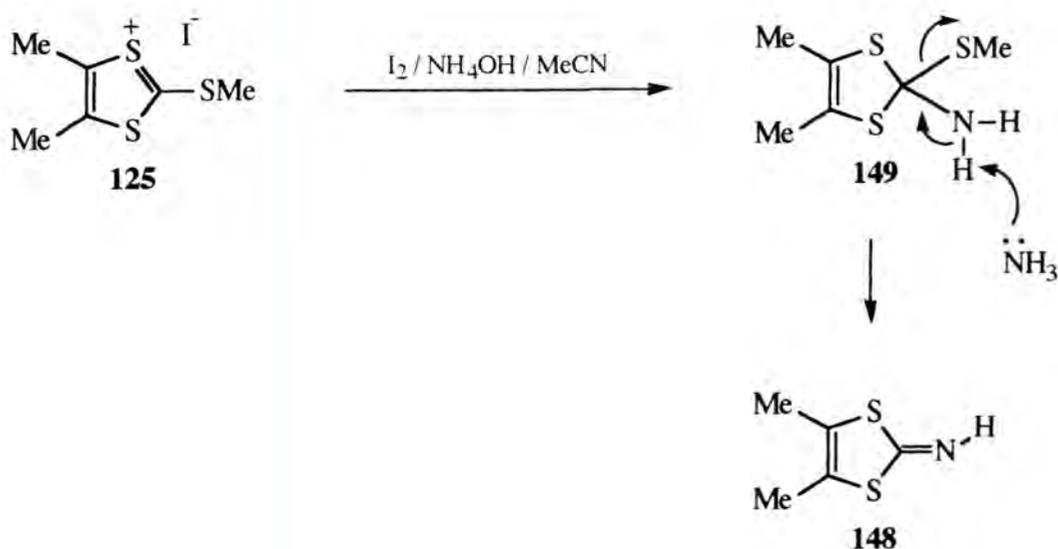
^aAcetonitrile, 10 equiv. ammonia.

Table 6. Yields of 1,4,2-Dithiazines.

The only imine which we have obtained was during ring expansion of dithiolium salt **125**. The main product was the expected dithiazine **135**, in 38% yield, along with imine **148**, in 8% yield, in which the methylthio group has been lost during nitrogen incorporation. Imine **148** has been obtained previously, by an alternative synthetic route.⁵⁶



The isolation of imine **148** was initially surprising, since the methylthio functionality of the precursor dithiolium salt **125** had been lost. A possible mechanism which explains the formation of this imine is given in Scheme 33.



Scheme 33

Amine adduct **149** is formed by initial nucleophilic attack by ammonia on C-2 of the dithiolium salt **125**. Under the reaction conditions, involving a large excess of ammonia, a proton is then removed from the amino group, with concerted loss of the methylthio fragment, to yield the observed imine by-product **148**. Fanghänel has noted the formation of an analogous imine product **100**, by reaction of strong mineral acid with a 1,4,2-dithiazine derivative (Section 1.4.3.5, Scheme 25).²⁵ Alternative mechanisms are likely to operate under these differing reaction conditions.

2.3.2 Discussion of Results.

The synthetic approach shown in Scheme 30 has yielded some interesting 1,4,2-dithiazine products and provided valuable information on the stabilities of less highly substituted derivatives. For the majority of cases, literature routes gave good yields of 1,3-dithiolium salt precursors. Salt **122** was found to be a notable exception; polymeric material predominated during its attempted synthesis.

Ring expansion of the dithiolium salts gave novel dithiazines **130**, **131**, **133**, **134**, **135** and **137**.⁴⁴ Dithiazine **101** had been recorded previously.²⁷ We also obtained NMR and MS evidence for the formerly unknown parent unsubstituted 1,4,2-dithiazine **55**, although it was not possible to isolate this interesting compound in a pure state. Of further note, the bicyclic dithiazine derivatives **130**, **131** and **133** are the first examples of two new heterocyclic systems.

The data presented in Table 6 (Section 2.3.1.2) show an emerging trend of decreasing 1,4,2-dithiazine yield as substituents are removed. The only major deviation from this trend appears to be compound **130**, isolated in only 12% yield, despite its high substituent loading. No obvious reason for this anomalous behaviour can be offered. For the remaining derivatives, as substituents with electron donating or withdrawing capabilities are replaced by hydrogen, decreases in product yield are observed. Once isolated, compounds **130**, **131**, **137** and **75** are air-stable for at least several months at room temperature. The remaining derivatives **133-135**, **101** and **55**, however, decompose at room temperature to yield numerous unidentified products (TLC evidence). Storage at 0°C was required to preserve these compounds for any length of time. The above observations may reflect a measure of anti-aromatic character development in these eight π -electron derivatives.

In general, yields of all 3-methylthio- and 3-hydro-1,4,2-dithiazines were found to be much lower (1-54%) than those of the 3-aryl derivatives (61-94%) described earlier (Table 5, Section 2.2.3). This may further reflect the unstable nature of less substituted derivatives. Concerted efforts were made to find optimum conditions for ring expansion

of the less substituted dithiolium cation salts. Contrary to evidence obtained for the phenyl-substituted derivatives investigated earlier, higher iodine concentrations were actually found to be detrimental to product yields. For example, optimum conditions for the synthesis of dithiazine **101** were not only a reduction to two molar equivalents of iodine, but also a much shorter reaction time of *ca.* 15 minutes (*cf.* two or more hours typically employed for other derivatives). An explanation for this may be that excess iodine reacts with the dithiazine **101**, leading to its destruction, possibly by oxidation. It appears, therefore, that large excesses of iodine are only beneficial for the synthesis of more stable 1,4,2-dithiazine derivatives.

Whilst attempting to isolate the parent dithiazine **55**, very mild conditions were employed. Iodine concentration was limited to 0.9 equivalents and the reaction was carried out at both 20°C and 0°C, with the only evidence for formation of **55** coming from reaction at the higher temperature. This indicates that there may be little scope to reduce the temperature used for the iodine-ammonia reaction, perhaps as the consequence of an activation energy barrier.

It is interesting to contrast the product types isolated from the iodine-ammonia and azide reactions for 2-alkylthio-1,3-dithiolium cation salts. As previously seen (Section 1.4.2.2), ring expansion of these salts by the azide route led to significant competition of reaction pathways, giving both dithiazines and corresponding imine isomers (Scheme 9). Imine isomers were sometimes the major isolated product. During ring expansion of 2-alkylthio-1,3-dithiolium salts by iodine-ammonia methodology, we have not observed the isomeric imine products. The iodine-ammonia route to dithiazines is clearly, therefore, more selective in this respect.

2.4 Spectroscopic and Molecular Modelling Studies on 1,4,2-Dithiazines.

This section details some of the characterisation studies which have been carried out on the new 1,4,2-dithiazine derivatives. Trends in spectroscopic data are discussed and related to previous findings. Additionally, the results of some molecular modelling

studies which we have undertaken are presented and discussed. The fundamental question of dithiazine structural proof is also addressed.

2.4.1 NMR Spectroscopy of 1,4,2-Dithiazines.

The possibility for nitrogen ring expansion of 1,3-dithiolium cation salts to give isomeric 1,4,2-dithiazine and 2-imino-1,3-dithioles by competing pathways has been noted.^{15,18} We wished to confirm unequivocally that our use of the iodine-ammonia reaction on 1,3-dithiolium cation substrates had indeed furnished the dithiazine isomers, rather than imino species.

We first explored this question by the use of NMR spectroscopy. A tentative indication that the isolated major reaction products were dithiazines came by comparison of the spectroscopic data of the supposed dithiazines with those of the minor imine product **148**, the isolation of which is described in Section 2.3.1.2. Significant non-equivalence of the methyl protons was observed for the dithiazines **111a-111e**, *ca.* 0.05 ppm typically separated the methyl singlets. Conversely, the methyl protons of imine **148** were found to be equivalent; a singlet in the NMR spectrum of **148** was observed. This suggests molecular symmetry in the imine **148**, due to rapid inversion of the imine nitrogen on the NMR time-scale; a recognised phenomenon.⁵⁷ This symmetry aspect was clearly absent from the dithiazine molecules, where methyl group non-equivalence would be predicted. However, this evidence was considered insufficient proof and we undertook more detailed NMR investigations.

The major conceivable products which can arise from nitrogen ring expansion of 3-aryl-4,5-dimethyl-1,3-dithiolium salts **110** are represented by 3-aryl-5,6-dimethyl-1,4,2-dithiazines **111** and 2-imino-4,5-dimethyl-1,3-dithioles **150** (Figure 2). The products of the ring expansion reaction were studied by proton-coupled ¹³C NMR spectroscopy.

The main carbon-proton couplings of interest for confirmation of the structural

identity of dithiazines **111** are those between atoms depicted by asterisks (Figure 2). These three-bond couplings, ($^3J_{CH}$), between hetero-ring C-3 and the protons *ortho* to the dithiazine substituent on the benzene ring, were determined for derivatives **111a** and **111c-111e**.

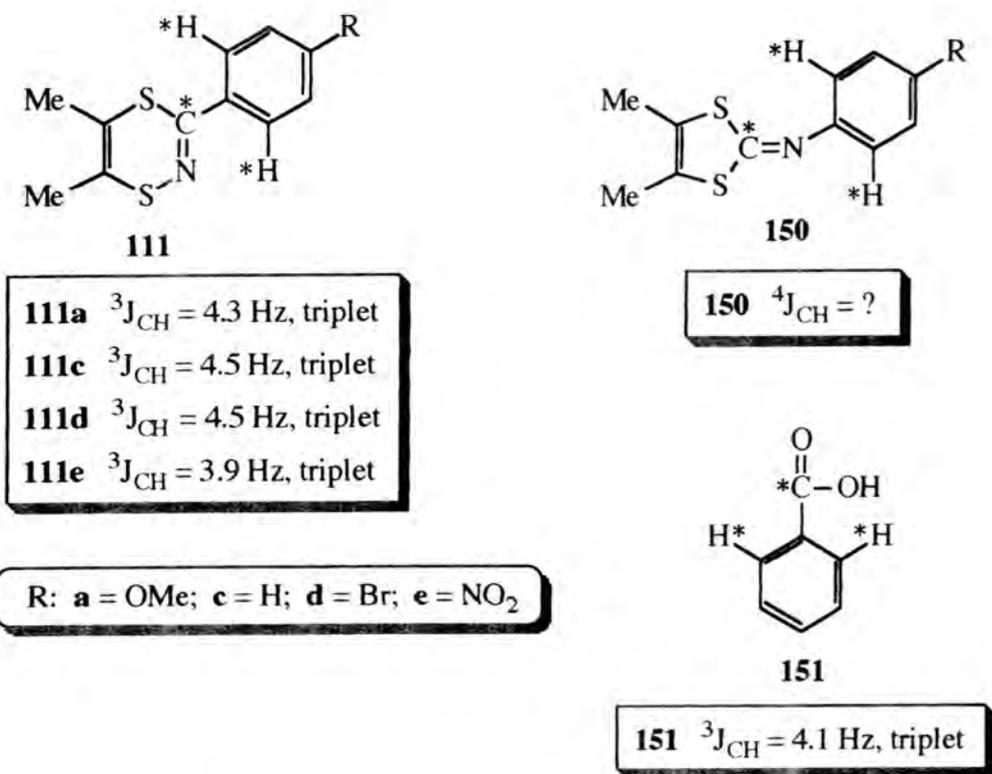


Figure 2. Proton-Coupled ^{13}C Spectroscopic Data.

As can be seen, the coupling results obtained bear great similarity to literature data^{30b} for the structurally-related benzoic acid **151**, in terms of both coupling constant values and multiplicity of carbon peaks.

If reaction products were imine isomers **150**, the diagnostic couplings of asterisked carbon and hydrogen atoms (Figure 2) would be through four atoms ($^4J_{CH}$), with a corresponding reduction in coupling constant by approximately one order of magnitude, to *ca.* 0.5 Hz. Additionally, these couplings would have to occur through nitrogen, a quadrupolar nucleus, which would significantly affect the bonded C-2 nucleus of interest

by a quadrupolar relaxation mechanism. Therefore, for the imine isomer, it is most unlikely that the $^4J_{\text{CH}}$ coupling would be observed, in contrast to the clean triplet signals actually seen. As a result of these NMR studies, we concluded that the dithiazine structures **111** were correct. Some time later, we obtained X-ray crystallographic data (Section 2.5), which confirmed unequivocally these conclusions.

2.4.2 Mass Spectroscopy of 1,4,2-Dithiazines.

Observed mass spectroscopic (MS) data for a range of 1,4,2-dithiazines are shown in Table 7. Radical ion abundance data are given. The data reveal some interesting trends. Abundances of the parent ions of 3-aryl-1,4,2-dithiazines **111a-111f** tend to be higher than those of the other substituted dithiazines **133 - 135**, **101** and **55**. This may be related to the greater stability of the aryl-bearing derivatives under MS conditions. Isothiazole (or thiazole) radical ions of the aryl-substituted derivatives invariably occur in far greater abundance than those derived from the remaining systems, indicating that desulphurisation is easier to achieve in the 3-aryl derivatives. In general, dithiete species predominate for the 3-hydro (**133** and **55**), 3-methylthio (**134**, **135** and **101**) and 3-dimethylamino (**137**) derivatives. For the partially saturated dithiazine **75**, the corresponding saturated dithietane fragment is seen. This may indicate that the primary reason for the observed fragmentation in eight- π dithiazines is the arrangement of heteroatoms in the ring, rather than any anti-aromatic character.

The most interesting observation is the occurrence of the parent dithiete species, **152**, observed for the fragmentation of dithiazines **101** and **55**, in 100% abundance (Scheme 34). This species may be in equilibrium with 1,2-dithioaldehyde **153**.

Dithiazine	Ionisation Mode	Parent	(Iso)thiazole	Dithiete
111a	CI	100%	100%	7%
111b	EI	26%	45%	69%
111c	EI	100%	35%	32%
111d	CI	100%	58%	9%
111e	EI	42%	29%	35%
111f	EI	34%	17%	60%
133	EI	15%	2%	12%
134	EI	9%	3%	53%
135	EI	100%	0%	44%
137	EI	58%	3%	53%
101	EI	28%	2%	100%
55	EI	48%	7%	100%
75	EI	39%	0%	54% ^a

^aDithietane fragment.

Table 7. Radical Ion Abundances (%) for some 1,4,2-Dithiazines.



Scheme 34

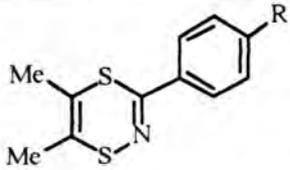
Radical ions **152** and **153** are anticipated to be highly reactive species and it is, therefore, notable to observe them in such high abundance in the mass spectrometer. The overall fragmentation characteristics of the parent 1,4,2-dithiazine **55** match those of other dithiazines. This provides further evidence for the first synthesis of compound **55** during the current work.

Other workers have examined the MS fragmentation of 1,4,2-dithiazines (Section 1.4.3.7, Scheme 26) and drawn the general conclusion that dithiete radical ions predominate over those of isothiazoles.²⁶ This observation was related to dithiazine

fragmentation under photolytic and thermolytic conditions.²⁷ On the basis of the new evidence presented in Table 7, however, it would appear that their conclusions may have been derived from an incomplete set of data. Our findings indicate that, for 3-aryl-1,4,2-dithiazines, isothiazole radical ion formation actually predominates over the formation of dithiete radical ions in several cases. It is, therefore, difficult to make generalisations about the MS fragmentation behaviour of 1,4,2-dithiazines, results of which have a significant dependence on the ring substituents.

2.4.3 Ultraviolet-Visible Spectroscopy of 1,4,2-Dithiazines.

The ultraviolet-visible (UV-VIS) spectra of a number of 1,4,2-dithiazine derivatives have been recorded. Data for 3-aryl derivatives **111a-111e** are presented in Table 8.

 111	λ_{max} (nm) ^a
111a R = OMe	382
111b R = Me	385
111c R = H	389
111d R = Br	393
111e R = NO ₂	432

^a Solvent, dichloromethane : hexane 1 : 1 (V/V).

Table 8. Long Wavelength UV-VIS Absorption Maxima for 1,4,2-Dithiazines **111**.

A correlation can be seen between the electronic properties of aryl substituents and the UV spectra. Bathochromic shifts are observed for increasing electron-withdrawing character of these substituents. This indicates conjugation between the substituent, aryl ring and heterocyclic core; highly electron-withdrawing substituents decrease the overall

π -electron density of the conjugated system. The most significant bathochromic shift occurred for the *para*-nitro derivative **111e**. Enhanced donor-acceptor behaviour across the π -bond framework is suggested, as indicated in Figure 3. Further evidence for conjugation between the aryl and heterocyclic rings of molecules **111** was obtained by X-ray crystallographic (Section 2.5) and solution electrochemical studies (Section 2.6). Ultraviolet spectroscopic data for 3-hydro-, 3-amino- and 3-alkylthio-1,4,2-dithiazines did not show any notable trends.

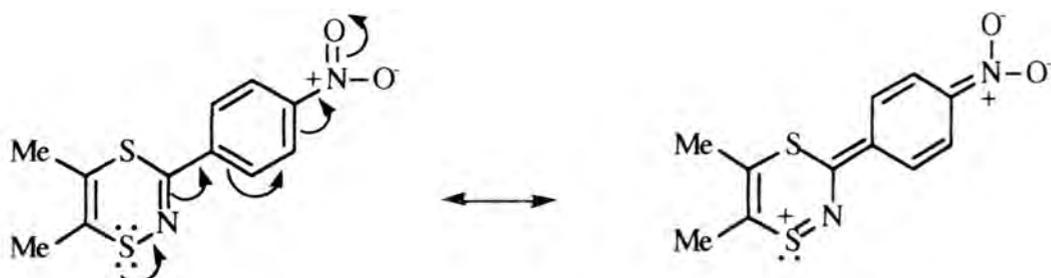
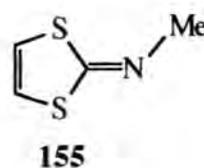
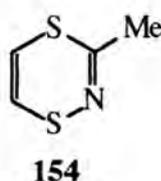


Figure 3

2.4.4 Molecular Modelling Studies on 1,4,2-Dithiazines.

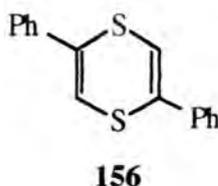
Molecular orbital calculations were carried out on the model compounds, 1,4,2-dithiazine **154** and isomeric imine species **155**, using the PM3 programme.⁵⁸ Heats of formation of compounds **154** and **155** were calculated as +130 and +179 kJ mol⁻¹ respectively. This indicates that dithiazine **154** is the more thermodynamically stable isomer and provides some basis to explain why nitrogen ring expansion reactions of 1,3-dithiolium cations in general lead to an observed predominance of dithiazine products over corresponding imine isomers.



2.5 X-Ray Crystallographic Studies on 1,4,2-Dithiazines.

We have obtained the first X-ray crystallographic data on the geometry of the eight π -electron 1,4,2-dithiazine ring.^{43,44} Single crystal X-ray diffraction studies of compounds **111a** and **130** confirm unequivocally that 1,4,2-dithiazines result from ring expansion of 1,3-dithiolium cation salts under the iodine-ammonia reaction methodology. Crystal structures of compounds **111a** and **130** are shown in Figure 4. Full crystallographic data are recorded in Appendix 1.

In both molecules, **111a** and **130**, the dithiazine ring adopts a boat conformation, by folding along the S(1)··S(4) axis. Fold angles of 50° and 48° were determined for compounds **111a** and **130**, respectively. This type of folding of the heterocyclic ring away from planarity has also been observed for 1,4-dithiin derivatives.⁵⁹ For example, X-ray analysis of 2,5-diphenyl-1,4-dithiin **156** reveals a boat conformation, with a fold angle of 47°.



These deviations from planar ring structures which have been observed for 1,4-dithiins and now for 1,4,2-dithiazines, are consistent with the eight π -electron characteristics of both heterocyclic systems. By bending away from a planar structure, the π -orbital overlap in the 1,4,2-dithiazine core is made less efficient, with the result that anti-aromatic character of the heterocycle is diminished, the system being thus stabilised. Indeed, many of the 1,4,2-dithiazines isolated during our studies have shown excellent stability during long term (> two years) storage under ambient conditions.

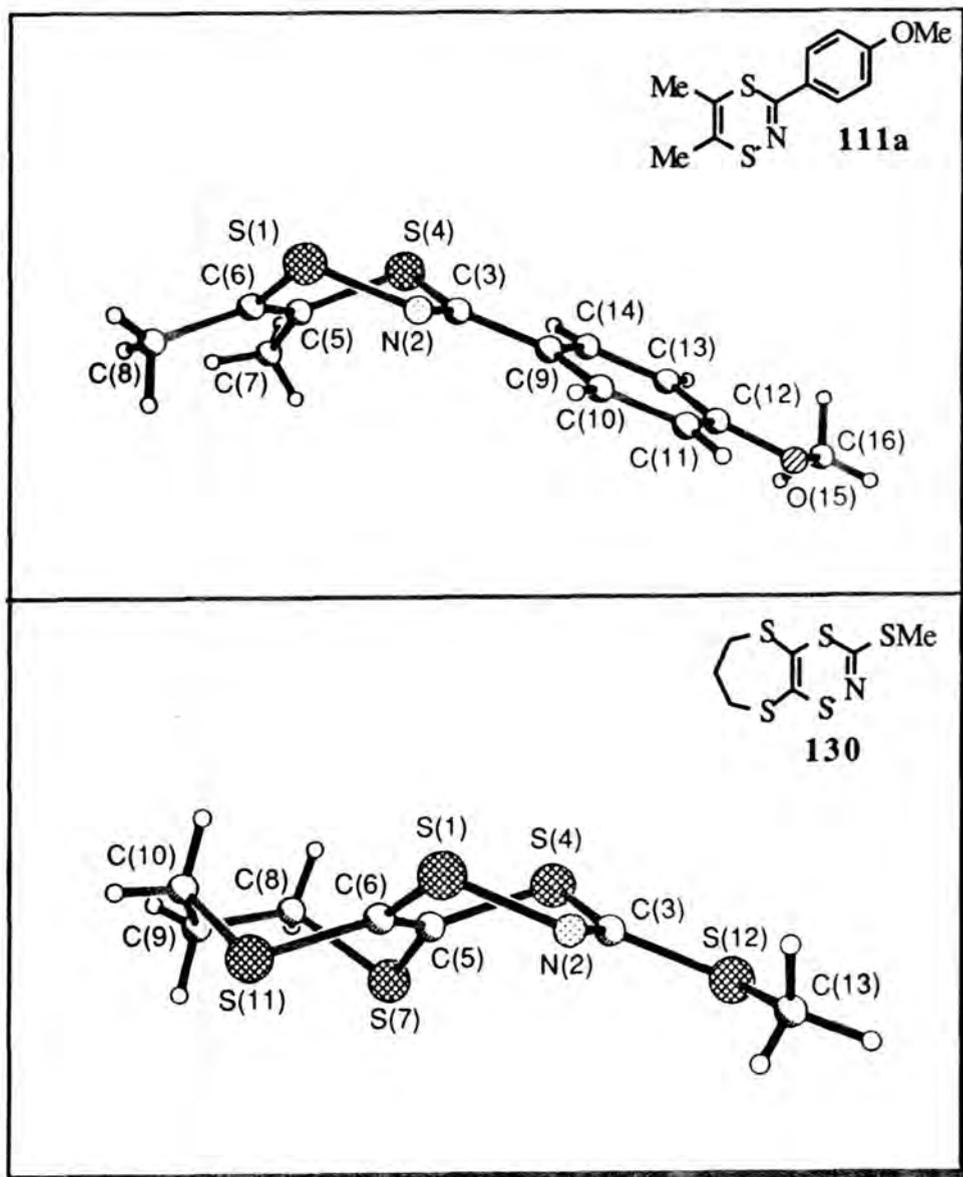


Figure 4. X-Ray Crystal Structures of 1,4,2-Dithiazines **111a** and **130**.

In both **111a** and **130** the substituents attached to C(3) are virtually coplanar with the S(1)-N(2)-C(3)-S(4) plane (plane A), thus maximising their conjugation with the N(2)=C(3) π -bond. In compound **111a**, plane A and the benzene ring form a dihedral angle of 2.9° , whilst the O(15)-C(16) bond is rotated out of the benzene ring plane by only 1.8° . This enables conjugation through the 3-aryl-1,4,2-dithiazines **111a-111e** and is reflected in their UV spectra (Section 2.4.3); *para*-substituents on the aryl ring led to wavelength shifts as the electronic properties of these substituents perturbed the π -conjugated system. Evidence for conjugation in dithiazines **111** was also found during

studies on their solution electrochemistry (Section 2.6).

In compound **130**, the seven-membered heterocycle adopts a chair conformation with folding along the S(7)⋯S(11) axis by 54° and along the C(8)⋯C(10) axis by 61°. Bond distances within the dithiazine ring are essentially the same in compounds **111a** and **130**. Interestingly, the N(2)=C(3) and C(5)=C(6) double bonds are localised, compared to standard values.⁶⁰ This again demonstrates the non-delocalised nature of the dithiazine core. The crystal packing of compounds **111a** and **130** reveals no specifically close intermolecular interactions; the only contact which is shorter than twice the Van der Waals radius of the sulphur atom (1.85-1.90 Å)³² is S(1)⋯S(4) in compound **130** (3.53 Å).

Molecular modelling predictions by other workers for 1,4,2-dithiazine ring geometry are shown in Table 2 (Section 1.4.3.8); results were derived from CNDO/2 calculations.²¹ S(1)⋯S(4) fold angle predictions of 14° and 11° were made for dithiazine derivatives **107** and **55**. Comparison of these predictions with our X-ray data shows that the actual fold angles are considerably larger (48-50°), albeit for different derivatives. The predicted S(1)⋯S(4) distances of 3.37-3.41 Å are smaller than that determined for compound **130** (3.53 Å) from crystallographic data. However, the conceptual prediction that the S(1)⋯S(4) distance may lie inside the sum of Van der Waals radii for two sulphur atoms is shown to be valid. Bond length predictions were generally in good agreement with our crystallographic data.

2.6 Solution Electrochemistry of 1,4,2-Dithiazines.

Prior to our work, studies on the solution electrochemistry of 1,4,2-dithiazine derivatives had not been reported. We have used cyclic voltammetry (CV) to evaluate the redox properties of 1,4,2-dithiazines in the solution state; full procedures are detailed in Chapter 6. Data for a range of eight π -electron 1,4,2-dithiazines and the partially saturated analogue **75** are recorded in Table 9. The cyclic voltammogram of a representative 3-aryl-1,4,2-dithiazine **111d**, and that of the partially saturated dithiazine

75, are recorded in Figures 5 and 6, respectively.

All eight π -electron 1,4,2-dithiazines were found to undergo single electron oxidations, E_1^{ox} , at potentials of between 0.84 and 1.27 V. This corresponds to oxidation of the 8π neutral molecules to 7π radical cations. The process is reversible for the 3-aryl derivatives **111a-111f**, but is irreversible for the 3-methylthio, 3-hydro and 3-amino derivatives **130**, **131**, **133-135** and **137**, for which the corresponding cathodic reduction, E_1^{red} , was seen only as a weak shoulder, was absent altogether, or was shifted to significantly lower potential.

Compound ^a	$E_1^{\text{ox}} / \text{V}$	$E_1^{\text{red}} / \text{V}$	$E_1^{1/2} / \text{V}$	$E_2^{\text{ox}} / \text{V}$	$\Delta E / \text{V}^b$
111a	1.12	0.97	1.05	1.70	0.65
111b^c	1.02	0.92	0.97	d	
111c	1.18	1.10	1.14	1.72	0.58
111d	1.18	1.12	1.15	1.72	0.57
111e	1.24	1.16	1.20	d	
111f	1.19	1.11	1.15	1.72	0.57
130	1.27	1.17	1.22	1.57	0.35
131	1.20	1.13	1.17	1.58	0.41
133	1.24	1.15	1.20	1.52	0.32
134	1.17	1.07	1.12	1.43	0.31
135	1.03	d		d	
137^e	0.84	0.60	f	1.42	
75	1.39	0.83	f	d	

^aCompound (*ca.* 10^{-3} mol dm⁻³) in anhydrous dichloromethane, electrolyte Bu₄N⁺PF₆⁻ (*ca.* 10^{-2} mol dm⁻³), Pt electrode, vs. Ag/AgCl, 20°C. ^b $\Delta E = E_2^{\text{ox}} - E_1^{1/2}$. ^cValidity of data is in doubt.

^dNot observed. ^eEvidence for $E_3^{\text{ox}} = 1.78$ V also. ^fNot applicable due to irreversibility of E_1 .

Table 9. Cyclic Voltammetric Data for 1,4,2-Dithiazine Derivatives.

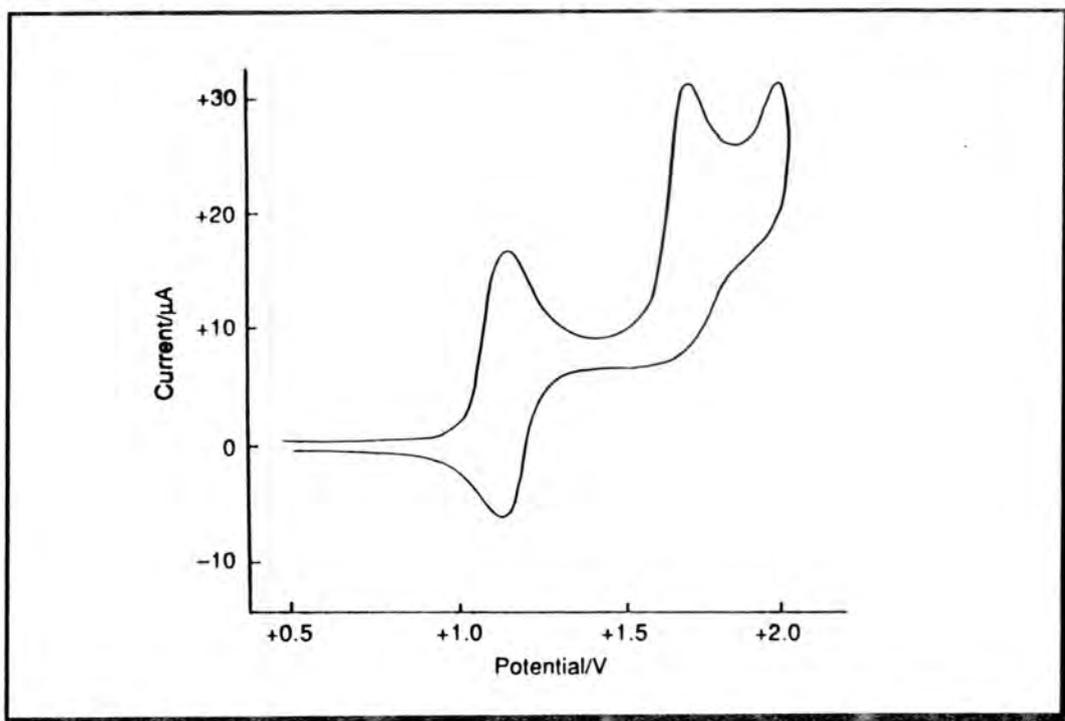


Figure 5. Cyclic Voltammogram of Compound 111d.

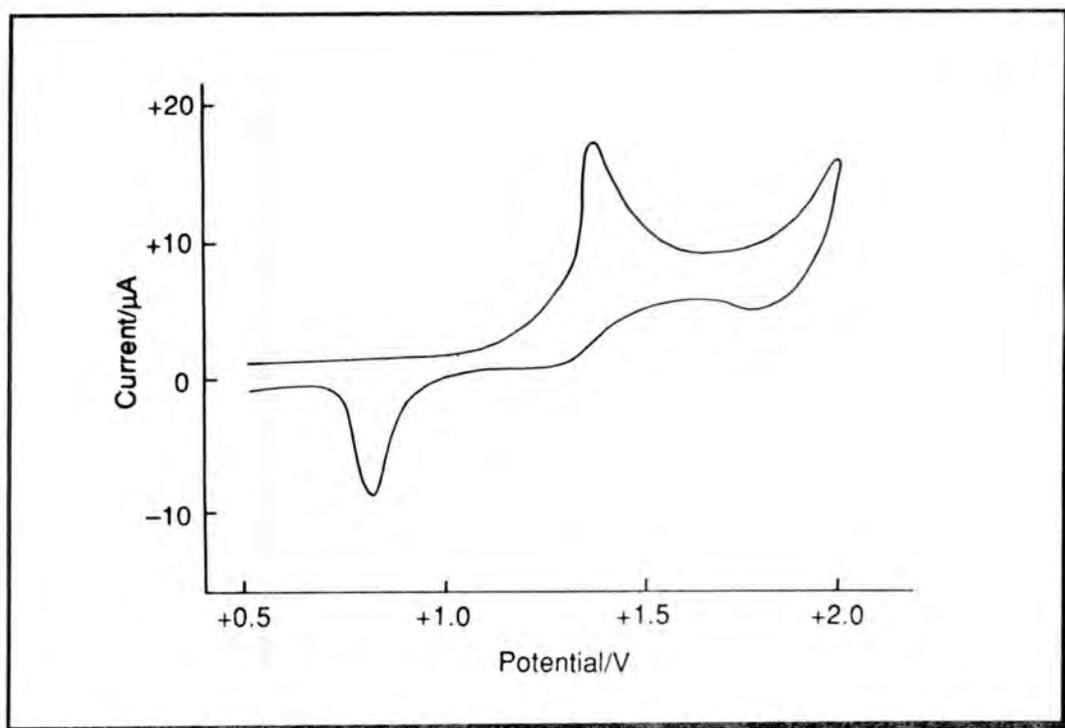


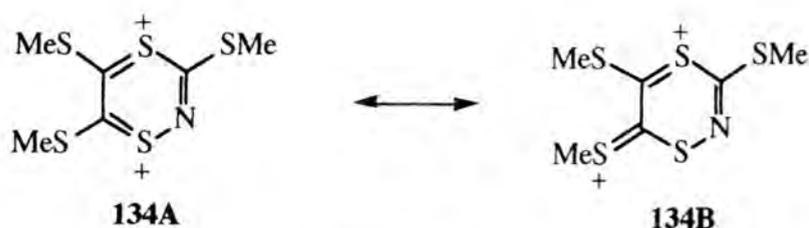
Figure 6. Cyclic Voltammogram of Compound 75.

With the exception of compound **111b**, where the validity of data is in question, the 3-aryl series **111a** and **111c-111e** displays a clear dependence of half-wave potential, $E_1^{1/2}$, upon the electronic nature of the substituents attached to the *para*-position of the aryl ring. The heterocycle was thus harder to oxidise when the electron withdrawing bromo (**111d**) or nitro (**111e**) substituents were present, in contrast to the relative ease of oxidation with a methoxy substituent (**111a**). These data suggest a conjugative effect between the *para*-aryl substituents and the heterocyclic core of the molecule, in agreement with results obtained for the solid-state conformation of the heterocycle (Section 2.5) and UV spectral properties (Section 2.4.3). 3-Phenyl and 3-thienyl derivatives **111c** and **111f** displayed virtually identical electrochemical properties, indicative of the electronic similarity of the phenyl and thienyl ring systems.

A second oxidation, E_2^{ox} , to form the six π -electron 1,4,2-dithiazine dication, is observed for the majority of derivatives (Table 9), compounds **111b**, **111e** and **135** being exceptions. This second oxidation is an irreversible process. Interestingly, the reduction peak, E_1^{red} , is still observed after scanning to a potential of 2.0 V (*i.e.* well beyond the potential for E_2^{ox}). This observation has two key implications: first that the 6π dication species does not decompose at higher potential in a chemical reaction with either solvent or dissolved oxygen. Secondly, that a co-proportionation process may be occurring; that is the 6π dication species is reduced by the neutral 8π molecule, *via* a single-electron transfer process, to form 7π radical cations. These radical cation species are then reduced to the neutral molecule in the observed E_1^{red} wave.

The tabulated difference, ΔE , between the first and second oxidation potentials in multi-stage redox systems can be correlated to coulombic repulsion in the dication redox stage.⁶¹ The values of ΔE were significantly reduced for derivatives **130**, **131**, **133** and **134**, indicating lowered coulombic repulsion for these species in their dication states. These derivatives all carry alkylthio substituents at positions C-5 and C-6 of the heterocyclic core. This implies that these substituents are involved in charge delocalisation, as shown for canonical structures **134A** and **134B** (Scheme 35), with canonical form **134B** reducing coulombic interaction of the positive charges and,

therefore, stabilising the dication oxidation state.



Scheme 35

The solution electrochemistry of 3-amino-1,4,2-dithiazine **137** was significantly different from that displayed by other 1,4,2-dithiazines studied. All observed oxidations of **137** were irreversible processes and the early onset of the first and second oxidation waves, at potentials of 0.84 and 1.42 V, is consistent with stabilisation of the radical cation and dication states by mesomeric release from the 3-dimethylamino substituent. A third oxidation wave, at 1.78 V, was also indicated; this may correspond to a radical trication state, resulting from loss of an electron from the 3-dimethylamino lone-pair of the intermediate dication redox stage.

Comparison of the data obtained for 1,4,2-dithiazines (Table 9) with those reported previously for 1,4-dithiin systems,⁵⁹ reveals that incorporation of a nitrogen atom into the heterocyclic core considerably increases the half-wave oxidation potentials of the system (*e.g.* for the parent, unsubstituted 1,4-dithiin, $E_1^{1/2}$ and $E_2^{1/2}$ occur at 0.69 and 1.16 V, respectively). This indicates that inductive electron withdrawal by the nitrogen atom in 1,4,2-dithiazine derivatives acts to destabilise both the radical cation and dication oxidation states.

The cyclic voltammetric behaviour of the related, partially saturated compound **75** has also been examined (Table 9, Figure 6). The redox properties exhibited by **75** are quite different from those of the eight π -electron dithiazines. A single oxidation peak is seen, at higher potential, with the accompanying cathodic reduction peak shifted to

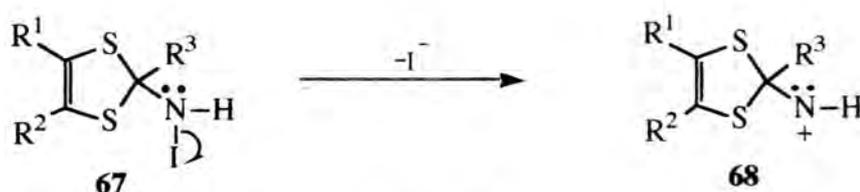
significantly lower potential; this is characteristic of a non-reversible redox process.

2.7 Mechanism of the Iodine-Ammonia Reaction.

2.7.1 Review of Existing Literature.

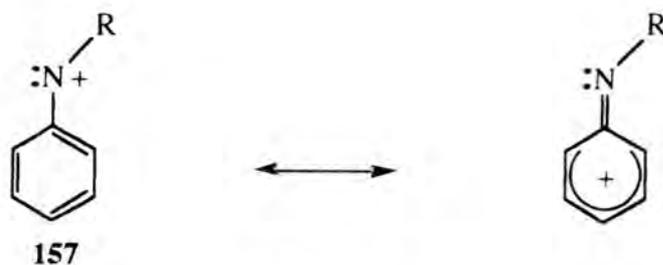
As described in Section 1.4.2.4, the workers who developed the iodine-ammonia route postulated that reaction occurred via a nitrenium ion intermediate (Scheme 13).²³ The main evidence offered for this intermediate was the observation that ring expansion of an unsymmetrical dithiazolium salt under both azide and iodine-ammonia conditions led to the formation of unique product isomers for each reaction (Scheme 14). Since nitrenes are established intermediates of azide methodology, a nitrenium ion intermediate was speculated for the iodine-ammonia route.

We have evaluated the key literature on nitrenium ion chemistry, specifically those reports dealing with the generation of nitrenium ions **68** from haloamine precursors **67**, implicated in the iodine-ammonia route (Scheme 36).



Scheme 36

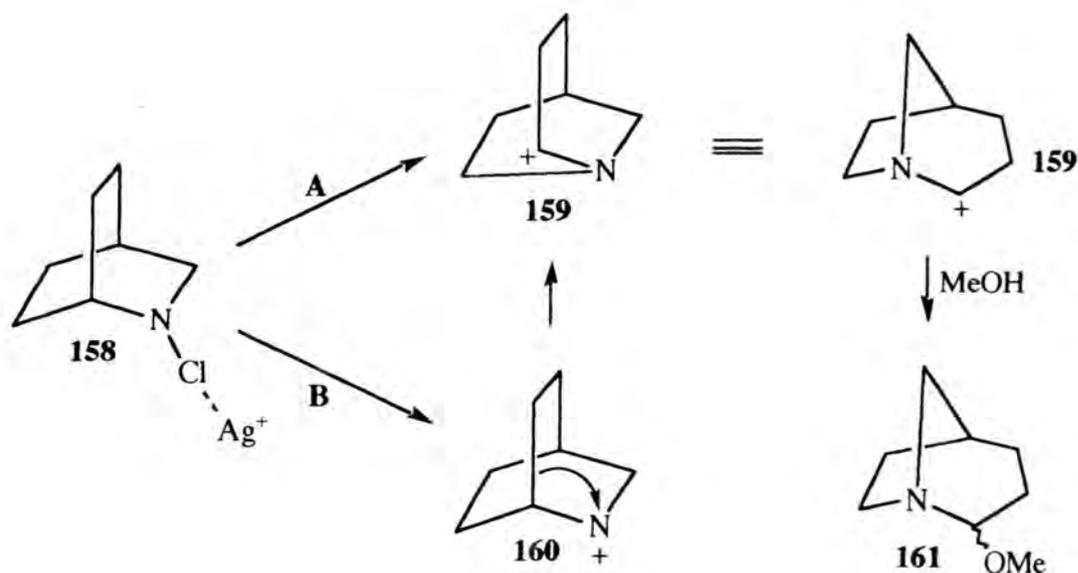
The existence of aryl nitrenium ions **157** seems to be agreed upon, evidence being supplied by both theoretical and experimental studies.⁶²⁻⁶⁴ These species, however, delocalise the formal positive charge on nitrogen over the aromatic ring, thus greatly stabilising these highly reactive intermediates (Scheme 37).⁶⁴



Scheme 37

For alkyl nitrenium ions this stabilisation method is not available. There is disagreement on whether alkyl nitrenium ions exist as discrete intermediates of haloamine heterolytic fission, or whether reaction products can be explained by alternative routes.

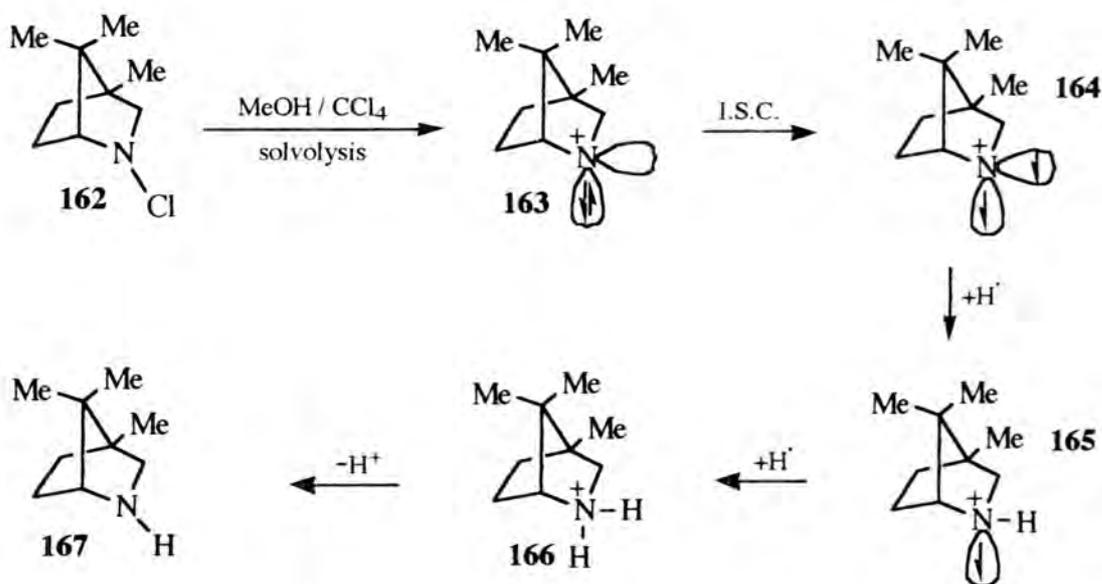
Gassman has carried out much research on whether nitrenium ions can be derived from alkyl haloamine substrates.⁶⁵ For the rearrangement of the alkyl haloamine *N*-chloroisoquinuclidine **158**, in refluxing methanolic silver nitrate, two possible pathways, **A** and **B** were envisaged (Scheme 38). The role of silver ions was to complex with the chlorine atom and thus further polarise the N-Cl bond, assisting the ionisation process.



Scheme 38

Path **A** represents a concerted process, migration of an alkyl group to the nitrogen atom, itself rendered electron deficient by halogen inductive withdrawal, concomitant with loss of chloride anion as silver chloride, to give carbocation **159**. Path **B** involves heterolytic fission of the N-Cl bond of **158** to give the nitrenium ion intermediate **160**, which rearranges to carbocation **159**, and is then trapped by the solvent to give observed ether **161**. Gassman concluded that it was not possible to determine which pathway was operating for this conversion. For a wide range of similar experiments, it was also impossible to differentiate between nitrenium or concerted reaction paths.

However, in related studies, evidence was offered for the formation of discrete nitrenium ions derived from alkyl haloamines by consideration of potential spin-states of the nitrenium ions.⁶⁵ Thus, haloamine **162** was solvolysed in hot methanolic carbon tetrachloride (Scheme 39).

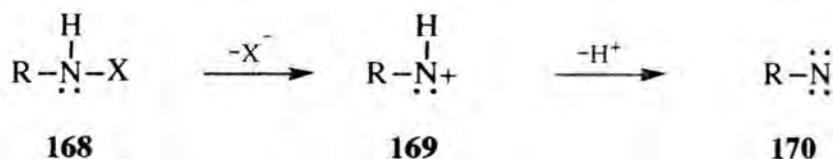


It was anticipated that under these reaction conditions, nitrenium ion **163** would be generated, in the singlet spin-state. It had been shown in separate studies that heavy atom solvents, *e.g.* carbon tetrachloride, could catalyse spin inversion.⁶⁶ Therefore, singlet-state ion **163** may undergo inter-system conversion (I.S.C.) to generate the triplet-state

nitrenium ion **164**. This intermediate was expected to participate in radical reactions with the solvent, specifically to abstract hydrogen atoms from methanol, to yield, sequentially, species **165** and **166**. Ammonium salt **166** was indeed formed under these reaction conditions, deprotonation of which gave amine **167**, in 59% yield. This approach was regarded by Gassman⁶⁵ and others⁶⁷ as offering strong proof for the existence of discrete nitrenium ion intermediates.

Some time later, however, Edwards and co-workers re-evaluated the question of nitrenium ions derived by heterolytic fission of haloamines,⁶⁸ and concluded that nitrenium ions were not formed from simple aliphatic chloramines at room temperature, even in the presence of species which may assist ionisation, such as silver ions. In addition, they stated that no heterolytic fission was observed at temperatures of 60-80°C and regarded decomposition at these temperatures to follow radical processes.

A further complication exists with respect to the concept of nitrenium ion generation from haloamines which bear hydrogen atoms, *e.g.* **168** (Scheme 40).



Scheme 40

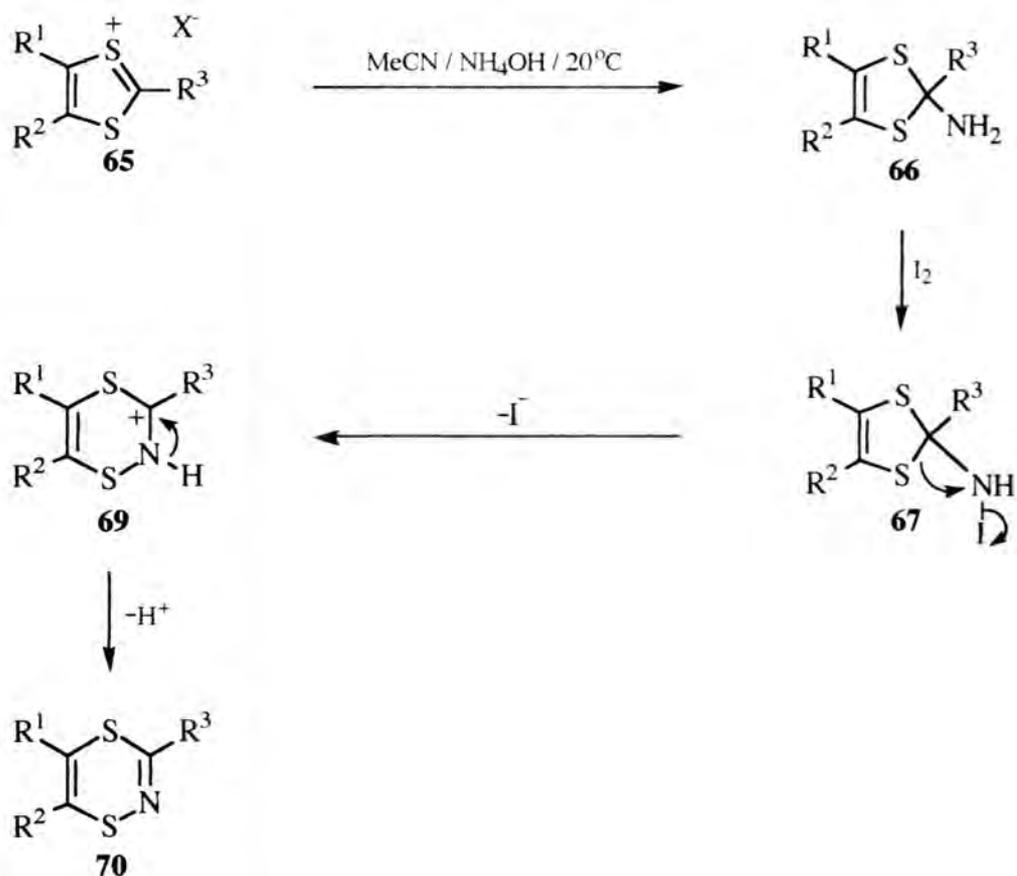
The nitrenium ion intermediate **169** may participate in subsequent reactions directly, or deprotonate to give a nitrene species **170**. The difficulties of selecting between nitrenium ion and nitrene intermediates in these situations has been acknowledged.⁶⁵ As previously seen, nitrene routes to 1,4,2-dithiazines (*via* azide methodology) are well established (Section 1.4.2.2). Of further relevance, the type of nitrenium ion **68** (Scheme 36) postulated as an intermediate for the iodine-ammonia reaction does indeed bear a hydrogen atom.

In summary, opinions on the generation of nitrenium ions by heterolytic fission of alkyl haloamine precursors are divided. Detailed studies have been interpreted diametrically by different workers. Competition between; i) homolytic, ii) heterolytic, iii) nitrene and iv) concerted processes may exist. One fact which does emerge from this uncertain picture is that the intermediate species of the first three processes, namely, amide radicals, nitrenium ions and nitrenes, are all high-energy intermediates with correspondingly high transition state energies and, therefore, activation energies. For a concerted process, employing migration to an electron-deficient nitrogen, with concomitant loss of halogen anion, a lower activation energy barrier may exist and act to favour this pathway.

2.7.2 Postulated Mechanism for the Iodine-Ammonia Reaction.

Having evaluated the literature on the derivation of nitrenium ions from alkyl haloamines (Section 2.7.1) and given consideration to the evidence provided for the participation of these intermediates in the iodine-ammonia reaction,²³ we have now published our own mechanistic interpretation,⁴⁴ as detailed in Scheme 41.

Initial nucleophilic attack by ammonia on C-2 of dithiolium cation salt **65** gives the amine **66**. Significant literature precedents¹⁶ and our own investigations (Section 2.2.4.1) support this proposal. Intermediate **66** then undergoes oxidative iodination to give the haloamine **67**. Up to this point, our mechanism is in agreement with that originally published.²³ In the next step, however, we favour a concerted process whereby a carbon-sulphur sigma bond (or sulphur lone-pair) migrates to the nitrogen centre which is rendered electron-deficient from induction by the attached halogen atom. This creates a new sulphur-nitrogen sigma bond, with concomitant loss of iodide anion. The resultant cationic intermediate **69** then deprotonates, in the presence of a large excess of ammonia, to give the dithiazine product **70**.



Scheme 41

The key advantage of this mechanistic proposal is that it is likely to follow a lower energy reaction coordinate, as the transition state does not involve a discrete high-energy species such as a nitrenium ion, nitrene or free-radical. The positive charge which develops on C-3 in the transition state, during conversion of intermediate **67** into intermediate **69**, is stabilised by the adjacent sulphur atom, in common with the nitrenium ion pathway. The concerted mechanism also takes account of the mild reaction conditions; it has been stated that room-temperature heterolysis of haloamines does not occur.⁶⁸

The concerted route also provides an explanation for product differences noted in the ring expansion of unsymmetrical dithiazolium salt **71** by azide and iodine-ammonia routes (Section 1.4.2.4, Scheme 14). A nitrene mechanism for the former, and concerted mechanism for the latter, may account for the unique products isolated.

Kinetic studies to support the mechanism in Scheme 41 have not been undertaken. We do, however, believe that the concerted route is less contentious than one which invokes nitrenium ion intermediates.²³

2.8 Conclusions.

The work described in this Chapter has demonstrated the effectiveness of the iodine-ammonia route for the synthesis of 1,4,2-dithiazines with less stabilising substituent groups. A wide range of new dithiazine derivatives have been isolated, including the first observation of the parent, unsubstituted 1,4,2-dithiazine itself. The majority of the dithiazine derivatives which we have synthesised do not carry phenyl substituents; reports of these derivatives were rare prior to our studies. Two novel bicyclic systems have also been obtained during our work.

As we have progressed the trend from mono-phenyl-1,4,2-dithiazines, to the parent heterocycle itself, the instability of the heterocyclic core has become apparent in reduced product yields and diminished stability of the derivatives under ambient storage conditions. This may reflect some increase in the anti-aromatic nature of the heterocyclic system.

The iodine-ammonia reaction has been optimised to give greatly improved dithiazine yields in most cases and we have proposed a reaction mechanism which takes account of both the existing knowledge in this area and the conditions under which reaction takes place. The reaction has been compared with the azide approach to 1,4,2-dithiazines and for the same substrate, the iodine-ammonia route gives significantly better yields of dithiazine, in far greater purity.

Detailed characterisation of the novel 1,4,2-dithiazines has included: NMR techniques to determine the isomeric identity of the ring expansion products as 1,4,2-dithiazines; X-ray crystal structure analysis of two 1,4,2-dithiazine derivatives which shows that the dithiazine ring exists in a boat conformation in the solid state; ultraviolet

spectroscopy which has shown correlations between the electronic properties of the substituents of some derivatives and the position of λ_{max} (consistent with the solid state structures confirmed by X-ray diffraction analysis), and cyclic voltammetry to explore the solution redox properties of these systems. Mass spectroscopic fragmentation patterns have been examined and compared for a range of derivative sub-classes.

CHAPTER 3

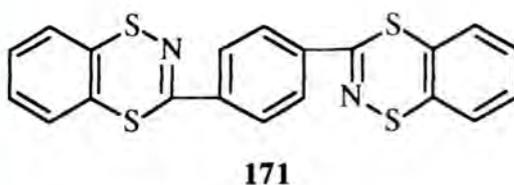
SYNTHESIS AND CHARACTERISATION OF BIS(1,4,2-DITHIAZINES) AND RELATED STUDIES

3.1 Introduction.

The work described in this Chapter concerns the application of methodologies developed in Chapter 2 to the synthesis of novel bis(1,4,2-dithiazine) derivatives. We also briefly examine some approaches to the synthesis of heterocyclic systems other than the dithiazine class.

3.2 Synthesis and Characterisation of Bis(1,4,2-dithiazine) Derivatives.

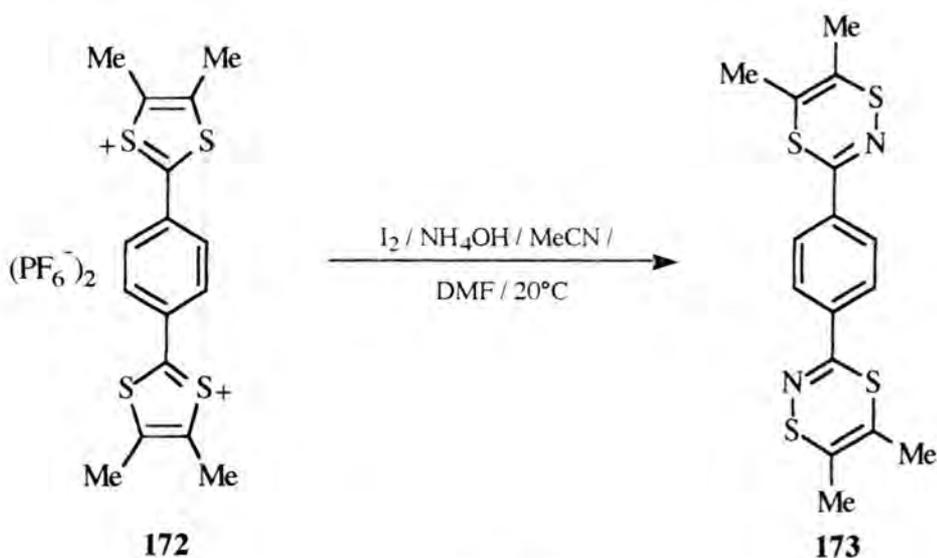
There is one literature report of a compound which contains two 1,4,2-dithiazine rings, *viz.* the bis(1,4,2-benzodithiazine) **171**,¹⁸ synthesised from the corresponding bis(1,3-dithiolium) dication salt by the azide route (Section 1.4.2.2).



We have explored nitrogen ring expansion of bis(1,3-dithiolium) salts,^{55,69-72} under iodine-ammonia conditions (Section 1.4.2.4), and characterised the resulting bis(1,4,2-dithiazines) by a variety of techniques.

3.2.1 Synthesis of a *para*-Phenylene-bis(1,4,2-dithiazine).

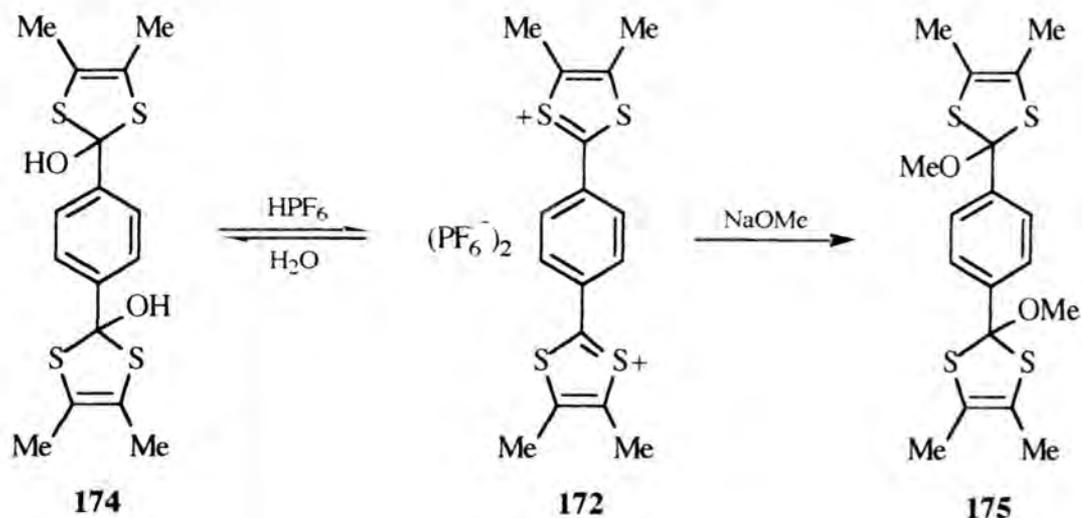
Bis(1,3-dithiolium) salt **172** was synthesised, in four steps, from *p*-xylene, following literature procedures (Scheme 42),^{71,73} and reacted under iodine-ammonia conditions (4 equivalents of iodine with respect to salt **172**), using dimethylformamide as co-solvent (salt **172** was sparingly soluble in acetonitrile). Bis(1,4,2-dithiazine) **173** was obtained in 44% yield, as an orange crystalline solid.



Scheme 42

Bis(hexafluorophosphate) salt **172** was water soluble, in contrast to other 1,3-dithiolium hexafluorophosphate salts, *e.g.* Section 2.2.1, salts **110a-110f**, which were insoluble. An aqueous solution of compound **172** could be re-precipitated as the bis(hexafluorophosphate) salt by the addition of excess hexafluorophosphoric acid. We postulate that, due to extended conjugation in dication salt **172**, the compound might be more reactive to nucleophiles, and be in equilibrium with diol **174**, thus explaining its solubility (Scheme 43). Alternatively, the behaviour of salt **172** under aqueous conditions may be explained simply by solvation phenomena.

Salt **172** was, however, insoluble in methanol and no evidence of comparable nucleophilic attack by the alcohol was observed at room temperature (TLC). Addition of sodium to the alcoholic suspension led to reaction, to afford the bis(1,3-dithiole) **175**, in 40% yield.



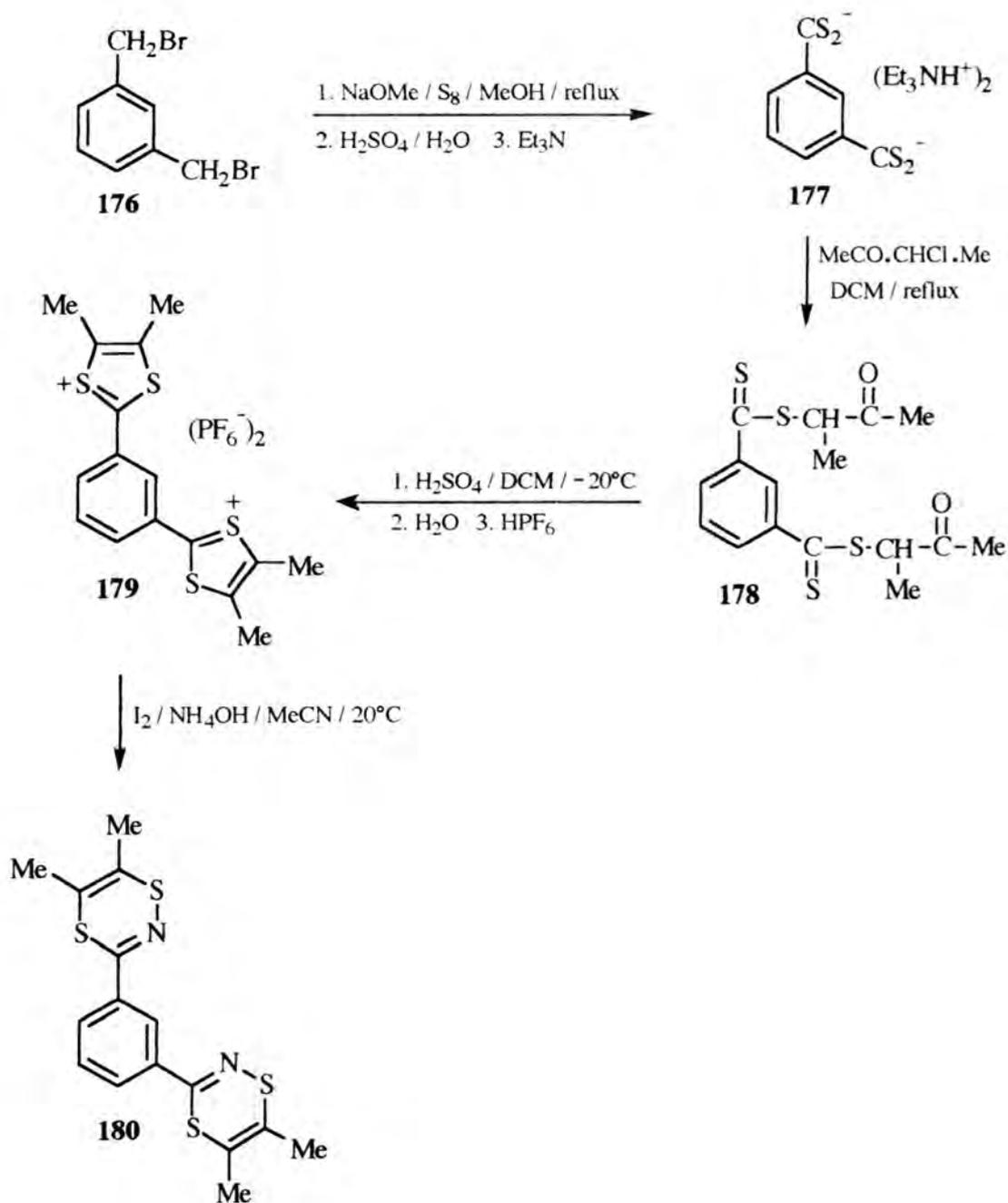
Scheme 43

3.2.2 Synthesis of a *meta*-Phenylene-bis(1,4,2-dithiazine).

Synthesis of the *meta*-analogue **180** was undertaken, by the procedure shown in Scheme 44. *m*-Dibromoxylene **176** was used to synthesise bis(dithiobenzoate) salt **177**,⁷² in 59% yield, following the literature route.³⁶ Alkylation of salt **177** with 3-chlorobutan-2-one afforded the novel bis(dithioester) **178**, in 73% yield. Salt **179** could not be obtained in pure form; addition of hexafluorophosphoric acid during work-up led to the formation of a pale precipitate which rapidly decolourised, indicating decomposition of the product salt. Fast isolation of the impure salt, however, followed by immediate reaction under iodine-ammonia conditions, led to the formation of *m*-bis(1,4,2-dithiazine) **180**, in overall yield of 2.1% from bis(dithioester) **178**. Bis(dithiazine) **180** was stable under ambient conditions.

3.2.3 Characterisation of Bis(1,4,2-dithiazine) Derivatives.

The solution electrochemistry of bis(1,4,2-dithiazines) **173** and **180** has been studied by cyclic voltammetry; results are collated in Table 10. The electrochemical properties of *p*-bis(dithiazine) **173** were similar to those of 3-aryl-1,4,2-dithiazine



Scheme 44

derivatives which we have studied (Section 2.6, Table 9). A reversible half wave oxidation, $E_1^{1/2}$, was observed, corresponding to oxidation of the neutral compound **173** to the bis(radical cation) redox stage. A second, irreversible oxidation, E_2^{ox} , to the bis(dication) redox stage was also noted for compound **173**. These results indicate that each dithiazine ring behaves as an independent and isolated electronic system in these redox processes, with no conjugative effects being observed through the connecting

benzene ring of the molecule.

m-Bis(1,4,2-dithiazine) **180** also showed a reversible first oxidation wave, at potentials comparable to the *para* analogue **173**. However, a second oxidation of compound **180** was not observed. This reluctance to undergo a second oxidation could be due to increased intramolecular coulombic repulsion in the *meta*-isomer **180**, compared with *para*-isomer **173**.

Compound ^a	$E_1^{\text{ox}} / \text{V}$	$E_1^{\text{red}} / \text{V}$	$E_1^{1/2} / \text{V}$	$E_2^{\text{ox}} / \text{V}$	$\Delta E / \text{V}^{\text{b}}$
173	1.25	1.09	1.17	1.74	0.57
180	1.24	1.05	1.15	c	

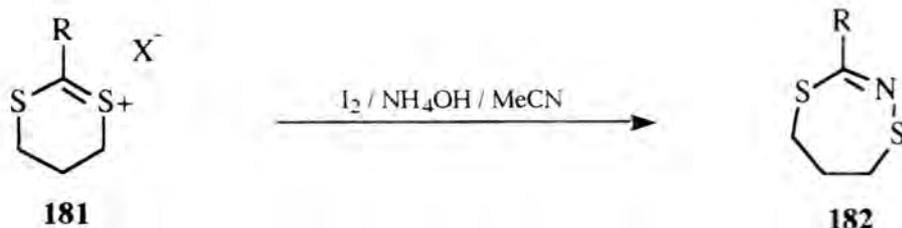
^aCompound (*ca.* 10^{-3} mol dm⁻³) in anhydrous dichloromethane, electrolyte Bu₄N⁺PF₆⁻ (*ca.* 10^{-2} mol dm⁻³), Pt electrode, vs. Ag/AgCl, 20°C. ^b $\Delta E = E_2^{\text{ox}} - E_1^{1/2}$. ^cNot observed.

Table 10. Cyclic Voltammetric Data for Bis(1,4,2-dithiazine) Derivatives.

The mass spectra of compounds **173** and **180** showed similar features; peaks were observed for the parent bis(dithiazine) (m/z 364), isothiazolodithiazine (m/z 332) and bis(isothiazole) (m/z 300) radical ions, resulting from sequential desulphurisation of the compounds. Peaks were detected (m/z 118) for the dithiete radical ion, derived from fragmentation of the dithiazine rings of compounds **173** and **180** into dithiete and nitrile species; various nitrile fragmentation products were also observed. These results are analogous to those obtained for 3-aryl-1,4,2-dithiazines (Section 2.4.2, Table 7).

3.3 Studies on the Synthesis of 1,4,2-Dithiazepines.

Ring expansion of 6-membered 1,3-dithianium cationic salts, **181**, under iodine-ammonia conditions, has been examined, with the objective of synthesising seven-membered 1,4,2-dithiazepine species **182** (Scheme 45); this would represent the first example of six- to seven-membered ring expansion using iodine-ammonia methodology.

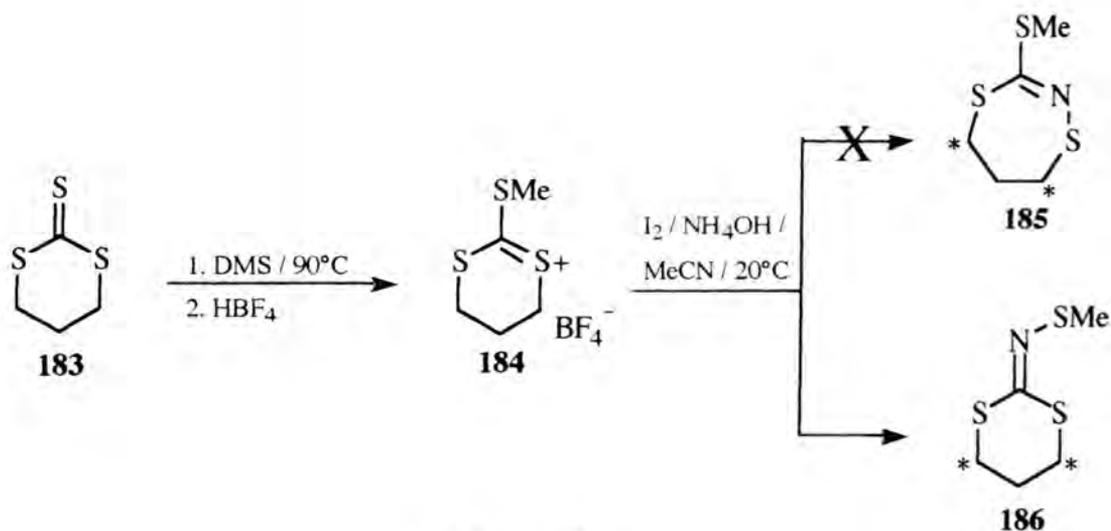


Scheme 45

Reaction of thiophosgene with propane-1,3-dithiol, using a modified literature procedure,⁷⁴ gave thione **183** in low purity and yield (< 20%). Conversely, reaction of carbon disulphide with sodium hydroxide solution, under phase-transfer conditions with tricaprilmethylammonium chloride as catalyst, followed by addition of 1,3-dibromopropane, afforded thione **183**, in *ca.* 60% yield.⁷⁵ It is notable that only a 30% yield of compound **183** was reported when *n*-tetrabutylammonium hydrogensulphate was used as the phase-transfer catalyst.⁷⁵

Thione **183** was alkylated with dimethyl sulphate,⁷⁶ to afford salt **184**, in 81% yield (Scheme 46). Reaction of **184** under iodine-ammonia conditions (2.5 equivalents of iodine), yielded a product, in 5% yield, whose analytical data (NMR, MS, elemental composition) fitted either isomer **185** or **186**. To establish the identity of the isolated product, we resorted to a variable temperature (VT) proton NMR study. At 22°C, the protons corresponding to the asterisked methylene groups of **185** or **186** (Scheme 46) were seen as two distinct triplets with a chemical shift difference of 0.083 ppm (Figure 7). For the dithiazepine isomer, **185**, raising the temperature at which the NMR data were collected would be expected to have little effect on these methylene triplets.

For the imine isomer **186**, however, raising the temperature would enable faster inversion of the imine nitrogen to occur, with the result that the asterisked methylene groups of **186** would become progressively more equivalent, leading to coalescence of the two distinct triplets. We observed that the triplets began to coalesce at *ca.* 50°C, with almost complete coalescence occurring by 70°C (Figure 7). Notably, the remaining proton signals of the molecule remained sharp throughout the experiments.



Scheme 46

These studies indicate that the isolated reaction product is imine isomer **186**. This is the first example we have seen where the iodine-ammonia reaction has led to imine formation with retention of the 2-substituent of the salt, although Yonemoto and Shibuya have reported the isolation of an analogous imine species **76** under these conditions (Section 1.4.2.4, Scheme 15). The formation of compound **186** may be attributable to the seven-membered ring isomer **185** being disfavoured.

Our isolation of isomer **186**, and its poor yield, are in contrast to results which we have obtained for reaction of the homologous salt **74**, where the ring expansion product **75** was obtained, in 42% yield (Section 2.3.1). Attempts were made to improve the product yield from reaction of salt **184**, by increasing the iodine stoichiometry to five equivalents; no isolable products were formed under these conditions.

Salt **184** was also reacted with sodium azide, using conditions described by Fanghänel (DMF, 0°C).¹⁹ No evidence for the formation of dithiazepine **185** or imine **186** was found (NMR and MS analysis), again indicating that the azide reaction is harder to control than the iodine-ammonia reaction (see also Section 2.2.4.2).

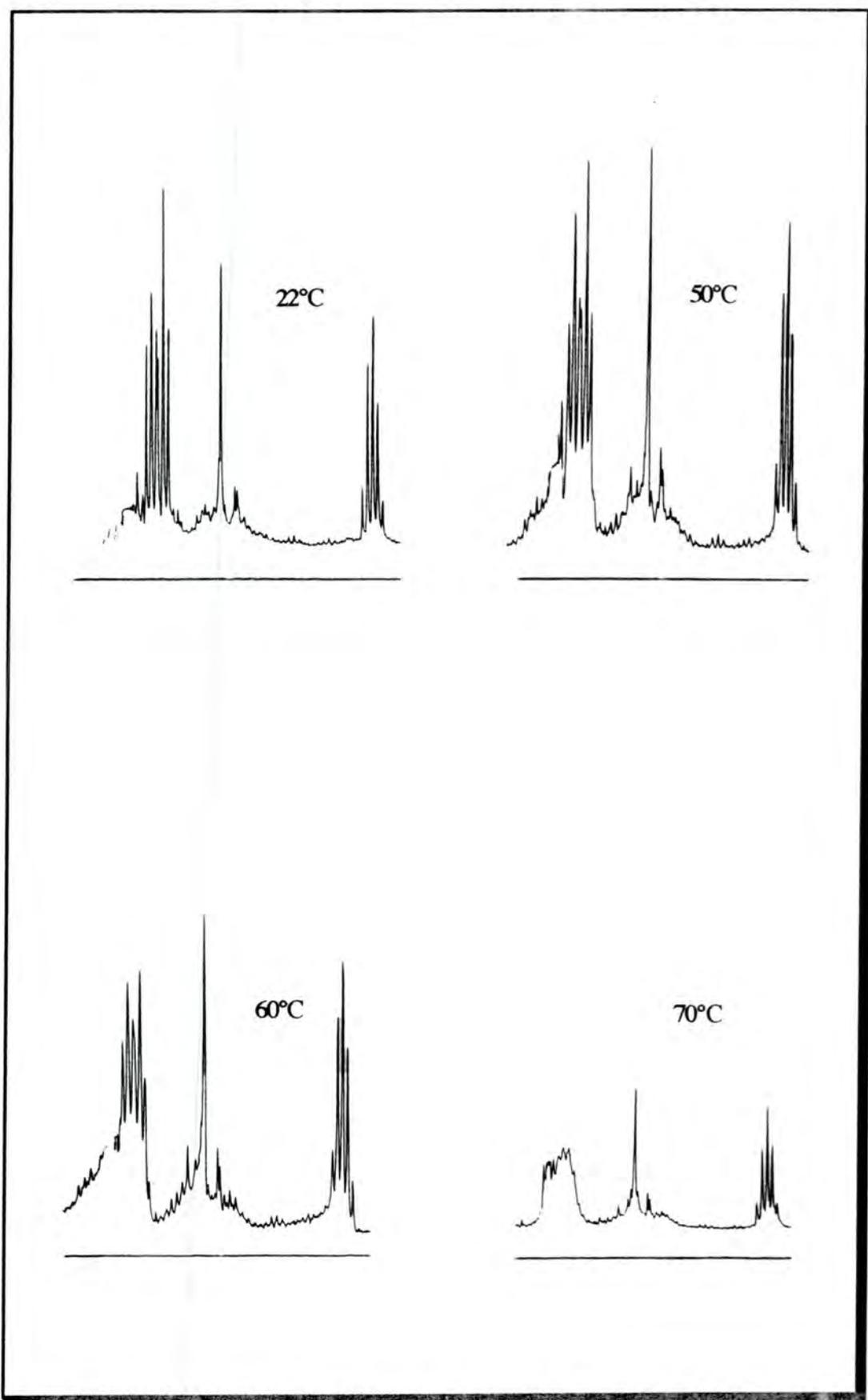


Figure 7. Variable Temperature NMR Spectra of Compound **186** (in C_6D_6).

3.4 Conclusions.

In this Chapter we have reported the synthesis of two novel bis(1,4,2-dithiazine) isomers, and explored the application of the iodine-ammonia reaction to synthesis of the dithiazepine heterocyclic system.

Bis(1,4,2-dithiazines) **173** and **180** were synthesised by the utilisation of methodology described in Chapter 2. These compounds displayed electrochemical and mass spectroscopic fragmentation characteristics similar to those of mono-1,4,2-dithiazine derivatives, with the exception that no second oxidation wave was observed for compound **180**.

Attempts to ring expand a six-membered cationic salt, under iodine-ammonia conditions, did not lead to formation of a dithiazepine derivative. Exocyclic nitrogen insertion furnished the alternative imine isomer **186**, identified by a variable temperature NMR study. This result implies that use of the iodine-ammonia route, to synthesise nitrogen-containing seven-membered heterocyclic systems, may not be feasible.

CHAPTER 4

THE REACTIONS OF 1,4,2-DITHIAZINES

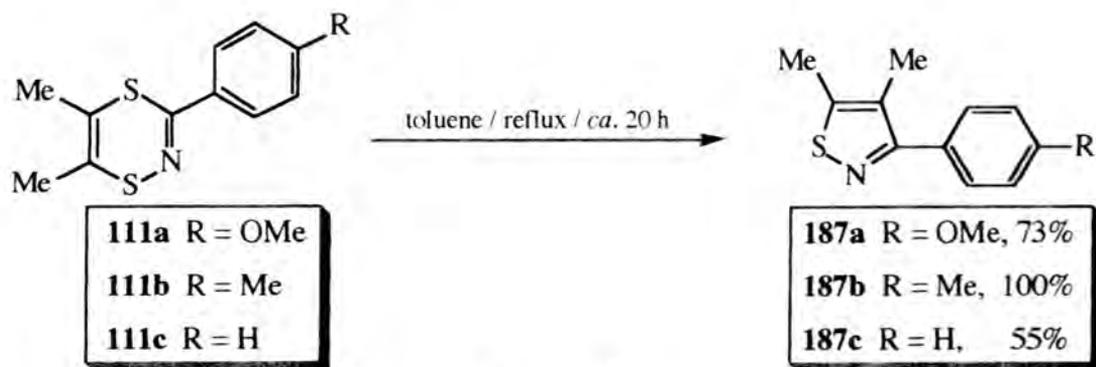
4.1 Introduction.

Having obtained a large range of 1,4,2-dithiazine derivatives, we next explored the chemistry which these compounds would undergo. As eight π -electron species, with multiple heteroatoms, the dithiazines were expected to display interesting chemical reactivity. Fanghänel *et al* have published some results on 1,4,2-dithiazine reactivity.^{21,25} Their main findings are reviewed in Chapter 1 (Section 1.4.3). In this Chapter, we build on these earlier studies, using our less substituted dithiazine derivatives to extend fundamental knowledge on the chemical reactivity of the 1,4,2-dithiazine system.

For clarity, the early part of this Chapter has been broken down into sections with specific themes, *i.e.* thermolytic, cycloaddition and photolytic reactions, in Sections 4.2, 4.3 and 4.4, respectively. Of necessity, there is some overlap between the contents of these sections. To briefly define terms: thermolytic reactions (Section 4.2) refer to thermally initiated reactions of 1,4,2-dithiazines where no trapping agents (*e.g.* dienophiles) are used. Section 4.3 deals with thermally initiated cycloaddition reactions, where trapping agents are employed to form cycloadducts with thermally-generated dithiazine fragments. Section 4.4 encompasses all photolytic experiments performed on 1,4,2-dithiazines, both with and without the use of trapping agents.

4.2 Thermolysis Reactions of 1,4,2-Dithiazines.

In this section, thermally induced reactions of dithiazines are described. Previous workers have obtained isothiazoles from the desulphurisation of 1,4,2-dithiazines, by heating them to 160-180°C in the absence of solvent,¹⁵ or by refluxing in a solvent, *e.g.* toluene,²⁰ (Section 1.4.3.1). We repeated some of this work on a range of 3-aryl-1,4,2-dithiazines **111a-111c** and obtained isothiazoles **187a-187c**, in yields of 55-100% (Scheme 47).

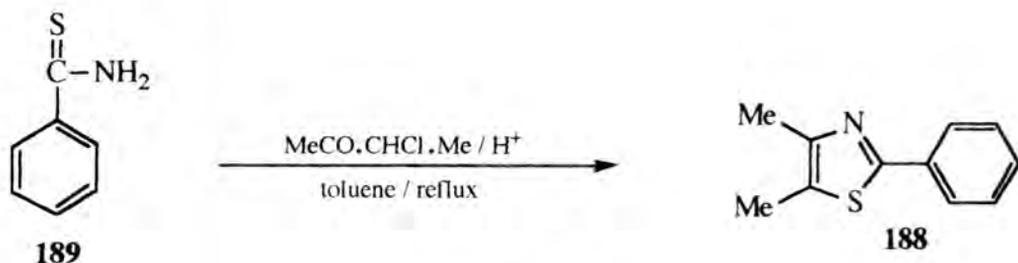


Scheme 47

Optimum reaction conditions were found to be 20-24 hours reflux in toluene. The isothiazoles were separated from elemental sulphur and by-products using chromatography on silica. Since routes to isothiazoles are uncommon,^{1a} this reaction may be of some utility for access to specifically-functionalised isothiazole derivatives.

We initially based our assignments of isothiazole structure mainly on literature precedent.¹⁵ The non-equivalence of methyl singlets was increased considerably in the proton NMR spectra of isothiazoles **187a-187c** (ca. 0.24 ppm separation) as compared to the dithiazine precursors **111a-111c** (ca. 0.05 ppm separation). This agreed with the isothiazole assignments, but the possibility of thiazole isomers, formed by desulphurisation of the S-1 position of dithiazines **111a-111c**, could not be ruled out. Extensive proton and carbon NMR studies on phenylthiazoles have been reported,⁷⁷ but no data could be found which confirmed unequivocally the isomeric structure of products **187a-187c**.

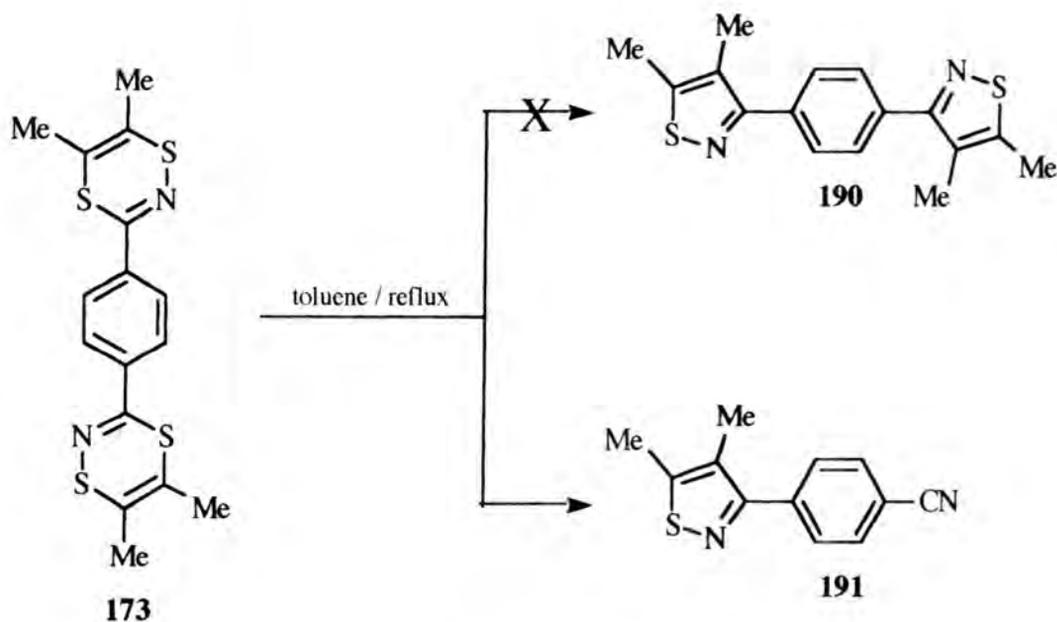
We therefore synthesised thiazole isomer **188** by an unambiguous literature route: reaction of thiobenzamide **189** with 3-chlorobutan-2-one afforded thiazole **188**, in 56% yield (Scheme 48).⁷⁸ Comparison of data for thiazole **188** and the corresponding desulphurisation product **187c** confirmed them to be different structural isomers (methyl group proton non-equivalence of only 0.08 ppm was noted for **188**). This established the identity of **187c** as 4,5-dimethyl-3-phenyl-isothiazole.



Scheme 48

Thermal desulphurisation of 1,4,2-dithiazines to give exclusively isothiazole isomers was, therefore, confirmed. Other workers have performed molecular modelling calculations on the relative ease of S-1 and S-4 desulphurisation in 1,4,2-dithiazines (Section 1.4.3.8, Table 4).²¹ A slight favourability for S-4 desulphurisation, to give isothiazoles, was predicted, which is in accord with our experimental data.

In a related experiment, thermolysis of a toluene solution of bis(1,4,2-dithiazine) **173** led, not to bis(isothiazole) **190**, but, unexpectedly, to the novel isothiazolonitrile **191** instead, in 69% yield (Scheme 49).



Scheme 49

Compound **191** was formed during 5 hours of refluxing in toluene, the reaction proceeding more rapidly than desulphurisation of 3-aryl-1,4,2-dithiazines **111a-111c**, where *ca.* 24 hours of refluxing was required to complete the reaction.

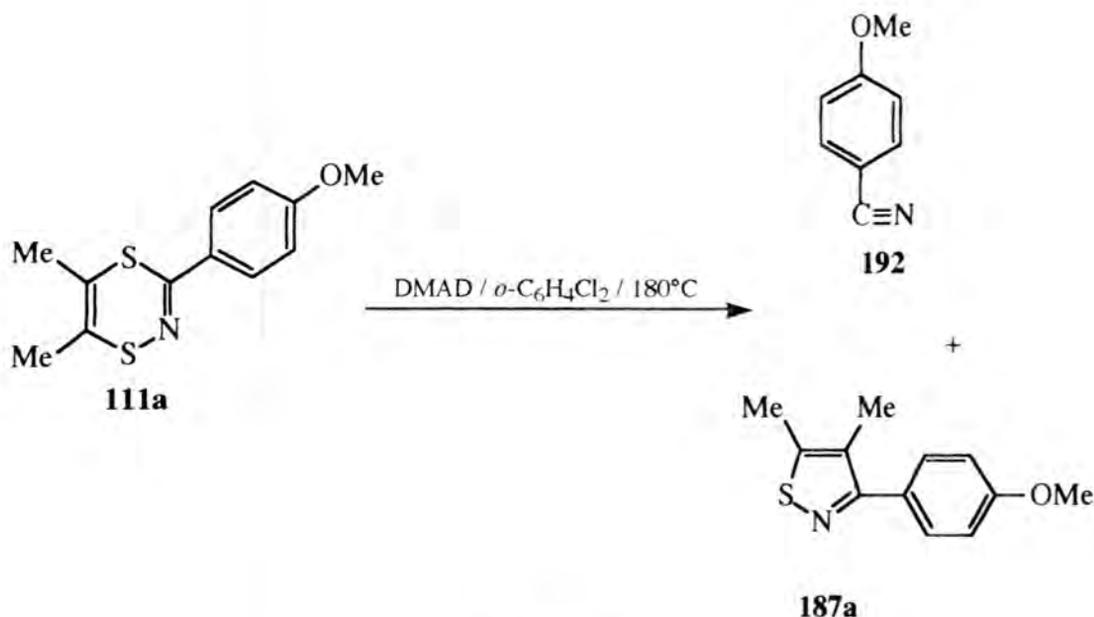
4.3 Cycloaddition Reactions of 1,4,2-Dithiazines.

This section describes thermally-induced cycloaddition reactions of 1,4,2-dithiazines. Thermal fragmentation products of the dithiazines are isolated as adducts with trapping agents. Other researchers have published findings in this area. Fanghänel *et al* described the trapping of a thermally-generated dithiete species with dimethyl fumarate, to give a 1,4-dithiin derivative (Section 1.4.3.1, Scheme 18).²⁵ Nakayama and co-workers have heated 1,4,2-benzodithiazines to high temperatures (180°C), in the presence of DMAD, to give 1,4-benzodithiin, which was suggested to have arisen by a stepwise, bimolecular reaction between the dithiazine and DMAD, with involvement of a zwitterionic intermediate **91** (Section 1.4.3.3).²⁸

Different workers have, therefore, interpreted the isolation of 1,4-dithiin products, from reaction of 1,4,2-dithiazines with dienophiles under thermal conditions, as arising by two alternative pathways *via* different intermediates. Fanghänel proposed a concerted route whereby dithiete intermediates are trapped with DMAD. Conversely, Nakayama postulated a stepwise route *via* a zwitterionic intermediate. An objective of our own studies was to ascertain which of these proposals was correct.

4.3.1 Synthetic Details.

Our initial studies used DMAD as the dienophile (Scheme 50), under reaction conditions similar to those reported by Nakayama, *i.e.* using *o*-dichlorobenzene as solvent at 180°C.²⁸

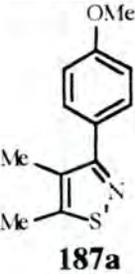
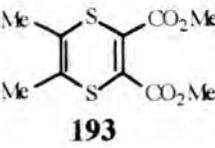
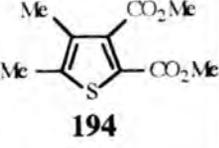


Scheme 50

Nitrile **192** was obtained in 38% yield, along with the desulphurisation product **187a**, in negligible yield. No evidence was found for the presence of 1,4-dithiin cycloadducts. We therefore modified the reaction conditions in an attempt to observe dithiin products (Table 11). With the exception of the by-product nitrile **192**, yields of all reaction products were extremely low. Some competition was observed between nitrile and sulphur elimination from the dithiazine, in common with our isolation of isothiazolonitrile **191** (Section 4.2).

Products **193** and **194** are believed to have arisen by the retro-Diels-Alder mechanism shown in Scheme 51. Nitrile loss from the 1,4,2-dithiazine gives dithiete intermediate **195**. Cycloaddition of the 1,2-dithioketone form **196** with DMAD results in the 1,4-dithiin product **193**. Thermal sulphur elimination from 1,4-dithiins has been observed previously,²⁷ thus explaining the observation of thiophene derivative **194** under the reaction conditions.

High resolution mass spectra confirmed the elemental composition of compounds **193** and **194**, but we were unable to obtain large enough quantities to characterise them fully (see, however, Section 4.4.2). No significant improvements to the yields of cycloaddition products could be made. These disappointing results agree with

Conditions ^a	Products & Yields (%)			
				
<i>o</i> -C ₆ H ₄ Cl ₂ , DMAD ^b 180°C, 0.5 h	trace	38%	nil	nil
toluene, DMAD ^b 111°C, 16 h	trace	8%	nil	trace
toluene, DMAD ^b 60°C, 115 h	trace	nil	trace	trace

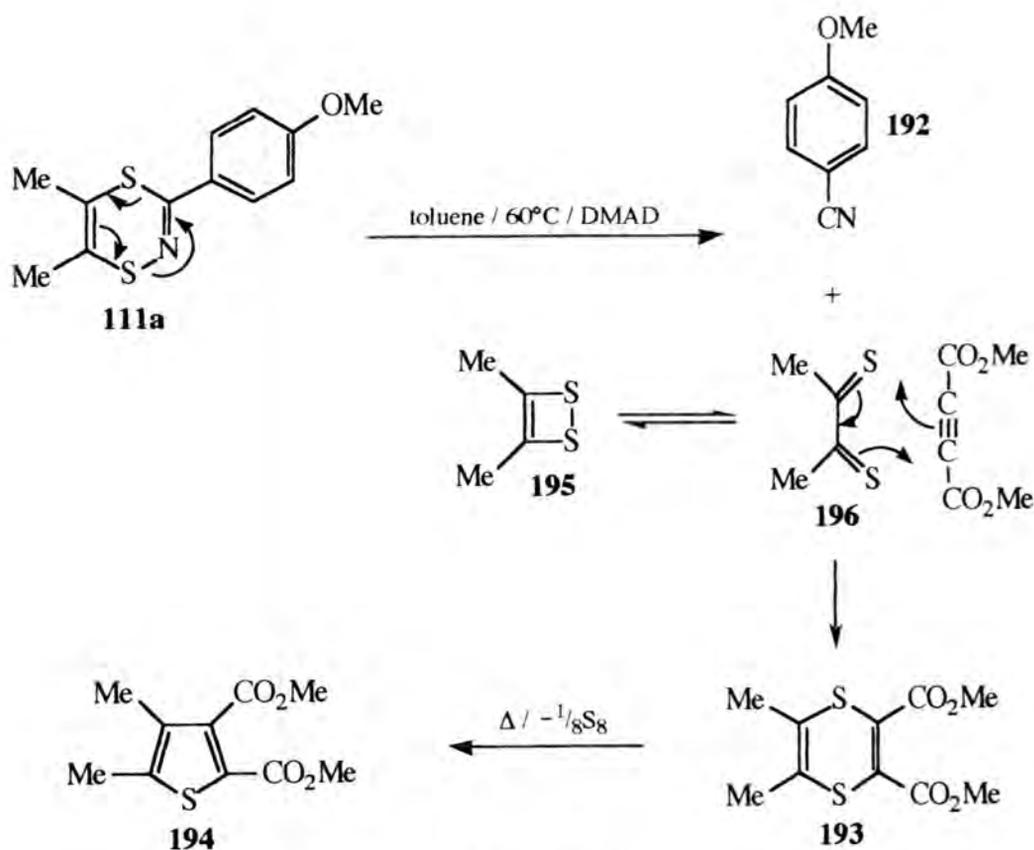
^a1,4,2-dithiazine **111a** (1 mmol). ^bDMAD (3 mmol).

Table 11. Results of Reactions Between DMAD and 1,4,2-Dithiazine **111a**.

earlier findings by Nakayama *et al* on reactions of mono-cyclic 1,4,2-dithiazines with DMAD during reflux in toluene; no cycloaddition products were observed.²⁰

When 1,4,2-dithiazine derivative **111a** was refluxed in *o*-dichlorobenzene at 180°C for three hours, in the absence of DMAD, significant quantities of nitrile **192** and isothiazole **187a**, in a 60:40 ratio, were seen in the proton NMR of the crude product mixture. This observation of nitrile formation in the absence of DMAD supports the route postulated by Fanghänel, involving dithiete intermediates (Section 1.4.3.1, Scheme 18).²⁵ The alternative stepwise bimolecular route which has been proposed (Section 1.4.3.3) involved attack by S-1 of the dithiazine on DMAD, followed by ring-closure to the 1,4-dithiin, with nitrile loss.²⁸ Our observation indicates strongly that independent fragmentation of 1,4,2-dithiazines to nitrile and dithiete fragments is occurring. The dienophile acts subsequently, to trap the dithiete fragment **195** in a Diels-Alder reaction.

Further evidence for this proposal was obtained by our isolation of isothiazolonitrile **191** (Section 4.2), this compound arising by thermally-induced desulphurisation and dithiete loss from precursor bis(1,4,2-dithiazine) **173**.

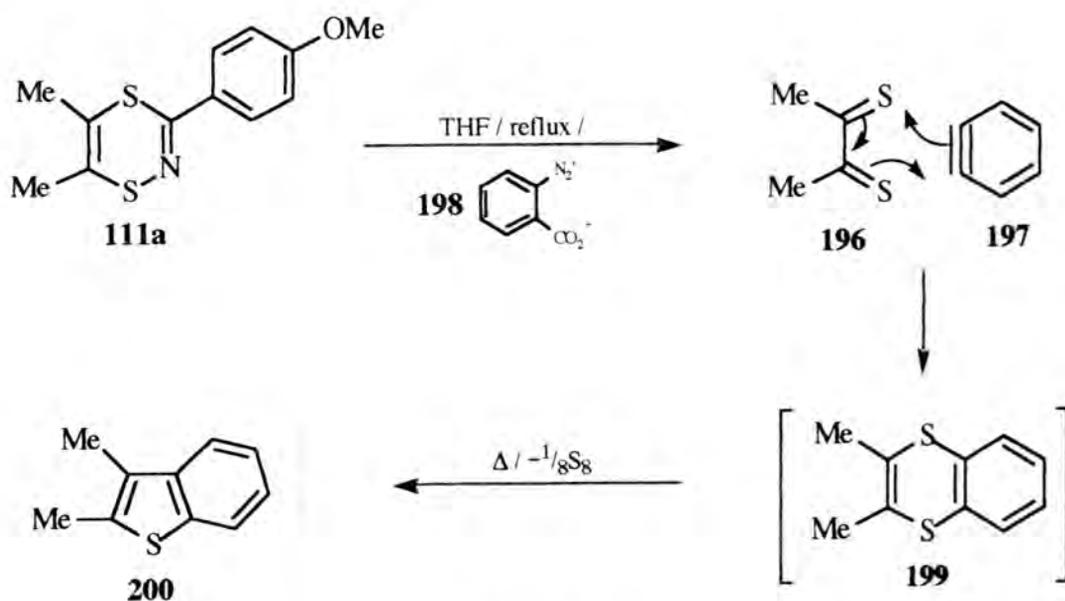


Scheme 51

Following the poor cycloadduct yields which were obtained with DMAD, we investigated alternative dienophiles, with a view to finding a more suitable trapping agent for intermediate dithietes. Reactions of benzyne, **197**, with heterocyclic systems have been comprehensively reviewed.⁷⁹

Benzyne precursor salt **198**⁸⁰ (four or eight equivalents) was decomposed, in aliquots, by addition to a refluxing tetrahydrofuran (THF) solution of 1,4,2-dithiazine **111a**, in a modified literature procedure (Scheme 52).⁸¹ Reaction of intermediate dithioketone **196** with benzyne would give 1,4-benzodithiin derivative **199**. This

product was, however, not observed. A small quantity of the desulphurisation product of **199**, *viz.* thiophene **200**, was the only material found. Total reflux time for these reactions was *ca.* 1.5 hours; isothiazole **187a** was not detected, but recovered dithiazine yields (*ca.* 40%) indicated decomposition of the heterocycle by benzyne had occurred.



Scheme 52

Reaction of the electron-deficient dienophile tetracyanoethene with 1,4,2-dithiazine **111a**, in toluene at 80°C for 24 hours, led to isolation of unreacted dithiazine (52%) and corresponding isothiazole **187a** (36%). Spectroscopic analysis (NMR, MS) of the crude product mixture gave no indication of cycloaddition product formation.

4.3.2 Discussion of Results.

From our studies, we conclude that thermally induced cycloaddition reactions of 1,4,2-dithiazines are particularly difficult to effect. Despite numerous modifications to the reaction conditions and variation of the trapping agents employed, cycloadducts were obtained only in very low yields (<5%), if at all. Indirect evidence for 1,2-dithiocarbonyl

intermediate formation was obtained by the isolation of nitrile products from many reactions, particularly those at elevated temperatures. The highly reactive nature of 1,2-dithiocarbonyl species is well documented.^{82,83} Self-polymerisation of these reactive intermediates may have occurred in preference to Diels-Alder reaction with the dienophiles. A further complication of these dithiazine reactions was the competition which existed between elimination of nitrile molecules and sulphur atoms, to give dithiocarbonyl species and isothiazoles, respectively.

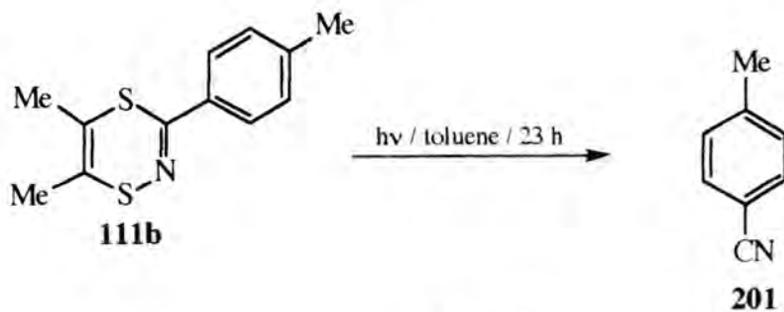
4.4 Photolysis Reactions of 1,4,2-Dithiazines.

This section describes the results of photolysis experiments which we have conducted on 1,4,2-dithiazines. The majority of reactions were carried out in the presence of trapping agents, with the intention of comparing our results under photolytic and thermolytic (Section 4.3) conditions.

4.4.1 Photolysis of 1,4,2-Dithiazines in the Absence of Dienophiles.

Photolysis of 1,4,2-dithiazine **111b**, in toluene for 23 hours, gave a quantitative yield of nitrile **201** (Scheme 53). Decreasing the reaction time to 2 hours gave a 15% yield of nitrile **201**, and 60% recovery of the dithiazine. The corresponding isothiazole product was not observed. Considerable deposits of brown film were seen on the walls of the quartz reaction tube, indicative of polymeric material, resulting from self-reaction of dithioketone intermediates in the absence of trapping agents.

These initial results are in contrast to those obtained for thermal reaction of dithiazines in the absence of trapping agents (Section 4.2). Photolysis of 3-aryl-1,4,2-dithiazines gave quantitative fragmentation to nitriles, whereas thermolysis gave isothiazoles in high yields. We expected, therefore, to see enhanced yields of cycloadducts under photolytic *cf.* thermolytic conditions (Section 4.3).

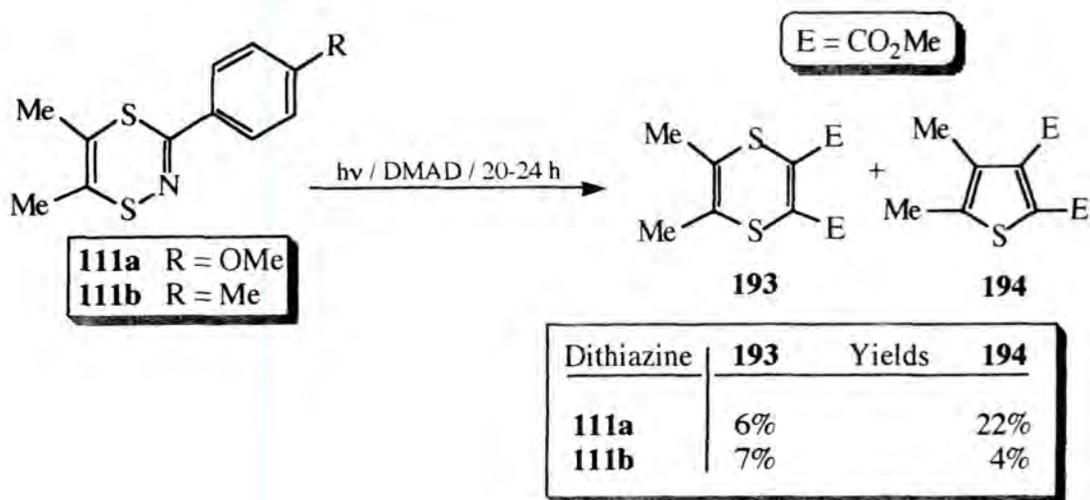


Scheme 53

We also irradiated isothiazole **187b** (obtained by dithiazine thermolysis) in toluene, for 24 hours, and recovered 96% of the isothiazole. This indicated that nitrile products seen under photolytic conditions were obtained directly from the dithiazine, not *via* isothiazole intermediates. Interestingly, a literature report describes the photochemical isomerisation of 2-arylthiazoles to 3-arylisothiazoles,⁸⁴ further confirming the stability of isothiazoles under photochemical conditions.

4.4.2 Photolysis of 1,4,2-Dithiazines in the Presence of Dienophiles.

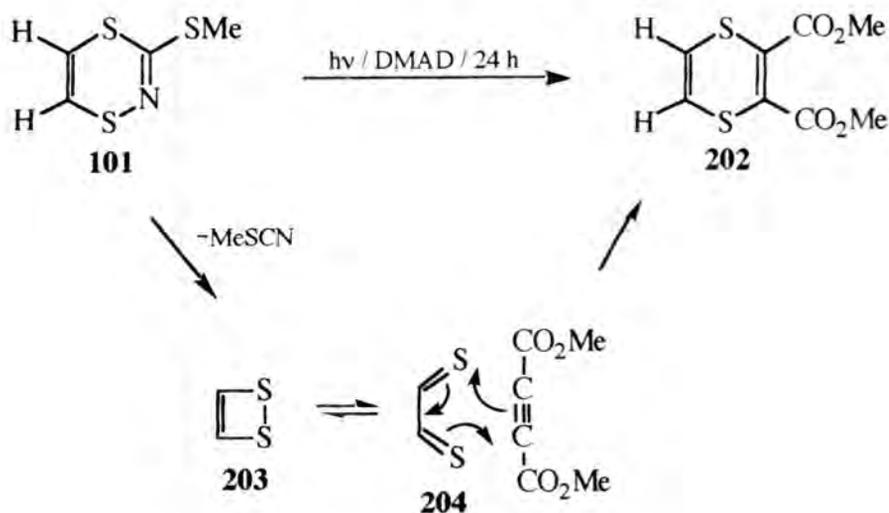
Toluene solutions of dithiazines **111a** and **111b** were irradiated in the presence of DMAD (10 molar equivalents) to trap photo-generated 1,2-dithiocarbonyl intermediates (Scheme 54). Yields of the 1,4-dithiin cycloadduct **193**, although still poor (6-7%), were a considerable improvement on those obtained under thermal trapping conditions (Section 4.3.1, Table 11). Significant yields of thiophene **194** were obtained from these photochemical trapping reactions (4-22%), probably as a result of photo-induced desulphurisation of 1,4-dithiin **193**, a recognised phenomenon.⁸⁵ The overall yields of cycloadducts for the reactions shown in Scheme 54 are, therefore, 11-28%. The extent of polymeric wall-film was much reduced in the presence of DMAD.



Scheme 54

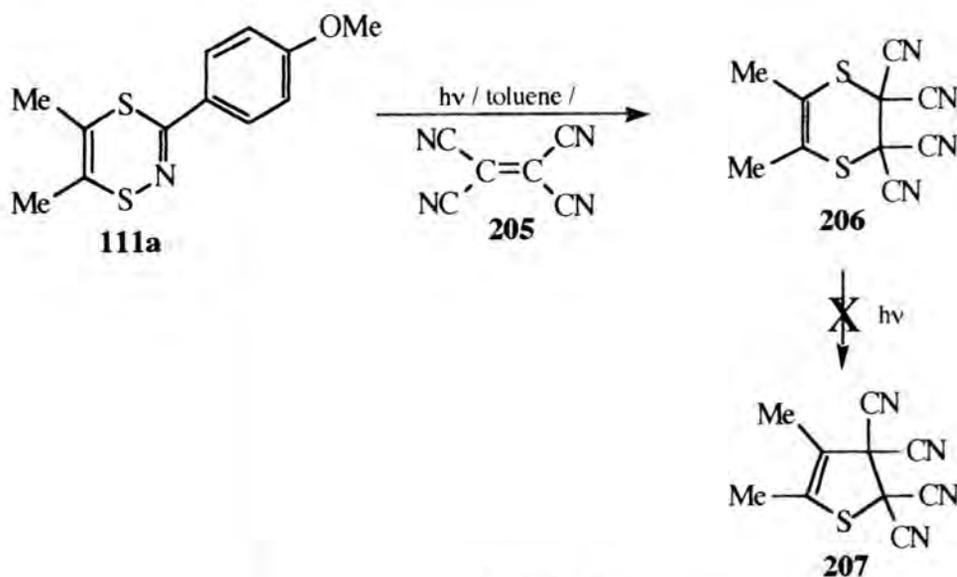
We have also examined the photolysis reaction of 1,4,2-dithiazine derivative **101**, with DMAD acting as both trapping agent and solvent (Scheme 55). 1,4-Dithiin **202** was isolated in *ca.* 4% yield. The observation of this cycloadduct provides evidence for the intermediacy of parent dithiete **203**, which reacts in a 4+2 cycloaddition in open-chain form **204**. A new route has, therefore, been found to enable studies to be carried out on the highly reactive four-membered heterocyclic system **203**. Photochemical fragmentation of 1,4,2-dithiazines, to give dithiete species such as **203**, may occur *via* free-radical or concerted (retro-Diels Alder) mechanisms. We have also noted the appearance of the radical ion of dithiete **203**, in high abundance, by fragmentation of dithiazine **101** under mass spectrometric conditions (Section 2.4.2, Table 7).

On repeating the photolysis of dithiazine **101**, in toluene as solvent, with DMAD, no trapped products were obtained. Much brown polymeric film was noted on the walls of the reaction vessel. Formation of cycloadducts, therefore, seems to be most efficient in the presence of neat dienophile for this particular reaction.



Scheme 55

When dithiazine **111a** was photolysed in toluene with tetracyanoethene **205** as trap, the 1,4-dithiin derivative **206** was isolated, in *ca.* 6% yield (Scheme 56).

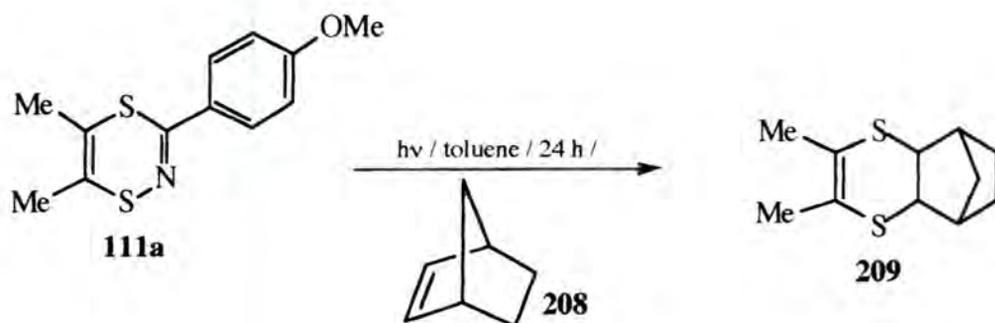


Scheme 56

Notably, the corresponding thiophene derivative **207**, which could form by photo-induced desulphurisation of dithiin **206**, was not observed. Since this dithiin species is a

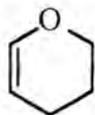
partially saturated analogue, no stabilisation of the desulphurisation product by aromatisation would occur, which may explain the absence of thiophene derivative **207** in this case.

Previous reports have suggested that 1,2-dithiocarbonyl species may form cycloadducts most readily under inverse-electron demand conditions.⁸⁶ Therefore, optimum reaction of 1,2-dithiocarbonyl species should occur with electron-rich and strained alkenes and alkynes. A toluene solution of dithiazine **111a** was photolysed with ten equivalents of norbornene **208**, for 24 hours (Scheme 57), but only a trace amount of dithiin adduct **209** was detected (MS evidence), the major product being the nitrile fragment. Large amounts of brown film were also seen on the walls of the reaction vessel. Using a thirty-fold excess of norbornene, the yield of dithiin **209** improved (*ca.* 30%), although it was not possible to isolate this product in analytically pure form. In agreement with some of our earlier findings, no corresponding partially saturated thiophene derivative was isolated during these experiments.



Scheme 57

No cycloadducts were obtained when pyran derivative **210** was used (without additional solvent) as the trapping agent during photolysis of dithiazine **111a**. Despite extended reaction time (37 hours), high dithiazine recovery was noted (*ca.* 50%).



210

4.4.3 Discussion of Results.

Examination of the photolytic reactions of 1,4,2-dithiazines has provided some interesting contrasts with thermally-induced processes. In the absence of trapping agents, photolysis leads to a predominance of nitrile extrusion from the heterocycle, presumably with associated formation of dithiete species. Thermolysis, however, gives predominantly isothiazoles, *via* sulphur extrusion (Section 4.2).

In the presence of trapping agents, photolysis of 1,4,2-dithiazines resulted in far more efficient formation of cycloadducts than was the case with thermal initiation (Section 4.3). Some generalisations can be made about the thermal and photochemical behaviour of (at least) 3-aryl-1,4,2-dithiazines. Thermal processes favour sulphur extrusion to yield isothiazoles, whilst photolytic processes favour fragmentation to afford nitriles and dithiete species. These dithiete species can be trapped by appropriate dienophiles to yield 1,4-dithiins.

Photolytic fragmentation of a 5,6-dihydro-1,4,2-dithiazine has opened up a new route to the parent dithiete heterocycle. This finding is in accord with mass spectroscopic data on this dithiazine derivative.

Our results were partially in agreement with literature precedent for 1,2-dithioketones to undergo Diels-Alder reactions most readily *via* inverse electron-demand processes. We obtained highest adduct yields (*ca.* 30%) with the electron-rich norbornene dienophile. Poorest adduct yields (6%) were obtained with the most electron-deficient dienophile, tetracyanoethene. Relatively good cycloadduct yields (28%) were also obtained, however, for the electron-deficient species DMAD.

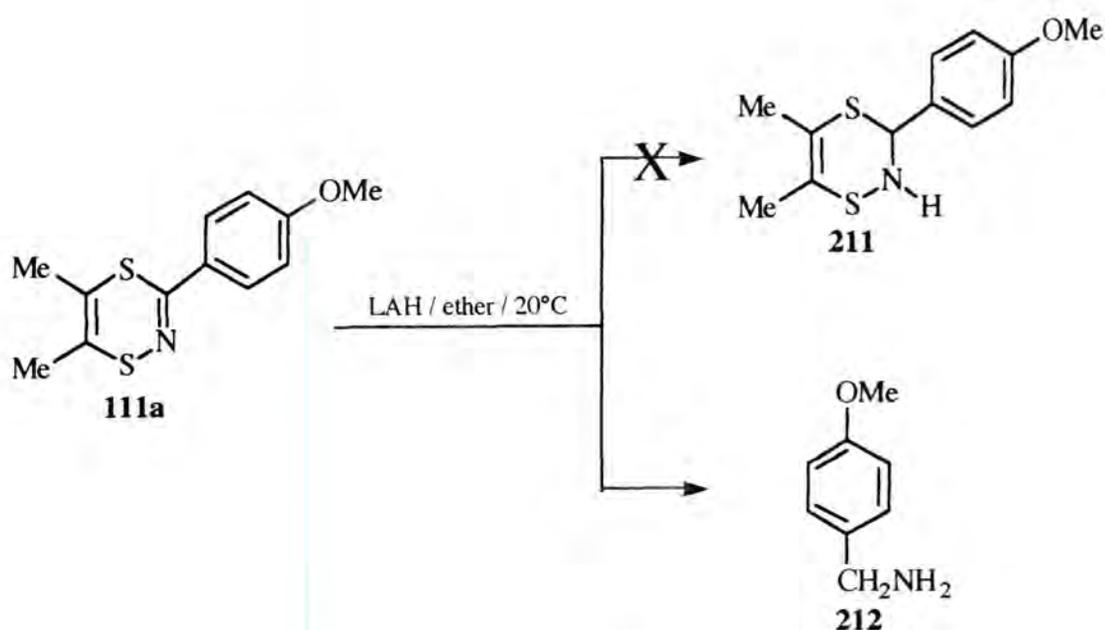


4.5 Reaction of 1,4,2-Dithiazines with Nucleophiles.

No reactions of 1,4,2-dithiazines with hydride nucleophiles have been reported in the literature, although there is one report on the reaction of a Grignard reagent with a 1,4,2-dithiazine; this work is described in Section 1.4.3.4.²⁵ This left considerable scope to examine the reactions of 1,4,2-dithiazine derivatives with nucleophilic species.

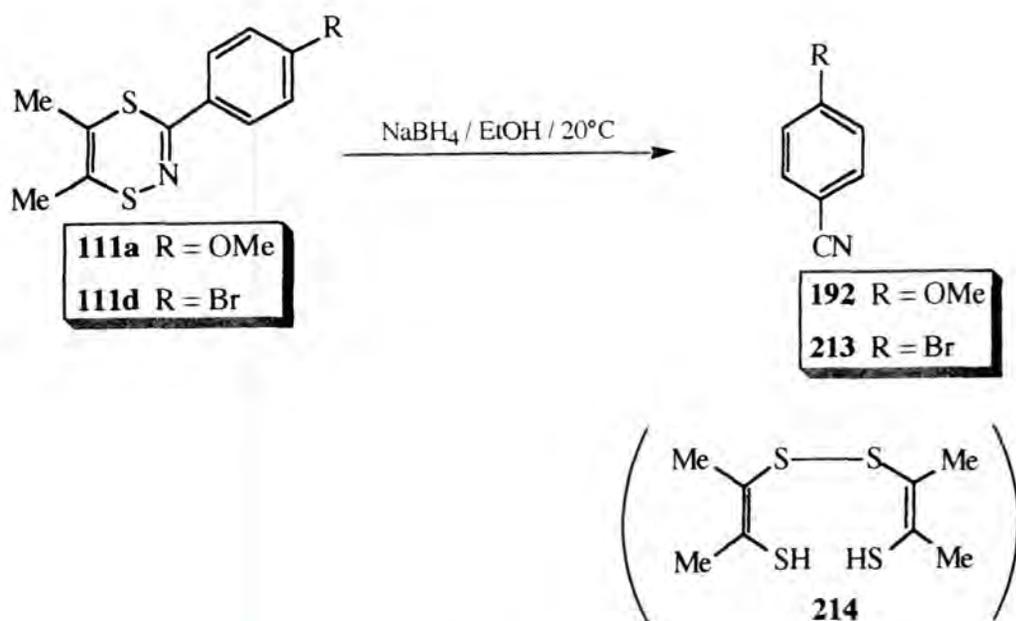
4.5.1 Synthetic Details.

We initially reacted dithiazine **111a** with two equivalents of lithium aluminium hydride (LAH). Reduced derivative **211** was not formed; the only product which we were able to isolate was the benzylamine **212**, in *ca.* 50% yield (Scheme 58). Clearly, the hydride nucleophile had led to cleavage of the 1,4,2-dithiazine ring, perhaps to give a benzonitrile which itself was reduced by LAH to afford **212**.



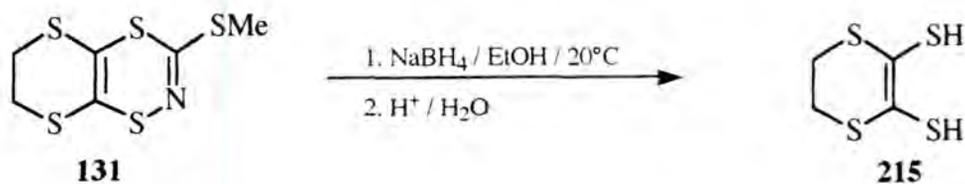
Scheme 58

Reaction of 1,4,2-dithiazines **111a** and **111d** with a less reactive hydride source, sodium borohydride (NaBH_4) (five equivalents), gave nitriles **192** and **213** in yields of 68% and 69%, respectively (Scheme 59). This indicated that the electronic properties of *para*-substituents on the aryl ring had no significant effect on the course of reaction. A small quantity (*ca.* 5%) of the disulphide **214** was also isolated from reaction of **111a** with the reducing agent. The isolation of benzonitriles using NaBH_4 bears similarity to the isolation of a benzylamine derivative with LAH (Scheme 58). With NaBH_4 , however, the nitriles were produced cleanly, in enhanced yields.



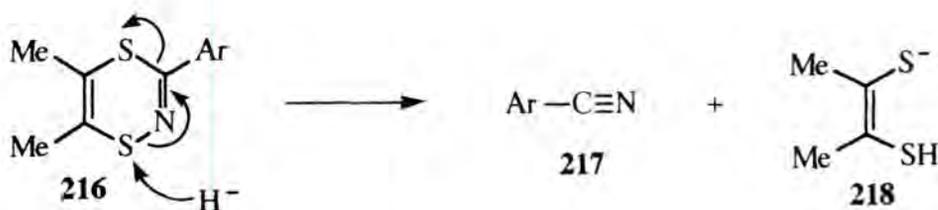
Scheme 59

Reaction of NaBH_4 with 3-methylthio-1,4,2-dithiazine derivative **131** was also examined (Scheme 60). Acidic work-up conditions were employed, to enable any intermediate thiolate salts to be isolated as thiols. This reaction proceeded in a less distinct manner than those of the 3-aryl dithiazines. Crude product analysis (NMR) indicated a multiplicity of minor reaction products. A trace amount of the 1,2-dithiol **215** was the only identifiable product.



Scheme 60

For these reactions, we postulate a mechanism which involves initial attack of the hydride ion on S-1 of 3-aryl dithiazine **216** (Scheme 61). Other workers have carried out modelling studies which show that S-1 of 1,4,2-dithiazines is the more electron-deficient sulphur atom (Section 1.4.3.8, Table 3), presumably due to inductive electron-withdrawal by the adjacent nitrogen atom in the ring.²¹

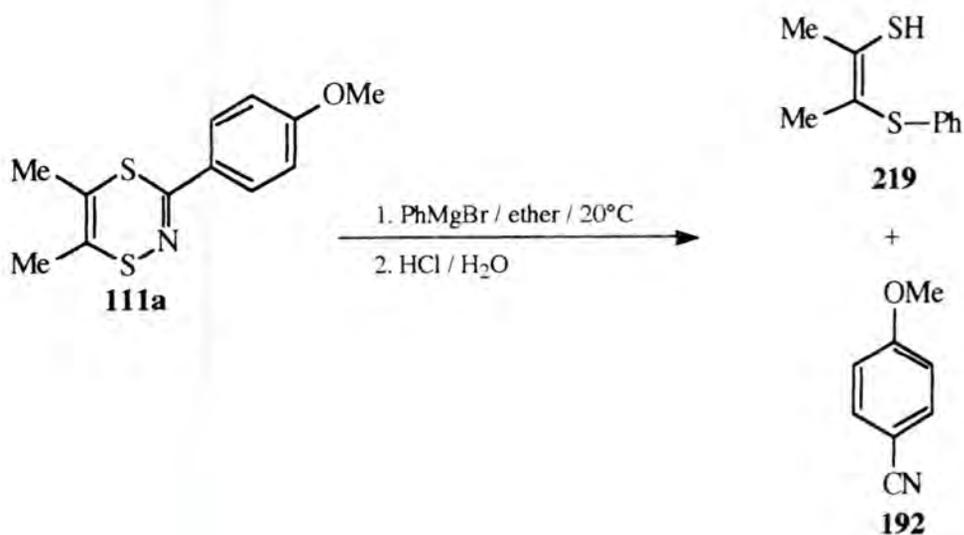


Scheme 61

Hydride attack leads to cleavage of the S-N bond and formation of the nitrile leaving group **217**. The other fragment **218**, is likely to be stabilised as a sodium salt prior to work-up. Proof for this mechanism was obtained by reaction of 1,4,2-dithiazines with carbon nucleophiles, described below; products included derivatives of thiolate species **218**. This mechanism is also supported by the isolation of disulphide **214**. This species may arise *via* attack of nucleophilic intermediate **218** on unreacted 1,4,2-dithiazine, in analogous fashion to the attack by hydride ion shown in Scheme 61.

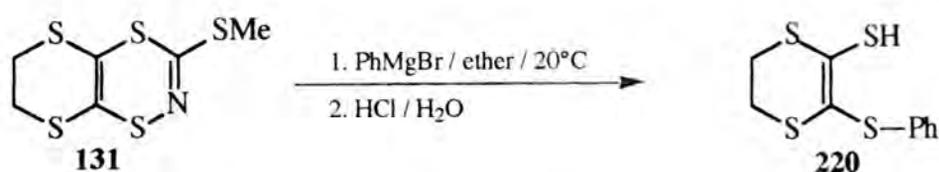
Reaction of Grignard reagents with 1,4,2-dithiazines was examined, with the objective of isolating sulphur-bearing fragments of dithiazine ring cleavage. Dithiazine

derivative **111a** was reacted with five equivalents of phenylmagnesium bromide at room temperature (Scheme 62). The phenylsulphide **219** was isolated in *ca.* 85% yield, along with the nitrile **192**. We anticipate that the formation of compound **219** follows the same mechanism as that proposed for hydride reagents (Scheme 61), the phenyl carbanion acting as nucleophile in this case.



Scheme 62

Analogously, phenylmagnesium bromide reacted with the 3-methylthio-1,4,2-dithiazine **131** (Scheme 63).

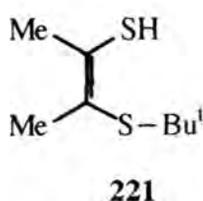


Scheme 63

The crude yield of sulphide **220** was *ca.* 75%. However, this compound proved

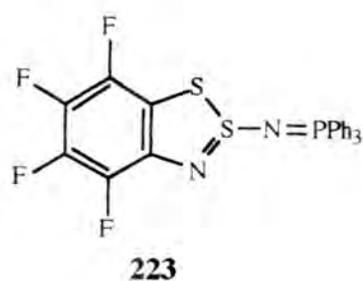
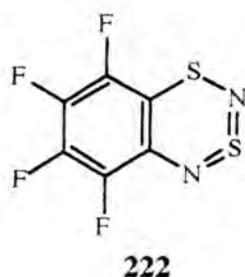
difficult to separate from reaction by-products and could not be obtained in analytically pure form.

Reaction of 1,4,2-dithiazine **111a** with *tert*-butyl magnesium chloride gave compound **221**. Initial reactions were carried out with five molar equivalents of the Grignard reagent, at room temperature, for 17 hours. An 11% yield of **221** resulted, along with 41% recovery of the dithiazine.



This reaction was appreciably slower than those of phenyl Grignard reagent on dithiazines. Yield of **221** was improved, to 23%, by the use of ten molar equivalents of the *t*-butyl Grignard reagent, reacting for 95 hours. Despite these poor yields, compound **221** could be readily obtained in excellent purity. The use of *tert*-butyl groups is an established method for protecting the thiol functionality.⁸⁷ Compound **221** may be viewed as a mono-protected 1,2-dithiol. This compound is a potentially versatile synthetic intermediate. Related work has recently been carried out by Barton *et al*, concerning 1,2-diols which are mono-protected with the *t*-butyl group.⁸⁸

We were prompted to examine the interaction of 1,4,2-dithiazines with phosphorus nucleophiles, following a literature report in which triphenylphosphine was reacted with the twelve π -electron dithiadiazine **222**.⁸⁹ This reaction led to formation of the iminophosphane species **223**.



Dithiazine **111a** was reacted with an equimolar quantity of triphenylphosphine, in toluene at 20°C. Chromatographic evidence (TLC) indicated that complete reaction of the dithiazine had taken place, but work-up gave unreacted **111a** and small, colourless crystals which were tentatively identified by X-ray diffraction studies as triphenylphosphine oxide, in an uncommon crystal habit,⁹⁰ although the X-ray data collected were of poor quality. Overall, these results indicate that the dithiazine and phosphine may form a reversible complex in solution.

4.5.2 Discussion of Results.

1,4,2-Dithiazines have been found to react with a range of carbon and hydrogen nucleophiles, with the occurrence of ring opening, in agreement with a literature report for the reaction of a 1,4,2-dithiazine with methylmagnesium iodide.²⁵

In general, higher yields of products have been observed for reactions involving 3-aryl dithiazines than for 3-methylthio derivatives. The mechanism we propose disagrees with that published by Fanghänel for the interaction of a 3-methylthio-1,4,2-dithiazine with a Grignard reagent (Section 1.4.3.4, Scheme 23). The possibility that different mechanistic pathways apply to alternatively-substituted dithiazines cannot be ruled out.

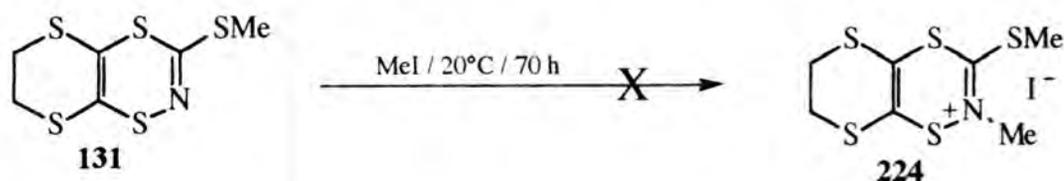
A range of interestingly functionalised 1,2-dithiol derivatives have been synthesised by reaction of dithiazines with Grignard reagents. It is envisaged that these compounds may be useful synthetic intermediates.

4.6 Reaction of 1,4,2-Dithiazines with Electrophiles.

Literature reports have shown that 1,4,2-dithiazines react with strong electrophiles, *e.g.* mineral acids, to give ring-contraction products, specifically 2-imino-1,3-dithioles (Section 1.4.3.5).²⁵ We now describe reactions of our novel 1,4,2-dithiazines with a range of electrophilic reagents.

4.6.1 Synthetic Details.

No reports on the interaction of 1,4,2-dithiazines with methylating agents are contained in the literature. Attempts made to methylate compound **131** with iodomethane resulted in no reaction: neither *N*-methyl, *e.g.* compound **224**, nor *S*-methyl salts were formed (Scheme 64). 1,4,2-Dithiazine **111a** was used for the remaining investigations; results are collated in Table 12.



Methylating Agent ^a	Conditions	Products
iodomethane	acetone, 56°C, 2 h	no reaction ^b
dimethyl sulphate	neat, 90°C, 5 min	trace / no reaction ^c
dimethyl sulphate	toluene, 111°C, 15 min	mixed salts ^d

^aMethylating agents used in large excess (> x10 molar). ^b96% recovery of dithiazine. ^cChromatographic evidence (TLC). ^dThree products indicated (NMR).

Table 12. Methylation of 1,4,2-Dithiazine **111a**.

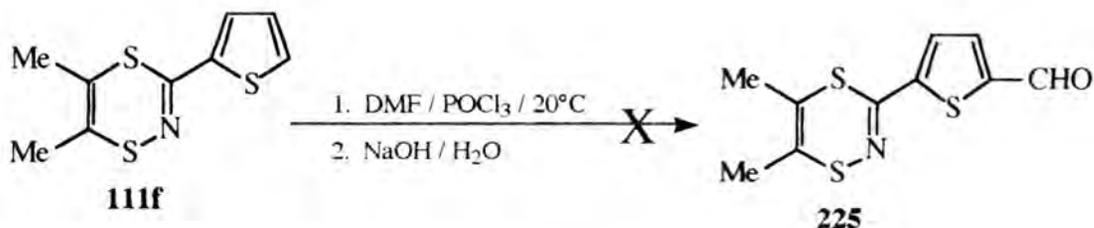
Iodomethane methylation of dithiazine **111a** was ineffective at both room temperature and during reflux in acetone; 96% recovery of starting material resulted after a two hour reflux period. Longer reflux times would have been likely to desulphurise the dithiazine. Reaction of **111a** with dimethyl sulphate (DMS), at 20°C or 90°C, was again found to be ineffective; TLC indicated little or no reaction had occurred.

When dithiazine **111a** was refluxed in a large excess of DMS, with toluene as solvent, the heterocycle was found to methylate. No evidence for unreacted starting material or the isothiazole by-product were seen in crude NMR spectra. Unfortunately, however, these spectra showed the presence of three or more methylation products. These products may correspond to the S-1, N-2 and S-4 methiodide salts, or to species bearing multiple methyl groups. Separation of the product mixture proved to be impossible.

Formylation of aromatic substituents on 1,4,2-dithiazines under Vilsmeier-Haack conditions⁹¹ has been examined. The electrophilic complex was pre-formed by reaction of *N,N*-dimethylformamide (DMF) with phosphorus oxychloride, using a modified literature procedure.⁹² Since the reaction is only applicable to activated, *i.e.* electron-rich substrates, the 3-thienyl-1,4,2-dithiazine derivative **111f** was used in initial studies. Reaction of thiophene under Vilsmeier conditions is known to give good yields of 2-formylthiophene (*ca.* 70%).⁹²

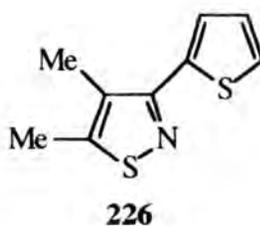
Dithiazine **111f** was dissolved in DMF and allowed to react with 1.5 molar equivalents of the Vilsmeier complex, at room temperature for 2 hours (Scheme 65). The dithiazine reacted completely, but at least six products resulted (NMR and TLC), with no evidence for compound **225**.

The 3-aryl-1,4,2-dithiazine **111a** was also reacted with the Vilsmeier complex, under conditions applied to the thienyl derivative **111f**. Dithiazine **111a** reacted completely; a complex product mixture resulted (NMR and TLC), indicating destruction of the heterocycle.



Scheme 65

Reaction of dithiazine derivative **111f** under Friedel Crafts acylation conditions was investigated briefly. The acylating complex was pre-formed by reaction of aluminium chloride with acetyl chloride, following a literature procedure.⁹³ Reactions were carried out with *ca.* 2 molar equivalents of the acylating complex, in chloroform, initially at room temperature. After three hours, the reaction mixture was worked up to yield recovered starting material (34%) and the novel isothiazole **226** (8%). This provided evidence for Lewis acid-catalysed desulphurisation of the dithiazine, particularly as the reaction was carried out at room temperature. Reaction at *ca.* 60°C led to a predominance of black polymeric material, with isothiazole **226** being isolated in a crude yield of *ca.* 11%.



We attempted to discover whether Lewis acids could bring about desulphurisation of dithiazines, as suggested by the isolation of compound **226**. A dichloromethane solution of dithiazine **111f** was stirred with a large excess of phosphorus oxychloride, for 20 minutes at room temperature. The dithiazine was recovered unchanged.

4.6.2 Discussion of Results.

In the majority of cases, reaction of 1,4,2-dithiazines with electrophilic reagents gave disappointing results. Selective methylation of the heterocycle was found to be very difficult to effect. Mild conditions and reagents gave no reaction, whilst more forceful conditions led to the formation of mixed products.

The aromatic substituents of 3-thienyl- and 3-aryl-1,4,2-dithiazines proved to be insufficiently reactive under both Friedel Crafts acylation and Vilsmeier-Haack formylation conditions. Comparison of NMR chemical shifts for the protons attached to substituent aromatic rings on these 1,4,2-dithiazines with those of the corresponding isothiazole species indicates that the dithiazine ring has a significantly electron-withdrawing effect on the substituent aromatic rings. The protons *ortho*- to the dithiazine substituent on the aromatic ring are considerably deshielded in comparison to the analogous isothiazole derivatives. This may explain the lack of reactivity shown by these aromatic substituents towards electrophiles.

The product mixtures obtained from these reactions showed that alternative reactions were taking place. Crude products were found to be complex mixtures, with much polymeric material often in evidence, particularly for reactions carried out at higher temperatures. We did not observe the clean formation of ring-contraction products from these electrophilic reactions, in contrast to the previous findings of other workers using different electrophiles (Section 1.4.3.5).²⁵ Some evidence was obtained for the occurrence of an alternative ring-contraction process; an isothiazole was isolated under Friedel Crafts acylation conditions. This may indicate Lewis-acid promoted desulphurisation of the 1,4,2-dithiazine system, although experiments to confirm this hypothesis were inconclusive.

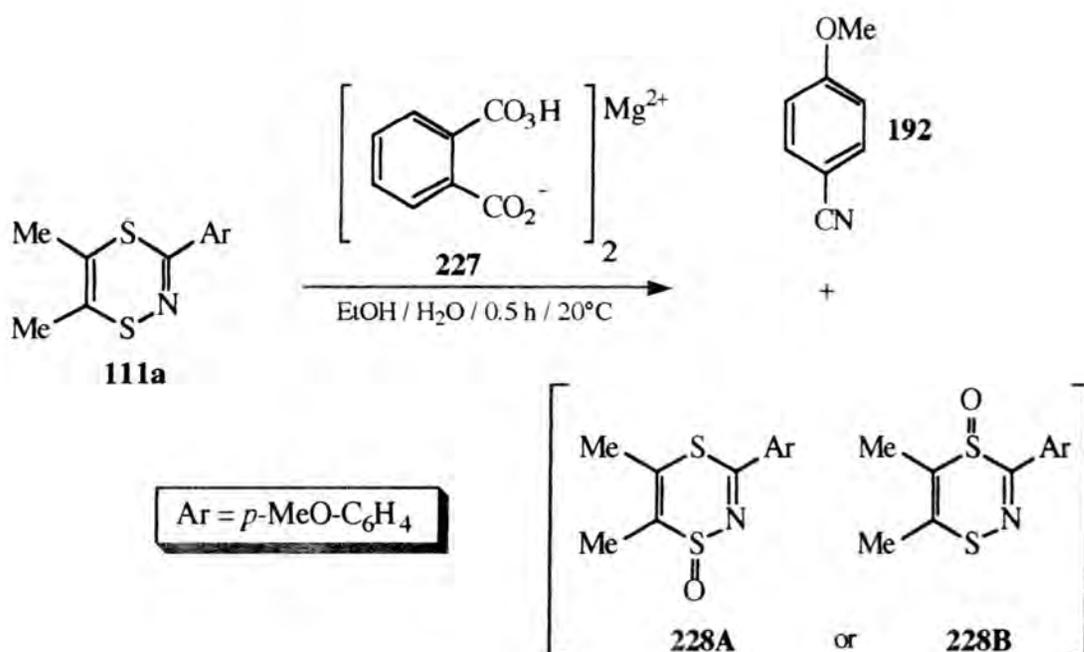
4.7 Reaction of 1,4,2-Dithiazines with Oxidising Agents.

There had been no reports on the chemical or electrochemical oxidation or reduction

of 1,4,2-dithiazines prior to our work. The electrochemical redox properties of the heterocycle have been discussed in Section 2.6, and its reactions with hydride reducing agents were evaluated in Section 4.5.1. We now turn attention to the reactions of 1,4,2-dithiazines with chemical oxidising agents.

4.7.1 Synthetic Details.

Reaction of dithiazine derivative **111a** with the magnesium salt of mono-peroxyphthalic acid **227** (MMPP)⁹⁴ is shown in Scheme 66. For this reaction, a quantity of MMPP supplying 1.1 molar equivalents of oxygen was employed, with the objective of synthesising a mono-oxide of the dithiazine.



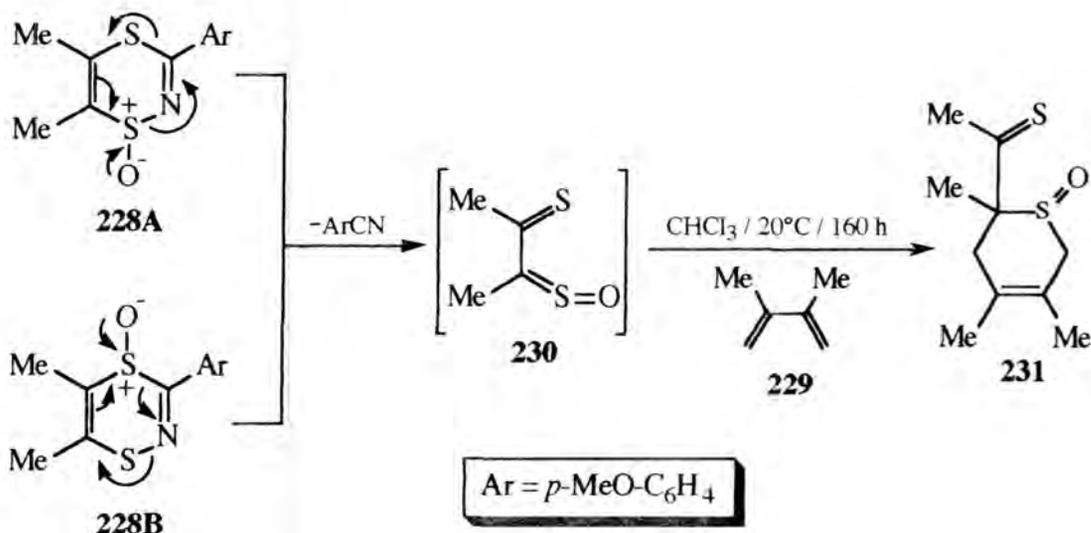
Scheme 66

Unexpectedly, nitrile **192** was obtained as a minor product, in 22% yield. The major reaction product was a mono-oxide of dithiazine **111a**, in a yield of 46%, to which we assign one of the sulfoxide isomer structures **228A** or **228B**, on the basis of analytical characterisation, and the findings discussed below.

Complete decomposition of compound **228** occurred after two days in chloroform, at room temperature. A quantitative yield of nitrile **192** was the only identifiable decomposition product. This provides strong evidence that the mono-oxide **228** is not an *N*-oxide; fragmentation of an *N*-oxide to the nitrile would involve rupture of not only the heterocyclic ring, but also an N-O bond. We also found that compound **228**, which was isolated as a cream coloured powder, itself decomposed under ambient storage conditions. Approximately 40% decomposition to the nitrile was noted after six days of storage. The relative instability of sulphoxides, *cf.* sulphones, is a recognised characteristic in related 1,4-dithiin systems.⁵⁹ The mass spectroscopic fragmentation pattern of compound **228** is analogous to its decomposition behaviour at room temperature. The radical ion of **228** is seen in very low abundance (*ca.* 5%), whilst that of the nitrile is seen in 100% abundance.

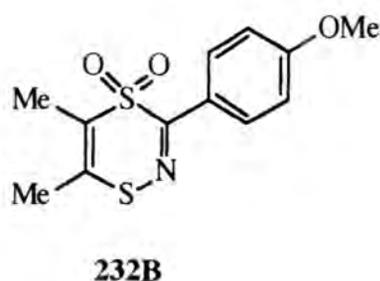
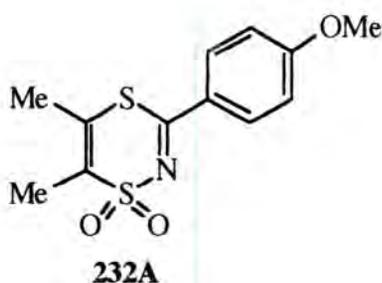
It has not been possible to determine which of the isomers **228A** or **228B** is the actual sulphoxide isolated. Plausible mechanisms for the fragmentation of either isomer, to give the nitrile product, can be envisaged. However, oxidation of sulphides to sulphoxides by peroxyacids is known to involve initial nucleophilic attack by sulphur on the oxidising agent.⁹⁵ Previous studies have indicated that S-4 of the 1,4,2-dithiazine system is more nucleophilic than S-1 (Section 1.4.3.8, Table 3).²¹ This would indicate that isomer **228B** is the more likely sulphoxide isomer.

It was anticipated that the sulphur-bearing fragment arising from decomposition of sulphoxide **228** may be a sulphine species.⁹⁶ Sulphoxide **228** was, therefore, reacted with dimethylbutadiene **229**, in an attempt to trap sulphine **230**, in a Diels-Alder reaction (Scheme 67). Mechanisms for the decomposition of either sulphoxide isomer, to give the same sulphine intermediate, are shown. Evidence was obtained (high resolution MS) for the formation of cycloadduct **231**, in low yield. This result clearly supports the intermediacy of sulphine **230**, and opens up a potential new route to these species.⁹⁶ Unfortunately, these observations do not provide any information on the isomeric identity of sulphoxide **228**.



Scheme 67

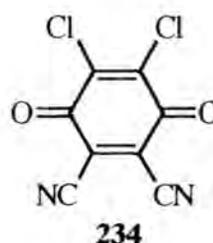
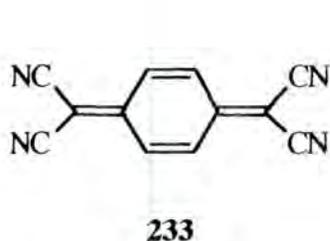
We next investigated the possibility of 1,4,2-dithiazine sulphone formation. Dithiazine **111a** was reacted with 2.2 equivalents of oxygen, supplied by MMPP, at reaction temperatures of between 20 and 50°C. Analysis of the product obtained indicated a dioxide species, in yields of 18-20%. This product was tentatively assigned as either sulphone **232A** or **232B**, by analogy with sulfoxide **228**.



The possibility that the product is a bis(sulphoxide) is thought to be unlikely by comparison with studies on 1,4-dithiin systems; sulphones are formed in significant preference to bis-sulphoxides.⁵⁹ Sulphone formation is, however, usually slower to bring about than sulfoxide formation.^{97a} The possibility of sulfoxide-*N*-oxide formation under the more vigorous reaction conditions cannot, therefore, be ruled out.

Spectroscopic data were unable to confirm unequivocally the identity of compound **232**, and X-ray quality crystals could not be obtained.

Oxidation of dithiazines by electron donation to acceptor molecules,⁹⁸ such as tetracyanoquinodimethane (TCNQ) **233** and dichlorodicyanobenzoquinone (DDQ) **234**, was briefly examined. Charge-transfer between dithiazines and these acceptor molecules was not observed.



4.7.2 Discussion of Results.

The studies described provide the first results on the chemical oxidation of 1,4,2-dithiazines. Reaction of the heterocycle with peroxyacids has enabled the selective isolation of mono- or dioxides of the system, dependent on the reaction conditions employed. The mono-oxide has been shown to be a sulfoxide and the dioxide is almost certainly a sulphone derivative, although ambiguity remains as to the absolute isomeric identities of these compounds.

In related work, we have shown that the sulfoxide species is capable of acting as a precursor to sulphines, the sulphine fragment being trapped by cycloadduct formation.

4.8 Hydrolysis of 1,4,2-Dithiazines.

The imine functionality of the 1,4,2-dithiazine ring, due to the non-delocalised nature of the heterocyclic core (Section 2.5), may be susceptible to hydrolysis. We have,

therefore, investigated the characteristics of 1,4,2-dithiazines under neutral, basic and acidic hydrolysis conditions.

4.8.1 Synthetic Details.

Dithiazine derivative **111a** was dissolved in a mixture of acetonitrile and water (90:10 v/v) and stirred at room temperature for 70 hours. Thin layer chromatography suggested that no reaction had taken place. The solution was then heated to reflux (80°C) for 24 hours. Column chromatography led to the isolation of recovered dithiazine **111a** (60%), nitrile **192** (9%) and isothiazole **187a** (7%). The nitrile was proposed to have arisen *via* nucleophilic attack by water on the dithiazine, leading to ring cleavage, analogous to the findings discussed in Section 4.5 for other nucleophilic species. The isothiazole presumably arises by thermally-induced desulphurisation of the dithiazine, as described in Section 4.2. Recovery of such a large proportion of the dithiazine after a prolonged period at elevated temperature indicates that the 1,4,2-dithiazine ring is resistant to hydrolysis under neutral conditions. Despite the non-delocalised nature of the heterocycle, the N(2)=C(3) double bond does not appear to behave as a typical imine.

To examine the behaviour of 1,4,2-dithiazines under basic conditions, an acetonitrile:water solution of derivative **111a** was stirred at room temperature with 100 molar equivalents of sodium hydroxide for one hour. No significant reaction was observed (TLC evidence). The solution was then refluxed for a further four hours. Decomposition of the heterocycle resulted, with the formation of five or more breakdown products (TLC). The only product isolated was nitrile **192**, in 15% yield. Again, this is suggestive of dithiazine ring fragmentation *via* initial nucleophilic attack by hydroxide ion.

Acidic hydrolysis conditions were also evaluated. An acetonitrile:water solution of dithiazine **111a**, containing ten molar equivalents of hydrochloric acid, was stirred at room temperature for 70 hours. Almost total reaction of the dithiazine was indicated by TLC analysis, but the only identifiable product was the dithiazine starting material,

recovered in 10% yield.

4.8.2 Discussion of Results.

Dithiazine derivative **111a** was resistant to hydrolysis under neutral and basic conditions at ambient temperature. Higher temperatures did little to initiate reaction under neutral conditions, but facilitated decomposition of the heterocycle in an alkaline environment. Conversely, the 1,4,2-dithiazine system appeared to be more susceptible to reaction in acidic media, even at room temperature, probably resulting in decomposition of the heterocycle.

4.9 Conclusions.

A comprehensive series of 1,4,2-dithiazine reactions has been examined in this Chapter. Some reactions progress readily and may be of synthetic value. Others were found to be difficult to bring about, with little scope for development.

Thermolysis of 1,4,2-dithiazines leads to the isolation of isothiazole species, in good to high yields, confirming the earlier observations of Fanghänel *et al.* A novel isothiazolonitrile species resulted from thermolysis of a bis(1,4,2-dithiazine) derivative.

Thermally-induced cycloaddition reactions of 1,4,2-dithiazines gave disappointing results. Extremely low yields of cycloadducts were isolated, but we were able to obtain supporting evidence for the intermediacy of dithiete species in these reactions.

Photolytically-induced cycloaddition reactions of 1,4,2-dithiazines were significantly more facile than those initiated thermally. Reasonable yields of products (1,4-dithiins and thiophenes) were obtained *via* trapping of dithietes with a variety of dienophiles. In general, the formation of dithiete species predominates under photolytic conditions, whilst thermal conditions effect desulphurisation of the dithiazine ring. Notably, we obtained evidence for the formation of the parent, unsubstituted dithiete

under photolytic conditions.

Reaction of 1,4,2-dithiazines with nucleophilic species leads to ring opening of the heterocycle, to afford 1,2-dithiol derivatives, some with potential as synthetic intermediates. In the majority of cases, reactions were found to occur more cleanly with 3-aryl substituted 1,4,2-dithiazines.

The interaction of dithiazine derivatives with a range of electrophilic species gave poor results. It was impossible to selectively methylate the dithiazine ring; either no reaction occurred or intractable mixtures of salts resulted. Attempts to formylate and acylate aromatic substituents of 1,4,2-dithiazine derivatives were unsuccessful; the aromatic substituents were rendered insufficiently reactive by electronic withdrawal of the dithiazine ring. Some evidence was obtained for Lewis acid-catalysed desulphurisation of dithiazines, to give isothiazoles.

1,4,2-Dithiazines reacted cleanly with peroxyacids, to selectively yield sulphoxides and sulphones (the sulphone assignment is tentative at present). The sulphoxide fragments into a sulphine intermediate, which can be trapped in a Diels-Alder reaction.

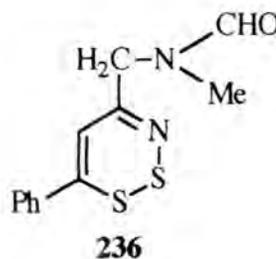
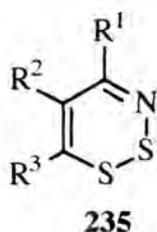
The dithiazine ring is highly resistant to hydrolytic cleavage under neutral conditions and reasonably resistant in strongly alkaline media. In strongly acidic conditions, however, decomposition of the heterocycle is thought to result.

CHAPTER 5

SYNTHESIS AND CHARACTERISATION OF 1,2,3-DITHIAZINE DERIVATIVES

5.1 Introduction.

Following studies on the synthesis, characterisation and reactivity of 1,4,2-dithiazines (Chapters 2, 3 and 4), our next synthetic target became the 1,2,3-dithiazine system **235**.



In common with the 1,4,2-isomer, the 1,2,3-dithiazine system is an eight π -electron heterocycle. Additionally, the three contiguous heteroatoms of the ring, incorporating the labile disulphide functional group, led to the expectation that derivatives of 1,2,3-dithiazines might be difficult to synthesis and handle.

Reflecting this, the 1,2,3-dithiazine system **235** is very rare; the first example being reported in 1989.⁹ Prior to our work, only five derivatives of the eight π system were known,⁹⁹ four of which are described in Chapter 1, Section 1.3, the remaining example being compound **236**. These derivatives were obtained by electrochemical synthesis, as described in Section 1.3; no chemical routes to eight π -electron 1,2,3-dithiazines had been reported.

An objective of our research was to develop the scope of the iodine-ammonia methodology, which we had used to synthesise 1,4,2-dithiazines, in the quest for further novel heterocyclic species. The 1,2,3-dithiazine system offered an opportunity to fulfil this objective.

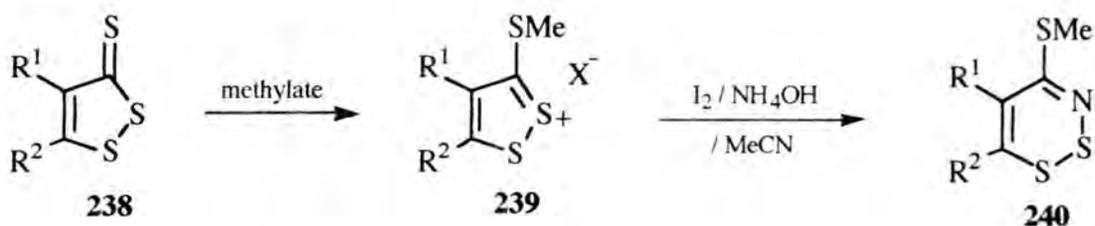
5.2 Synthesis of 1,2,3-Dithiazine Derivatives.

5.2.1 Synthetic Details.

A potential route to 1,2,3-dithiazines first became apparent by the serendipitous isolation of a by-product arising from alkylation of the zincate species **142**, as shown in Section 2.3.1.1, Scheme 31. Along with the expected thione **139**, column chromatography led to the isolation of a small quantity of the isomeric 1,2-dithiole-3-thione derivative **237** (1.4%).



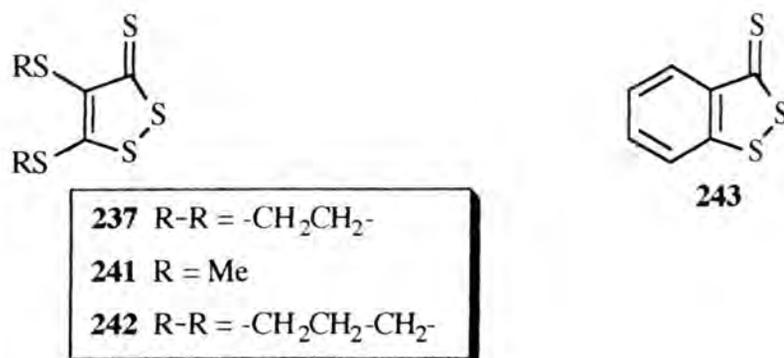
We rationalised that methylation of 1,2-dithiole-3-thione species, such as **238**, would yield 1,2-dithiolium cation salt **239**, ring expansion of which, using iodine-ammonia methodology, could then afford the 1,2,3-dithiazine system **240** (Scheme 68). The development of this synthetic approach is described in the following sections.



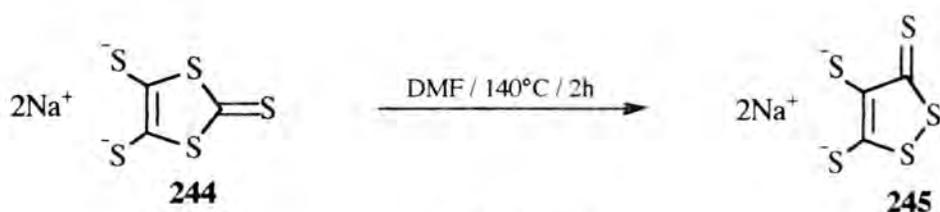
Scheme 68

5.2.1.1 Synthesis of 1,2-Dithiole-3-thiones.

The synthesis of target thiones **237** and **241-243** was examined.

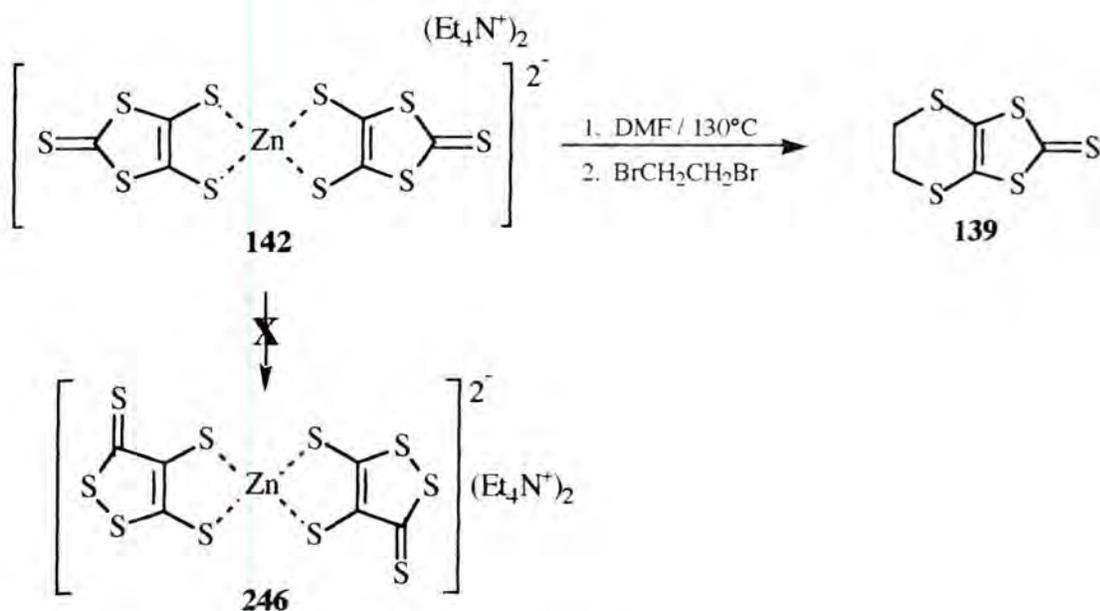


A number of approaches to thiones **237**, **241** and **242** were explored, with the aim of finding the most expedient route. It has been shown that dithiolate species **244** can be isomerised to **245**, by heating in DMF (Scheme 69).¹⁰⁰



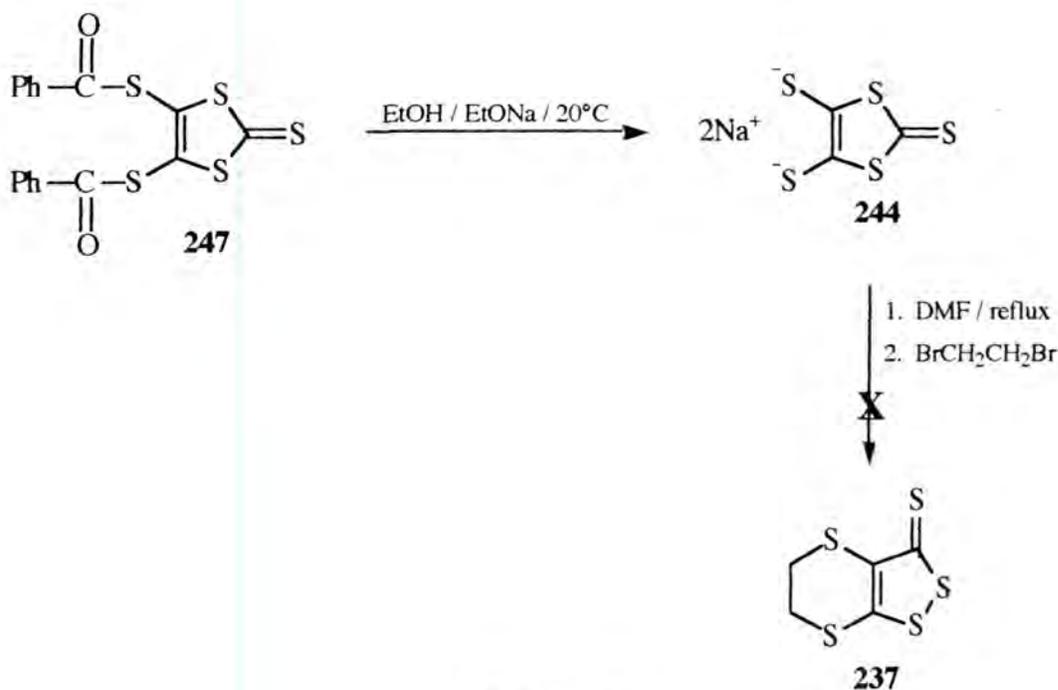
Scheme 69

However, when we heated zincate salt **142** at 130°C in DMF for 4 hours, followed by addition of dibromoethane, the only isolated product was the 1,3-dithiole derivative **139** (Scheme 70). This suggested that isomerisation of zincate salt **142** to salt **246** did not occur under the conditions which isomerise disodium salt **244** into salt **245**.



Scheme 70

Similarly, thione **237** was not obtained when disodium salt **244** was formed *in situ* from di(thioester) **247**,¹⁰¹ and the mixture then refluxed in DMF for 4 hours, followed by addition of dibromoethane (Scheme 71); low yields of isomer **139** resulted.

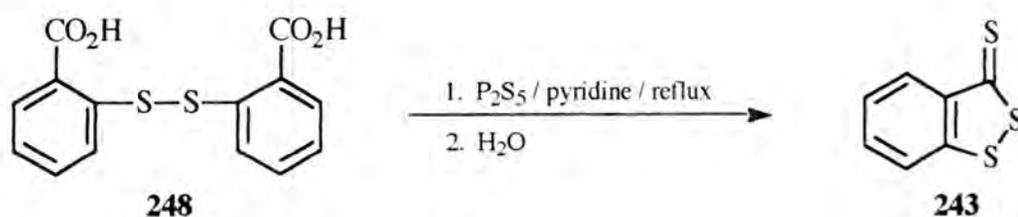


Scheme 71

Direct thermal isomerisation of 2-thione **139** into 3-thione **237** did not occur; refluxing **139** in DMF resulted in progressive destruction of the compound, although this isomerisation has been reported to occur under photochemical conditions.¹⁰²

We therefore resorted to using zincate salt **246**, obtained in 62% yield *via* thermal isomerisation of the disodium dithiolate salt **244**, in DMF at 140°C, following a modified literature procedure.¹⁰⁰ This route has the advantage that, depending upon the alkylating agent chosen, salt **246** may be used to synthesise a range of 3-thione derivatives. Thus, reaction of **246** with a variety of mono- and di-functional alkyl halides, refluxing in acetonitrile, led to the isolation of 1,2-dithiole-3-thiones **237**,¹⁰³ **241**,¹⁰³ and **242**,¹⁰³ in yields of 72, 44 and 18%, respectively.

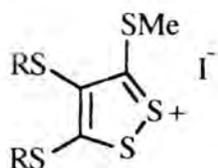
1,2-Benzodithiole-3-thione **243** was obtained in 77% yield by reaction of phosphorus pentasulphide with the commercially-available aryldisulphide derivative **248**, following the literature procedure (Scheme 72).¹⁰⁴



Scheme 72

5.2.1.2 Synthesis of 1,2-Dithiolium Cation Salts.

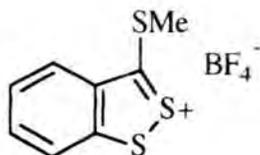
1,2-Dithiolium cation salts are a well-established class of compounds.^{16,105} Following synthesis of thiones **237** and **241-243**, attempts were made to synthesise 1,2-dithiolium salts **249-253**.



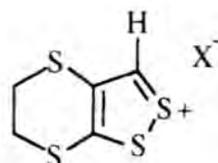
249 R = Me

250 R-R = -CH₂CH₂-

251 R-R = -CH₂CH₂CH₂-



252

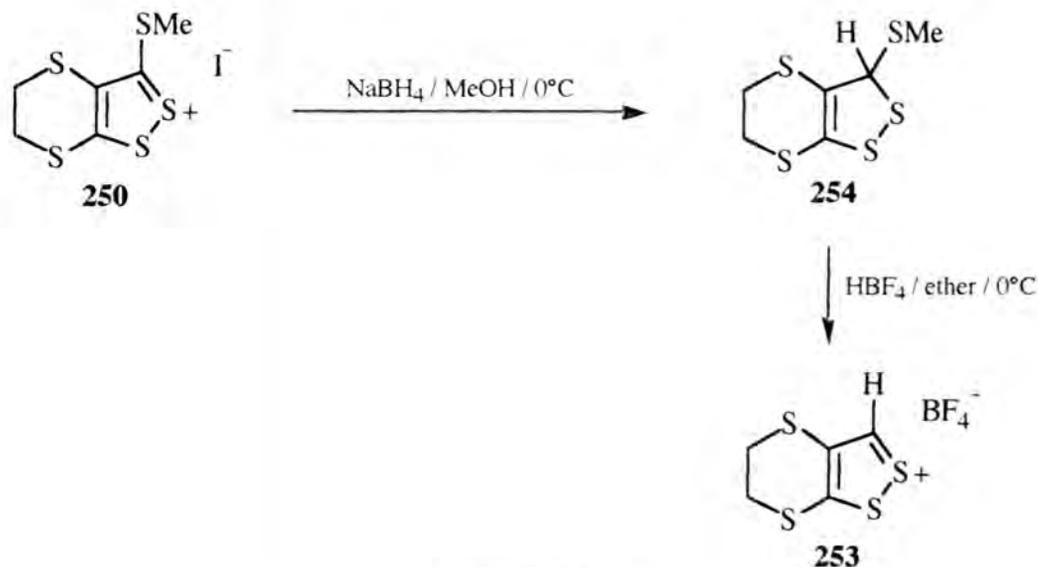


253

Refluxing acetone solutions of thiones **241**, **237** and **242** were methylated with iodomethane, following a modified literature procedure;¹⁰³ significant improvement to product yields was effected by extending the reaction time from 4 hours,¹⁰³ to *ca.* 24 hours. Methiodide salts **249**,¹⁰⁶ **250**¹⁰³ and **251**¹⁰³ were thus obtained in yields of 90, 82 and 52%, respectively. It is notable that methylation of these 3-thiones occurs readily with iodomethane, whereas 2-thione isomeric analogues typically require more forceful conditions, *i.e.* dimethyl sulphate at *ca.* 100°C.^{48,49}

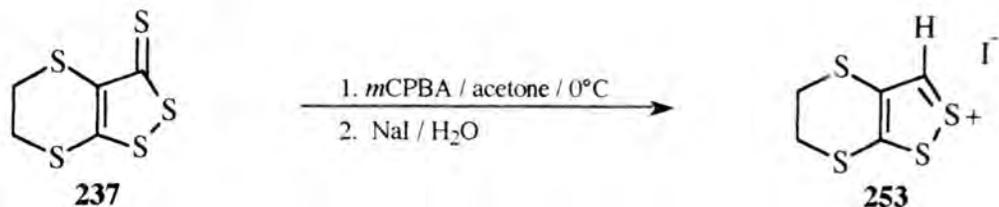
Compound **252** was obtained, in 97% yield, by methylation of thione **243** with dimethyl sulphate, following the literature.¹⁰⁷ Interestingly, compound **243** could not be methylated with iodomethane, under a range of conditions.

The synthesis of 1,2-dithiolium salt **253** was more challenging. An inefficient route to salt **253** (X = BF₄), which proceeds *via* methiodide salt **250**, has been reported by Papavassiliou and co-workers (Scheme 73).⁴⁹ The overall yield for conversion of salt **250** to **253** (as the tetrafluoroborate salt) was quoted as 10%, however, based upon the weights of starting materials and products given in the experimental of that paper, the yield is only 5.4%. Numerous attempts made by us to replicate this procedure resulted in failure. Reaction of salt **250** with sodium borohydride did not give the expected dithiole species **254**; a complex, multi-component mixture (NMR and TLC evidence), probably containing ring-opened products, was obtained and could not be purified under the reported procedure.⁴⁹ Notably, protons of the dithioethylene group were not observed in the ¹H NMR spectra of crude product mixtures, indicating degradation of the heterocycle.



Scheme 73

We therefore explored an alternative approach to salt **253**, and have developed a straightforward route from thione **237** (Scheme 74).



Scheme 74

Reaction of thione **237** with *m*-chloroperoxybenzoic acid (*m*CPBA) yielded the crude hydrogensulphate salt of **253**, which upon addition of aqueous sodium iodide furnished the desired compound **253**, as the iodide salt, in 34% yield.^{105,108} This salt is highly insoluble in water and a range of common organic solvents. It is stable when stored under ambient conditions, whereas the isomeric 1,3-dithiolium cation salt **123** (Section 2.3.1.1) requires storage at $<5^\circ\text{C}$.⁴⁸

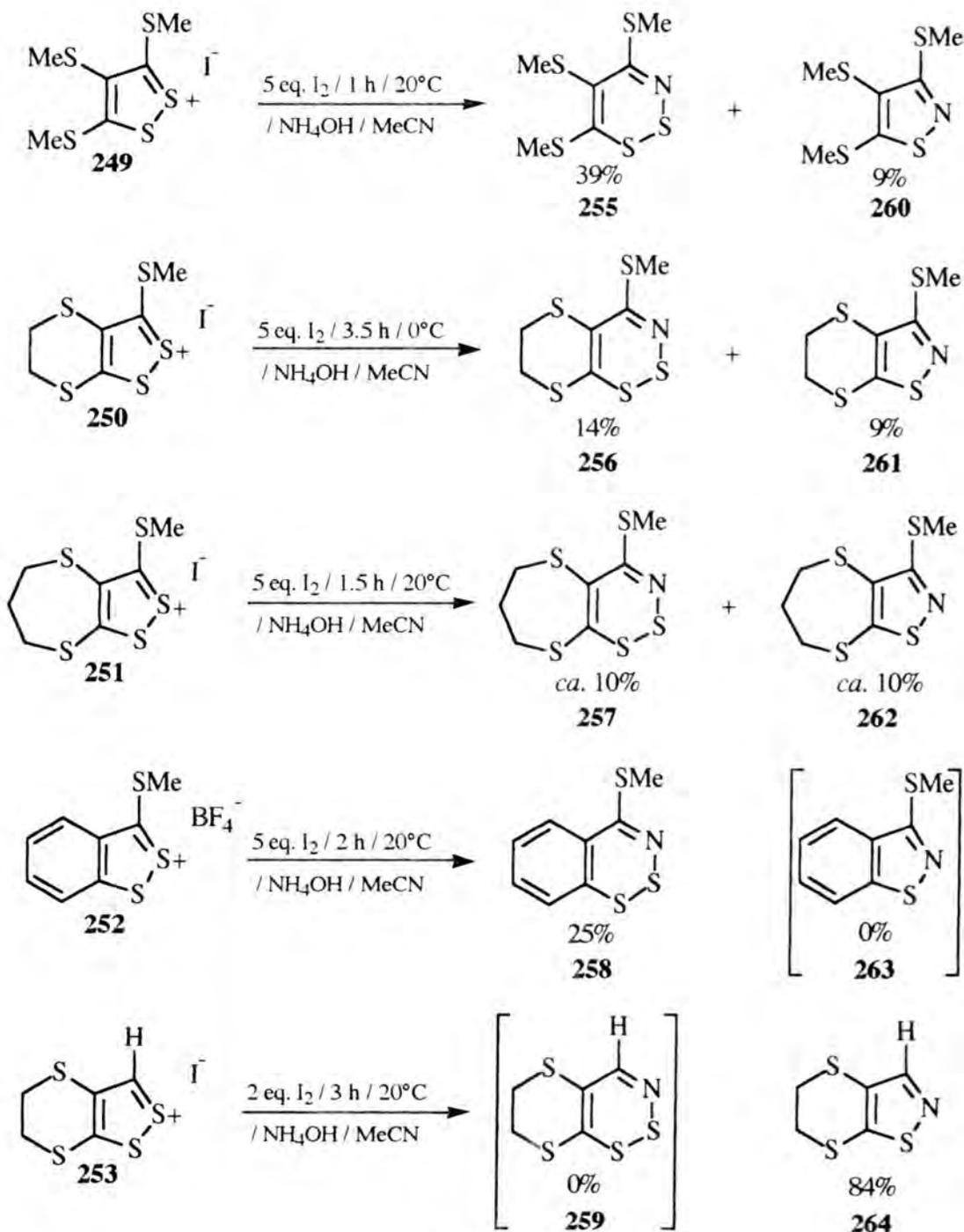
5.2.1.3 Synthesis of 1,2,3-Dithiazine Derivatives.

Salts **249-253** were reacted under iodine-ammonia conditions, with the objective of isolating corresponding 1,2,3-dithiazines **255-259**. Exhaustive attempts were made to find optimum reaction conditions; results are shown in Scheme 75.

Novel 1,2,3-dithiazines **255-258** were isolated in yields of between *ca.* 10 and 39%; 4-hydro dithiazine **259** was not observed. Isothiazoles **260-262** and **264**¹⁰⁹ were also isolated from these reactions, in yields of 9-84%. Benzisothiazole **263** was, however, not formed during reaction of benzodithiolium salt **252**. Precursor thiones **237**, **241** and **243** were also obtained, in low yields (< 10%), from product mixtures resulting from reaction of salts **250**, **249** and **252**, respectively, probably as a result of demethylation of these salts under the reaction conditions.

Lower reaction temperatures were examined with the aim of eliminating isothiazole formation, these species presumably arising *via* desulphurisation of dithiazine products under the reaction conditions. In general, lower reaction temperatures (-20-0°C) did not prevent isothiazole formation, but reduced the overall yields of isothiazole and dithiazine products. Reaction of salt **250** was, however, exceptional; the highest yield of dithiazine **256** (14%) was obtained from reaction at 0°C. Conversely, when salt **250** was reacted at 40°C, isolation of isothiazole **261** and thione **237** resulted, in yields of 58 and 14%, respectively; dithiazine **256** was not observed under these conditions.

Following observations on reactions of 1,3-dithiolium cation salts (Section 2.3.1.2), it was expected that higher yields of potentially unstable 1,2,3-dithiazines may be obtained by reducing the iodine stoichiometry used in the ring expansion reaction, from 5 equivalents to 1-2 equivalents; for reactions of salts **250** and **252** this led to significantly diminished yields of dithiazine products. Isothiazole **264** was, however, obtained in 84% yield, from salt **253**, using only 2 equivalents of iodine in the iodine-ammonia reaction.



Scheme 75

Ring expansion of salt **251** under iodine-ammonia conditions proceeded less distinctly; some evidence was obtained for dithiazine **257** (NMR) and isothiazole **262** (NMR and MS), but insufficient quantities of both compounds were isolated to enable full characterisation.

Chloroform solutions of 1,2,3-dithiazines **255**, **256** and **258** extruded sulphur during storage at room temperature, to give opaque solutions. Removal of colloidal sulphur by filtration afforded quantitative yields of corresponding isothiazole derivatives **260**, **261** and **263**, respectively. These desulphurisation reactions have been monitored by NMR experiments, to determine the time required for total conversion to isothiazoles (Section 5.3.1). NMR data for the corresponding benzothiazole analogue of compound **263** are given in Section 6.5.1, confirming these species as different structural isomers.

Reaction of salt **249**, under conditions similar to those shown in Scheme 75, also led to the isolation of a compound tentatively assigned as 1,2-thiazoline-3-thione **265** [$\nu(\text{NH}) = 3460 \text{ cm}^{-1}$, amine], in 21% yield. These compounds are known to be in equilibrium with the corresponding 3-imino-1,2-dithiole species **266** (Scheme 76).^{107,110-112} Imine **266** is analogous to imine **148**, isolated during ring expansion of a 1,3-dithiolium cation salt (Section 2.3.1.2, Scheme 33). A similar mechanism to that proposed in Scheme 33 may operate to form imine **266**, which could then isomerise to the isolated thiazoline **265**.



Scheme 76

5.2.2 Discussion of Results.

We have established a reproducible procedure for the synthesis of a range of 1,2-dithiolium cation salts **249-251** and **253**, derived from precursor zincate species **246**. Notably, a synthetic approach to cationic salt **253** has been developed¹⁰⁹ which is a significant improvement on the original literature route.⁴⁹

Ring expansion of 1,2-dithiolium cation salts **249-253**, under iodine-ammonia conditions, furnished novel 1,2,3-dithiazine derivatives **255-258**, representing the first synthesis of this heterocyclic system by a chemical method (*cf.* electrochemical route, Section 1.3). The confirmation of the 1,2,3-dithiazine structures is discussed in Sections 5.3 and 5.4.

For the majority of ring expansion reactions, both dithiazine and isothiazole products were separated from crude reaction mixtures; it is postulated that desulphurisation of the dithiazines to isothiazoles under the reaction conditions was occurring. The conversion of chloroform solutions of 1,2,3-dithiazine derivatives to isothiazoles supports the proposal that the dithiazines act as intermediates of isothiazole formation. Conditions which were required to bring about desulphurisation of the 1,2,3- and 1,4,2-dithiazine systems are markedly different. Whilst spontaneous desulphurisation of 1,2,3-dithiazines in chloroform solution at room temperature was noted, 1,4,2-dithiazines require a period of refluxing in toluene (Section 4.2). The greater facility of 1,2,3-dithiazines to undergo desulphurisation may result from lability of the iminodisulphide functionality in this heterocycle, or may indicate a measure of thermodynamic instability in the system, arising from anti-aromatic character.

5.3 Characterisation of 1,2,3-Dithiazine Derivatives.

Characterisation of 1,2,3-dithiazines **255-258** has presented a significant analytical challenge. None of the derivatives was crystalline, thus preventing the use of X-ray diffraction studies. Spectroscopic (NMR, MS, UV-VIS) and electrochemical (CV) analysis, described in this section, combined with mechanistic appraisal (Section 5.4), have been used to provide clear evidence for these novel 1,2,3-dithiazines.

5.3.1 NMR Spectroscopy of 1,2,3-Dithiazines.

The desulphurisation reactions of 1,2,3-dithiazines **255**, **256** and **258**, to afford

isothiazole derivatives **260**, **261** and **263**, respectively, have been studied, as a function of time, using ^1H NMR spectroscopy. A representative series of spectra, showing conversion of dithiazine **256** into isothiazole **261**, is shown in Figure 8. Clean conversion of the dithiazines was observed, with the corresponding isothiazoles being formed in quantitative yields. Downfield shifts of methylthio protons were seen, upon sulphur extrusion from the dithiazine derivatives, e.g. 2.36 to 2.66 ppm for the conversion of dithiazine **256** into isothiazole **261**, consistent with development of aromatic character in the isothiazole products.

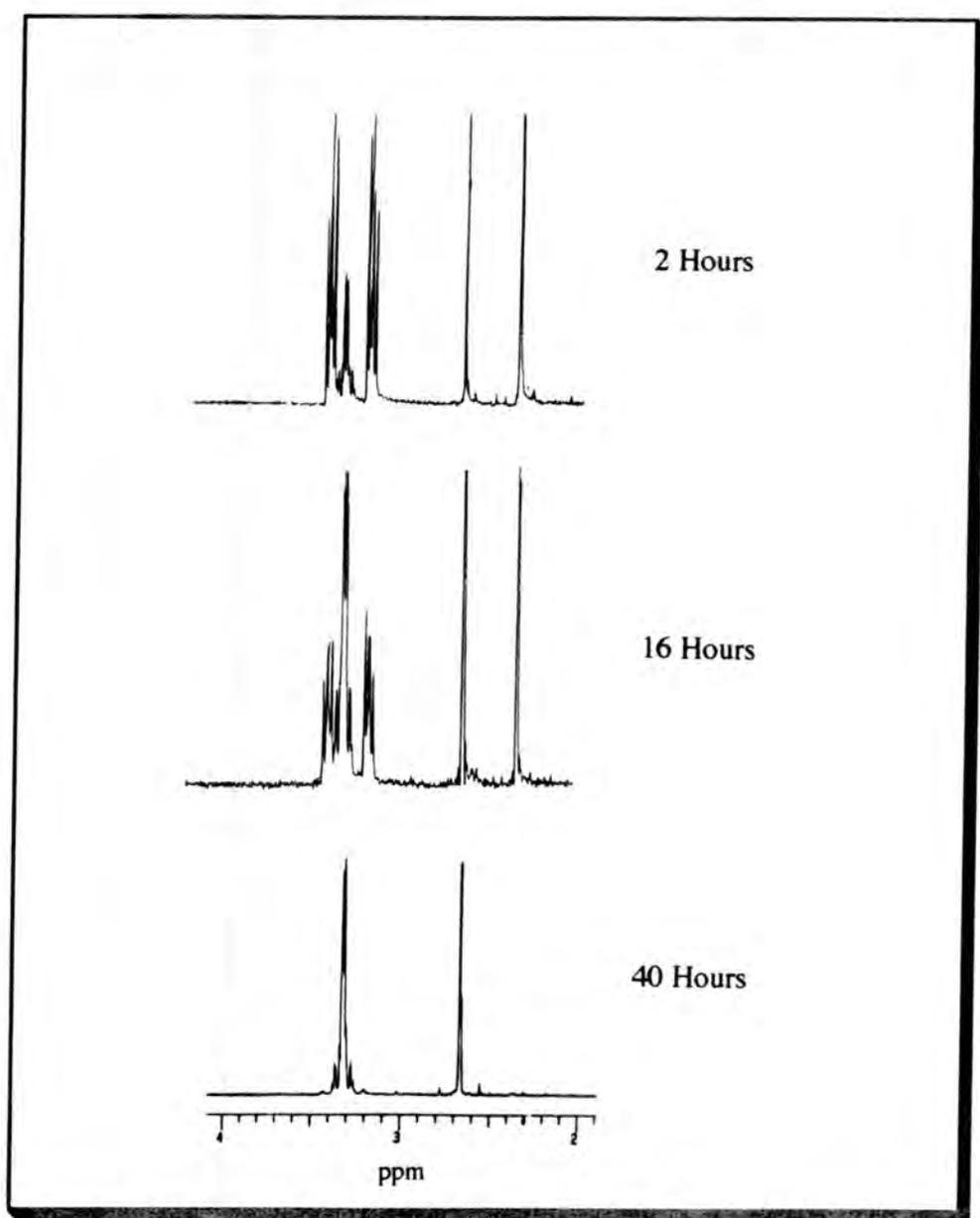


Figure 8. Time-Dependent ^1H NMR Spectra Showing Desulphurisation of 1,2,3-Dithiazine **256** to Yield Isothiazole **261** (20°C). (Methyl signals truncated).

Analogous sets of time-resolved spectra were obtained for the desulphurisation of 1,2,3-dithiazines **255**, **256** and **258**, enabling estimates to be made for total reaction times under identical conditions (20°C in deuteriochloroform), complete conversion to corresponding isothiazoles occurring in: <48, 30 and 99 hours, respectively. Greater relative stability of 1,2,3-benzodithiazine **258** is thus indicated, in accord with its isolation in the absence of corresponding benzisothiazole **263** (Section 5.2.1.3).

5.3.2 Mass Spectroscopy of 1,2,3-Dithiazines.

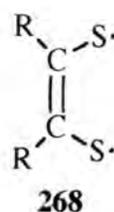
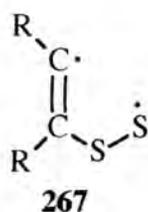
Mass spectroscopic data for 1,2,3-dithiazines **255-258** are presented in Table 13. Abundances of parent radical ions varied considerably between derivatives; this may be due in part to decomposition of the dithiazines, to isothiazoles, prior to analysis. The high parental abundance for dithiazine **258** may, however, again be an indication of enhanced stability in this compound.

Dithiazine	Ionisation Mode	Parent	Isothiazole	Dithiete
255	DCI	62%	100%	0%
256	EI	4%	100%	0%
257	EI	0%	72%	0%
258	EI	100%	42%	0%

Table 13. Radical Ion Abundances (%) for 1,2,3-Dithiazines **255-258**.

Isothiazole radical ions were observed for all dithiazine derivatives. In contrast to results obtained for 1,4,2-dithiazine derivatives (Section 2.4.2), no dithiete radical ions were seen in the mass spectra of 1,2,3-dithiazines **255-258**. Free-radical or ionic mechanisms can be postulated for the loss of nitrile fragments from 1,2,3-dithiazine species. For a free-radical process, the resultant diradical intermediate **267** would have an unpaired electron located on a carbon atom, in contrast with the analogous intermediate

for 1,4,2-dithiazine fragmentation, **268**, where unpaired electrons reside only on sulphur atoms, prior to cyclisation to dithiete species. This latter situation is favoured by the ability of sulphur atoms to stabilise radical states more readily than carbon atoms.¹¹³ (The same argument can be applied to ionic mechanisms, where zwitterionic analogues of intermediates **267** and **268** would be formed). Thus, the relative instability of intermediate **267** may account for the absence of dithiete fragments in the mass spectra of 1,2,3-dithiazine derivatives **255-258**.



5.3.3 Solution Electrochemistry of 1,2,3-Dithiazines.

Solution electrochemistry of 1,2,3-dithiazine derivatives **255**, **256** and **258** has been studied by cyclic voltammetry; data are presented in Table 14 and a representative voltammogram, of derivative **258**, is shown in Figure 9.

Compound ^a	$E_1^{\text{ox}} / \text{V}$	$E_1^{\text{red}} / \text{V}$	$E_1^{1/2} / \text{V}$	$E_2^{\text{ox}} / \text{V}$	$\Delta E / \text{V}^{\text{b}}$
255	1.27	1.21	1.24	1.64	0.40
256	1.28	1.19	1.24	1.58	0.34
258	1.37	1.31	1.34	1.68	0.34

^aCompound (*ca.* 10^{-3} mol dm⁻³) in anhydrous dichloromethane, electrolyte Bu₄N⁺PF₆⁻ (*ca.* 10^{-2} mol dm⁻³), Pt electrode, vs. Ag/AgCl, 20°C. ^b $\Delta E = E_2^{\text{ox}} - E_1^{1/2}$.

Table 14. Cyclic Voltammetric Data for 1,2,3-Dithiazine Derivatives.

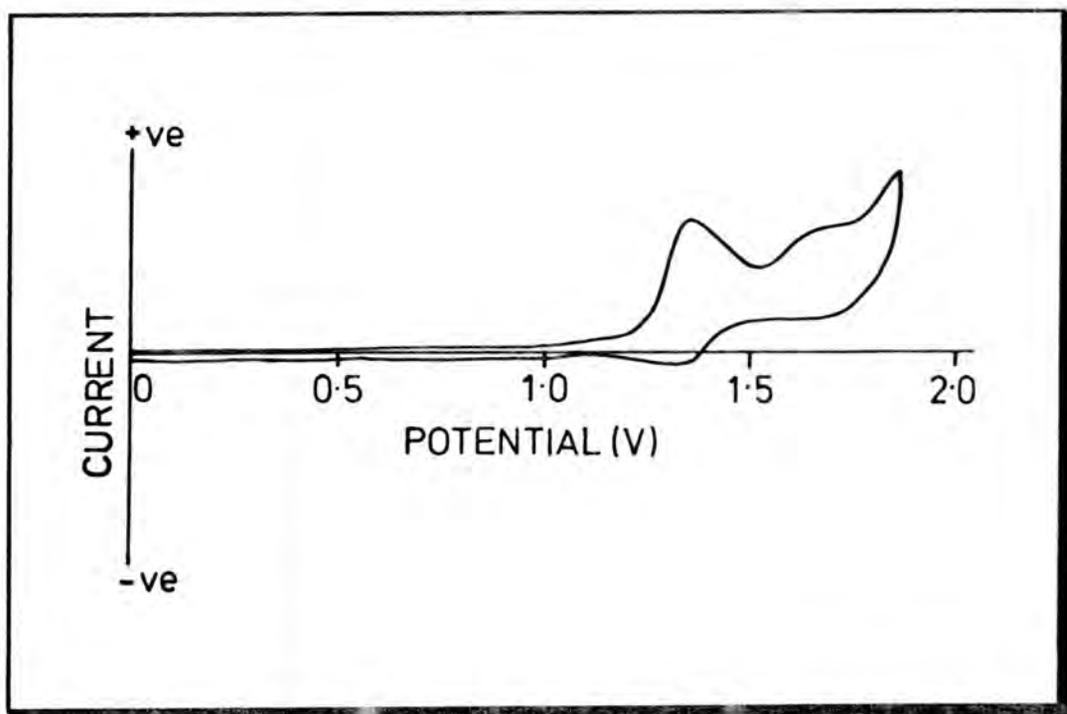


Figure 9. Cyclic Voltammogram of Compound **258**.

1,2,3-Dithiazines **255**, **256** and **258** showed similar electrochemical properties in the solution state. Single electron oxidations, E_1^{ox} , occurred at potentials of between 1.27 and 1.37 V, corresponding to oxidation of the 8π neutral molecules to 7π radical cations. This was an irreversible process for all derivatives studied; corresponding cathodic reduction peaks, E_1^{red} , were observed only as weak shoulders. A second oxidation, E_2^{ox} , was observed for all derivatives, to form 6π dication systems, this oxidation being an irreversible process also. Data for the 1,2,3-benzodithiazine **258** show that it is slightly harder to oxidise than derivatives **255** and **256**; this may be due to the ability of the latter derivatives to distribute positive charge on additional exocyclic sulphur atoms and thus stabilise the radical cation and dication redox stages.

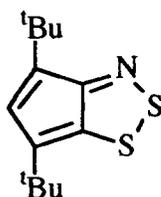
Comparison of the electrochemical data for 1,2,3-dithiazines **255** and **256** with their corresponding 1,4,2-dithiazine isomers **134** and **131**, respectively, is of great interest (Section 2.6, Table 9). Overall, the electrochemical properties of both isomeric heterocyclic systems show quite remarkable similarities; both systems are oxidised irreversibly and sequentially to radical cations and thence to dications, with weak first

wave reduction shoulders being seen. In general, oxidation of the 1,4,2-dithiazine system is a little easier to bring about, *i.e.* E_1^{ox} values of 1.17-1.20 V were recorded for compounds **134** and **131**. The coincident behaviour of compounds **255** and **256** with 1,4,2-dithiazines **134** and **131** provides strong additional proof for the identity of the former compounds as being derivatives of the electronically-related eight π -electron 1,2,3-dithiazine system.

We have also examined the electrochemical behaviour of isothiazole derivative **264**. This heterocycle was significantly harder to oxidise to the radical cation stage than 1,2,3-dithiazine derivatives **255**, **256** and **258**; E_1^{ox} for compound **264** occurred at 1.60 V, reflecting the stability of the six π -electron isothiazole ring.

5.3.4 Ultraviolet-Visible Spectroscopy of 1,2,3-Dithiazines.

The 1,2,3-iminodisulphide arrangement of heteroatoms is very rare; few literature reports are available with which comparisons of data can be made. The iminodisulphide group is, however, present in 1,2,3-dithiazole derivatives, examples being compounds **223**⁸⁹ (Section 4.5.1) and **269**.¹¹⁴ Both compounds show long-wave bands in their UV-VIS spectra, at 513 (weak absorption) and 525 nm, respectively.



269

For 1,2,3-dithiazine derivatives **255** and **256**, we observe weak absorptions at 473 and 490 nm, respectively, although no corresponding absorption was seen for 1,2,3-benzodithiazine derivative **258**. Notably, these long-wave absorptions were absent from

the spectra of isothiazole derivatives **261**, **263** and **264**, indicating that this is a spectral property of the iminodisulphide group, rather than of the iminosulphide group present in isothiazoles.

5.3.5 Discussion of Results.

The question of 1,2,3-dithiazine structural proof has been addressed by the application of various analytical techniques. Quantitative transformation of 1,2,3-dithiazine derivatives, into corresponding isothiazoles, has been studied over time by NMR spectroscopy. Mass spectra of 1,2,3-dithiazine derivatives did not show fragmentation to dithiete species, in contrast to MS fragmentation patterns for 1,4,2-dithiazine derivatives. These findings have been rationalised by consideration of the intermediates which would arise upon extrusion of nitriles from 1,2,3- and 1,4,2-dithiazines.

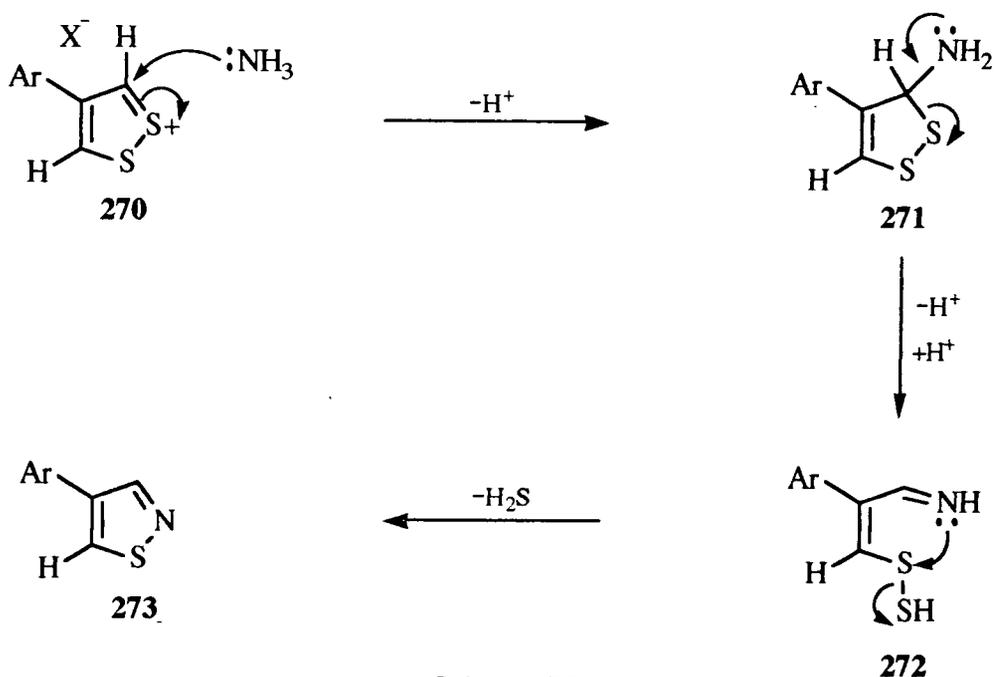
Comparison of the solution electrochemistry displayed by 1,2,3-dithiazine derivatives, with their isomeric 1,4,2-dithiazine analogues, showed great similarities. These findings are attributed to the eight π -electron complements possessed by both heterocyclic systems. Ultraviolet-visible spectra of 1,2,3-dithiazine derivatives showed some correlation with features of related 1,2,3-dithiazole systems; long-wave absorptions were seen for both heterocyclic classes.

Significant evidence which supports the assignment of 1,2,3-dithiazine structure to compounds **255-258** has, therefore, been obtained by analytical characterisation. Further proof is offered in the next section, where possible reaction mechanisms are considered.

5.4 Reaction Mechanism for 1,2-Dithiolium Salts Under Iodine-Ammonia Conditions.

It is well established that the reaction of a wide variety of 1,2-dithiolium cation salts with anhydrous ammonia leads to the formation of isothiazole derivatives.^{16,115,116}

Olofson *et al* reported a general route to isothiazoles which proceeded by reaction of ethanolic solutions of 1,2-dithiolium cation salts with ammonia, under anhydrous conditions.¹¹⁵ Significantly, the vast majority of reactions were carried out at reflux and/or products were isolated by vacuum distillation ($\geq 98^\circ\text{C}$), to give isothiazole derivatives in yields of 7-89%. A number of mechanistic proposals were put forward, all of which involved scission of the disulphide group of the dithiolium cation as a result of reaction with ammonia. On the basis of studies carried out, an addition-elimination pathway was suggested to explain the formation of isothiazole products (Scheme 77).¹¹⁵



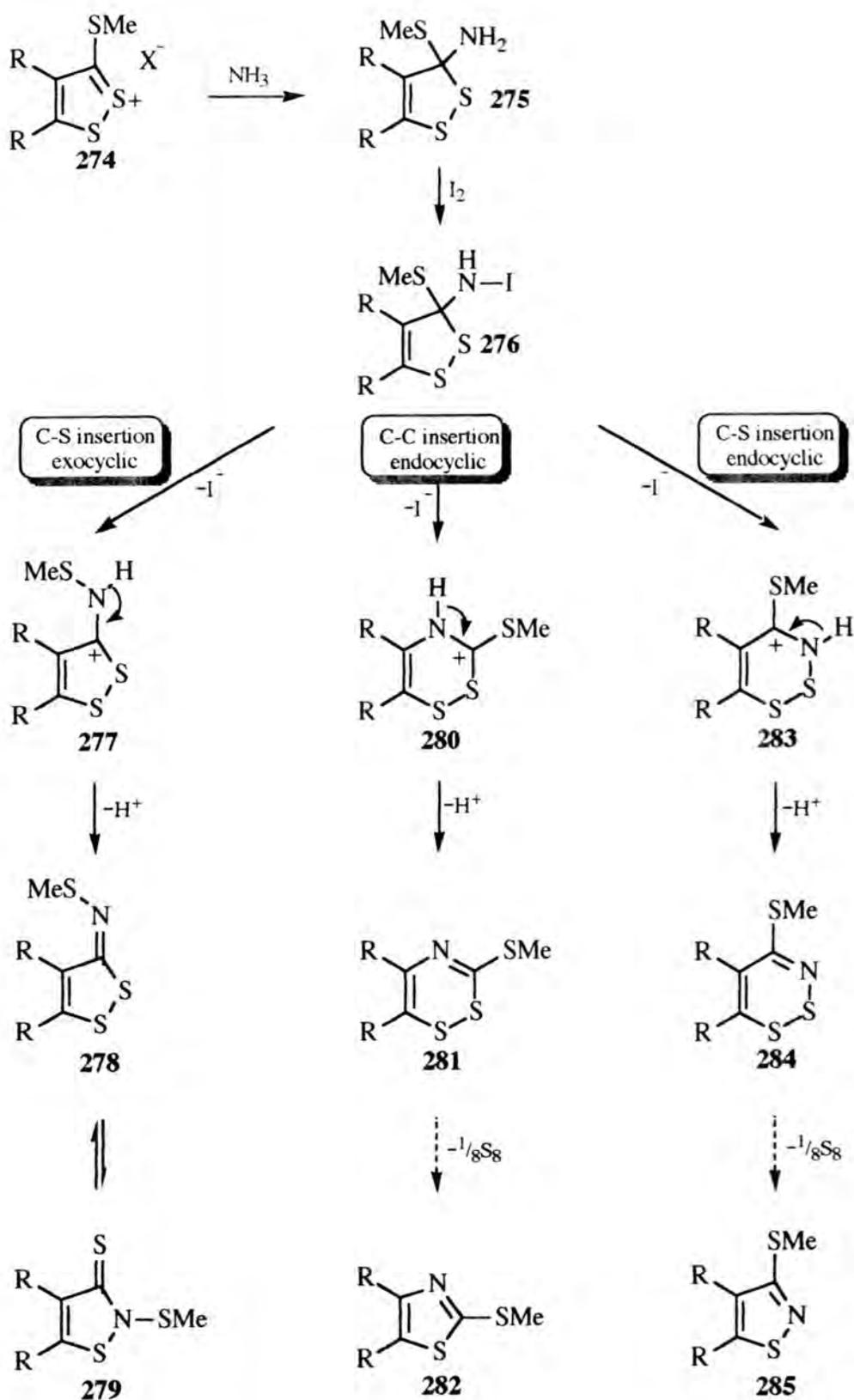
Nucleophilic attack by ammonia on C-3 of 4-aryl-1,2-dithiolium cation **270** gives the amine adduct **271**, which undergoes ring cleavage to imine **272**. Ring closure then occurs, *via* loss of a sulphhydryde anion, with deprotonation, to form the aromatic isothiazole derivative **273**.

Whilst this mechanism could be used to explain our own observation of 3-hydro isothiazole derivative **264**, where the corresponding intermediate 1,2,3-dithiazine **259** was not detected, it does not account for our observation of 1,2,3-dithiazines **255-258**,

and their subsequent conversion to isothiazoles **260-263**. Neither of the proposed intermediates **271** or **272** (assuming that they could be isolated) fit the spectroscopic data obtained for 1,2,3-dithiazine derivatives **255-258** (NMR, IR, MS). The mechanism published by Olofson and co-workers requires the loss of hydrogen sulphide during the ring closure step (**272** to **273**), but detection of hydrogen sulphide is not described in their report. In our own work, the extrusion of elemental sulphur from 1,2,3-dithiazine derivatives, to yield isothiazoles, has been observed.

Clearly, therefore, the mechanism postulated by Olofson *et al* for the formation of isothiazoles from reaction of 1,2-dithiolium cation salts with ammonia does not fit our experimental findings. Two possible reasons may account for this; first, the reactions of Olofson *et al* were conducted under anhydrous conditions, whereas our experiments involved aqueous ammonia solution in the presence of iodine; alternative mechanisms may operate under these different reaction conditions. A second explanation is that intermediate 1,2,3-dithiazines which may have been formed during the experiments of Olofson *et al* were desulphurised by the reaction conditions, *i.e.* refluxing in ethanol, or during product isolation by vacuum distillation at temperatures of 98-135°C.¹¹⁵ In our own studies we have noted the spontaneous desulphurisation of 1,2,3-dithiazines at room temperature (Section 5.2.1.3).

To explain the formation of products isolated from our reactions of 1,2-dithiolium cation salts with iodine and aqueous ammonia solution, we favour a mechanism analogous to that proposed for reaction of 1,3-dithiolium cation salts under similar conditions (Section 2.7.2, Scheme 41).^{43,44} Nucleophilic attack by ammonia (Scheme 78) on 1,2-dithiolium salt **274** gives the intermediate amine **275**, as proposed by Olofson *et al* (*cf.* compound **271**, Scheme 77).¹¹⁵ In the presence of iodine, however, oxidative iodination of amine **275** can then occur, to afford haloamine **276**. This haloamine is capable of undergoing three possible modes of concerted nitrogen insertion, with concomitant loss of iodide anion.



Scheme 78

The first possibility involves nitrogen insertion into the exocyclic C3-SMe sigma bond, to give intermediate **277**, which then deprotonates to 3-imino-1,2-dithiole **278**. As previously described, these species are in equilibrium with the corresponding 1,2-thiazoline-3-thione isomer **279** (Section 5.2.1.3, Scheme 76).^{107,110-112} However, for either of these isomers **278** or **279**, there is no obvious way of losing elemental sulphur from the molecules, as we have observed with our reaction products (Section 5.2.1.3). Desulphurisation of heterocycle **278** or **279** would lead to the formation of a four-membered ring, and loss of the thione sulphur atom from compound **279** would be an unlikely occurrence. Despite the many studies on the isomerisation and chemistry of these compounds,^{107,110-112} no reports of their desulphurisation were found. We conclude, therefore, that the exocyclic carbon-sulphur bond insertion mechanism does not explain the products which we have isolated.

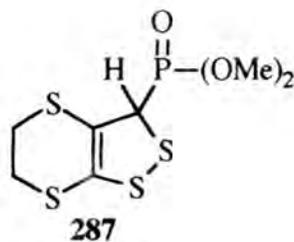
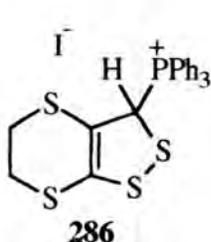
A second mechanistic possibility is endocyclic insertion of nitrogen into the C3-C4 bond of compound **276** to give, after deprotonation of intermediate **280**, 1,2,4-dithiazine derivative **281** (Scheme 78). This would require initial cleavage of a carbon-carbon sigma bond, an energetically more difficult proposition than cleavage of a carbon-sulphur sigma bond.^{97b} For reactions of 2-aryl-1,3-dithiolium cation salts under identical reaction conditions (Section 2.2.1), no evidence for the imine products of nitrogen insertion into carbon-carbon sigma bonds was found. 1,2,4-Dithiazine derivatives are themselves rare species (Section 1.2)^{1c,5} and it is notable that desulphurisation of compound **281** would lead to thiazole derivative **282**, whereas the reaction of 1,2-dithiolium salts with ammonia is known to give isothiazole products,^{16,115,116} albeit under anhydrous conditions without the presence of iodine. After consideration of the above factors we, therefore, discount the possibility that reaction occurs *via* endocyclic insertion of nitrogen into the carbon-carbon bond.

The remaining mechanism, which is consistent with all the available data, involves endocyclic insertion of nitrogen into the S2-C3 sigma bond of haloamine **276**, to give cationic intermediate **283** which, after deprotonation, furnishes 1,2,3-dithiazine derivative **284** (Scheme 78). This pathway builds on the earlier precedent for endocyclic

nitrogen insertion into carbon-sulphur bonds of 1,3-dithiolium cation salts under iodine-ammonia conditions (Sections 2.2.1.4 and 2.3.1.2).^{43,44} The products of reaction which we have obtained are explained satisfactorily by this mechanism; desulphurisation of 1,2,3-dithiazine species **284** leads to the formation of isothiazole **285**. We therefore favour the pathway *via* intermediate **283**, as it is consistent with the products which we have obtained from reaction of 1,2-dithiolium salts under iodine-ammonia conditions.¹⁰⁹

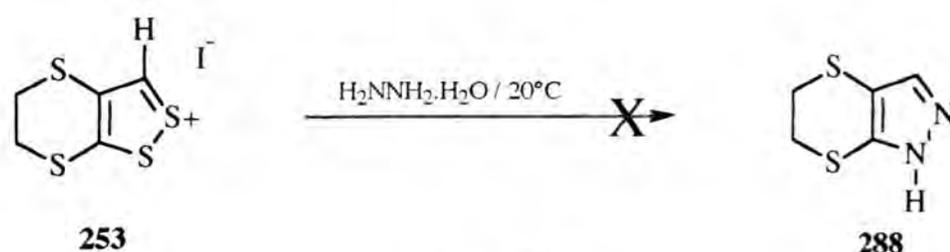
5.5 Related Chemical Studies.

Some additional reactions of 1,2-dithiolium cation salts and 1,2,3-dithiazine derivatives have been examined. The interaction of salt **253** with phosphorus nucleophiles was investigated, with a view to preparing Wittig and Wittig-Horner reagents. Analogous reagents derived from 1,3-dithiolium cation salts have proved to be of value in the synthesis of extended tetrathiafulvalene derivatives.^{48,117} Addition of either triphenylphosphine, or trimethylphosphite and sodium iodide, to a suspension of methiodide salt **253** in acetonitrile at 20°C, standard conditions for the 1,3-dithiolium isomer **123**,^{48,117} gave intractable product mixtures, with no evidence for the formation of desired phosphonium salt **286** or phosphonate ester **287**, respectively.



Reaction of hydrazine hydrate with 1,2-dithiolium cation salts has been reported to give pyrazoles.¹⁰⁵ However, reaction of methiodide salt **253** with hydrazine monohydrate failed to give the expected pyrazole derivative **288** (Scheme 79); no isolable products were obtained. 1,2-Dithiolium cation salts are decomposed by bases in the

presence of water;¹⁰⁵ moisture impurities in the hydrazine source used may have thus led to failure of the reaction.

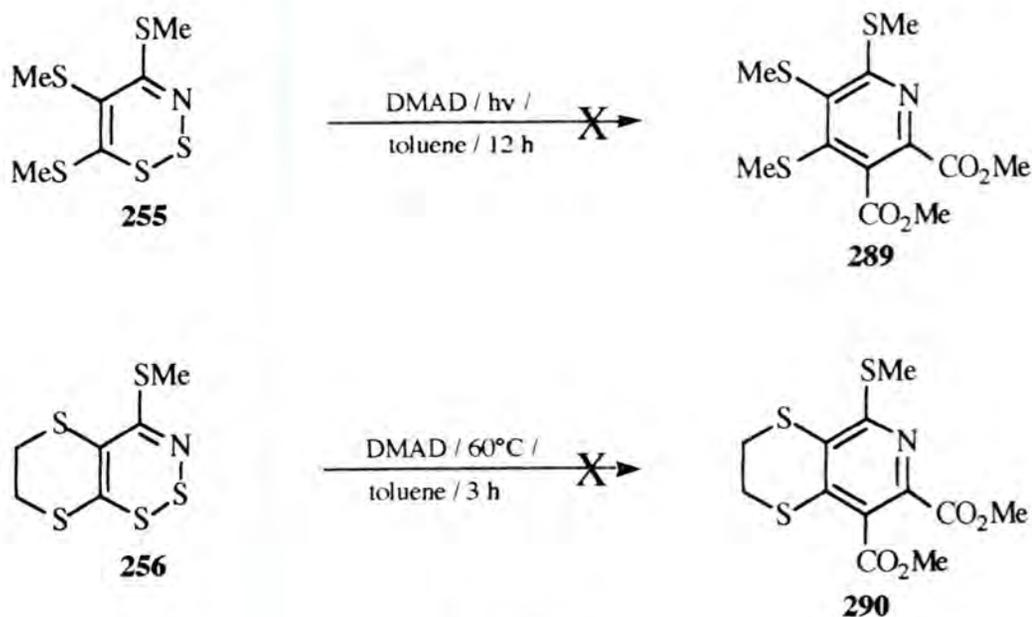


Scheme 79

1,2-Dithiolium cation salt **250** reacted with two equivalents of 7,7,8,8-tetracyano-*p*-quinodimethane (TCNQ, **233**) in acetonitrile, to afford a salt of stoichiometry **250**-(TCNQ)₂, in 31% yield. The product salt is an organic semiconductor ($\sigma_{\pi} = 2 \times 10^{-3} \text{ Scm}^{-1}$), based on two-probe measurements of compressed pellets, and contains the TCNQ radical anion, as determined by infrared spectroscopy, *i.e.* $\nu(\text{CN}) = 2186 \text{ cm}^{-1}$ which is diagnostic of anionic TCNQ.¹¹⁸ Attempts to prepare similar charge-transfer compounds from methiodide salt **253** and TCNQ were unsuccessful, possibly due to the insolubility of salt **253** in acetonitrile and a range of other common organic solvents.

Some reactions of 1,2,3-dithiazine derivatives have also been examined. Attempts to methylate 1,2,3-dithiazine derivative **258** with both iodomethane and dimethyl sulphate at 20°C led to the formation of multiple products (TLC evidence), which could not be separated. Similarly, the reaction of dithiazine **258** with *m*-chloroperoxybenzoic acid at 20°C led to the formation of a number of products (TLC evidence), the only identifiable one being isothiazole **263**, in trace amount (NMR and MS evidence).

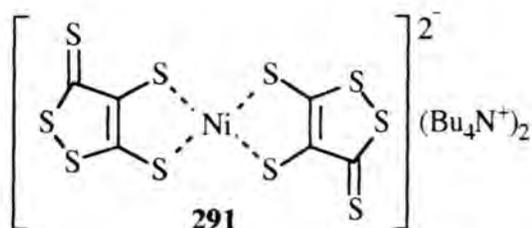
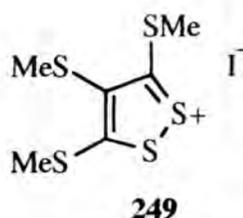
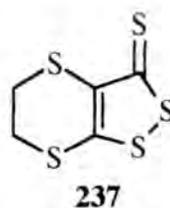
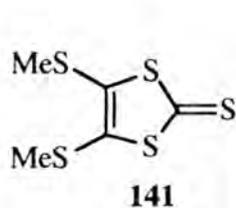
Cycloaddition reactions of DMAD with 1,2,3-dithiazines **255** and **256**, under photochemical and thermal conditions, respectively, were investigated (Scheme 80). No evidence to suggest formation of the expected pyridine derivatives **289** or **290** was found by analysis of crude product mixtures (NMR and MS).



5.6 X-Ray Crystallographic Studies on 1,2-Dithiole-3-thione Derivative **237**.

The X-ray crystal structure of thione **237** was obtained for several reasons. There is currently much interest in organosulphur heterocycles which are able to form intermolecular S...S contacts in the solid state,¹¹⁹⁻¹²¹ and compound **237**, with several peripheral sulphur atoms, was seen as a likely candidate for possession of these features. The study of non-bonded close contacts between chalcogen atoms is fundamental to the development of electron donors for use in organic metals.^{98,122} Additionally, a comparison of the molecular dimensions in the neutral compound **237** with those published for the related neutral 1,3-dithiole structure **141**,¹²³ cationic 1,2-dithiolium salt **249**,¹⁰⁶ and anionic nickelate salt **291**,¹⁰⁰ would provide new information on the distribution of electrons in 1,2-dithiole systems generally.

Needle-shaped crystals of compound **237** were obtained from chloroform solution. X-Ray analysis showed that there are two symmetry-independent conformations in the structure of compound **237**, conformations **237A** and **237B**.¹⁰⁹ The crystal structure of compound **237**, showing the atom numbering scheme, is illustrated in Figure 10; full crystallographic data are recorded in Appendix 1.



The 1,2-dithiole ring in both conformers **237A** and **237B** is essentially planar; the maximum deviations from a least squares plane defined by the 1,2-dithiole ring atoms are 0.04 and 0.01 Å, respectively. Conformations **237A** and **237B** have very similar bond lengths and angles, except for the dithioethylene bridge, the carbon atoms of which, in conformation **B**, show large displacement factors, explaining the apparent shortening of its C3'-C4' bond (1.38 Å, *cf.* C3-C4 = 1.51 Å in conformation **A**). Similar features in dithioethylene bridges of related structures have been reported previously.^{122,124}

The conjugated C=C and C=S bonds within structure **237** are longer (C2-C5 = 1.369, C2'-C5' = 1.375, C1-S1 = 1.662 and C1'-S1' = 1.659 Å) than the non-conjugated C=C and C=S bonds of the related 1,3-dithiole-2-thione structure **141** (values of 1.352 and 1.647 Å, respectively).¹²³ This implies that intramolecular π -electron delocalisation is occurring in the α,β -unsaturated thione functionality of compound **237**. The S2-S3 and S2'-S3' bond lengths of conformations **237A** and **237B** are 2.047 and 2.049 Å, respectively; similar to those observed in 1,2-dithiolium cation salt **249** (2.024 Å)¹⁰⁶ and other 1,2-dithiolium cation salts.¹²⁵ These values are consistent with single bond character of the disulphide group in both the neutral and cationic systems.

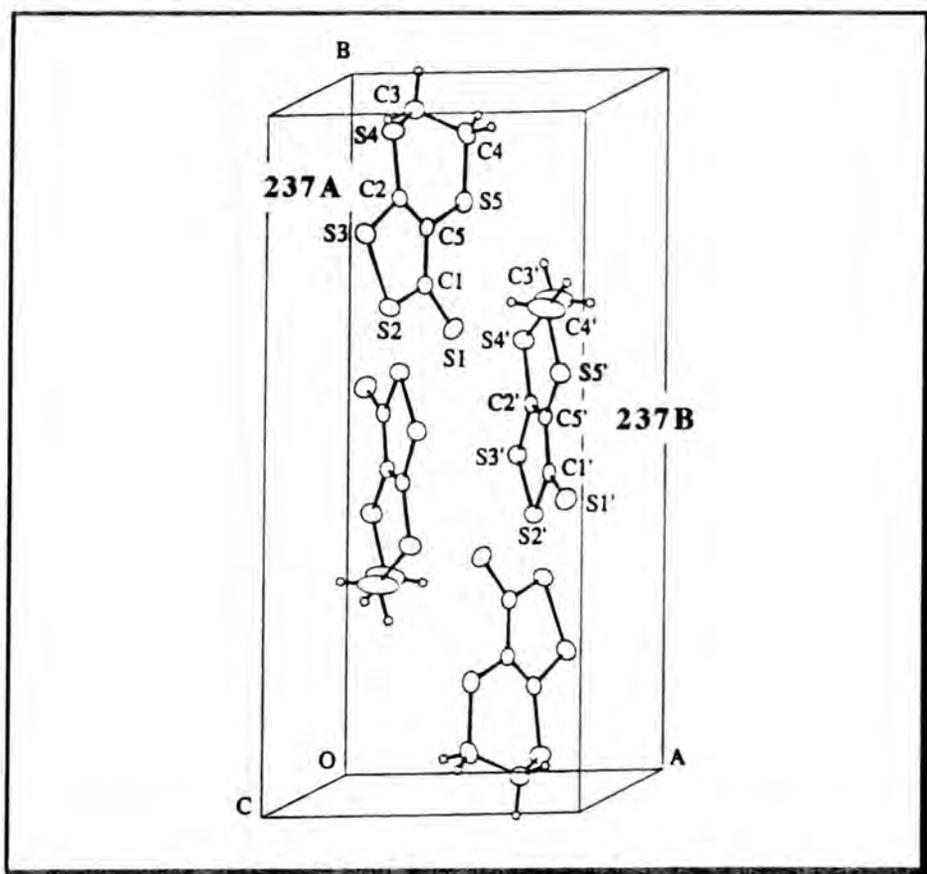


Figure 10. X-Ray Crystal Structure of Compound **237**, Showing the Atom Numbering Scheme.

A comparison of the bond lengths of compound **237** with those reported for the dithiolate ligands in nickelate salt **291**¹⁰⁰ reveals significant differences in the C=C and C-S lengths; the C=S bond lengths are comparable in both compounds. The C-S⁻ bond lengths in salt **291** are shortened, relative to **237**, to 1.68-1.73 Å, by coordination of the thiolate anions to the nickel atom, and the C=C bond distance in salt **291** is lengthened to 1.42 Å; these findings are consistent with more fully developed π -electron delocalisation in the structure of bis(dithiolate) **291**.

The structure of compound **237** reveals several intermolecular S---S contact distances which are significantly shorter than the accepted sum of Van der Waals radii for sulphur atoms (3.7-3.8 Å).³² The shortest non-bonded contact is 3.357 Å, between S1 and S3'. The close intermolecular S---S interactions present in structure **237** are identified in Figure 11 (only the unique contacts are indicated). Compound **237**,

therefore, exemplifies a growing family of organosulphur heterocycles which have solid state structures that are characterised by a three-dimensional network of non-bonded S---S interactions.¹¹⁹⁻¹²¹

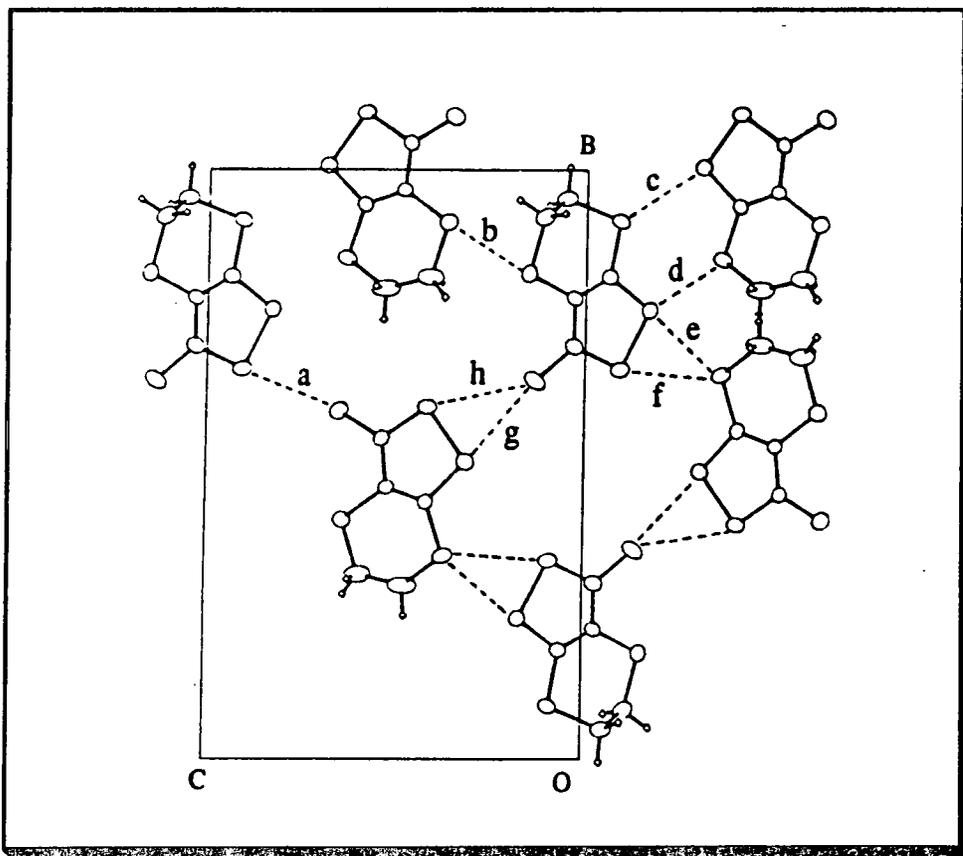


Figure 11. X-Ray Crystal Structure of Compound **237**, Viewed Down the A-Axis.

Intermolecular S---S distances (Å) are as follows: a, 3.786; b, 3.447; c, 3.506; d, 3.668; e, 3.385; f, 3.827; g, 3.357 and h, 3.766. Additional unique contacts (not shown) are: (S1---S5'), 3.719; (S1'---S3), 3.725 and (S1'---S4) 3.731.

5.7 Conclusions.

Reliable routes have been developed to enable synthesis of 1,2-dithiolium cation salts **249-253**. Nitrogen ring-expansion of these salts, under iodine-ammonia conditions, has led to the isolation of novel 1,2,3-dithiazine derivatives **255-258**, in yields of 10-39%, along with lower yields of isothiazole products in the majority of examples studied. This route represents the first chemical synthesis of the rare 1,2,3-

dithiazine heterocyclic system. Chloroform solutions of 1,2,3-dithiazines **255-258** desulphurised spontaneously at room temperature to furnish corresponding isothiazole derivatives **260-263**. Ring expansion of 3-hydro-1,2-dithiolium cation salt **253** under iodine-ammonia conditions was anomalous; only the isothiazole product **264** was obtained, in 84% yield.¹⁰⁹

1,2,3-Dithiazine derivatives **255-258** have been characterised by a variety of techniques. The time-dependence of dithiazine desulphurisation, to afford isothiazoles, has been examined by NMR spectroscopy. Mass spectroscopic fragmentation patterns of 1,2,3-dithiazines are different to those of 1,4,2-dithiazine derivatives; these findings have been related to the differing arrangements of heteroatoms in the two heterocyclic systems. Solution electrochemical properties of 1,2,3-dithiazine derivatives and their equivalent 1,4,2-dithiazine isomers show great similarities; we postulate that these findings reflect the eight π -electron compliments possessed by both heterocyclic systems. Ultraviolet-visible spectroscopy of 1,2,3-dithiazine derivatives has shown some features in common with structurally-related 1,2,3-dithiazole derivatives.

A mechanism for the reaction of 1,2-dithiolium cation salts under iodine-ammonia conditions has been proposed¹⁰⁹ which builds on the precedent of our earlier studies with 1,3-dithiolium cation salts.^{43,44}

Reaction of salt **250** with TCNQ led to the formation of a charge-transfer complex of 1:2 donor:acceptor stoichiometry; this complex showed semiconducting electrical properties. The X-ray crystal structure of 1,2-dithiole-3-thione derivative **237** has been solved.¹⁰⁹ The compound is characterised by a three-dimensional array of non-bonded intermolecular close S---S contacts. The data obtained have contributed to fundamental understanding of electronic distribution in the 1,2-dithiole system.

CHAPTER 6

EXPERIMENTAL

6.1 General Procedures.

M.p.s were recorded on a Kofler hot-stage microscope apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer model 547, 577 and 1600-FTIR spectrometers; samples were either mullied, embedded in KBr discs, or analysed as thin films between KBr plates, as indicated. Solution-state UV spectra were recorded on a Kontron Uvikon 930 instrument, with solvents as indicated. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AMX 500 (500.139 and 125.770 MHz), Bruker AC 250 (250.134 and 62.896) and Varian Gemini 200 (199.975 and 50.284 MHz) instruments, operating at the frequencies quoted in parentheses, for hydrogen and carbon nuclei, respectively. Chemical shifts are quoted in ppm, relative to tetramethylsilane (TMS) as internal reference. All coupling constants, J , are quoted in Hz. Mass spectra were obtained on a VG 7070E instrument, operating at 70 eV, with ionisation modes as indicated; ammonia was used as the impinging gas for chemical ionisation mode. Elemental analyses were performed on a Carlo-Erba Strumentazione.

TLC analyses were performed using Merck pre-coated silica (0.2 mm) aluminium backed sheets. Column chromatography was carried out using Merck silica gel (70-230 mesh) or alumina (70-230 mesh), the latter neutralised by pre-soaking in ethyl acetate for 24 h; eluent solvents are as indicated. Nitrogen was dried by passing through a column of P_2O_5 ; reactions were routinely carried out under nitrogen, unless otherwise stated. Solvents were dried over and distilled from the following reagents, under a dry nitrogen atmosphere: tetrahydrofuran and diethyl ether (sodium metal); acetone (K_2CO_3); toluene (LiAlH_4); chlorocarbons (P_2O_5); acetonitrile (CaH_2); methanol (magnesium methoxide) and ethanol (magnesium ethoxide). All other reagents were reagent grade and used as supplied, unless otherwise stated.

Cyclic voltammetry (CV) experiments were performed in a one-compartment cell with platinum working and counter electrodes and a silver-silver chloride reference electrode. Measurements were made with a BAS 100 Electrochemical Analyser and were compensated for internal resistance. The cell contained a solution of the test compound (*ca.* 10^{-3} mol dm^{-3}), with oven-dried (120°C) tetrabutylammonium hexafluorophosphate

(ca. 10^{-2} mol dm⁻³) as supporting electrolyte, in anhydrous dichloromethane.

Conductivity measurements on powdered samples were obtained using the two-probe technique; samples were manually compressed between two steel probes and the resistance of the sample monitored with a Fluka 8000A Digital Multimeter.

Photolysis reactions were carried out in 1 cm diameter quartz tubes, in either dry toluene or neat dienophile, as stated, with substrate concentration of ca. 0.3 mol dm⁻³. The sealed tube was placed 30 cm from a Variac 270 (1 kW, 4 A) ultraviolet lamp. The tube contents were not externally cooled and solution temperatures of 35-40°C were recorded during irradiation.

6.2 Experimental Procedures for Chapter 2.

6.2.1 Experimental for Section 2.2.

Triethylammonium *p*-methoxydithiobenzoate 108a was prepared by a modified literature procedure, from *p*-bromoanisole, magnesium and carbon disulphide (40% yield).³⁵ M.p. 73-74°C (lit.¹²⁶ 70-71°C).

Triethylammonium *p*-methylthiobenzoate 108b was prepared by a modified literature procedure, from *p*-bromotoluene, magnesium and carbon disulphide (14% yield).³⁵ M.p. 110°C (lit.¹²⁶ 54-56°C).

Piperidinium dithiobenzoate 108c was prepared by the literature procedure, from benzyl bromide, elemental sulphur and sodium methoxide (49% yield).³⁶ M.p. 94-96°C (lit.¹²⁷ 96-97.5°C).

Triethylammonium *p*-bromodithiobenzoate 108d was prepared by the literature procedure, from *p*-bromobenzyl bromide, elemental sulphur and sodium methoxide (39% yield).³⁶ M.p. 67-69°C (lit.¹²⁶ m.p. not recorded for triethylammonium salt).

Triethylammonium α -thienyldithiocarboxylate 108f was prepared by literature

procedures, from thiophene, ⁿbutyl lithium and carbon disulphide (34% yield).^{34,35} M.p. 60-63°C (lit.³⁵ m.p. not recorded).

1-[4-Bromophenyl(thiocarbonyl)] piperidine 117 was isolated from reaction of *p*-bromodithiobenzoic acid **108d** with piperidine, as a cream crystalline solid (48% yield). M.p. 114-117°C (from ethanol) (lit.⁴⁰ 105-108°C) [Found: *m/z* (EI) 282.98991. Calc. for C₁₂H₁₄BrNS: 283.00301]; ν_{\max} (C₄Cl₆, mull)/cm⁻¹ 2945, 1495, 1480, 1445, 1435, 1395, 1290, 1240, 1135 and 900; δ_{H} (250 MHz, CDCl₃) 7.48 (2 H, d, J 8), 7.16 (2 H, d, J 8), 4.33 (2 H, t, J 5), 3.51 (2 H, t, J 5), 1.79 (4 H, t, J 6) and 1.57 (2 H, d, J 5).

Bis(*p*-methoxythiobenzoyl) disulphide 118 was isolated as a by-product of the synthesis of *p*-methoxydithiobenzoate salt **108a**, as a bright orange powder (*ca.* 2% yield). M.p. 162-163°C (from carbon disulphide-hexane) (lit.⁴² 160°C).

Triethylammonium *p*-nitrodithiobenzoate 108e.³⁹

A mixture of elemental sulphur (1.48 g, 46 mmol) and sodium methoxide [from sodium (1.06 g, 46 mmol)] in dry methanol (250 ml) was refluxed with stirring for 2.5 h under nitrogen. *p*-Nitrobenzyl bromide (5.0 g, 23 mmol) was dissolved in hot, dry methanol (100 ml) and added dropwise to the refluxing mixture over 1 h. The mixture was then refluxed for a further 18 h, after which it was cooled, and solvent evaporated under reduced pressure. (The remainder of the work-up was carried out under a nitrogen atmosphere). The residue was dissolved in water (60 ml), and the solution filtered and acidified with dilute sulphuric acid (*ca.* 2 mol dm⁻³, 3 ml) to yield *p*-nitrodithiobenzoic acid as a pungent red oil. This oil was extracted into dichloromethane (3 x 50 ml) and the combined extracts dried (MgSO₄) and filtered. The solution was cooled to 0°C and triethylamine added (9.8 ml, 70 mmol). The solution was then stirred at 20°C for 3 h, after which solvent was evaporated at reduced pressure to give a brown oil. This oil was triturated with hexane (2 x 100 ml), and the resulting solid re-dissolved in dichloromethane (20 ml). The solution was added dropwise to rapidly stirring ether (300

ml) to give a brown solid, which was dried *in vacuo* to afford salt **108e** (1.90 g, 27%) as a dark brown powder, m.p. 78-80°C (Found: C, 51.8; H, 6.8; N, 9.1. $C_{13}H_{20}N_2O_2S_2$ requires C, 52.0; H, 6.7; N, 9.3%); ν_{\max} (KBr)/ cm^{-1} 2980, 2640, 1520, 1335, 1025, 910, 845 and 750; δ_H (250 MHz, $CDCl_3$) 8.30 (2 H, d, J 9), 8.07 (2 H, d, J 9), 3.13 (6 H, q, J 7) and 1.32 (9 H, t, J 7).

3-Oxobutan-2-yl *p*-methoxydithiobenzoate 109a.

This material is representative of the dithioesters prepared. A solution of 3-chlorobutan-2-one (11.2 g, 105 mmol) in dry dichloromethane (50 ml) was added dropwise over 0.8 h to a stirred solution of salt **108a** (15.0 g, 53 mmol) in dry dichloromethane (250 ml) at 20°C. Stirring was continued for 22 h at 20°C, after which solvent was removed under reduced pressure and the residue chromatographed on a silica column, eluted with dichloromethane, to afford compound **109a** (5.2 g, 39%) as a viscous red oil (Found: C, 56.5; H, 5.5. $C_{12}H_{14}O_2S_2$ requires C, 56.7; H, 5.6%); m/z (CI) 255 ($M^+ + 1$); ν_{\max} (thin film)/ cm^{-1} 2965, 1715, 1595, 1505, 1170, 1040, 880 and 830; δ_H (250 MHz, $CDCl_3$) 8.10 (2 H, d, J 9), 6.89 (2 H, d, J 9), 4.92 (1 H, q, J 7), 3.86 (3 H, s), 2.32 (3 H, s) and 1.56 (3 H, d, J 7).

3-Oxobutan-2-yl *p*-methyldithiobenzoate 109b.

Following the procedure described for compound **109a**, a solution of salt **108b** (10.3 g, 38 mmol) and 3-chlorobutan-2-one (8.1 g, 76 mmol) in dry dichloromethane (250 ml) was stirred for 12 h at 20°C and refluxed for a further 3 h to afford compound **109b** (5.6 g, 62%) as a red semi-solid, m.p. *ca.* 30°C (Found: C, 60.0; H, 5.4. $C_{12}H_{14}OS_2$ requires C, 60.5; H, 5.9%); m/z (CI) 239 ($M^+ + 1$); ν_{\max} (KBr)/ cm^{-1} 2940, 1720, 1600, 1245, 1180, 1050, 880 and 820; δ_H (250 MHz, $CDCl_3$) 7.95 (2 H, d, J 8), 7.19 (2 H, d, J 8), 4.91 (1 H, q, J 7), 2.37 (3 H, s), 2.32 (3 H, s) and 1.56 (3 H, d, J 7).

3-Oxobutan-2-yl dithiobenzoate 109c.

Following the procedure described for compound **109a**, a solution of salt **108c** (9.9 g, 41 mmol) and 3-chlorobutan-2-one (8.5 g, 80 mmol) in dry dichloromethane (500 ml) was stirred for 18 h at 20°C to afford compound **109c** (7.9 g, 86%) as a red oil [Found: C, 57.3; H, 5.5%; m/z (CI) 225.0428. $C_{11}H_{12}OS_2$ requires C, 58.9; H, 5.4%; m/z 225.0408]; ν_{\max} (thin film)/ cm^{-1} 2940, 1720, 1450, 1360, 1235, 1045, 870 and 765; δ_H (250 MHz, $CDCl_3$) 8.01 (2 H, d, J 8), 7.55 (1 H, t, J 7), 7.39 (2H, t, J 8), 4.90 (1 H, q, J 7), 2.33 (3 H, s) and 1.60 (3 H, d, J 7). This material was used without further purification.

3-Oxobutan-2-yl *p*-bromodithiobenzoate 109d.

Following the procedure described for compound **109a**, a solution of salt **108d** (8.1 g, 24 mmol) and 3-chlorobutan-2-one (7.8 g, 73 mmol) in dry dichloromethane (400 ml) was stirred for 17 h at 20°C to afford compound **109d** (5.4 g, 74%) as a viscous red oil [Found: C, 43.9; H, 3.4%; m/z (CI) 302.9287. $C_{11}H_{11}BrOS_2$ requires C, 43.6; H, 3.7%; m/z 302.9513]; ν_{\max} (thin film)/ cm^{-1} 2935, 1720, 1580, 1480, 1230, 1045, 880 and 825; δ_H (250 MHz, $CDCl_3$) 7.86 (2 H, d, J 8), 7.51 (2 H, d, J 8), 4.82 (1 H, q, J 7), 2.30 (3 H, s) and 1.56 (3 H, d, J 8).

3-Oxobutan-2-yl *p*-nitrodithiobenzoate 109e.

Following the procedure described for compound **109a**, a solution of salt **108e** (2.3 g, 7.5 mmol) and 3-chlorobutan-2-one (2.4 g, 23 mmol) in dry dichloromethane (150 ml) was stirred for 19 h at 20°C and a further 6 h at reflux to afford compound **109e** (1.05 g, 52%) as a viscous red oil (Found: C, 49.2; H, 4.1; N, 4.8. $C_{11}H_{11}NO_3S_2$ requires C, 49.1; H, 4.1; N, 5.2%); m/z (EI) 269 (M^+); (CI) 270 ($M^+ + 1$); ν_{\max} (thin film)/ cm^{-1} 3110, 2935, 1720, 1525, 1345, 1050, 845 and 750; δ_H (250 MHz, $CDCl_3$) 8.22 (2 H, d, J 9), 8.08 (2 H, d, J 9), 4.82 (1 H, q, J 7), 2.35 (3 H, s) and 1.61 (3 H, d, J 7).

3-Oxobutan-2-yl α -thienyldithiocarboxylate **109f**.

Following the procedure described for compound **109a**, a solution of salt **108f** (15.9 g, 61 mmol) and 3-chlorobutan-2-one (19.5 g, 183 mmol) in dry dichloromethane (200 ml) was stirred at 20°C for 72 h to afford compound **109f** (12.8 g, 91%) as a red crystalline solid, m.p. 37-38°C (Found: C, 47.3; H, 4.5. C₉H₁₀OS₃ requires C, 46.9; H, 4.4%); *m/z* (CI) 231 (M⁺ + 1); ν_{\max} (thin film)/cm⁻¹ 3100, 2980, 1720, 1505, 1405, 1350, 1250 and 1045; δ_{H} (250 MHz, CDCl₃) 7.82 (1 H, d, J 5), 7.66 (1 H, d, J 5), 7.11 (1 H, t, J 5), 4.88 (1 H, q, J 7), 2.30 (3 H, s) and 1.54 (3 H, d, J 7).

2-(*p*-Methoxyphenyl)-4,5-dimethyl-1,3-dithiolium hexafluorophosphate **110a**.

This material is representative of the 1,3-dithiolium cation salts prepared. A solution of dithioester **109a** (4.2 g, 16.5 mmol) in dry chloroform (10 ml) was added dropwise with stirring over 0.3 h to sulphuric acid (20 ml, conc.) at -20°C. The solution was then stirred at between -15 and -5°C for a further 2.5 h after which it was warmed to 20°C and added dropwise to water (400 ml). Hexafluorophosphoric acid (60%, 15 ml, 99 mmol) was then added with stirring. The resultant precipitate was extracted into dichloromethane (6 x 80 ml) and the combined organic layers were washed with water, dried (MgSO₄) and then partially evaporated under reduced pressure to a volume of *ca.* 100 ml. This solution was then added to ether (500 ml), with stirring, to produce a precipitate which was filtered off and washed with ether (3 x 50 ml). The precipitate was dried *in vacuo* to afford salt **110a** (5.0 g, 79%) as a yellow powder, m.p. 214-217°C (Found: C, 37.8; H, 3.4. C₁₂H₁₃F₆OPS₂ requires C, 37.7; H, 3.4%); *m/z* (FAB, MeOH) 237 (M⁺); ν_{\max} (KBr)/cm⁻¹ 1595, 1300, 1275, 1180, 960, 835, 595 and 550; δ_{H} (250 MHz, CF₃CO₂H) 8.0 (2 H, d, J 9), 7.3 (2 H, d, J 9), 4.1 (3 H, s) and 2.8 (6 H, s).

4,5-Dimethyl-2-(*p*-methylphenyl)-1,3-dithiolium hexafluorophosphate 110b.

Following the procedure for salt **110a**, a solution of dithioester **109b** (4.8 g, 20 mmol) in dry chloroform (20 ml) was added to sulphuric acid (20 ml, conc.) over 0.5 h at -20°C and stirred for a further 1 h at -20 to -5°C. Addition of the mixture to water (300 ml) followed by addition of hexafluorophosphoric acid (60%, 14.7 ml, 100 mmol) afforded salt **110b** (3.6 g, 49%) as a yellow powder, m.p. 152°C (decomp.) (Found: C, 39.6; H, 3.5. C₁₂H₁₃F₆PS₂ requires C, 39.3; H, 3.6%); *m/z* (DCI, MeCN) 222 (M⁺ + 1); ν_{\max} (KBr)/cm⁻¹ 1600, 1525, 1300, 1195, 840, 815sh, 735 and 560; δ_{H} (250 MHz, CDCl₃) 7.80 (2 H, d, J 8), 7.41 (2 H, d, J 8), 2.73 (6 H, s) and 2.48 (3 H, s).

4,5-Dimethyl-2-phenyl-1,3-dithiolium hexafluorophosphate 110c.

Following the procedure for salt **110a**, dithioester **109c** (6.9 g, 31 mmol) was added to sulphuric acid (22 ml, conc.) over *ca.* 0.3 h at -20°C and stirred for a further 2 h at -15 to -10°C. Addition of the mixture to water (150 ml) followed by addition of hexafluorophosphoric acid (60%, 8.8 ml, 60 mmol) afforded salt **110c** (6.0 g, 55%) as a cream powder, m.p. 225-227°C (decomp.) (Found: C, 37.3; H, 3.0. C₁₁H₁₁F₆PS₂ requires C, 37.5; H, 3.1%); *m/z* (FAB, glycerol) 207 (M⁺); ν_{\max} (C₄Cl₆, mull)/cm⁻¹ 1455, 1405, 1340, 1320, 1300, 1035, 770 and 690; δ_{H} (250 MHz, CF₃CO₂H) 8.1-7.7 (5 H, m) and 2.8 (6 H, s).

2-(*p*-Bromophenyl)-4,5-dimethyl-1,3-dithiolium hexafluorophosphate 110d.

Following the procedure for salt **110a**, a solution of dithioester **109d** (4.6 g, 15.2 mmol) in dry chloroform (30 ml) was added to sulphuric acid (40 ml, conc.) over *ca.* 0.3 h at -20°C and stirred for a further 3 h at -15 to -10°C. Addition of the mixture to water (300 ml) followed by addition of hexafluorophosphoric acid (60%, 9.0 ml, 61 mmol) afforded salt **110d** (5.7 g, 87%) as a bright yellow powder, m.p. 208-209°C (decomp.) (Found: C, 31.0; H, 2.4. C₁₁H₁₀BrF₆PS₂ requires C, 30.6; H, 2.3%); ν_{\max} (KBr)/cm⁻¹ 1585, 1540, 1410, 1300, 1080, 1010, 965 and 835; δ_{H} (250 MHz,

CF₃CO₂H) 7.98 (2 H, d, J 9), 7.85 (2 H, d, J 9) and 2.8 (6 H, s).

4,5-Dimethyl-2-(*p*-nitrophenyl)-1,3-dithiolium hexafluorophosphate 110e.

Following the procedure for salt **110a**, a solution of dithioester **109e** (0.83 g, 3.1 mmol) in dry chloroform (10 ml) was added to sulphuric acid (10 ml, conc.) over *ca.* 0.3 h at -20°C and stirred for a further 2.5 h at -15 to -5°C. Addition of the mixture to water (300 ml) followed by addition of hexafluorophosphoric acid (60%, 2.8 ml, 19 mmol) afforded salt **110e** (0.96 g, 78%) as a pale orange powder, m.p. 229-230°C (decomp.) (Found: C, 33.0; H, 2.6; N, 3.4. C₁₁H₁₀F₆NO₂PS₂ requires C, 33.3; H, 2.5; N, 3.5%); ν_{\max} (KBr)/cm⁻¹ 1615, 1535, 1370, 1355, 1325, 1300, 840 and 745; δ_{H} (250 MHz, CF₃CO₂H) 8.7 (2 H, d, J 9), 8.2 (2 H, d, J 9) and 2.9 (6 H, s).

4,5-Dimethyl-2-(α -thienyl)-1,3-dithiolium hexafluorophosphate 110f.

Following the procedure for salt **110a**, a solution of dithioester **109f** (2.0 g, 8.6 mmol) in dry dichloromethane (20 ml) was added to sulphuric acid (30 ml, conc.) over 0.2 h at -20°C and stirred for a further 1 h at -20 to -10°C. Addition of the mixture to water (500 ml) followed by addition of hexafluorophosphoric acid (60%, 7.4 ml, 50 mmol) afforded salt **110f** (1.92 g, 62%) as an ochre powder, m.p. 135-136°C (decomp.) (Found: C, 30.0; H, 2.5. C₉H₉F₆PS₃ requires C, 30.2; H, 2.5%); m/z (FAB, MeCN) 213 (M⁺); ν_{\max} (KBr)/cm⁻¹ 3130, 1535, 1415, 1370, 1030, 835, 745 and 550; δ_{H} (250 MHz, CD₃CN) 8.12 (1 H, br s), 8.02 (1 H, br s), 7.36 (1 H, br s) and 2.62 (6 H, s).

3-(*p*-Methoxyphenyl)-5,6-dimethyl-1,4,2-dithiazine 111a.

This material is representative of the 1,4,2-dithiazines prepared. To a stirred solution of 1,3-dithiolium cation salt **110a** (2.2 g, 5.6 mmol) and iodine (3.6 g, 28 mmol) in acetonitrile (150 ml) was added dropwise ammonia solution (33%, 4.9 ml, 84 mmol) at 20°C. After being stirred for 21 h, the solution was added to water (300 ml) and the resultant aqueous solution extracted with dichloromethane (3 x 60 ml). The organic layers were combined, washed with water (2 x 200 ml), dried (MgSO₄) and

evaporated under reduced pressure to give the crude product which was chromatographed on a silica column eluted with dichloromethane-hexane (1:3 v/v). A yellow band was collected from which solvent was removed *in vacuo* to afford compound **111a** (1.23 g, 87%) as a yellow crystalline solid, m.p. 56-58°C (Found: C, 57.1; H, 5.1; N, 5.2. C₁₂H₁₃NOS₂ requires C, 57.3; H, 5.2; N, 5.6%); *m/z* (CI) 252 (M⁺ + 1); ν_{\max} (KBr)/cm⁻¹ 2920, 1605, 1505, 1260, 1175, 1030, 920 and 830; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 382; δ_{H} (250 MHz, CDCl₃) 7.95 (2 H, d, J 9), 6.89 (2 H, d, J 9), 3.83 (3 H, s), 2.10 (3 H, s) and 2.05 (3 H, s); δ_{C} (250 MHz, CDCl₃) 163.1, 161.9, 130.9, 129.9, 128.4, 121.5, 113.6, 55.2, 20.7 and 18.7.

5,6-Dimethyl-3-(*p*-methylphenyl)-1,4,2-dithiazine 111b.

Following the procedure for compound **111a**, ammonia solution (33%, 1.2 ml, 20 mmol) was added to a solution of 1,3-dithiolium cation salt **110b** (0.73 g, 2 mmol) and iodine (1.27 g, 10 mmol) in acetonitrile (100 ml). The resultant mixture was stirred for 2.5 h at 20°C to afford compound **111b** (0.39 g, 83%) as a bright orange crystalline solid, m.p. 52-53°C (Found: C, 61.3; H, 5.5; N, 5.7. C₁₂H₁₃NS₂ requires C, 61.2; H, 5.6; N, 6.0%); *m/z* (EI) 235 (M⁺); (CI) 236 (M⁺ + 1); ν_{\max} (KBr)/cm⁻¹ 2915, 1610, 1225, 1175, 915, 820, 790 and 580; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 385 and 266; δ_{H} (500 MHz, CDCl₃) 7.89 (2 H, d, J 8), 7.19 (2 H, d, J 8), 2.37 (3 H, s), 2.10 (3 H, s) and 2.06 (3 H, s); δ_{C} (500 MHz, CDCl₃) 163.9, 141.7, 133.3, 130.9, 129.2, 128.4, 121.7, 21.5, 20.9 and 18.8.

5,6-Dimethyl-3-phenyl-1,4,2-dithiazine 111c.

Following the procedure for compound **111a**, ammonia solution (33%, 0.33 ml, 5.7 mmol) was added to a solution of 1,3-dithiolium cation salt **110c** (200 mg, 0.57 mmol) and iodine (360 mg, 2.85 mmol) in acetonitrile (20 ml). The resultant mixture was stirred for 1.5 h at 20°C to afford compound **111c** (110 mg, 87%) as an orange oil [Found: C, 59.9; H, 5.2; N, 5.8%; *m/z* (EI) 221.0295. C₁₁H₁₁NS₂ requires C, 59.7; H, 5.0; N, 6.3%; *m/z* 221.0333]; ν_{\max} (thin film)/cm⁻¹ 2920, 1545, 1450, 1225, 1070, 915, 755 and 685; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 389; δ_{H} (250 MHz, CDCl₃) 8.02-

7.37 (5 H, m), 2.12 (3 H, s) and 2.07 (3 H, s); δ_C (250 MHz, $CDCl_3$) 162.8, 135.5, 130.8, 130.2, 128.2, 127.9, 120.9, 20.5 and 18.5.

3-(*p*-Bromophenyl)-5,6-dimethyl-1,4,2-dithiazine 111d.

Following the procedure for compound **111a**, ammonia solution (33%, 0.27 ml, 4.6 mmol) was added to a solution of 1,3-dithiolium cation salt **110d** (200 mg, 0.46 mmol) and iodine (0.29 g, 2.3 mmol) in acetonitrile (20 ml). The resultant mixture was stirred for 1 h at 20°C to afford compound **111d** (130 mg, 94%) as a bright yellow crystalline solid, m.p. 58-59°C (Found: C, 43.7; H, 3.3; N, 4.3. $C_{11}H_{10}BrNS_2$ requires C, 44.0; H, 3.4; N, 4.7%); m/z (CI) 302 and 300 ($M^+ + 1$, isotopes); ν_{max} (KBr)/ cm^{-1} 2910, 1480, 1390, 1215, 1070, 1010, 910 and 830; λ_{max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 393; δ_H (250 MHz, $CDCl_3$) 8.02 (2 H, d, J 9), 7.65 (2 H, d, J 9), 2.12 (3 H, s) and 2.07 (3 H, s); δ_C (250 MHz, $CDCl_3$) 161.5, 134.3, 131.3, 130.3, 129.4, 125.6, 120.6, 20.6 and 18.5.

5,6-Dimethyl-3-(*p*-nitrophenyl)-1,4,2-dithiazine 111e.

Following the procedure for compound **111a**, ammonia solution (33%, 0.25 ml, 4.3 mmol) was added to a solution of 1,3-dithiolium cation salt **110e** (170 mg, 0.43 mmol) and iodine (0.27 g, 2.15 mmol) in acetonitrile (20 ml). The resultant mixture was stirred for 3 h at 20°C to afford compound **111e** (70 mg, 61%) as an orange-red solid, m.p. 128-129°C (Found: C, 49.6; H, 3.7; N, 10.5. $C_{11}H_{10}N_2O_2S_2$ requires C, 49.6; H, 3.8; N, 10.5%); m/z (EI) 266 (M^+); (CI) 267 ($M^+ + 1$); ν_{max} (KBr)/ cm^{-1} 2920, 1605, 1530, 1355, 920, 860, 850 and 755; λ_{max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 432; δ_H (250 MHz, $CDCl_3$) 8.24 (2 H, d, J 8), 8.15 (2 H, d, J 8), 2.11 (3 H, s) and 2.06 (3 H, s); δ_C (250 MHz, $CDCl_3$) 160.6, 149.2, 141.2, 130.7, 129.5, 123.7, 120.5, 20.8 and 18.6.

5,6-Dimethyl-3-(α -thienyl)-1,4,2-dithiazine 111f.

Following the procedure for compound **111a**, ammonia solution (33%, 6.8 ml, 120 mmol) was added to a solution of 1,3-dithiolium cation salt **110f** (4.3 g, 12 mmol) and iodine (4.5 g, 36 mmol) in acetonitrile (200 ml). The resultant mixture was stirred for 17 h at 20°C to afford compound **111f** (2.34 g, 86%) as an orange oil (Found: C, 47.9; H, 4.0; N, 6.2. C₉H₉NS₃ requires C, 47.5; H, 4.0; N, 6.2%); m/z (EI) 227 (M⁺); (CI) 228 (M⁺ + 1); ν_{\max} (thin film)/cm⁻¹ 3090, 2920, 1615, 1540, 1420, 1230, 1050 and 830; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 396 and 293; δ_{H} (250 MHz, CDCl₃) 7.62 (1 H, d, J 5), 7.43 (1 H, d, J 6), 7.03 (1 H, t, J 4), 2.09 (3 H, s) and 2.06 (3 H, s); δ_{C} (500 MHz, CDCl₃) 156.5, 140.4, 131.8, 130.8, 129.8, 127.3, 121.5, 20.6 and 18.8.

6.2.2 Experimental for Section 2.3.

2-Methylthio-5,6,7-trihydro[1,4]dithiepine[2,3-d]-1,3-dithiolium

tetrafluoroborate 120 was prepared by literature procedures, in two steps, from zincate salt **142** and 1,3-dibromopropane (*via* thione **138**) (100% overall yield).⁴⁷ M.p. 148-152°C (lit.⁴⁷ m.p. not recorded).

2-Methylthio-5,6-dihydro[1,4]dithiino[2,3-d]-1,3-dithiolium

tetrafluoroborate 121 was prepared by literature procedures, in two steps, from zincate salt **142** and 1,2-dibromoethane (*via* thione **139**) (76% overall yield).⁴⁸ M.p. 127°C (lit.⁴⁸ 124-126°C).

5,6-Dihydro[1,4]dithiino[2,3-d]-1,3-dithiolium tetrafluoroborate 123 was prepared by the literature procedure, from salt **121** (90% yield).⁴⁸ M.p. *ca.* 120°C (decomp.) [lit.⁴⁸ 110°C (decomp.)].

2,4,5-Tris(methylthio)-1,3-dithiolium tetrafluoroborate 124 was prepared by literature procedures, in two steps, from zincate salt **142** and iodomethane (*via* thione **141**) (76% overall yield).⁴⁹ M.p. 127-129°C (lit.⁴⁹ m.p. not recorded).

4,5-Dimethyl-2-methylthio-1,3-dithiolium iodide 125 was prepared by literature procedures, in three steps, from the potassium salt of O-ethylxanthic acid and 3-chlorobutan-2-one (*via* xanthate ester **146** and thione **145**) (42% overall yield).⁵² M.p. 93-95°C (lit.⁵¹ m.p. not recorded).

4,5-Dimethyl-2-dimethylamino-1,3-dithiolium hexafluorophosphate 127 was prepared by a modified literature procedure, in two steps, from the sodium salt of *N,N*-dimethylaminodithiocarbamic acid and 3-chlorobutan-2-one (*ca.* 70% overall yield).⁵⁴

2-Methylthio-1,3-dithiolium iodide 128 was prepared by a modified literature procedure, from vinylene trithiocarbonate, **143**, and iodomethane (87% yield).⁵⁰ M.p. 124-127°C (decomp.) [lit.⁵⁰ 131-132°C (decomp.)].

1,3-Dithiolium tetrafluoroborate 129 was prepared by a modified literature procedure, from salt **128** (79% yield).⁴⁸ Rather than melt, the material decomposed over a wide temperature range (lit.⁵⁵ m.p. 128-130°C).

3-Methylthio-1,4,2-dithiazine 101 was prepared by a modified literature procedure from 1,3-dithiolium cation salt **128** under iodine-ammonia conditions (2 equivalents of iodine) (26% yield).²³ Spectroscopic data found: ν_{\max} (thin film)/cm⁻¹ 3040, 2930, 1550, 1510, 970, 915, 800 and 670; δ_{H} (250 MHz, CDCl₃) 6.91 (1 H, d, J 7), 6.33 (1 H, d, J 7) and 2.54 (3 H, s) [lit.²⁷ ν_{\max} (thin film)/cm⁻¹ 3040, 2935, 1610 and 1560; δ_{H} 6.96 (1 H, d, J 6.5), 6.36 (1 H, d, J 6.5) and 2.50 (3 H, s)].

4,5-Dihydro-2-methylthio-1,3-dithiolium iodide 74 was prepared by a modified literature procedure, from ethylene trithiocarbonate, **144**, and iodomethane (71% yield).⁵⁰ M.p. 99-101°C (lit.²³ m.p. not recorded).

5,6-Dihydro-3-methylthio-1,4,2-dithiazine 75 was prepared by a modified literature procedure from salt **74** under iodine-ammonia conditions (5 equivalents of iodine) (42% yield).²³ Spectroscopic data found: δ_{H} (250 MHz, CDCl₃) 3.38 (2 H, m), 3.27 (2 H, m) and 2.40 (3 H, s); δ_{C} (250 MHz, CDCl₃) 149.3, 28.6, 26.9 and 13.9

[lit.²³ δ_{H} (CDCl₃) 3.5-3.1 (4 H, m) and 2.38 (3 H, s); δ_{C} (CDCl₃) 149.3, 28.6, 26.9 and 13.9].

[1,4]Dithiolo-1,3-dithiole-2-thione 140 was prepared by the literature procedure, from zincate salt **142** and diiodomethane (*ca.* 25% yield).⁴⁹ M.p. 149-153°C (lit.⁴⁹ m.p. not recorded).

Bis(tetraethylammonium)-bis(4,5-dithiolato-1,3-dithiole-2-thione) zincate 142 was prepared by the literature procedure, from carbon disulphide, sodium and *N,N*-dimethylformamide (62% yield).⁴⁶ M.p. *ca.* 205-208°C (lit.⁴⁶ 200-205°C).

2-Imino-4,5-dimethyl-1,3-dithiole 148 was isolated as a by-product from the reaction of 1,3-dithiolium cation salt **125** under iodine-ammonia conditions, as an oily red solid (*ca.* 8% yield).²³ M.p. *ca.* 55-65°C (lit.⁵⁶ m.p. not recorded for free imine) (Found: C, 41.2; H, 4.8; N, 9.2. Calc. for C₅H₇NS₂: C, 41.3; H, 4.9; N, 9.6%); *m/z* (EI) 145 (M⁺); (CI) 146 (M⁺ + 1).

4,5-Dimethyl-2-methylseleno-1,3-dithiolium tetrafluoroborate 126.

4,5-Dimethyl-1,3-dithiole-2-selenone⁵³ (1.22 g, 5.8 mmol) and dimethyl sulphate (15 ml, 160 mmol) were heated with stirring for 0.2 h at 80°C. The resultant solution was cooled and tetrafluoroboric acid (54%, 4.8 ml, 35 mmol) was added with stirring. Slow addition of ether (300 ml) formed a precipitate which was filtered and washed with ether (3 x 50 ml). The precipitate was dried *in vacuo* to afford salt **126** (1.73 g, 96%) as a pale yellow crystalline solid, m.p. 90-93°C; δ_{H} (250 MHz, CDCl₃) 3.11 (3 H, s) and 2.67 (6 H, s).

3-Methylthio-6,7,8-trihydro[1,4]dithiepine[2,3-e]-1,4,2-dithiazine 130.

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 0.88 ml, 15 mmol) was added to a solution of 1,3-dithiolium cation salt **120** (510 mg, 1.5 mmol) and iodine (950 mg, 7.5 mmol) in acetonitrile (30 ml). The resultant

mixture was stirred for 1 h at 20°C to afford compound **130** (50 mg, 12%) as a yellow crystalline solid, m.p. 125-127°C (Found: C, 31.5; H, 3.4; N, 4.9. C₇H₉NS₅ requires C, 31.4; H, 3.4; N, 5.2%); *m/z* (EI) 267 (M⁺); (CI) 268 (M⁺ + 1); ν_{\max} (KBr)/cm⁻¹ 2920, 1530, 1410, 1280, 975, 920, 865 and 845; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 374, 282 and 264; δ_{H} (250 MHz, CDCl₃) 2.74 (4 H, m), 2.49 (3 H, s) and 2.28 (2 H, m); δ_{C} (500 MHz, CDCl₃) 165.1, 141.9, 122.2, 33.7, 33.2, 32.7 and 16.8.

3-Methylthio-6,7-dihydro[1,4]dithiino[2,3-e]-1,4,2-dithiazine 131.

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 0.9 ml, 15.3 mmol) was added to a solution of 1,3-dithiolium cation salt **121** (500 mg, 1.53 mmol) and iodine (980 mg, 7.7 mmol) in acetonitrile (30 ml). The resultant mixture was stirred for 2 h at 20°C to afford compound **131** (210 mg, 54%) as a yellow oil [Found: *m/z* (CI) 253.9277. C₆H₇NS₅ requires 253.9260]; ν_{\max} (thin film)/cm⁻¹ 2930, 1525, 1410, 1285, 980, 920, 850 and 730; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 312sh and 291; δ_{H} (250 MHz, CDCl₃) 3.29 (4 H, m) and 2.53 (3 H, s); δ_{C} (500 MHz, CDCl₃) 165.4, 124.8, 113.7, 30.5, 29.9 and 17.1.

6,7-Dihydro[1,4]dithiino[2,3-e]-1,4,2-dithiazine 133.

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 0.6 ml, 9.6 mmol) was added to a solution of 1,3-dithiolium cation salt **123** (270 mg, 0.96 mmol) and iodine (122 mg, 0.96 mmol) in acetonitrile (80 ml). The resultant mixture was stirred for 0.7 h at 20°C to afford compound **133** (50 mg, 25%) as a yellow oil [Found: C, 27.9; H, 2.3; N, 5.5%; *m/z* (CI) 207.9259. C₅H₅NS₄ requires C, 29.0; H, 2.4; N, 6.8%; *m/z* 207.9383]; ν_{\max} (thin film)/cm⁻¹ 2920, 1560, 1410, 1285, 910, 855, 780 and 745; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 291 and 249; δ_{H} (250 MHz, CDCl₃) 8.35 (1 H, s) and 3.30 (4 H, m); δ_{C} (250 MHz, CDCl₃) 154.2, 119.5, 110.1, 29.8 and 29.3.

3,5,6-Tris(methylthio)-1,4,2-dithiazine 134.

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 1.9 ml, 32 mmol) was added to a solution of 1,3-dithiolium cation salt **124** (1.06 g, 3.2 mmol) and iodine (2.03 g, 16 mmol) in acetonitrile (30 ml). The resultant mixture was stirred for 2.5 h at 20°C to afford compound **134** (0.31 g, 38%) as an orange oil [Found: m/z (CI) 255.9855. $C_6H_9NS_5$ requires 255.9417]; ν_{\max} (thin film)/ cm^{-1} 2920, 1525, 1425, 1310, 965, 915, 850 and 735; λ_{\max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 371sh and 264; δ_H (250 MHz, $CDCl_3$) 2.54 (3 H, s), 2.49 (3 H, s) and 2.44 (3 H, s); δ_C (250 MHz, $CDCl_3$) 163.6, 137.5, 122.1, 17.9, 17.9 and 16.9.

5,6-Dimethyl-3-methylthio-1,4,2-dithiazine 135.

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 5.9 ml, 100 mmol) was added to a solution of 1,3-dithiolium cation salt **125** (3.0 g, 10 mmol) and iodine (6.4 g, 50 mmol) in acetonitrile (150 ml). The resultant mixture was stirred for 4 h at 20°C to afford compound **135** (0.74 g, 38%) as an orange solid, m.p. 42–44°C (Found: C, 37.9; H, 4.6; N, 7.5. $C_6H_9NS_3$ requires C, 37.7; H, 4.7; N, 7.3%); m/z (EI) 191 (M^+); (CI) 192 ($M^+ + 1$); ν_{\max} (KBr)/ cm^{-1} 2920, 1535, 1435, 1185, 1090, 940, 765 and 750; λ_{\max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 360 and 304; δ_H (250 MHz, $CDCl_3$) 2.82 (3 H, s), 2.06 (3 H, s) and 2.02 (3 H, s); δ_C (250 MHz, $CDCl_3$) 157.9, 122.5, 122.1, 23.5, 13.9 and 13.4.

5,6-Dimethyl-3-dimethylamino-1,4,2-dithiazine 137.

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 3.5 ml, 60 mmol) was added to a solution of 1,3-dithiolium cation salt **127** (1.9 g, 6 mmol) and iodine (1.5 g, 12 mmol) in acetonitrile (50 ml). The resultant mixture was stirred for 23 h at 20°C to afford compound **137** (0.74 g, 65%) as a yellow oil (Found: C, 44.3; H, 6.4; N, 15.1. $C_7H_{12}N_2S_2$ requires C, 44.6; H, 6.4; N, 14.9%); m/z (EI) 188 (M^+); (CI) 189 ($M^+ + 1$); ν_{\max} (thin film)/ cm^{-1} 2915, 1550, 1355, 1255, 1115, 1065, 915 and 805; λ_{\max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 321 and 281; δ_H (200 MHz, $CDCl_3$) 3.06 (6 H, s), 2.03 (3 H, s) and 2.00 (3 H, s); δ_C (500 MHz, $CDCl_3$)

163.6, 136.1, 121.9, 40.3, 20.6 and 18.4.

1,4,2-Dithiazine 55.

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 0.71 ml, 12.1 mmol) was added to a solution of 1,3-dithiolium cation salt **129** (230 mg, 1.21 mmol) and iodine (140 mg, 1.1 mmol) in acetonitrile (50 ml). The resultant mixture was stirred for 0.5 h at 20°C to afford compound **55** (*ca.* 2 mg, 1%) as an orange oil [Found: m/z (EI) 116.9769. $C_3H_3NS_2$ requires 116.9707]; m/z (EI) 117 (M^+), 90 (dithiete); (CI) 118 ($M^+ + 1$), 86 (isothiazole + 1); δ_H (250 MHz, $CDCl_3$) 8.05 (1 H, s), 6.57* (1 H, d, J 5) and 6.10* (1 H, d, J 5). *(Due to the presence of olefinic impurity peaks, these assignments are tentative).

6.3 Experimental Procedures for Chapter 3.

6.3.1 Experimental for Section 3.2.

***p*-Phenylene-bis(4,5-dimethyl-1,3-dithiolium hexafluorophosphate) 172** was prepared by modified literature procedures, in four steps, from *p*-xylene, *N*-bromosuccinimide and azoisobutyronitrile (9% overall yield).^{36,71,73} M.p. 184-187°C (decomp.) (lit.⁷¹ m.p. not recorded for hexafluorophosphate salt).

***m*-Phenylene-bis(triethylammonium dithiocarboxylate) 177** was prepared by a modified literature procedure, from α,α' -dibromo-*m*-xylene, **176**, elemental sulphur and sodium methoxide (59% yield).³⁶ M.p. [for bis(piperidinium) salt] 129-135°C (lit.⁷² 140°C).

***p*-Phenylene-bis(5,6-dimethyl-1,4,2-dithiazine) 173.**

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 0.3 ml, 4.9 mmol) was added to a solution of bis(1,3-dithiolium cation) salt **172** (154 mg, 0.25 mmol) and iodine (130 mg, 1 mmol) in acetonitrile-*N,N*-dimethylformamide (75 ml, 4:1 v/v). The resultant mixture was stirred for 2 h at 20°C to afford compound **173** (40 mg, 44%) as an orange solid, m.p. 142-145°C (Found: C, 53.2; H, 4.3; N, 7.6. C₁₆H₁₆N₂S₄ requires C, 52.7; H, 4.4; N, 7.7%); *m/z* (DEI, toluene) 364 (M⁺); (DCI) 365 (M⁺ + 1); ν_{\max} (KBr)/cm⁻¹ 2910, 1490, 1405, 1230, 1120, 915, 860 and 840; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 417, 294 and 252sh; δ_{H} (250 MHz, CDCl₃) 8.02 (4 H, s), 2.10 (6 H, s) and 2.05 (6 H, s); δ_{C} (500 MHz, CDCl₃) 162.5, 138.0, 130.8, 128.4, 121.3, 21.0 and 18.8.

***p*-Phenylene-bis(2-methoxy-4,5-dimethyl-1,3-dithiole) 175.**

To a suspension of bis(1,3-dithiolium cation) salt **172** (313 mg, 0.5 mmol) in dry methanol (15 ml) was added sodium (46 mg, 2 mmol). The mixture was stirred for 72 h at 20°C, after which solvent was removed under reduced pressure. The residue was chromatographed on a neutral alumina column, eluted with dichloromethane, to collect a yellow band. Removal of solvent *in vacuo* afforded compound **175** (80 mg, 40%) as a yellow waxy solid (Found: C, 54.1; H, 5.6. C₁₈H₂₂O₂S₄ requires C, 54.2; H, 5.6%); ν_{\max} (thin film)/cm⁻¹ 2930, 2860, 1440, 1410, 1280, 1205, 1070 and 890; δ_{H} (250 MHz, CDCl₃) 7.81 (4 H, s), 3.46 (6 H, s) and 1.97 (12 H, s).

***m*-Phenylene-bis(3-oxobutan-2-yl dithiocarboxylate) 178.**

Following the procedure described for compound **109a** (Section 6.2.1), a solution of salt **177** (2.73 g, 6.3 mmol) and 3-chlorobutan-2-one (2.69 g, 25.2 mmol) in dry dichloromethane (150 ml) was stirred for 5 h at reflux, followed by 68 h at 20°C to afford compound **178** (1.70 g, 73%) as a viscous red oil [Found: C, 51.1; H, 4.9%; *m/z* (EI) 369.9941. C₁₆H₁₈O₂S₄ requires C, 51.9; H, 4.9%; *m/z* 370.0189]; ν_{\max} (thin film)/cm⁻¹ 2930, 1710, 1585, 1445, 1355, 1045, 855 and 795; δ_{H} (250 MHz, CDCl₃) 8.57 (1 H, s), 8.17 (2 H, d, J 8), 7.44 (1 H, t, J 8), 4.89 (2 H, q, J 6), 2.35 (6 H, s) and 1.60 (6

H, d, J 6).

***m*-Phenylene-bis(4,5-dimethyl-1,3-dithiolium hexafluorophosphate) 179.**

Following the procedure for salt **110a** (Section 6.2.1), a solution of dithioester **178** (740 mg, 2 mmol) in dry dichloromethane (10 ml) was added to sulphuric acid (20 ml, conc.) over 0.3 h at -20°C and stirred for a further 1 h at -20 to -10°C. Addition of the mixture to water (300 ml) followed by addition of hexafluorophosphoric acid (60%, 2.0 ml, 14 mmol) afforded a pale precipitate of salt **179** which began to darken immediately. The precipitate was filtered off rapidly and washed with water (2 x 50 ml). This material was used immediately, for the preparation of bis(1,4,2-dithiazine) **180**, without further purification or characterisation.

***m*-Phenylene-bis(5,6-dimethyl-1,4,2-dithiazine) 180.**

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 1.2 ml, 20 mmol) was added to a solution of bis(1,3-dithiolium cation) salt **179** (from above preparation, quantity unknown) and iodine (0.76 g, 6 mmol) in acetonitrile (150 ml). The resultant mixture was stirred for 18 h at 20°C to afford compound **180** [15 mg, 2.1%, in two steps from bis(dithioester) **178**] as a yellow solid, m.p. 65-68°C (Found: C, 53.1; H, 4.5; N, 8.1. C₁₆H₁₆N₂S₄ requires C, 52.7; H, 4.4; N, 7.7%); *m/z* (EI) 364 (M⁺); (CI) 365 (M⁺ + 1); ν_{\max} (KBr)/cm⁻¹ 2915, 1530, 1145, 1015, 895, 805, 775 and 680; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 397, 269 and 231; δ_{H} (250 MHz, CDCl₃) 8.60 (1 H, s), 8.08 (2 H, d, J 8), 7.43 (1 H, t, J 8), 2.12 (6 H, s) and 2.06 (6 H, s); δ_{C} (500 MHz, CDCl₃) 162.7, 136.2, 130.7, 130.6, 128.7, 128.0, 121.2, 20.8 and 18.7.

6.3.2 Experimental for Section 3.3.

1,3-Dithiane-2-thione 183 was prepared by a modified literature procedure, from carbon disulphide, sodium hydroxide solution, tricaprilmethylammonium chloride and 1,3-dibromopropane (*ca.* 60% yield).⁷⁵ M.p. 73-76°C (lit.⁷⁵ 80°C).

2-Methylthio-1,3-dithianium tetrafluoroborate **184**.

A suspension of thione **183** (5.0 g, 33 mmol) in dimethyl sulphate (20 ml, 210 mmol) was heated with stirring for 0.3 h at 90°C. The resultant solution was cooled and tetrafluoroboric acid (54%, 13.6 ml, 100 mmol) added with stirring. Slow addition of ether (300 ml) formed a precipitate which was filtered and washed with ether (4 x 50 ml). The precipitate was dried *in vacuo* to afford salt **184** (6.8 g, 81%) as a pale cream powder, m.p. 125-129°C (Found: C, 21.6; H, 4.0. C₅H₉BF₄S₃ requires C, 23.8; H, 3.6%); *m/z* (DEI, MeOH) 165 (M⁺, cation); ν_{\max} (thin film)/cm⁻¹ 3030, 1670, 1422, 1282, 1235, 1024, 907 and 866. This material was used without further purification.

2-(*N*-Methylthioimino)-1,3-dithiane **186**.

Following the procedure for compound **111a** (Section 6.2.1), ammonia solution (33%, 5.9 ml, 100 mmol) was added to a solution of 1,3-dithianium cation salt **184** (2.52 g, 10 mmol) and iodine (3.17 g, 25 mmol) in acetonitrile (200 ml). The resultant mixture was stirred for 2.5 h at 20°C to afford compound **186** (90 mg, 5%) as a pale yellow oil (Found: C, 33.7; H, 5.1; N, 7.5. C₅H₉NS₃ requires C, 33.5; H, 5.1; N, 7.8%); *m/z* (EI) 179 (M⁺); (CI) 180 (M⁺ + 1); ν_{\max} (thin film)/cm⁻¹ 2915, 1644, 1518, 1471, 1417, 1301, 935 and 743; δ_{H} (250 MHz, CDCl₃) 3.17 (2 H, t, J 7), 3.09 (2 H, t, J 7), 2.78 (3 H, s) and 2.19 (2 H, quintet, J 7); δ_{C} (200 MHz, CDCl₃) 154.1, 30.5, 29.8, 23.0 and 22.1.

6.4 Experimental Procedures for Chapter 4.

6.4.1 Experimental for Section 4.2.

4,5-Dimethyl-3-phenylisothiazole 187c was prepared by thermolysis of 1,4,2-dithiazine **111c** in dry toluene for 17 h at 111°C (55% yield). Selected spectroscopic data found: ν_{\max} (thin film)/cm⁻¹ 3057, 2921, 1540, 1448, 1360, 1008, 769 and 699; δ_{H} (250 MHz, CDCl₃) 7.61 (2 H, d, J 7), 7.42 (3 H, m), 2.43 (3 H, s) and 2.19 (3 H, s); δ_{C} (250 MHz, CDCl₃) 168.3, 158.2, 136.6, 129.2, 128.3, 12.4 and 12.0 (lit.⁸⁴

spectroscopic data not recorded).

4,5-Dimethyl-2-phenylthiazole 188 was prepared by a modified literature procedure, from thiobenzamide, **189**, and 3-chlorobutan-2-one (56% yield).⁷⁸ Selected spectroscopic data found: ν_{\max} (thin film)/ cm^{-1} 3061, 2919, 1546, 1461, 1243, 1001, 761 and 689; δ_{H} (250 MHz, CDCl_3) 7.84 (2 H, d, J 7), 7.31 (3 H, m), 2.32 (3 H, s) and 2.24 (3 H, s); δ_{C} (200 MHz, CDCl_3) 162.5, 148.6, 133.4, 128.6, 128.1, 125.8, 125.4, 14.2 and 10.6 (lit.⁸⁴ spectroscopic data not recorded).

3-(*p*-Methoxyphenyl)-4,5-dimethylisothiazole 187a.

This material is representative of the isothiazoles prepared. A solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) in dry toluene (5 ml) was refluxed for 18 h. Solvent was removed under reduced pressure and the residue chromatographed on a silica column, eluted with dichloromethane, to afford compound **187a** (160 mg, 73%) as a pale yellow oil [Found: C, 65.3; H, 5.6; N, 6.2%; m/z (CI) 237.1109 ($\text{M}^+ + 18$). $\text{C}_{12}\text{H}_{13}\text{NOS}$ requires C, 65.7; H, 6.0; N, 6.4%; m/z 237.1062]; ν_{\max} (thin film)/ cm^{-1} 2960, 1615, 1520, 1400, 1295, 1250, 1175 and 1035; λ_{\max} (CH_2Cl_2 -hexane 1:1 ν/ν)/nm 298 and 265; δ_{H} (250 MHz, CDCl_3) 7.56 (2 H, d, J 9), 6.95 (2 H, d, J 9), 3.81 (3 H, s), 2.42 (3 H, s) and 2.19 (3 H, s); δ_{C} (500 MHz, CDCl_3) 168.1, 159.8, 158.0, 129.9, 129.6, 129.4, 114.0, 55.3, 12.5 and 12.1.

4,5-Dimethyl-3-(*p*-methylphenyl)isothiazole 187b.

Following the procedure for compound **187a**, a solution of 1,4,2-dithiazine **111b** (235 mg, 1 mmol) in dry toluene (5 ml) was refluxed for 22 h to afford compound **187b** (203 mg, 100%) as a pale yellow crystalline solid, m.p. 33-34°C (Found: C, 70.6; H, 6.5; N, 6.5. $\text{C}_{12}\text{H}_{13}\text{NS}$ requires C, 70.9; H, 6.5; N, 6.9%); m/z (EI) 203 (M^+); (CI) 204 ($\text{M}^+ + 1$); ν_{\max} (thin film)/ cm^{-1} 2920, 1450, 1360, 1230, 1180, 1010, 815 and 730; λ_{\max} (CH_2Cl_2 -hexane 1:1 ν/ν)/nm 295 and 260; δ_{H} (250 MHz, CDCl_3) 7.51 (2 H, d, J 8), 7.24 (2 H, d, J 8), 2.43 (3 H, s), 2.38 (3 H, s) and 2.20 (3 H, s); δ_{C} (500 MHz,

CDCl₃) 168.4, 158.1, 138.3, 133.8, 129.2, 129.1, 128.8, 21.1, 12.6 and 12.0.

3-(*p*-Cyanophenyl)-4,5-dimethylisothiazole 191.

Following the procedure for compound **187a**, a solution of bis(1,4,2-dithiazine) **173** (100 mg, 0.27 mmol) in dry toluene (15 ml) was refluxed for 5 h to afford compound **191** (40 mg, 69%) as a white crystalline solid, m.p. 111-114°C [Found: C, 62.8; H, 4.6; N, 11.1%; *m/z* (EI) 214.0463. C₁₂H₁₀N₂S requires C, 67.3; H, 4.7; N, 13.1%; *m/z* 214.0565]; ν_{\max} (KBr)/cm⁻¹ 2920, 2230, 1180, 1145, 1015, 860, 830 and 555; λ_{\max} (CH₂Cl₂-hexane 1:1 v/v)/nm 291, 270 and 234; δ_{H} (250 MHz, CDCl₃) 7.75 (4 H, s), 2.50 (3 H, s) and 2.24 (3 H, s); δ_{C} (500 MHz, CDCl₃) 166.0, 159.6, 140.6, 132.2, 129.4, 129.0, 118.7, 112.1, 12.4 and 12.1.

6.4.2 Experimental for Section 4.3.

***p*-Methoxybenzotrile 192** was obtained by thermolysis of 1,4,2-dithiazine **111a**, in *o*-dichlorobenzene at 180°C, in the presence of DMAD (38% yield). M.p. 59°C (lit.¹²⁸ 57-58°C). Compound **192** was also obtained from various other reactions detailed in Chapter 4.

Benzenediazonium-2-carboxylate 198 was prepared by the literature procedure, from anthranilic acid and isoamyl nitrite.⁸⁰

2,3-Dimethyl-benzo[d]thiophene 200 was prepared by a modified literature procedure, from reaction of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) with benzyne (8 molar equivalents, generated *via* salt **198**) in refluxing tetrahydrofuran (*ca.* 8 mg, 5% yield).⁸¹ Spectroscopic data found: *m/z* (EI) 162.0563. C₁₀H₁₀S requires 162.0503 (lit.¹²⁹ no comparable data recorded).

6.4.3 Experimental for Section 4.4.

***p*-Methylbenzonitrile 201** was obtained by photolysis of 1,4,2-dithiazine **111b**, in dry toluene, under standard conditions (Section 6.1) for 23 h (100% yield). M.p. *ca.* 25°C (lit.¹³⁰ 28°C).

Dimethyl-5,6-dimethyl-1,4-dithiin-2,3-dicarboxylate 193.

This procedure is representative of the photolytic trapping reactions carried out. A solution of 1,4,2-dithiazine **111b** (100 mg, 0.42 mmol) and dimethyl acetylenedicarboxylate (DMAD) (0.52 ml, 4.2 mmol) in dry toluene (3 ml) was irradiated under standard conditions (Section 6.1) for 24 h. Solvent and unreacted DMAD were removed *in vacuo* and the residue chromatographed on a silica column, eluted with dichloromethane, to afford compound **193** (8 mg, 7%) as a yellow oil [Found: C, 53.6; H, 5.2%; m/z (EI) 260.0075. $C_{10}H_{12}O_4S_2$ requires C, 46.1; H, 4.6%; m/z 260.0177]; ν_{\max} (thin film)/ cm^{-1} 2952, 1725, 1571, 1434, 1250, 1075, 1015 and 760; δ_H (250 MHz, $CDCl_3$) 3.83 (6 H, s) and 2.05 (6 H, s).

Dimethyl-4,5-dimethylthiophene-2,3-dicarboxylate 194.

Following the procedure for compound **193**, a solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) and DMAD (1.24 ml, 10 mmol) in dry toluene (3 ml) was irradiated under standard conditions for 20 h to afford compound **194** (51 mg, 22%) as a yellow oil [Found: C, 55.6; H, 5.4%; m/z (EI) 228.0270. $C_{10}H_{12}O_4S$ requires C, 52.6; H, 5.3%; m/z 228.0456]; ν_{\max} (thin film)/ cm^{-1} 2952, 1732, 1471, 1436, 1286, 1243, 1091 and 1034; δ_H (250 MHz, $CDCl_3$) 3.93 (3 H, s), 3.83 (3 H, s), 2.37 (3 H, s) and 2.09 (3 H, s).

Dimethyl-1,4-dithiin-2,3-dicarboxylate 202.

Following the procedure for compound **193**, a solution of 1,4,2-dithiazine **101** (344 mg, 2.11 mmol) in DMAD (3 ml, 24 mmol) was irradiated under standard

conditions for 24 h to afford compound **202** (*ca.* 20 mg, 4%) as a yellow oil [Found: m/z (EI) 232.0263. $C_8H_8O_4S_2$ requires 231.9864]; ν_{\max} (thin film)/ cm^{-1} 2980, 1680, 1434, 1265, 1106, 904, 728 and 660; δ_H (250 MHz, $CDCl_3$) 6.41 (2 H, s) and 3.83 (6 H, s).

2,2,3,3-Tetracyano-5,6-dimethyl-1,4-dithiin 206.

Following the procedure for compound **193**, a solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) and tetracyanoethene (1.92 g, 15 mmol) in dry toluene (2 ml) was irradiated under standard conditions for 25 h to afford compound **206** (*ca.* 16 mg, 6%) as an orange oily solid [Found: m/z (EI) 246.0002. $C_{10}H_6N_4S_2$ requires 246.0034]; δ_H (250 MHz, $CDCl_3$) 3.60 (6 H, s).

5,6-Dihydro-2,3-dimethyl-norbornyl[2,3-e]-1,4-dithiin 209.

Following the procedure for compound **193**, a solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) and norbornene (2.82 g, 30 mmol) in dry toluene (1 ml) was irradiated under standard conditions for 23 h to afford compound **209** (*ca.* 70 mg, 33%) as a yellow oil [Found: C, 52.5; H, 6.8%; m/z (EI) 212.0426. $C_{11}H_{16}S_2$ requires C, 62.2; H, 7.6%; m/z 212.0693]; ν_{\max} (thin film)/ cm^{-1} 2952, 2869, 1448, 1368, 1198, 1083, 909 and 733; δ_H (250 MHz, $CDCl_3$) 3.28 (s) and 2.6-1.1 (complex pattern due to overlap).

6.4.4 Experimental for Section 4.5.

***p*-Methoxybenzylamine 212** was obtained from reaction of 1,4,2-dithiazine **111a** with lithium aluminium hydride (*ca.* 50% yield). Spectroscopic data found: δ_H (250 MHz, $CDCl_3$) 7.23 (2 H, d, J 8), 6.87 (2 H, d, J 8) and 3.80 (5 H, s) [lit.¹³¹ δ_H (60 MHz) 7.2 (2 H, d), 6.8 (2 H, d), 3.8 (5 H, s) and 1.4 (2 H, s).

***p*-Bromobenzonitrile 213** was obtained from reaction of 1,4,2-dithiazine **111d** with sodium borohydride (69% yield). M.p. 113-114°C (lit.¹³² 113°C).

2,3-Dihydro-1,4-dithiin-5,6-dithiol 215 was obtained from reaction of 1,4,2-dithiazine **131** with sodium borohydride (trace yield). Spectroscopic data found: *m/z* (CI) 183 ($M^+ + 1$) (lit.¹³³ the di-potassium salt of compound **215** has been prepared by an alternative synthetic procedure).

Bis(but-2-ene-3-thiol-2-yl)-disulphide 214.

Sodium borohydride (190 mg, 5 mmol) was added to a solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) in dry ethanol (20 ml) and the mixture stirred for 95 h at 20°C, after which water (200 ml) was added. The mixture was extracted with diethyl ether (3 x 50 ml) and the organic layers combined and dried ($MgSO_4$). Solvent was removed under reduced pressure and the residue chromatographed on a silica column, eluted with dichloromethane-hexane (1:1 v/v), to collect a pale yellow band. Solvent was removed *in vacuo* to afford compound **214** (ca. 6 mg, 5%) as a yellow oily solid [Found: *m/z* (EI) 237.9999. $C_8H_{14}S_4$ requires 237.9978]; δ_H^* (250 MHz, $CDCl_3$) 1.61 (6 H, s) and 1.59 (6 H, s). *(Tentative assignment due to impurity peaks).

2-Phenylthio-but-2-ene-3-thiol 219.

This procedure is representative of the reactions carried out between 1,4,2-dithiazines and Grignard reagents. To a stirred solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) in dry diethyl ether (20 ml) was added phenylmagnesium bromide solution (3.0 M in ether, 1.7 ml, 5 mmol) and the mixture stirred for 18 h at 20°C. Hydrochloric acid solution (ca. 0.1 M, 100 ml) was added and the mixture extracted into dichloromethane (3 x 50 ml). The combined organic layers were washed with water (2 x 100 ml) and dried ($MgSO_4$). Solvent was removed under reduced pressure and the residue chromatographed on a silica column, eluted with dichloromethane-hexane (1:3 v/v), to collect a pale orange band. Solvent was removed *in vacuo* to afford compound

219 (ca. 170 mg, 87%) as a pale orange oil [Found: C, 62.0; H, 6.2%; m/z (EI) 196.0226. $C_{10}H_{12}S_2$ requires C, 61.2; H, 6.2%; m/z 196.0381]; ν_{\max} (thin film)/ cm^{-1} 3070, 2920, 1585, 1480, 1440, 1025, 740 and 685; δ_H (250 MHz, $CDCl_3$) 7.38-7.14 (5 H, m), 3.94 (1 H, s), 2.15 (3 H, s) and 1.97 (3 H, s).

2,3-Dihydro-5-phenylthio-1,4-dithiin-6-thiol 220.

Following the procedure for compound **219**, a solution of 1,4,2-dithiazine **131** (290 mg, 1.14 mmol) in dry diethyl ether (20 ml) and phenylmagnesium bromide solution (3.0 M in ether, 1.9 ml, 5.7 mmol) was stirred for 23 h at 20°C to afford compound **220** (ca. 220 mg, 75%) as a viscous orange oil [Found: m/z (EI) 257.9642. $C_{10}H_{10}S_4$ requires 257.9665]; δ_H (250 MHz, $CDCl_3$) 7.44-7.15 (5 H, m) and 3.44-3.21 (4 H, m).

2-^tButylthio-but-2-ene-3-thiol 221.

Following the procedure for compound **219**, a solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) in dry diethyl ether (20 ml) and *tert*-butylmagnesium chloride solution (2.0 M in ether, 5.0 ml, 10 mmol) was stirred for 95 h at 20°C to afford compound **221** (40 mg, 23%) as a pale yellow waxy solid [Found: C, 53.2; H, 8.3%; m/z (EI) 176.0666. $C_8H_{16}S_2$ requires C, 54.5; H, 9.1%; m/z 176.0693]; ν_{\max} (thin film)/ cm^{-1} 2950, 2910, 1580, 1455, 1365, 1215, 1150 and 1065; δ_H (250 MHz, $CDCl_3$) 2.15 (3 H, s), 2.09 (3 H, s) and 1.40 (9 H, s).

6.4.5 Experimental for Section 4.6.

4,5-Dimethyl-3-(α -thienyl)isothiazole 226.

Acetyl chloride (4 ml, 56 mmol) was added to aluminium chloride (1.3 g, 10 mmol) in dry chloroform (20 ml) and stirred until complete dissolution had taken place, whereupon it was added dropwise, with stirring, to a solution of 1,4,2-dithiazine **111f** (0.99 g, 4.4 mmol) in dry chloroform (10 ml). The reaction was stirred for 3 h at 20°C

after which water (200 ml) was added. The mixture was extracted with dichloromethane (4 x 70 ml) and the organic layers combined, washed with water to neutral pH, and dried (MgSO_4). Solvent was removed under reduced pressure and the residue chromatographed on a silica column, eluted with dichloromethane, to collect unreacted compound **111f** (340 mg, 34%), followed by a pale orange band. Solvent was removed *in vacuo* to afford compound **226** (70 mg, 8%) as a brown oil [Found: C, 48.2; H, 4.0; N, 5.2%; m/z (EI) 194.9964. $\text{C}_9\text{H}_9\text{NS}_2$ requires C, 55.3; H, 4.6; N, 7.2%; m/z 195.0176]; ν_{max} (thin film)/ cm^{-1} 3105, 2925, 1550, 1445, 1385, 1235, 910 and 710; δ_{H} (250 MHz, CDCl_3) 7.44 (1 H, d, J 4), 7.37 (1 H, d, J 5), 7.11 (1 H, t, J 4), 2.45 (3 H, s) and 2.34 (3 H, s); δ_{C} (250 MHz, CDCl_3) 161.4, 130.0, 127.9, 127.4, 127.3, 126.6, 125.3, 12.6 and 11.9.

6.4.6 Experimental for Section 4.7.

3-(*p*-Methoxyphenyl)-5,6-dimethyl-1,4,2-dithiazine-*S*-oxide **228**.^{*}

A solution of magnesium monoperoxyphthalic acid (MMPP) (80%, 340 mg, 0.55 mmol) in ethanol-water (10 ml, 1:1 v/v) was added dropwise, with stirring, to a solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) in ethanol (20 ml). Stirring was continued for 0.5 h at 20°C, after which the reaction was added to water (200 ml) and the mixture extracted with dichloromethane (3 x 50 ml) and diethyl ether (1 x 50 ml). The combined organic layers were washed with water (1 x 200 ml) and dried (MgSO_4). Solvent was removed under reduced pressure and the residue chromatographed on a silica column, eluted with dichloromethane, to afford compound **192** (29 mg, 22%). Elution was continued, with dichloromethane-ethanol (98:2 v/v), to afford, after *in vacuo* removal of solvent, compound **228** (124 mg, 46%) as a cream powder, m.p. 78-79°C (Found: C, 53.5; H, 5.0; N, 4.8. $\text{C}_{12}\text{H}_{13}\text{NO}_2\text{S}_2$ requires C, 53.9; H, 4.9; N, 5.2%); m/z (EI) 267 (M^+); ν_{max} (KBr)/ cm^{-1} 2973, 1603, 1503, 1310, 1250, 1111, 1021 and 835; δ_{H} (250 MHz, CDCl_3) 8.05 (2 H, d, J 9), 6.94 (2 H, d, J 9), 3.87 (3 H, s), 2.28 (3 H, s) and 2.18 (3 H, s); δ_{C} (250 MHz, CDCl_3) 163.0, 138.0, 137.0, 131.0, 130.1, 114.5, 114.3,

55.6, 20.6 and 11.1. *(S-1 or S-4 -Oxide regiochemistry undefined).

5-Hydro-3,4,6-trimethyl-6-thioacetyl-2H-thiopyran-1-oxide 231.

A solution of 1,4,2-dithiazine-S-oxide **228** (ca. 20 mg, 0.07 mmol) and 2,3-dimethyl-1,3-butadiene (2 ml, 18 mmol) in chloroform (5 ml) was allowed to stand for 160 h at 20°C. Solvent and unreacted diene were removed *in vacuo* to afford a brown oil, containing compound **231** (trace yield) [Found: m/z (CI) 217.0797, C₁₀H₁₆OS₂ requires 217.0721].

3-(p-Methoxyphenyl)-5,6-dimethyl-1,4,2-dithiazine-S,S-dioxide 232.#

A solution of magnesium monoperoxyphthalic acid (80%, 680 mg, 1.1 mmol) in ethanol-water (15 ml, 1:1 v/v) was added dropwise, with stirring, to a solution of 1,4,2-dithiazine **111a** (251 mg, 1 mmol) in ethanol (20 ml). Stirring was continued for 0.5 h at 20°C and 0.1 h at 50°C. Aqueous work-up conditions identical to those described for compound **228** were employed. Column chromatography on silica with dichloromethane as eluent afforded compound **192** (48 mg, 36%). Elution was continued with dichloromethane-methanol (98:2 v/v) to afford compound **232** (58 mg, 20%) as a cream solid, m.p. 163-165°C (Found: C, 50.4; H, 4.6; N, 5.1. C₁₂H₁₃NO₃S₂ requires C, 50.9; H, 4.6; N, 4.9%); m/z (DCI) 284 (M⁺ + 1); ν_{\max} (KBr)/cm⁻¹ 2923, 1601, 1535, 1508, 1306, 1139, 851 and 530; δ_{H} (250 MHz, CDCl₃) 8.00 (2 H, d, J 9), 6.97 (2 H, d, J 9), 3.89 (3 H, s), 2.35 (3 H, s) and 2.26 (3 H, s); δ_{C} (250 MHz, CDCl₃) 164.8, 158.0, 133.6, 130.1, 127.0, 114.5, 112.0, 55.7, 20.6 and 12.3. #(S,S-1,1 or S,S-4,4 -Dioxide regiochemistry undefined).

6.5 Experimental Procedures for Chapter 5.

6.5.1 Experimental for Section 5.2.

Bis(tetraethylammonium)-bis(4,5-dithiolato-1,2-dithiole-3-thione) zincate 246 has been reported previously.¹⁰⁰ Herein, a modified procedure is described which enables convenient access to compound **246**. To a stirred mixture of sodium (11.5 g, 0.5 mol) (cut into small pieces by the use of a cheese-grater),¹³⁴ in carbon disulphide (135 ml, 2.2 mol) at 0°C, *N,N*-dimethylformamide (150 ml, 1.9 mol) was added dropwise with stirring over 0.2 h. The mixture was allowed to warm to 20°C and stirred for a further 115 h. A small amount of residual sodium was removed by filtration through a glass wool plug. Excess carbon disulphide was removed by distillation and the remaining mixture was then heated at 130-140°C for 2 h. The mixture was cooled and methanol (200 ml) then water (250 ml) were added with stirring. A solution of zinc chloride (10.0 g, 0.07 mol) in ammonia solution (33%, 250 ml) and methanol (250 ml) was then added to the reaction mixture with stirring. A solution of tetraethylammonium bromide (26.5 g, 0.13 mol) in water (125 ml) was then added dropwise with stirring over 0.2 h. This caused the crude zincate salt **246** to precipitate as a dark oil, which was separated and allowed to solidify. It was then purified by stirring in ether (1000 ml) overnight, whereupon it broke up into a fine brown precipitate. This precipitate was filtered off and washed consecutively with water (1000 ml), propan-2-ol (200 ml) and ether (300 ml). Drying *in vacuo* afforded salt **246** as a brown powder (27.7 g, 62%).

4,5-Bis(benzoylthio)-1,3-dithiole-2-thione 247 was prepared by the literature procedure, from carbon disulphide, sodium and *N,N*-dimethylformamide.⁴⁶ Compound **247** was used to generate 4,5-dithiolato-1,3-dithiole-2-thione disodium salt **244**, according to the literature procedure.¹⁰¹

3,4,5-Tris(methylthio)-1,2-dithiolium iodide 249 was prepared by literature procedures, in two steps, from zincate salt **246** and iodomethane (*via* thione **241**) (40% overall yield).¹⁰³ M.p. 158-159°C (lit.¹⁰⁶ 156°C).

3-Methylthio-5,6-dihydro[1,4]dithiino[2,3-d]-1,2-dithiolium iodide 250 was prepared by literature procedures, in two steps, from zincate salt **246** and 1,2-dibromoethane (*via* thione **237**) (59% overall yield).¹⁰³ M.p. 160-162°C (lit.¹⁰³ 160°C).

3-Methylthio-5,6,7-trihydro[1,4]dithiepine[2,3-d]-1,2-dithiolium iodide 251 was prepared by literature procedures, in two steps, from zincate salt **246** and 1,3-dibromopropane (*via* thione **242**) (9% overall yield).¹⁰³ M.p. 178-180°C (lit.¹⁰³ 184°C).

3-Methylthio-benzo[d]-1,2-dithiolium tetrafluoroborate 252 was prepared by literature procedures, in two steps, from 2,2'-dithiodibenzoic acid, **248**, and phosphorus pentasulphide (*via* thione **243**) (75% overall yield).^{104,107} M.p. 126-129°C (decomp.) (lit.¹⁰⁷ m.p. not recorded).

5,6-Dihydro[1,4]dithiino[2,3-d]-1,2-dithiolium iodide 253.

This material has been reported previously (as the tetrafluoroborate salt), synthesised by a low yielding and non-reproducible approach.⁴⁹ Herein, an alternative procedure is described which enables reproducible access to compound **253**, in improved yield. Thione **237** (0.5 g, 2.2 mmol) was dissolved in acetone and cooled to 0°C. A solution of *m*-chloroperoxybenzoic acid (50%, 2.3 g, 6.7 mmol) in acetone (20 ml) was added dropwise with stirring over 2 min. Stirring at 0°C was maintained for 0.5 h, whence the precipitate which formed was filtered off and washed with ether (3 x 30 ml). After drying *in vacuo* the crude product was converted into the iodide salt as follows. The solid was dissolved in water (100 ml), the solution was filtered and the filtrate added, with stirring, to a solution of sodium iodide (1.7 g, 11 mmol) in water (20 ml). The resultant precipitate was filtered off and washed with acetone (2 x 30 ml) and ether (3 x 30 ml). Drying *in vacuo* afforded salt **253** (0.24 g, 34%) as an orange solid, m.p. 181-184°C (Found: C, 18.8; H, 1.5. C₅H₅S₄I requires C, 18.8; H, 1.6%); *m/z* (FAB, glycerol) 193 (M⁺, cation); ν_{\max} (KBr)/cm⁻¹ 3045, 2945, 1405, 1335, 1280,

1175, 1020 and 865; δ_{H} (250 MHz, d_6 -DMSO) 10.1 (1 H, br s) and 3.55-3.27 (4 H, m).

4,5,6-Tris(methylthio)-1,2,3-dithiazine 255.

This material is representative of the 1,2,3-dithiazines prepared. To a stirred solution of 1,2-dithiolium cation salt **249** (180 mg, 0.5 mmol) and iodine (320 mg, 2.5 mmol) in acetonitrile (100 ml) was added dropwise ammonia solution (33%, 0.29 ml, 5 mmol). Stirring was continued for 1 h at 20°C, after which water (200 ml) was added and the mixture extracted with dichloromethane (3 x 70 ml). The combined organic layers were washed with water (1 x 200 ml), dried (MgSO_4) and evaporated at reduced pressure at 25°C maximum. The resultant oil was chromatographed on a silica column, eluted with dichloromethane-hexane (1:3 v/v). An orange band was collected, from which solvent was removed *in vacuo* at $\leq 25^\circ\text{C}$, to afford compound **255** (50 mg, 39%) as a red oil [Found: m/z (DEI, toluene) 254.9464. $\text{C}_6\text{H}_9\text{NS}_5$ requires 254.9339]; ν_{max} (thin film)/ cm^{-1} 2920, 1490, 1445, 1310, 1270, 1110, 870 and 730; λ_{max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 473w, 336, 283, 257 and 236; δ_{H} (250 MHz, CDCl_3) 2.56 (3 H, s), 2.36 (3 H, s) and 2.28 (3 H, s).

3,4,5-Tris(methylthio)isothiazole 260.

Following isolation of compound **255** above, column elution was continued, to collect a yellow band. Solvent was removed *in vacuo* at $\leq 25^\circ\text{C}$, to afford compound **260** (10 mg, 9%) as an orange oil [Found: m/z (EI) 222.9745. $\text{C}_6\text{H}_9\text{NS}_4$ requires 222.9618]; ν_{max} (nujol mull)/ cm^{-1} 1605, 1580, 1290, 1270, 1120, 1070, 1040 and 955; δ_{H} (250 MHz, CDCl_3) 2.60 (6 H, s) and 2.29 (3 H, s). Compound **260** could also be obtained, in quantitative yield, by desulphurisation of a chloroform solution of compound **255**, over *ca.* 48 h at 20°C.

4-Methylthio-6,7-dihydro[1,4]dithiino[2,3-e]-1,2,3-dithiazine 256.

Following the procedure for compound **255**, ammonia solution (33%, 0.59 ml, 10 mmol) was added to a solution of 1,2-dithiolium cation salt **250** (370 mg, 1 mmol) and iodine (630 mg, 5 mmol) in acetonitrile (130 ml). The resultant mixture was stirred for 3.5 h at 0°C to afford, after work-up and column chromatography on silica, eluted with dichloromethane-hexane (1:1 v/v), compound **256** (35 mg, 14%) as a red solid, m.p. 122-125°C [Found: C, 30.5; H, 3.0; N, 5.2%; m/z (EI) 252.9505. $C_6H_7NS_5$ requires C, 28.4; H, 2.8; N, 5.5%; m/z 252.9182]; ν_{max} (KBr)/ cm^{-1} 2925, 1495, 1460, 1410, 1265, 1105, 850 and 710; λ_{max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 490w, 379, 284 and 231; δ_H (250 MHz, $CDCl_3$) 3.40 (2 H, t, J 6), 3.18 (2 H, t, J 6) and 2.37 (3 H, s).

3-Methylthio-5,6-dihydro[1,4]dithiino[2,3-d]isothiazole 261.

Following isolation of compound **256** above, column elution was continued, to collect a yellow band. Solvent was removed *in vacuo* at $\leq 20^\circ C$, to afford compound **261** (20 mg, 9%) as a yellow solid, m.p. 56-58°C [Found: C, 31.2; H, 3.0; N, 5.3%; m/z (EI) 220.9440. $C_6H_7NS_4$ requires C, 32.6; H, 3.2; N, 6.3%; m/z 220.9461]; ν_{max} (thin film)/ cm^{-1} 2925, 1470, 1430, 1355, 1265, 1055, 930 and 880; λ_{max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 436, 295, 265 and 230; δ_H (250 MHz, $CDCl_3$) 3.32 (4 H, m) and 2.66 (3 H, s). Compound **261** could also be obtained, in quantitative yield, by desulphurisation of a chloroform solution of compound **256**, over *ca.* 30 h at 20°C.

4-Methylthio-6,7,8-trihydro[1,4]dithiepino[2,3-e]-1,2,3-dithiazine 257.

Following the procedure for compound **255**, ammonia solution (33%, 0.25 ml, 4.2 mmol) was added to a solution of 1,2-dithiolium cation salt **251** (160 mg, 0.42 mmol) and iodine (270 mg, 2.1 mmol) in acetonitrile (30 ml). The resultant mixture was stirred for 1.5 h at 20°C to afford, after work-up and column chromatography on silica, eluted with dichloromethane-hexane (1:1 v/v), compound **257** (*ca.* 11 mg, 10%) as an orange oily solid, in a mixture with compound **262**. Spectroscopic data found for compound **257**: δ_H^* (250 MHz, $CDCl_3$) 3.35 (2 H, t, J 6), 3.21 (2 H, t, J 6) and 2.50 (2 H, m). *(Partial and tentative assignment due to impurity peaks).

3-Methylthio-5,6,7-trihydro[1,4]dithiepine[2,3-d]isothiazole 262.

Compound **262** (ca. 10 mg, 10%) was obtained as a mixture with compound **257**, from the preceding reaction. Spectroscopic data found for compound **262**: m/z (EI) 235 (M^+); (CI) 236 ($M^+ + 1$); δ_H^\dagger (250 MHz, $CDCl_3$) 2.96 (2 H, t, J 6), 2.89 (2 H, t, J 6), 2.61 (3 H, s) and 2.50 (2 H, m). \dagger (Tentative assignment due to impurity peaks).

4-Methylthio-benzo[e]-1,2,3-dithiazine 258.

Following the procedure for compound **255**, ammonia solution (33%, 2.4 ml, 40 mmol) was added to a solution of 1,2-dithiolium cation salt **252** (1.14 g, 4 mmol) and iodine (2.54 g, 20 mmol) in acetonitrile (150 ml). The resultant mixture was stirred for 2 h at 20°C to afford compound **258** (215 mg, 25%) as an orange oil [Found: C, 47.6; H, 3.5; N, 7.1%; m/z (DEI, toluene) 212.9672. $C_8H_7NS_3$ requires C, 45.0; H, 3.3; N, 6.6%; m/z 212.9741]; ν_{max} (thin film)/ cm^{-1} 3060, 2925, 1580, 1505, 1290, 1195, 955 and 755; λ_{max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 426, 313, 267sh and 235; δ_H (250 MHz, $CDCl_3$) 7.76 (1 H, d, J 8), 7.49-7.28 (3 H, m) and 2.49 (3 H, s).

3-Methylthio-benzo[d]isothiazole 263.

A solution of 1,2,3-dithiazine **258** in deuteriochloroform was held at 20°C for ca. 100 h, after which a yellow precipitate of elemental sulphur (crude m.p. 85-95°C, lit.¹³⁵ 112.8°C) was separated by filtration. *In vacuo* removal of solvent from the filtrate afforded compound **263** (quantitative yield)[#] as a yellow oil [Found: C, 48.7; H, 3.6; N, 7.2%; m/z (EI) 181.0218. $C_8H_7NS_2$ requires C, 53.0; H, 3.9; N, 7.7%; m/z 181.0020]; ν_{max} (thin film)/ cm^{-1} 3065, 2930, 1595, 1465, 1290, 1250, 995 and 760; λ_{max} (CH_2Cl_2 -hexane 1:1 v/v)/nm 427, 314 and 246; δ_H (500 MHz, $CDCl_3$) 7.88 (1 H, d, J 9), 7.83 (1 H, d, J 9), 7.47 (1 H, t, J 9), 7.37 (1 H, t, J 9) and 2.78 (3 H, s); δ_C (500 MHz, $CDCl_3$) 159.4, 151.7, 133.6, 128.0, 124.4, 122.7, 119.9 and 13.3. (Comparative data for 2-methylthio-benzo[d]-thiazole¹³⁶ δ_C [60 MHz, d_6 -DMSO] 167.4, 152.5, 134.2, 126.0, 123.9, 121.4, 120.7 and 15.5). [#](Based on NMR evidence).

5,6-Dihydro[1,4]dithiino[2,3-d]isothiazole 264.

Following the procedure for compound **255**, ammonia solution (33%, 0.44 ml, 7.5 mmol) was added to a solution of 1,2-dithiolium cation salt **253** (240 mg, 0.75 mmol) and iodine (190 mg, 1.5 mmol) in acetonitrile (100 ml). The resultant mixture was stirred for 3 h at 20°C to afford compound **264** (110 mg, 84%) as an orange crystalline solid, m.p. 44-46°C [Found: C, 34.2; H, 2.8; N, 7.3%; m/z (EI) 174.9568. $C_5H_5NS_3$ requires C, 34.3; H, 2.9; N, 8.0%; m/z 174.9585]; ν_{max} (KBr)/ cm^{-1} 2920, 1415, 1365, 1285, 1180, 855, 770 and 485; λ_{max} (CH₂Cl₂-hexane 1:1 v/v)/nm 436, 310, 258, 250 and 226; δ_H (250 MHz, CDCl₃) 8.07 (1 H, s) and 3.30 (4 H, AA'BB'); δ_C (250 MHz, CDCl₃) 155.2, 146.2, 120.5, 28.4 and 26.0.

4,5-Dimethylthio-1,2-thiazoline-3-thione 265.

Following the procedure for compound **255**, ammonia solution (33%, 0.82 ml, 14 mmol) was added to a solution of 1,2-dithiolium cation salt **249** (500 mg, 1.36 mmol) and iodine (860 mg, 6.8 mmol) in acetonitrile (100 ml). The resultant mixture was stirred for 2.5 h at 20°C, followed by aqueous work-up and chromatography on a silica column, eluted with dichloromethane-hexane (1:3 v/v). Coloured bands were collected in the following order of elution; red, orange and yellow, corresponding to compounds **265**, **255** and **260**, respectively. Solvent was removed *in vacuo* from the red fraction to afford compound **265** (60 mg, 21%) as a red solid, m.p. 93-95°C [Found: C, 29.4; H, 3.2; N, 11.5%; m/z (DEI) 208.9311. $C_5H_7NS_4$ requires C, 28.7; H, 3.4; N, 6.7%; m/z 208.9461]; ν_{max} (KBr)/ cm^{-1} 3460, 2920, 1410, 1330, 1310, 1160, 880 and 825; δ_H (250 MHz, CDCl₃) 2.72 (3 H, s) and 2.65 (3 H, s).

TCNQ Salt of 1,2-Dithiolium Cation 250.

A mixture of the iodide salt of 1,2-dithiolium cation **250** (50 mg, 0.14 mmol) and 7,7,8,8-tetracyano-*p*-quinodimethane (58 mg, 0.28 mmol) were dissolved in boiling acetonitrile (15 ml). The solution was cooled to 20°C to afford a precipitate of salt **250-(TCNQ)₂** (28 mg, 31%) as a black powder (Found: C, 55.3; H, 2.3; N, 17.8. $C_{30}H_{15}N_8S_5$ requires C, 55.6; H, 2.3; N, 17.3%); ν_{max} (KBr)/ cm^{-1} 2186 (the

remainder of the spectrum comprises a series of broad bands, typical of an organic conductor); σ_{rt} (two-probe, compressed pellet)/ Scm^{-1} 2×10^{-3} .

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APPENDIX 1

X-RAY CRYSTALLOGRAPHIC DATA

A.1.1 Crystallographic Data for:

3-(*p*-Methoxyphenyl)-5,6-dimethyl-1,4,2-dithiazine 111a.

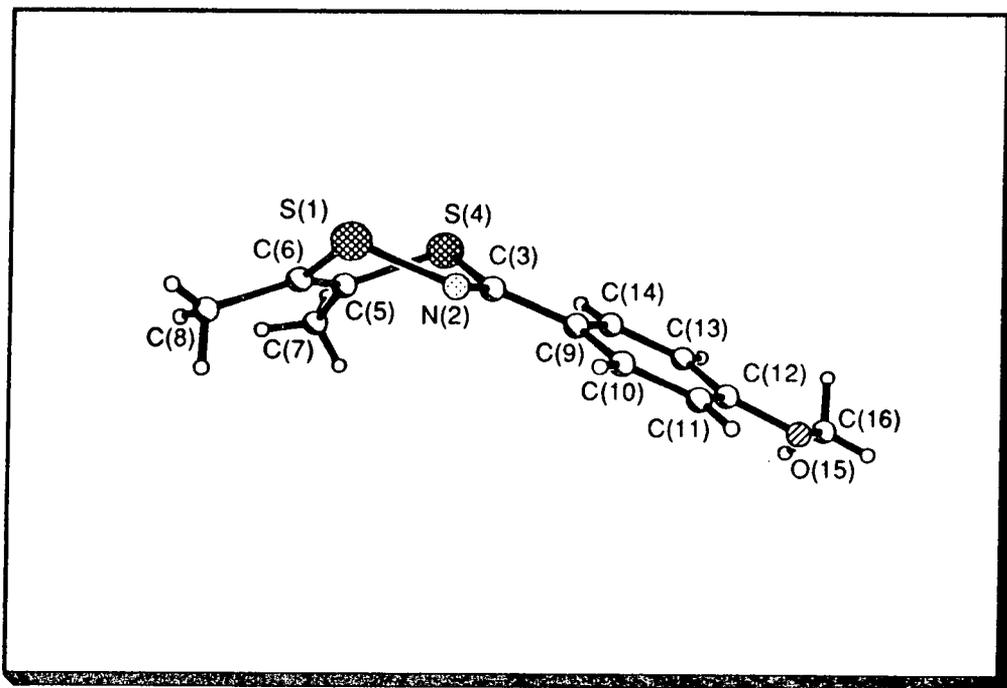


Figure 12. X-Ray Crystal Structure of Compound 111a, Showing Atom Numbering.

Crystal Data for Compound 111a.

Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	14.226(2)
b/Å	10.896(2)
c/Å	8.142(2)
β/(°)	104.44(2)
U/Å ³	1222.1(3)
Z	4
D _c /g cm ⁻³	1.37
Formula	C ₁₂ H ₁₃ NOS ₂
Crystal size/mm	0.20 x 0.62 x 0.85
M	251.4
F(000)	528

Data Collection for Compound 111a.

$\mu(\text{MoK}\alpha)/\text{cm}^{-1}$	4.13
max. $2\theta(^{\circ})$	50
Unique reflections	2133
Reflections with $I > 2\sigma(I)$	1899
Absorption correction:	
Transmission factors, min., max.	0.5203/0.6857

Refinement Details for Compound 111a.

No. of ψ -scans (reflections) used	140(8)
Refined parameters	197
R	0.047
$R_G = wR$	0.066
Goodness-of-fit	2.50
Weighting scheme, g^a	0.0004
Residual difference feature, max. (min.), $e/\text{\AA}^{-3}$	0.21 (-0.26)
$^a[\text{Weighting scheme } w^{-1} = \sigma^2(F) + gF^2 \text{ was used}].$	

Additional Details for Compound 111a.

X-Ray measurements for compound **111a** were performed on a Siemens R3m/V four-circle diffractometer with graphite-monochromated Mo-K α radiation ($\lambda = 0.71069 \text{ \AA}$) at room temperature. Reflection intensities were measured by the Wyckoff (limited ω) scan technique and corrected for absorption by a semi-empirical method (based on ψ -scan method). The structure was solved by direct methods and refined by full-matrix least-squares using the SHELX^{TL} PLUS suite of programmes.¹³⁷ All non-hydrogen atoms were refined anisotropically; all hydrogen atoms were located from a difference Fourier map and refined in isotropic approximation. Additional material available from the Cambridge Crystallographic Data Centre comprises thermal parameters, hydrogen atom coordinates and all bond lengths and angles.

Selected Bond Lengths (\AA) for Compound 111a.

S(1)-N(2)	1.709(2)	C(3)-C(9)	1.477(3)
N(2)-C(3)	1.274(3)	C(5)-C(7)	1.498(4)
C(3)-S(4)	1.785(2)	C(6)-C(8)	1.504(3)
S(4)-C(5)	1.762(2)	C(12)-O(15)	1.361(3)
C(5)-C(6)	1.336(3)	O(15)-C(16)	1.419(3)
C(6)-S(1)	1.752(2)		

Selected Bond Angles (°) for Compound 111a.

N(2)-S(1)-C(6)	105.1(1)	N(2)-C(3)-C(9)	120.6(2)
S(1)-N(2)-C(3)	119.2(2)	S(4)-C(3)-C(9)	116.5(1)
N(2)-C(3)-S(4)	122.9(2)	S(4)-C(5)-C(7)	114.9(2)
C(3)-S(4)-C(5)	100.5(1)	C(6)-C(5)-C(7)	125.2(2)
S(4)-C(5)-C(6)	119.9(2)	C(5)-C(6)-C(8)	124.9(3)
S(1)-C(6)-C(5)	119.5(2)	S(1)-C(6)-C(8)	115.3(2)
C(3)-C(9)-C(10)	119.8(2)	C(11)-C(12)-O(15)	115.6(2)
C(3)-C(9)-C(14)	122.3(2)	C(13)-C(12)-O(15)	124.6(2)
C(10)-C(9)-C(14)	117.9(2)	C(12)-C(13)-C(14)	119.3(2)
C(9)-C(10)-C(11)	120.8(2)	C(13)-C(14)-C(9)	121.8(2)
C(10)-C(11)-C(12)	120.3(2)	C(12)-O(15)-C(16)	117.6(2)
C(11)-C(12)-C(13)	119.8(2)		

Atomic Coordinates ($\times 10^4$) for Compound 111a.

Atom	x	y	z
S(1)	8588(1)	5244(1)	2188(1)
N(2)	7402(1)	5262(2)	2283(3)
C(3)	6840(2)	6097(2)	1493(3)
S(4)	7233(1)	7260(1)	272(1)
C(5)	8357(2)	7659(2)	1645(3)
C(6)	8962(2)	6779(2)	2417(3)
C(7)	8523(3)	9009(3)	1918(6)
C(8)	9934(2)	7000(4)	3630(5)
C(9)	5811(1)	6142(2)	1553(3)
C(10)	5457(2)	5287(2)	2532(3)
C(11)	4508(2)	5333(2)	2640(3)
C(12)	3885(2)	6225(2)	1765(3)
C(13)	4212(2)	7049(2)	751(3)
C(14)	5173(2)	6998(2)	659(3)
O(15)	2970(1)	6211(2)	1997(2)
C(16)	2309(2)	7113(3)	1137(5)

A.1.2 Crystallographic Data for:

3-Methylthio-6,7,8-trihydro[1,4]dithiepine[2,3-e]-1,4,2-dithiazine 130.

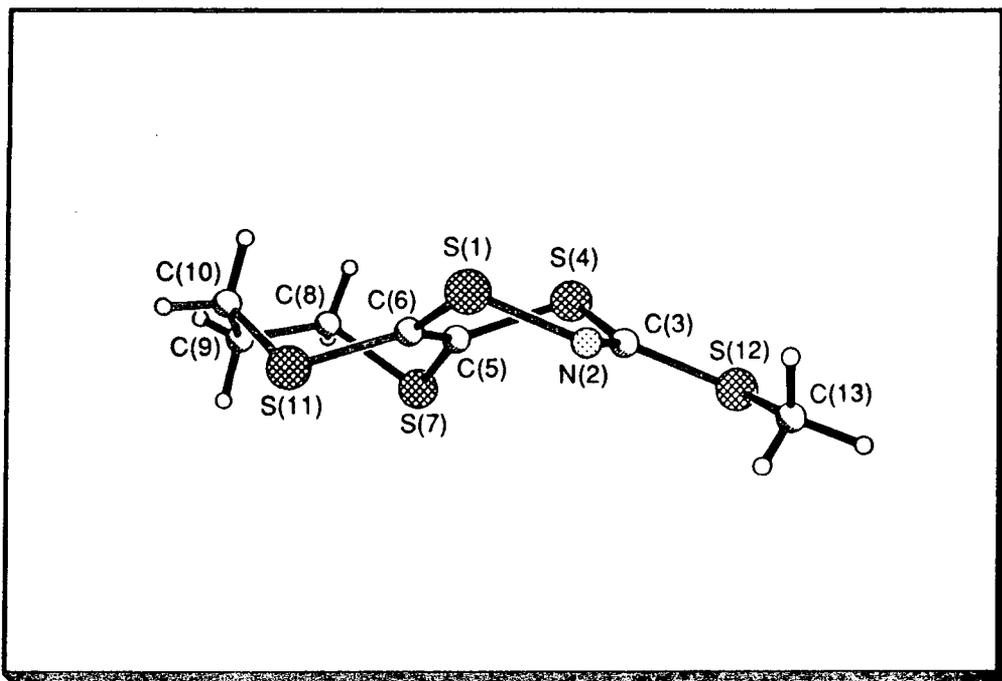


Figure 13. X-Ray Crystal Structure of Compound 130, Showing Atom Numbering.

Crystal Data for Compound 130.

Crystal system	monoclinic
Space group	$P2_1/c$
$a/\text{\AA}$	8.509(2)
$b/\text{\AA}$	8.540(2)
$c/\text{\AA}$	15.732(3)
$\beta/^\circ$	93.36(2)
$U/\text{\AA}^3$	1141.3(4)
Z	4
$D_c/\text{g cm}^{-3}$	1.56
Formula	$C_7H_9NS_5$
Crystal size/mm	0.3 x 0.5 x 0.5
M	267.5
$F(000)$	552

Data Collection for Compound 130.

$\mu(\text{MoK}\alpha)/\text{cm}^{-1}$	9.69
max. $2\theta(^{\circ})$	55
Unique reflections	2616
Reflections with $I > 2\sigma(I)$	2062
Absorption correction:	
Transmission factors, min., max.	0.2989/0.3297

Refinement Details for Compound 130.

No. of ψ -scans (reflections) used	360(10)
Refined parameters	154
R	0.039
$R_G = wR$	0.051
Goodness-of-fit	1.80
Weighting scheme, g^a	0.0003
Residual difference feature, max. (min.), $e/\text{\AA}^{-3}$	0.36 (-0.24)
^a [Weighting scheme $w^{-1} = \sigma^2(F) + gF^2$ was used].	

Additional Details for Compound 130.

Equipment, radiation, collection, solution and refinement details for compound **130** are identical to those described for compound **111a** (Section A.1.1). Additional material available from the Cambridge Crystallographic Data Centre comprises thermal parameters, hydrogen atom coordinates and all bond lengths and angles.

Selected Bond Lengths (\AA) for Compound 130.

S(1)-N(2)	1.707(2)	C(5)-S(7)	1.757(3)
N(2)-C(3)	1.265(3)	C(6)-S(11)	1.753(3)
C(3)-S(4)	1.784(3)	S(7)-C(8)	1.812(4)
S(4)-C(5)	1.767(3)	C(8)-C(9)	1.499(5)
C(5)-C(6)	1.352(4)	C(9)-C(10)	1.518(5)
C(6)-S(1)	1.749(3)	C(10)-S(11)	1.822(4)
C(3)-S(12)	1.748(3)	S(12)-C(13)	1.798(4)

Selected Bond Angles (°) for Compound 130.

N(2)-S(1)-C(6)	104.6(1)	C(6)-C(5)-S(7)	126.3(2)
S(1)-N(2)-C(3)	119.0(2)	C(5)-C(6)-S(11)	125.7(2)
N(2)-C(3)-S(4)	126.4(2)	S(1)-C(6)-S(11)	112.5(1)
C(3)-S(4)-C(5)	99.5(1)	C(5)-S(7)-C(8)	103.9(1)
S(4)-C(5)-C(6)	119.8(2)	S(7)-C(8)-C(9)	116.1(2)
S(1)-C(6)-C(5)	121.6(2)	C(8)-C(9)-C(10)	114.9(3)
N(2)-C(3)-S(12)	122.7(2)	C(9)-C(10)-S(11)	117.0(3)
S(4)-C(3)-S(12)	110.9(1)	C(10)-S(11)-C(6)	104.1(2)
S(4)-C(5)-S(7)	113.7(1)		

Atomic Coordinates (x 10⁴) for Compound 130.

Atom	x	y	z
S(1)	1519(1)	4083(1)	3087(1)
S(4)	1227(1)	6170(1)	1433(1)
S(7)	3775(1)	8269(1)	2086(1)
S(11)	3794(1)	6186(1)	3941(1)
S(12)	1554(1)	3351(1)	420(1)
N(2)	1626(3)	3240(3)	2108(1)
C(3)	1492(3)	4097(3)	1452(2)
C(5)	2534(3)	6692(3)	2301(2)
C(6)	2581(3)	5828(3)	3023(2)
C(8)	3304(4)	9734(4)	2864(3)
C(9)	4021(4)	9497(4)	3748(3)
C(10)	3300(5)	8178(5)	4242(2)
C(13)	1549(5)	1279(4)	625(3)

A.1.3 Crystallographic Data for:

5,6-Dihydro[1,4]dithiino[2,3-d]-1,2-dithiole-3-thione 237.

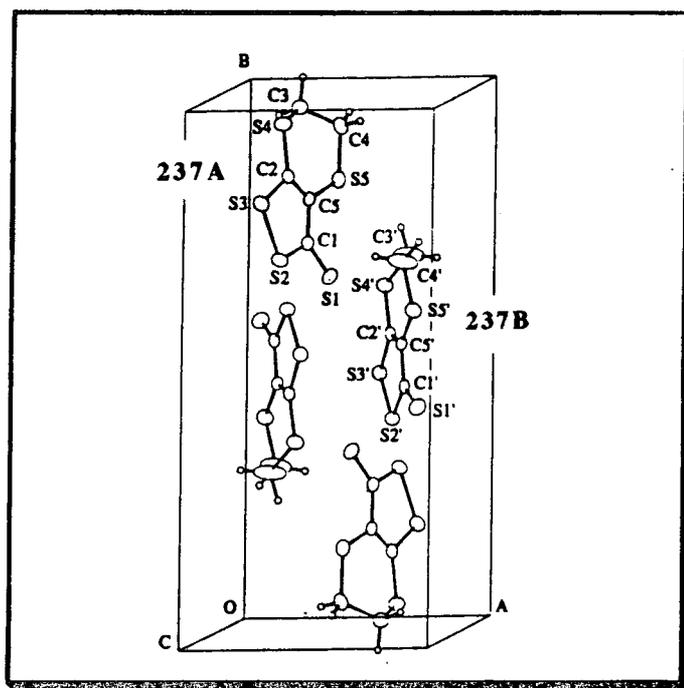


Figure 14. X-Ray Crystal Structure of Compound 237, Showing Atom Numbering.

Crystal Data for Compound 237.

Crystal system	monoclinic
Space group	$P2_1/a$
$a/\text{\AA}$	8.205(1)
$b/\text{\AA}$	17.610(4)
$c/\text{\AA}$	12.086(1)
$\beta/^\circ$	108.36(1)
$U/\text{\AA}^3$	1657.4
Z	8
$D_c/\text{g cm}^{-3}$	1.80
Formula	$C_5H_4S_5$
Crystal size/mm	0.28 x 0.14 x 0.10
M	224.42
$F(000)$	912

Data Collection for Compound 237.

$\mu(\text{MoK}\alpha)/\text{cm}^{-1}$	12.6
max. $2\theta(^{\circ})$	60
Unique reflections	4106
Observed reflections with $F_0 > 3\sigma F_0$	2479
Absorption correction:	
Transmission factors, min., max.	0.652/1.445

Refinement Details for Compound 237.

Number of parameters	182
Final R	0.046
Final R'	0.056
Parameter shift/e.s.d. (max.)	0.004
Weighting scheme	$w = 1 / [\alpha^2 (F_0) + 0.0005 (F_0)]$
Residual electron density, $e/\text{\AA}^{-3}$	-0.20 to 0.27

Additional Details for Compound 237.

X-Ray measurements for compound **237** were carried out at 300°K using Mo-K α radiation ($\lambda = 0.71069\text{\AA}$). The structure was solved by direct methods (SHELXS 86)¹³⁸ and refined by least-squares analysis¹³⁹ (anisotropic for non-hydrogens). The data were collected on an Enraf-Nonius FAST area detector diffractometer positioned at the window of a rotating anode generator. Full details of data collection and refinement, atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

Selected Bond Lengths (\AA) for Compound 237.

Conformer 237A		Conformer 237B	
C(1)-S(1)	1.662(6)	C(1')-S(1')	1.659(7)
S(3)-S(2)	2.047(4)	S(3')-S(2')	2.049(4)
C(1)-S(2)	1.731(7)	C(1')-S(2')	1.731(7)
C(2)-S(3)	1.736(6)	C(2')-S(3')	1.731(6)
C(2)-S(4)	1.728(6)	C(2')-S(4')	1.738(6)
C(3)-S(4)	1.824(7)	C(3')-S(4')	1.779(9)
C(4)-S(5)	1.786(7)	C(4')-S(5')	1.794(9)
C(5)-S(5)	1.753(6)	C(5')-S(5')	1.748(6)
C(5)-C(1)	1.423(7)	C(5')-C(1')	1.433(7)
C(5)-C(2)	1.369(6)	C(5')-C(2')	1.375(7)
C(4)-C(3)	1.511(8)	C(4')-C(3')	1.375(10)

Selected Bond Angles (°) for Compound 237.

Conformer 237A		Conformer 237B	
C(1)-S(2)-S(3)	97.0(3)	C(1')-S(2')-S(3')	97.5(3)
C(2)-S(3)-S(2)	94.1(3)	C(2')-S(3')-S(2')	93.9(3)
C(3)-S(4)-C(2)	100.9(3)	C(3')-S(4')-C(2')	100.8(4)
C(5)-S(5)-C(4)	102.9(3)	C(5')-S(5')-C(4')	102.4(4)
S(2)-C(1)-S(1)	119.1(4)	S(2')-C(1')-S(1')	119.9(4)
C(5)-C(1)-S(1)	126.9(4)	C(5')-C(1')-S(1')	126.4(5)
C(5)-C(1)-S(2)	114.0(4)	C(5')-C(1')-S(2')	113.7(4)
S(4)-C(2)-S(3)	113.1(3)	S(4')-C(2')-S(3')	113.2(4)
C(5)-C(2)-S(3)	117.6(4)	C(5')-C(2')-S(3')	118.1(4)
C(5)-C(2)-S(4)	129.3(4)	C(5')-C(2')-S(4')	128.7(5)
C(4)-C(3)-S(4)	113.5(4)	C(4')-C(3')-S(4')	120.8(7)
C(3)-C(4)-S(5)	114.7(4)	C(3')-C(4')-S(5')	120.3(7)
C(1)-C(5)-S(5)	115.6(4)	C(1')-C(5')-S(5')	116.0(4)
C(2)-C(5)-S(5)	127.1(4)	C(2')-C(5')-S(5')	127.2(4)
C(2)-C(5)-C(1)	117.3(5)	C(2')-C(5')-C(1')	116.8(5)

Selected Intermolecular Non-Bonded S...S Distances for Compound 237.

S(2')-S(1)	3.766	S(3')-S(1)	3.357
S(5')-S(1)	3.719	S(4')-S(2)	3.827
S(1')-S(2)	3.786	S(4')-S(3)	3.385
S(3')-S(4)	3.506	S(1')-S(3)	3.725
S(1')-S(4)	3.731	S(4')-S(4)	3.909
S(5')-S(5)	3.447	S(2')-S(5)	3.892

Fractional Atomic Coordinates for Compound 237.

Atom	x	y	z
S(1)	0.35729(16)	0.64169(8)	0.13530(13)
S(2)	0.09966(15)	0.66033(7)	-0.09379(12)
S(3)	0.00226(15)	0.76064(7)	-0.17288(11)
S(4)	0.10581(16)	0.91264(7)	-0.08992(12)
S(5)	0.39208(13)	0.82199(7)	0.15416(11)
S(1')	0.21880(16)	0.59062(8)	0.64547(12)
S(2')	0.26388(14)	0.59774(7)	0.41427(12)
S(3')	0.29265(14)	0.50770(7)	0.31459(11)
S(4')	0.29023(16)	0.34770(7)	0.36958(12)
S(5')	0.23803(16)	0.40992(7)	0.63308(11)
C(1)	0.24127(48)	0.69922(25)	0.03121(40)
C(2)	0.13556(47)	0.81642(24)	-0.06287(38)
C(3)	0.20937(56)	0.95129(27)	0.05533(46)
C(4)	0.38703(55)	0.91968(28)	0.11352(47)
C(5)	0.24510(45)	0.77998(23)	0.03149(37)
C(1')	0.24487(43)	0.54597(24)	0.53132(38)
C(2')	0.27625(44)	0.44045(24)	0.41505(37)
C(3')	0.21806(118)	0.29645(36)	0.47218(67)
C(4')	0.27284(105)	0.31583(37)	0.58832(62)
C(5')	0.25521(43)	0.46548(23)	0.51746(37)
H(3A)	0.13903(56)	0.93979(27)	0.10333(46)
H(3B)	0.21823(56)	1.00536(27)	0.04891(46)
H(4A)	0.45230(55)	0.92520(28)	0.06058(47)
H(4B)	0.43968(55)	0.94888(28)	0.18265(47)
H(3'A)	0.25083(118)	0.24448(36)	0.46785(67)
H(3'B)	0.09510(118)	0.30029(36)	0.44646(67)
H(4'A)	0.21714(105)	0.28167(37)	0.62685(62)
H(4'B)	0.39454(105)	0.30724(37)	0.61608(62)

APPENDIX 2

**RESEARCH COLLOQUIA, SEMINARS,
LECTURES AND CONFERENCES**

A.2.1 List of Research Colloquia, Seminars and Lectures.

There follows a list of research colloquia, seminars and lectures given by invited speakers during the period of the author's registration for postgraduate study at the University of Durham.

* Denotes presentations attended by the author.

Denotes speakers specifically invited for the postgraduate training programme.

A.2.1.1 Academic Year 1990-1991.

- 11.10.90 Dr. W. A. MacDonald (I.C.I. Wilton)
Materials for the Space Age.
- 24.10.90* Dr. M. Bochmann# (University of East Anglia)
Synthesis, Reactions and Catalytic Activity of Cationic Titanium Alkyls.
- 26.10.90* Prof. R. Soulen# (South Western University, Texas)
Preparation and Reactions of Bicycloalkenes.
- 31.10.90* Dr. R. Jackson# (University of Newcastle upon Tyne)
New Synthetic Methods: α -Amino Acids and Small Rings.
- 01.11.90* Dr. N. Logan (University of Nottingham)
Rocket Propellants.
- 06.11.90* Dr. P. Kocovsky# (University of Uppsala)
Stereo-Controlled Reactions Mediated by Transition and Non-Transition Metals.
- 07.11.90 Dr. D. Gerrard# (British Petroleum)
Raman Spectroscopy for Industrial Analysis.
- 08.11.90* Dr. S. K. Scott (University of Leeds)
Clocks, Oscillations and Chaos.

- 14.11.90* Prof. T. Bell# (S.U.N.Y., Stony Brook, New York)
Functional Molecular Architecture and Molecular Recognition.
- 21.11.90 Prof. J. Pritchard (Queen Mary and Westfield College, London)
Copper Surfaces and Catalysts.
- 28.11.90 Dr. B. J. Whitaker# (University of Leeds)
Two-Dimensional Velocity Imaging of State-Selected
Reaction Products.
- 29.11.90* Prof. D. Crout (University of Warwick)
Enzymes in Organic Synthesis.
- 05.12.90* Dr. P. G. Pringle# (University of Bristol)
Metal Complexes with Functionalised Phosphines.
- 13.12.90 Prof. A. H. Cowley (University of Texas)
New Organometallic Routes to Electronic Materials.
- 15.01.91 Dr. B. J. Alder (Lawrence Livermore Labs., California)
Hydrogen in all its Glory.
- 17.01.91 Dr. P. Sarre (University of Nottingham)
Comet Chemistry.
- 24.01.91 Dr. P. J. Sadler (Birkbeck College, London)
Design of Inorganic Drugs: Precious Metals, Hypertension and HIV.
- 30.01.91* Prof. E. Sinn# (University of Hull)
Coupling of Little Electrons in Big Molecules. Implications for the
Active Sites of Metalloproteins and other Macromolecules.
- 31.01.91 Dr. D. Lacey (University of Hull)
Liquid Crystals.
- 06.02.91* Dr. R. Bushby# (University of Leeds)
Biradicals and Organic Magnets.
- 14.02.91* Dr. M. C. Petty (University of Durham)
Molecular Electronics.
- 20.02.91 Prof. B. L. Shaw# (University of Leeds)
Syntheses with Coordinated, Unsaturated Phosphine Ligands.

- 28.02.91* Dr. J. Brown (University of Oxford)
Can Chemistry Provide Catalysts Superior to Enzymes?
- 06.03.91 Dr. C. M. Dobson[#] (University of Oxford)
NMR Studies of Dynamics in Molecular Crystals.
- 07.03.91 Dr. J. Markam (I.C.I. Pharmaceuticals)
DNA Fingerprinting.
- 07.03.91* Prof. K. Mullen (Max Planck Institute)
New Aromatic Compounds for Polymer Synthesis.
- 24.04.91 Prof. R. R. Schrock (Massachusetts Institute of Technology)
Metal-Ligand Multiple Bonds and Metathesis Initiators.
- 25.04.91 Prof. T. Hudlicky (Virginia Polytechnic Institute)
Biocatalysis and Symmetry Based Approaches to the Efficient
Synthesis of Complex Natural Products.
- 20.06.91 Prof. M. S. Brookhart (University of North Carolina)
Olefin Polymerisations, Oligomerisations and Dimerisations Using
Electrophilic Late Transition Metal Catalysts.
- 29.07.91 Dr. M. A. Brimble (Massey University, New Zealand)
Synthetic Studies Towards the Antibiotic Griseusin-A.
- A.2.1.2** Academic Year 1991-1992.
- 17.10.91* Dr. J. A. Salthouse (University of Manchester)
Son et Lumiere: A Demonstration Lecture.
- 31.10.91 Dr. R. Keeley (Metropolitan Police, Forensic Science Dept.)
Modern Forensic Science.
- 06.11.91 Prof. B. F. G. Johnson[#] (University of Edinburgh)
Cluster-Surface Analogies.
- 07.11.91 Dr. A. R. Butler (University of St. Andrews)
Traditional Chinese Herbal Drugs: a Different Way of Treating Disease.

- 13.11.91* Prof. D. Gani[#] (University of St. Andrews)
The Chemistry of PLP-Dependent Enzymes.
- 20.11.91 Dr. R. More O'Ferrall[#] (University College, Dublin)
Some Acid-Catalysed Rearrangements in Organic Chemistry.
- 28.11.91 Prof. I. M. Ward (University of Leeds, I.R.C.)
The SCI Lecture. Science and Technology of Orientated Polymers.
- 04.12.91* Prof. R. Grigg[#] (University of Leeds)
Palladium-Catalysed Cyclisation and Ion-Capture Processes.
- 05.12.91* Prof. A. L. Smith (formerly of Unilever)
Soap, Detergents and Black-Puddings.
- 11.12.91* Dr. W. D. Cooper[#] (Shell Research)
Colloid Science: Theory and Practice.
- 22.01.92 Dr. K. D. M. Harris[#] (University of St. Andrews)
Understanding the Properties of Solid Inclusion Compounds.
- 29.01.92* Dr. A. Holmes[#] (University of Cambridge)
Cycloaddition Reactions in the Service of the Synthesis of
Piperidine and Indolizidine Natural Products.
- 30.01.92* Dr. M. Anderson (Shell Research, Sittingbourne)
Recent Advances in the Safe and Selective Chemical Control
of Insect Pests.
- 12.02.92* Prof. D. E. Fenton[#] (University of Sheffield)
Polynuclear Complexes of Molecular Clefs as Models for
Copper Bio-sites.
- 13.02.92* Dr. J. Saunders (Glaxo Group Research Ltd.)
Molecular Modelling in Drug Discovery.
- 19.02.92* Prof. E. J. Thomas[#] (University of Manchester)
Applications of Organostannanes to Organic Synthesis.
- 20.02.92* Prof. E. Vogel (University of Cologne)
The Musgrave Lecture. Porphyrins: Molecules of
Interdisciplinary Interest.

- 25.02.92 Prof. J. F. Nixon (University of Sussex)
The Tilden Lecture. Phospha-Alkynes: New Building Blocks in Inorganic and Organometallic Chemistry.
- 26.02.92 Prof. M. L. Hitchman[#] (University of Strathclyde)
Chemical Vapour Deposition.
- 05.03.92 Dr. N. C. Billingham (University of Sussex)
Degradable Plastics - Myth or Magic?
- 11.03.92* Dr. S. E. Thomas[#] (Imperial College)
Recent Advances in Organoiron Chemistry.
- 12.03.92* Dr. R. A. Hann (I.C.I. Imagedata)
Electronic Photography - An Image of the Future.
- 18.03.92* Dr. H. Maskill[#] (University of Newcastle upon Tyne)
Concerted or Stepwise Fragmentation in a Deamination-Type Reaction.
- 07.04.92 Prof. D. M. Knight (University of Durham, Dept. of Philosophy)
Interpreting Experiments: the Beginning of Electrochemistry.
- 13.05.92* Dr. J.-C. Gehret (Ciba Geigy, Basel)
Some Aspects of Industrial Agrochemical Research.
- A.2.1.3** Academic Year 1992-1993.
- 15.10.92 Dr. M. Glazer and Dr. S. Tarling (U. of Oxford & Birkbeck College)
The Chemist's Role as an Expert Witness in Patent Litigation.
- 20.10.92 Dr. H. E. Bryndza (Dupont Central Research)
Synthesis, Reactions and Thermochemistry of Metal (Alkyl) Cyanide Complexes and Their Impact on Olefin Hydrocyanation Catalysis.
- 22.10.92 Prof. A. Davies (University College, London)
The Ingold-Albert Lecture. The Behaviour of Hydrogen as a Pseudometal.
- 28.10.92 Dr. J. K. Cockcroft (University of Durham)
Recent Developments in Powder Diffraction.

- 29.10.92 Dr. J. Emsley (Imperial College, London)
The Shocking History of Phosphorus.
- 04.11.92 Dr. T. P. Kee (University of Leeds)
Synthesis and Coordination Chemistry of Silylated Phosphites.
- 05.11.92* Dr. C. J. Ludman (University of Durham)
Explosions: A Demonstration Lecture.
- 11.11.92* Prof. D. Robins[#] (University of Glasgow)
Pyrrolizidine Alkaloids: Biological Activity, Biosynthesis and Benefits.
- 12.11.92 Prof. M. R. Truter (University College, London)
Luck and Logic in Host-Guest Chemistry.
- 18.11.92 Dr. R. Nix[#] (Queen Mary College, London)
Characterisation of Heterogeneous Catalysts.
- 25.11.92* Prof. Y. Vallée (University of Caen)
Reactive Thiocarbonyl Compounds.
- 25.11.92* Prof. L. D. Quin[#] (University of Massachusetts, Amherst)
Fragmentation of Phosphorus Heterocycles as a Route to Phosphoryl
Species with Uncommon Bonding.
- 26.11.92* Dr. D. Humber (Glaxo, Greenford)
AIDS - The Development of a Novel Series of HIV Inhibitors.
- 02.12.92 Prof. A. F. Hegarty (University College, Dublin)
Highly Reactive Enols Stabilised by Steric Protection.
- 02.12.92* Dr. R. A. Aitken[#] (University of St. Andrews)
The Versatile Cycloaddition Chemistry of $\text{Bu}_3\text{P} \cdot \text{CS}_2$.
- 03.12.92 Prof. P. Edwards (University of Birmingham)
The SCI Lecture. What is a Metal?
- 09.12.92 Dr. A. N. Burgess[#] (I.C.I. Runcorn)
The Structure of Perfluorinated Ionomer Membranes.
- 20.01.93 Dr. D. C. Clary[#] (University of Cambridge)
Energy Flow in Chemical Reactions.

- 21.01.93* Prof. L. Hall (University of Cambridge)
NMR - Window to the Human Body.
- 27.01.93* Dr. W. Kerr (University of Strathclyde)
Development of the Pauson-Khand Annulation Reaction: Organocobalt Mediated Synthesis of Natural and Unnatural Products.
- 28.01.93* Prof. J. Mann (University of Reading)
Murder, Magic and Medicine.
- 03.02.93* Prof. S. M. Roberts (University of Exeter)
Enzymes in Organic Synthesis.
- 10.02.93* Dr. D. Gillies# (University of Surrey)
NMR and Molecular Motion in Solution.
- 11.02.93* Prof. S. Knox (University of Bristol)
The Tilden Lecture. Organic Chemistry at Polynuclear Metal Centres.
- 17.02.93 Dr. R. W. Kemmitt# (University of Leicester)
Oxatrimethylenemethane Metal Complexes.
- 18.02.93 Dr. I. Fraser (I.C.I. Wilton)
Reactive Processing of Composite Materials.
- 22.02.93 Prof. D. M. Grant (University of Utah)
Single Crystals, Molecular Structure and Chemical-Shift Anisotropy.
- 24.02.93 Prof. C. J. M. Stirling# (University of Sheffield)
Chemistry on the Flat-Reactivity of Ordered Systems.
- 10.03.93 Dr. P. K. Baker (University College of North Wales, Bangor)
Chemistry of Highly Versatile 7-Coordinate Complexes.
- 11.03.93 Dr. R. A. Y. Jones (University of East Anglia)
The Chemistry of Wine Making.
- 17.03.93* Dr. R. J. K. Taylor# (University of East Anglia)
Adventures in Natural Product Synthesis.
- 24.03.93* Prof. I. O. Sutherland# (University of Liverpool)
Chromogenic Reagents for Cations.

- 13.05.93 Prof. J. A. Pople (Carnegie-Mellon University, Pittsburgh)
The Boys-Rahman Lecture. Applications of Molecular Orbital Theory.
- 21.05.93 Prof. L. Weber (University of Bielefeld)
Metallophospha-Alkenes as Synthons in Organometallic Chemistry.
- 24.05.93* Dr. A. Bader (Aldrich Chemical Co.)
The Adventures of a Chemist Collector.
- 24.05.93* Dr. A. Bader (Aldrich Chemical Co.)
Josef Loschmidt.
- 01.06.93 Prof. J. P. Konopelski (University of California, Santa Cruz)
Synthetic Adventures with Enantiomerically Pure Acetals.
- 02.06.93 Prof. F. Ciardelli (University of Pisa)
Chiral Discrimination in the Stereospecific Polymerisation
of Alpha Olefins.
- 07.06.93 Prof. R. S. Stein (University of Massachusetts)
Scattering Studies of Crystalline and Liquid Crystalline Polymers.
- 16.06.93 Prof. A. K. Covington (University of Newcastle upon Tyne)
Use of Ion Selective Electrodes as Detectors in Ion Chromatography.
- 17.06.93 Prof. O. F. Nielsen (University of Copenhagen)
Low-Frequency IR and Raman Studies of Hydrogen Bonded Liquids.

A.2.2 List of Conferences Attended.

There follows a list of conferences attended by the author during his period of registration for postgraduate study at the University of Durham.

- April 1991 Royal Society of Chemistry, Perkin Division.
One Day Meeting.
University of Leeds.

- April 1991 Royal Society of Chemistry.
150th Anniversary Annual Chemical Congress.
Imperial College, London.
- September 1991 Royal Society of Chemistry.
Autumn Meeting.
University of York.
- June 1992 15th International Symposium on the Organic Chemistry
of Sulfur (ISOCS 15).
University of Caen, France.
A poster was presented entitled: "Synthesis of Novel
Heterocycles of the Dithiazine Class by Ring Expansion
of Dithiolium Cations."
- December 1992 26th Annual Stereochemical Symposium.
University of Sheffield.
- January 1993 I.C.I. Medicinal Chemistry Workshop.
Macclesfield.
- April 1993 North East Chemistry Graduate Symposium.
University of Newcastle upon Tyne.
An oral presentation was delivered entitled: "Preparation and
Reactions of 1,4,2-Dithiazines and Related Heterocycles."
- June 1993 Science & Engineering Research Council.
Graduate School (C.R.A.C.).
University of Stirling.
- July 1993 Royal Society of Chemistry, Perkin Division.
8th Postgraduate Heterocyclic Symposium.
University of Birmingham.
An oral presentation was delivered entitled: "Synthesis and
Reactions of Dithiazines and Related Heterocyclic Systems."

APPENDIX 3

PUBLICATIONS

Some of the work described in this thesis has been published as follows:

1. M. R. Bryce, G. R. Davison, J. A. K. Howard and A. S. Batsanov,
J. Chem. Soc., Chem. Commun., 1992, 478.
Synthesis and Redox Properties of Substituted 1,4,2-Dithiazines: X-Ray Crystal Structure of 3-(4-Methoxyphenyl)-5,6-dimethyl-1,4,2-dithiazine.
2. M. R. Bryce, G. R. Davison, A. S. Batsanov and J. A. K. Howard,
J. Chem. Soc., Perkin Trans. 1, 1992, 2295.
Substituted 1,4,2-Dithiazines: Synthesis by Ring Expansion of 1,3-Dithiolium Cations, Solution Redox Properties and X-Ray Crystal Structures of a Monocyclic and a Bicyclic Derivative.
3. M. R. Bryce, G. R. Davison, A. J. Moore, M. B. Hursthouse and K. M. A. Malik,
Tetrahedron, 1992, **48**, 8143.
Synthetic, Structural and Electrochemical Studies on the 1,2-Dithiole-3-thione System: Preparation and Reactions of the 5,6-Dihydro-1,2-dithiolo[4,5-b][1,4]dithiin-3-ium Cation.

