STUDIES OF NEW TYPES OF

1,6,6aλ^4-TRIHETERAPENTALENES

being a Thesis

presented by

Robin Hamish Nicol

to the

University of St Andrews

in application for

THE DEGREE OF DOCTOR OF PHILOSOPHY

DECLARATION

I declare that this thesis is based on the results of experiments carried out by me, that it is of my own composition, and that it has not been submitted previously in application for a higher degree.

November 1983 Robin H. Nicol

CERTIFICATE

I hereby certify that Robin Hamish Nicol, B.Sc., has spent eleven terms at research work under by supervision, has fulfilled the conditions of the Resolution of the University Court, 1967 No 1, and is qualified to submit the accompanying thesis in application for the Degree of Doctor of Philosophy.

Director of Research

UNIVERSITY CAREER

I entered the University of St Andrews in October 1976, and subsequently graduated with Upper Second Class Honours in Chemistry in July 1980.

In October 1980 I was awarded a Research Studentship by the Science Research Council, and from then until July 1983 I carried out the work which is embodied in this thesis. This work was undertaken in the Department of Chemistry, University of St Andrews, under the supervision of Professor D.H. Reid.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to Professor D.H. Reid for his advice, guidance and continued interest in my work.

I would like to thank Professor Lord Tedder and Professor Wyatt for making available the laboratory facilities in the Department of Chemistry, University of St Andrews, and to the technical staff for their invaluable assistance.

Thanks are also due to Miss C. Finlay, Mr I. Nairn and Miss J. Rhodes for their help in preparing the type-script of this thesis.

Finally, I should like to thank the Science Research Council for the award of a Research Studentship.

EXPLANATORY NOTE

This thesis is divided into three sections Parts A, B and C. Each part is divided into a number of principal sections each prefixed by an Arabic numeral.

Part A consists of a review of the relevant background literature.

Part B consists of a discussion of the results obtained.

Part C consists of the experimental details of the results discussed in Part B, and is complementary to Part B.

Where reference is made to the chemical literature, this is indicated by a number in superscript, a key to which can be found at the end of this thesis. The structural formulae which have been reproduced for illustrative purposes have been assigned Arabic numerals, which correspond to those which have been assigned to the relevant compounds in the text. The structure keys to Parts A and B are distinct. The structure key to Part C is the same as that for Part B.

SUMMARY

The main aim of the project was to study new types of 1,6,6a λ^4- triheterapentalenes.

Attempted syntheses of 4,5-dihydro- 3,4-dimethyl- 5-methylimino- 1,2,4- thiadiazole (1) from 5- amino-3-methyl- 1,2,4-thiadiazole and 5-chloro- 3- methyl- 1,2,4-thiadiazole proved unsuccessful. Methylation of 5-chloro- 3-methyl- 1,2,4-thiadiazole with methyl fluorosulphonate followed by reaction with ethanolic methylamine solution gave 2,5-dihydro- 2,3-dimethyl- 5-methylimino- 1,2,4-thiadiazole (2) as the major product.

5-Amino- 1,2,4-thiadiazole, 5-amino- 3-methyl- 1,2,4-thiadiazole and 5-amino- 3-phenyl- 1,2,4-thiadiazole reacted with 1,3-dibromopropane in dimethylformamide solution to give salts (3) which, on deprotonation, afforded 5,6-dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (4), 5,6-dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (5) and 5,6-dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (6). The reactions of 5,6-dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (4) and 5,6-dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (5) with nitriles were investigated as a possible synthetic route to new types of 1,3,4,6-tetraaza- 6aλ^4-thiapentalenes (7). In general these reactions resulted in the replacement of hydrogen cyanide or acetonitrile from compounds (4) and (5) respectively, by the reactant nitrile. Some reactions of nitriles with 5,6-dihydro- 3-methyl-

4H-pyrimido [1,2-d] [1,2,4] thiadiazole (5) which did not proceed in this manner are discussed.

Thermolysis reactions of 5,6-dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazoles in various solvents were investigated. 5,6-Dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (5) decomposed in boiling tetralin (1,2,3,4-tetrahydronaphthalene) to give hexahydropyrimidine- 2-thione (8), but did not decompose in boiling toluene. 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (4) and 5,6-dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (6) also decomposed in boiling tetralin to give hexahydropyrimidine- 2-thione (8). In boiling toluene, 5,6-dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (4) decomposed to give a product formulated as the thione (9).

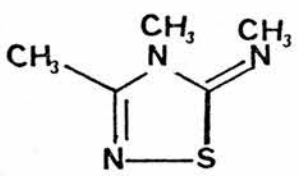
Two possible mechanisms for the reactions of 5,6-dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (5) with nitriles are discussed. Although absolutely conclusive differentiation between them is not possible on the basis of the available data it seems most probable with reference to the thermolysis behaviour of compound (5) that reactions with nitriles are bimolecular in nature, and involve a triheterapentalene intermediate (Scheme 1).

5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazoles formed 1:1 adducts (10) with the heterocumulenes carbon disulphide, carbon diselenide, methyl isothiocyanate, phenyl isothiocyanate, and phenyl isocyanate. The structures of these adducts are discussed in the light of their low solubility in organic solvents, their ^{1}H nmr and mass spectra, and the X-ray

crystal structure data of the phenyl isothiocyanate adduct of compound (5).

The thermolysis reactions of the heterocumulene adducts were studied. The carbon disulphide adducts fragmented to give the starting materials and some 5,6-dihydro- 4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)-thione (11). The carbon diselenide adduct of 5,6-dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (5) broke down in boiling toluene to give, in good yield, 5,6-dihydro-4 H-pyrimido [2,1-c] [2,1,4] thiaselenazole-3 (3H)-selenone (12).

An alternative synthesis of 5,6-dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazoles, of limited applicability, has been developed, involving the reaction of nitriles with the dithiazole-3-thione (11) (Scheme 2).



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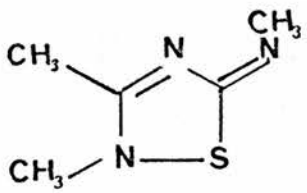

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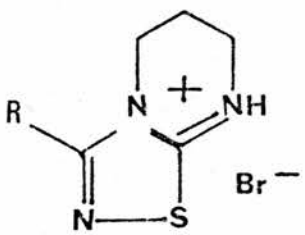
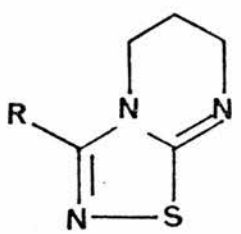
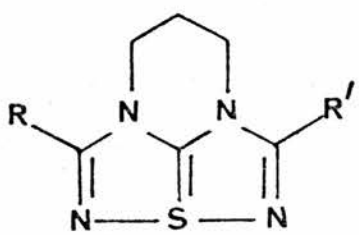


(3; R=H, Me, Ph)



(4; R=H)
(5; R=Me)
(6; R=Ph)



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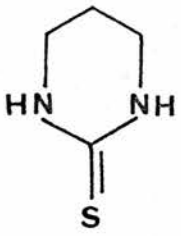

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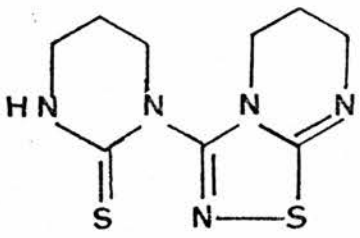

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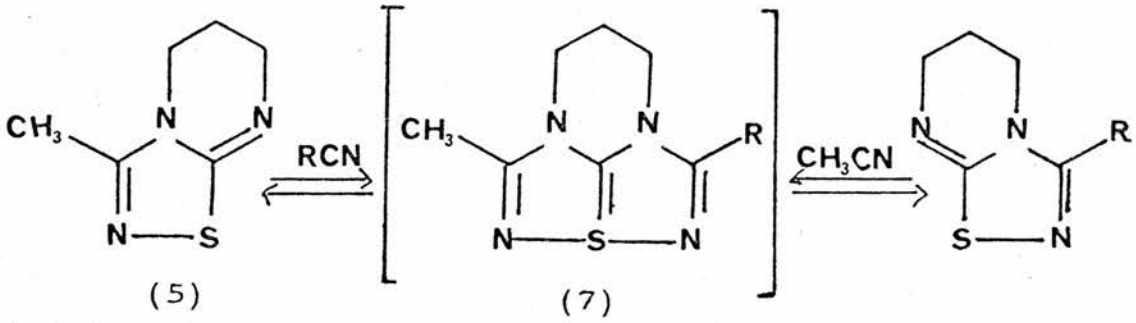

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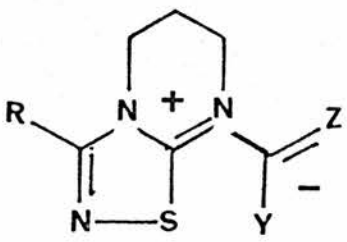
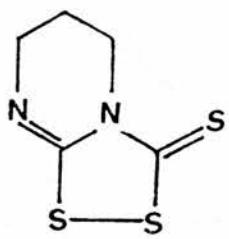
Scheme 1



(10)
Z = O, S, Se
Y = S, Se, NR



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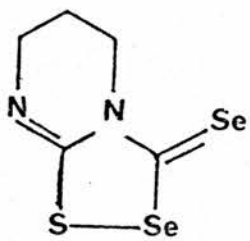

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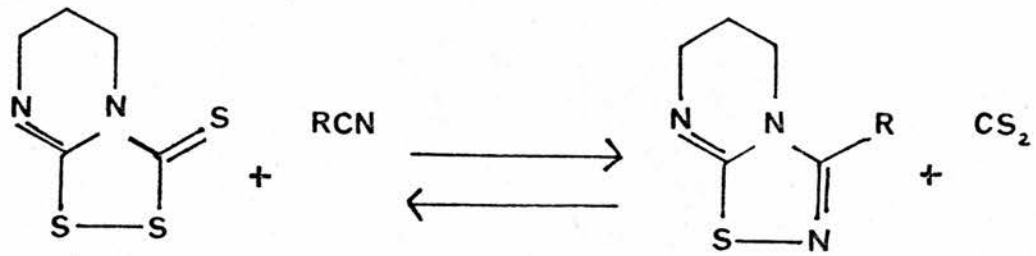


(11)

Scheme 2

CONTENTS

Part A

INTRODUCTION

Introduction

A large part of the work described in this thesis was concerned with the synthesis of new types of triheterapentalene structure, and it is the object of this section to review the literature relevant to that work. Reviews of the chemistry of triheterapentalenes have been written by Lozac'h[87], Klingsberg[88], Reid[89], Beer[86,90,91], Laever[92], Davis[93] and Pedersen[137].

1 Structure and Bonding in 1,6,6aλ^4 - Triheterapentalenes.

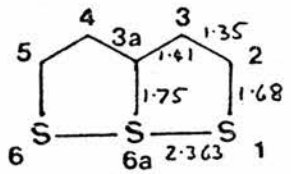
(a) Structural Studies of 1,6,6aλ^4 - Triheterapentalenes.

(1) X-Ray crystallography *

X-ray crystallography has played an important part in the elucidation of triheterapentalene structure in the solid state. From a comparison of the interatomic distances found in triheterapentalenes with bond length information already in the literature, it has been possible to determine whether there is a significant bonding interaction between two adjacent atoms and also what bond order exists between those atoms.

An X-ray crystal structure determination of 1,6,6aλ^4 - trithiapentalene (1)[22] showed that the molecule was planar, possessed C_{2v} symmetry, and that the three sulphur atoms were collinear. The S-S bond distances (2.363 Å) are approximately 10% longer than the average distance found for a two-electron covalent, S-S bond (2.10 Å)[23], but considerably shorter than the sum of the Van der Waal's radii of two sulphur atoms (3.70 Å)[24]. This indicates that there is an equal bonding interaction between S(6a)-S(6), and S(6a)-S(1). The C(2)-S(1) and C(5)-S(6) (1.68 Å), and C(3a)-S(6a)

* In this section some bonds have been omitted from diagrams for clarity.



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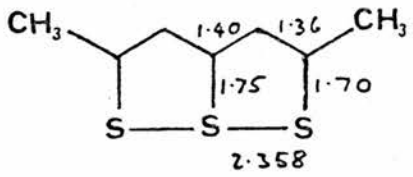
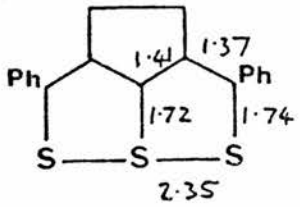


(2)

(1.75 Å) bond distances are shorter than the carbon-sulphur single bond length (1.81 Å)[24] but greater than the carbon-sulphur double bond length (1.61 Å)[24] suggesting bond orders greater than unity. The bonding in 1,6,6aλ^4 - triheterapentalenes involves a delocalised 10π -electron system (see later) and hence the bond lengths in the remainder of the carbon skeleton are very similar to those found in naphthalene[25], which possesses an analogous 10 π-electron system. Symmetrical arrangements of bond lengths were also found for the symmetrically substituted 1,6,6a λ^4 -trithiapentalenes (2)[26,27,28], (3)[29] and (4)[30]. However compounds



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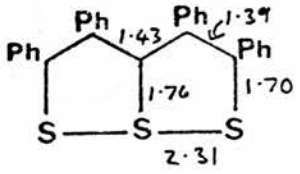

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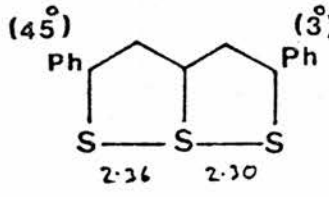
(5)[31], (6)[32] and (7)[33] have unequal S-S bond distances, due to intermolecular effects within the crystal lattice.



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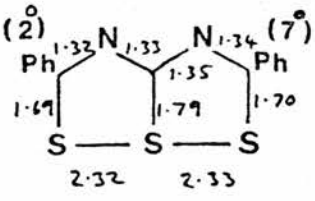

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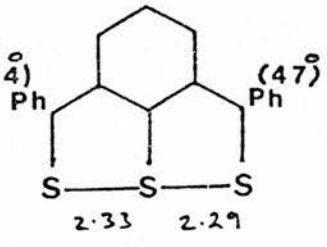
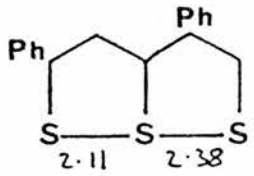


(7)

In trithiapentalene (5), the phenyl groups are twisted at angles of 45^{o} and 3^{o} to the plane of the molecule, presumably due to weak intermolecular interactions. The aza analogue (6) is also unsymmetrical, again probably as a result of intermolecular forces involving the phenyl groups. The S-S bond distances (2.32 Å, 2.33 Å) are similar to those of the corresponding trithiapentalene (5) (2.36 Å, 2.30 Å), and the C-N bond distances (1.32, 1.33, 1.35 and 1.34 Å) are similar to the C-N bond distances found in pyridine (1.34 Å)[34]. Therefore it may be assumed that compound (6) is bicyclic.

The inequality of the S-S distances in compound (7) is probably due to both intramolecular steric hindrance and intermolecular forces in the crystal lattice.

Generally, unsymmetrically substituted triheterapentalenes have unequal bond lengths eg compounds (8)[35], (9)[36] and (10)[37]. This shows that the S-S bond distances are particularly sensitive to



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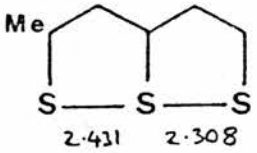

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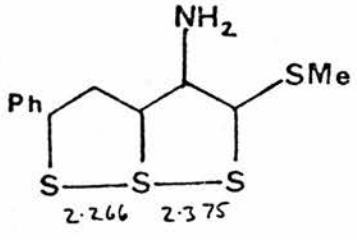


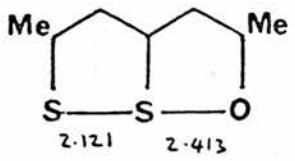
(10)

intramolecular perturbation such as substitution. However it is noteworthy that although individual S-S bond distances may vary by as much as 0.4 Å, the sum of the S(1)-S(6a) and S(6a)-S(6)

bond distances remains fairly constant at ca 4.7 Å, steric effects notwithstanding.

X-ray structure determinations carried out on oxygen, selenium and nitrogen analogues of 1,6,6aλ^4-trithiapentalenes have confirmed the planar, bicyclic structure of these compounds.

Replacement of sulphur by oxygen in the three-centre bonded sequences [eg (11)][38] leads to a stronger S-S interaction than in the corresponding trithiapentalene (2), and a weak S-O interaction; although this type of compound may still be regarded as bicyclic as the S-O distance (2.41 Å) is considerably less than the sum of the Van der Waal's radii (3.25 Å). Compound (12)[39] illustrates the generality of the



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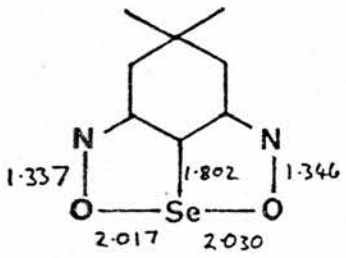
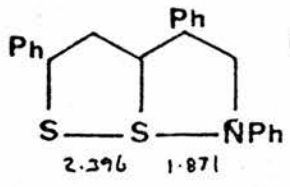


(12)

bonding in triheterapentalenes in that compounds containing oxygen atoms at positions 1 and 6 and a selenium atom at position (6a) may also be regarded as bicyclic. Replacement of one or both of the lateral atoms in a trithiapentalene by nitrogen has a marked effect on the bond lengths in the three-centre bond eg compounds (13)[40], (14)[41] and (15)[42].



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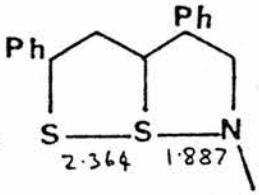

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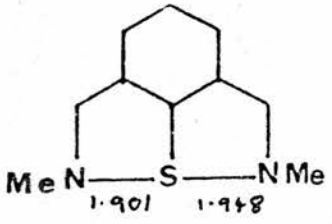
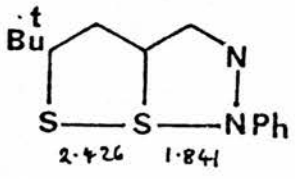


(15)

3-Quinolinyl

In the planar 6,6aλ^4 -dithia-1-azapentalene (13), the S-S-N sequence was found to be almost linear with an S-N bond length of 1.871 Å, which should be contrasted with the two-electron, covalent S-N bond distance of 1.74 Å[24] and the sum of the Van der Waal's radii for sulphur and nitrogen, 3.35 Å[24]. The S-S and S-N bond distances in (14) show how substituents on the N(1) atom can affect the bonding interactions in the S-S-N sequence. In compound (15) there is a slight departure from C_{2V} symmetry, probably due to strain caused by the trimethylene bridge and intermolecular crystal interactions. The average S-N bond length of 1.925 Å in compound (15) is approximately 10% greater than a normal S-N covalent bond length (1.74 Å)[24], indicating that the S-N bond order is similar to the S-S bond order found in trithiapentalenes.

From studies of the bond lengths in the 6,6a-dithia-1,2-diazapentalenes (16)[43] and (17)[44] these compounds can be seen to have similar S-S and S-N bond distances to the corresponding bonds in compounds (13) and (14), and therefore can be regarded as bicyclic structures. The effect of ring substituents on the S-S and S-N bond distances is apparent.



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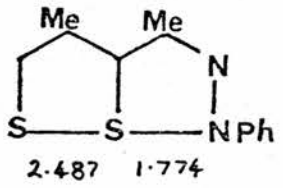
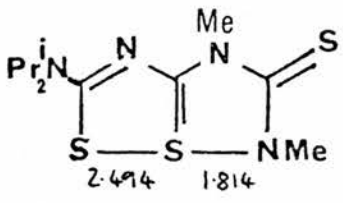
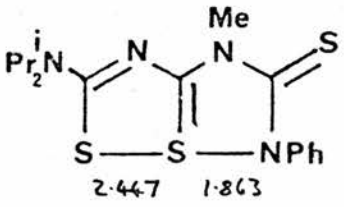


(17)

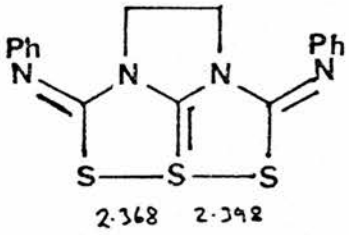
Recent X-ray crystal structure determinations have shown that the aza triheterapentalenes (18)[45], (19)[46] and (20)[47] can also be regarded as bicyclic. The S-S bond distances in compounds (18) and (19) are 2.494 Å and 2.447 Å respectively and, the S-N bond distances 1.814 Å and 1.863 Å respectively. These values should be compared with the corresponding values for the bond distances in compounds (13), (14), (16) and (17). The average S-S bond distance (2.385 Å) in compound (20) is similar to that found in trithiapentalenes eg compounds (1), (2) and (3). These compounds are of interest because they are



(18)



(19)



(20)

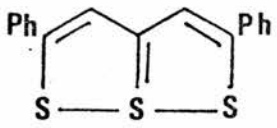
examples of triheterapentalenes containing exocyclic double bonds. The asymmetry of compound (20) is probably due to intermolecular strain induced by the dimethylene bridge.

A summary of the crystal structure data of many other triheterapentalenes has been published by Hordvik[48].

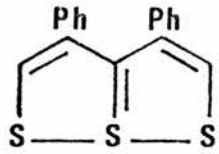
(2) NMR Spectroscopy

The ^1H nmr spectra of all symmetrically substituted 1,6,6a λ^4-triheterapentalenes[49,50] show that there is magnetic equivalence of the ring protons (or substituents) at C(2) and C(5), and at C(3) and C(4), indicating that these compounds have real or time-averaged C_{2V} symmetry in solution. 2,5-Diphenyl-1,6,6a λ^4-trithiapentalene (5)[49] and the 3,4-diphenyl isomer

(21)[51] show this symmetry in solution even though they have unequal S-S bond lengths in the solid state. The triheterapentalenes (22[52], 23[53] and 24[54]) also

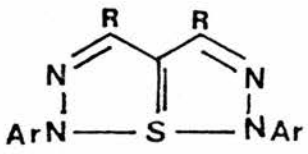


(5)

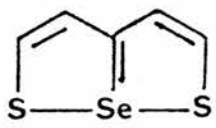


(21)

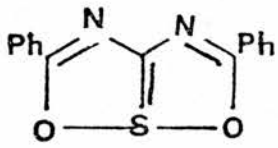
show real or time-averaged C_{2V} symmetry in solution. This symmetry probably results from intermolecular forces being averaged out in solution.



(22)

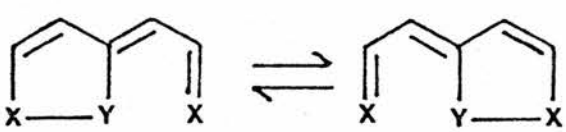


(23)



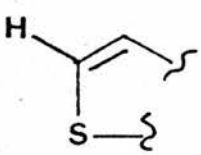
(24)

This observed equivalence could however arise from two rapidly interconverting valence tautomers (25a) and (25b), this interconversion results in time-averaged C_{2V} symmetry[55]. The ^1H nmr spectra of several compounds were studied at temperatures down to -60 °C[56-58], with no observed departure from C_{2V} symmetry. This would tend to suggest a symmetrical bonding pattern in the molecules but cannot be taken as conclusive evidence as the interconversion (25a)⇌(25b) may still be fast on the nmr time scale at -60 °C.

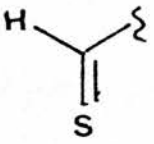


(25a) (25b)

Reid and co-workers[50] have compared the chemical shift of the 2-H protons in 1,6,6aλ^4-trithiapentalenes with the chemical shift of the thioformyl proton in stable heterocyclic thioaldehydes[59,60]. The thioformyl proton is normally in the region δ 10.4-11.2 and even when the thioformyl group is polarised in the sense $=CHS^-$ it does not resonate at higher field than δ10.2. The chemical shift found for the 2-H protons in trithiapentalenes is generally in the region δ 8.5-9.4, suggesting a environment (26a) rather than (26b). However this cannot be taken as conclusive as the resonance at δ 8.5-9.4 could be the average of two signals.



(26a)



(26b)

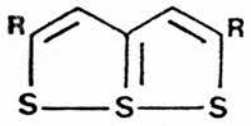
The chemical shift values observed for the ring protons in triheterapentalenes suggest the presence of a ring current due to π-electron delocalisation. The deshielding increases from oxa[61] to aza[62] to thia[63] analogues. From the ^{1}H nmr data Lozac'h[63] has estimated that the ring current in 2,5-dimethyl-1,6,6a λ^4-trithiapentalene (2) is about 65% of that in naphthalene.

^{13}C nmr studies tend to support the idea that symmetrically substituted trithiapentalenes have C_{2V} symmetry in solution [64,65] as carbons (2) and (5), and (3) and (4) are found to be equivalent. Here again however, this equivalence could be due to

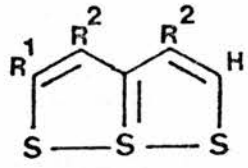
the time-averaging of two signals.

(3) Miscellaneous Spectroscopic Techniques

Clark and co-workers[66,67] have studied trithiapentalenes in the solid state using X-ray photoelectron spectroscopy to measure the sulphur (2s and 2p) molecular core binding energies. The results obtained for the trithiapentalenes (1) and (2) indicate that there are



(1;R=H)
(2;R=Me)

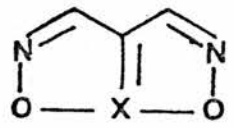


(9; R^1=Me, R^2=H)
(21; R^1=H, R^2=Ph)

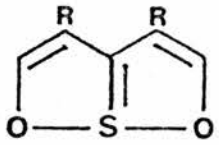
two types of sulphur present in each compound in a ratio of 2:1. Therefore these compounds possess symmetrical structures. On the other hand the sulphur core binding energies for compounds (9) and (21) showed the presence of three types of sulphur, and therefore these compounds have an unsymmetrical structure. These results agree with the X-ray crystallographic data for compounds (1,2,9 and 21). The results of a similar investigation by Lindberg[68] suggests that 2,5-dimethyl- 1,6,6aλ^4- trithiapentalene (2) has an unsymmetrical structure. This discrepancy is due to broad lines in the ESCA which could not be fully resolved. A more recent study on (2)[140] showed a symmetrical, bicyclic structure.

Gas-phase p.e. spectra of the 1,6-dioxa-6aλ^4-thia-2,5-diazapentalene (27) and its selenium and tellurium analogues (28 and 29) have been studied[69]. These showed that the

molecules have C_{2V} symmetry.



(28; X=S)
(29; X=Se)
(30; X=Te)



(31a; R=H)
(31b; R=D)

From rotational transitions observed in various vibrational states in the microwave spectra of 1,6-dioxa-6aλ^4-thiapentalene (31a) and its 3,4-dideuterio derivative (31b) several modes of vibration of the molecules have been assigned[70]. The results were consistent with the molecules having C_{2V} symmetry.

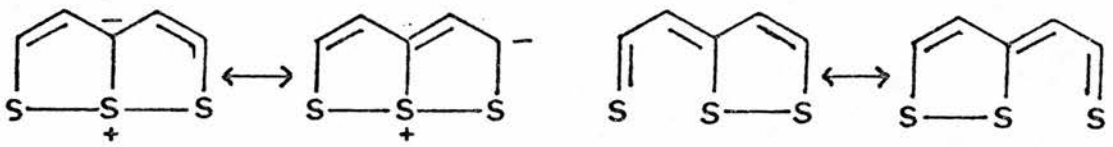
Infra-red and ultra-violet spectroscopy are of little general value in determining the structure of triheterapentalenes.

(b) Theories of Bonding in 1,6,6aλ^4-Triheterapentalenes.

For a theory of the bonding in 1,6,6a λ^4-triheterapentalenes to be successful it must explain the unique features of these molecules such as their planarity, the tendency towards collinearity of the three heteroatoms, and the distances between adjacent heteroatoms that indicate a bond-order of less than unity.

Various theories have been proposed to account for the bonding in such structures. They have succeeded in varying degrees. One early explanation described the 1,6,6a λ^4-trithiapentalenes as having the sulphonium ylid structure (32a)[71]. However, charge delocalisation of this structure would

give (32b), implying that electrophilic attack should occur at position 2. This is in conflict with the observed attack of electrophiles at position 3[72,73]. Another theory described 1,6,6a λ^4-trithiapentalenes as having "single bond - no bond resonance" between structures (33a) and (33b)[74-76].

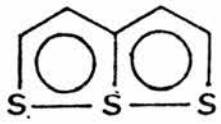


(32a) (32b) (33a) (33b)

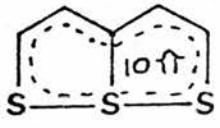
Other proposals required the central heteroatom to undergo valence shall expansion allowing its d-orbitals to participate in π-bonding[77,78]. Early Extended Huckel Calculations indicated that d-orbital utilization was required for the closest correlation with experimental results. However more recent calculations[67,79] using ab inito and CNDO methods suggest that d-orbital participation on the central sulphur atom of trithiapentalenes, and in other triheterapentalenes, is not important.

The present, generally accepted theory of bonding in trithiapentalenes describes the three sulphur atoms being held together by a four-electron three-centre bond with superimposed π-bonding[80] over the two rings. Three atomic p-orbitals, one from each of the sulphur atoms, are combined to form three molecular orbitals; one bonding, one non-bonding and one antibonding. The electron density of the fully occupied bonding molecular orbital is spread over all three sulphurs, while the non-bonding orbital, which is also doubly occupied, has its

charge localised mainly on the lateral atoms. The antibonding molecular orbital is vacant. Thus the three sulphur atoms are in effect held together by only one filled bonding molecular orbital which is consistent with the unusually long S-S bond lengths observed. Superimposed on this sigma bond skeleton is a delocalised 10π-electron system. Each carbon atom and the central sulphur atom donate one electron and the two lateral sulphur atoms each contribute a pair of electrons to the π-system. The stabalisation gained by the whole structure from this π-bonding is not expected to be large as the equilibrium distance for the three-centre bond is attained when p_π-p_π overlap is still small. Thus 1,6,6a λ^4-trithiapentalenes can be formulated as (34a or b).



(34a)



(34b)

The concept of electron-rich three-centre bonding is familiar in inorganic chemistry to describe the bonding in the polyhalide ions eg I_3^- [81,82], Br_3^- [141,141] and other hypervalent species eg XeF_2 [143], and in organic chemistry to describe the transition state for S_N2 displacement at a saturated carbon atom[83]. In the linear triiodide ion the bond lengths (2.90-2.93 Å). are approximately 9% longer than I-I distance found in molecular iodine[81,82]. A similar degree of bond elongation (10%) is observed between the sulphur atoms in trithiapentalenes and normal covalent S-S distances. Four-electron three-centre

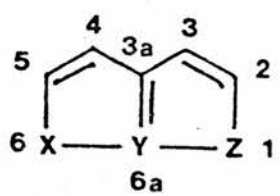
bonding may be used to describe the bonding in all triheterapentalenes synthesised to date.

So far there are no reports of the isolation of a triheterapentalene with C_{2V} symmetry where the central atom is a first-row element (eg oxygen or nitrogen). This does not necessarily mean that participation of empty d orbitals is essential in the three centre bond. That no such systems have been isolated could be due to the fact that the overlap provided by 2p orbitals of the central atoms is not sufficient for a stabilisation of the three-centre bond.

(c) Variations of the 1,6,6a λ^4-Triheterapentalene Structure.

1,6,6a λ^4-Triheterapentalenes comprise a large number of compounds based on structure (35), in which X and Z are heteroatoms of Groups V and VI (eg O, S, Se, NR) and Y is a second or lower-row element of Group VI (S, Se, Te). Aza analogues of (35) are known in which one or more ring carbon atoms are replaced by nitrogen atoms. Triheterapentalenes containing as many as 5 nitrogen atoms have been synthesised.

X-Ray crystallography has shown the generality of the trithiapentalene structure and that triheterapentalenes (35) are also planar, with heteroatoms X, Y and Z approximately collinear. There is some degree of bonding between the three heteroatoms, namely four-electron three-centre bonding in which Y contributes 2 electrons to the bond, and X and Z each donate one electron. Y is regarded as

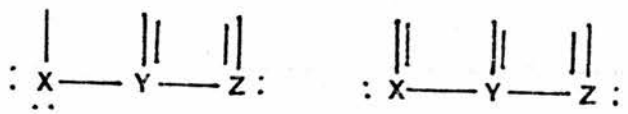


(35)

Y= S, Se, Te
X, Z= O, S, Se, NR

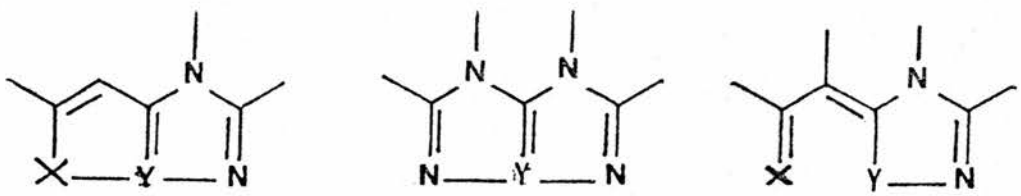
having a singly occupied P_Z orbital, and X and Z as having a doubly occupied P_Z orbital available for p_π-p_π conjugative interaction with neighbouring ring atoms (cf thiophene and pyrrole). The carbon atoms denote one electron each, thus forming a delocalised 10 -electron system over the two rings.

Variations of the triheterapentalene structure may be formulated which contain the three-centre bonded elements (36) and (37).



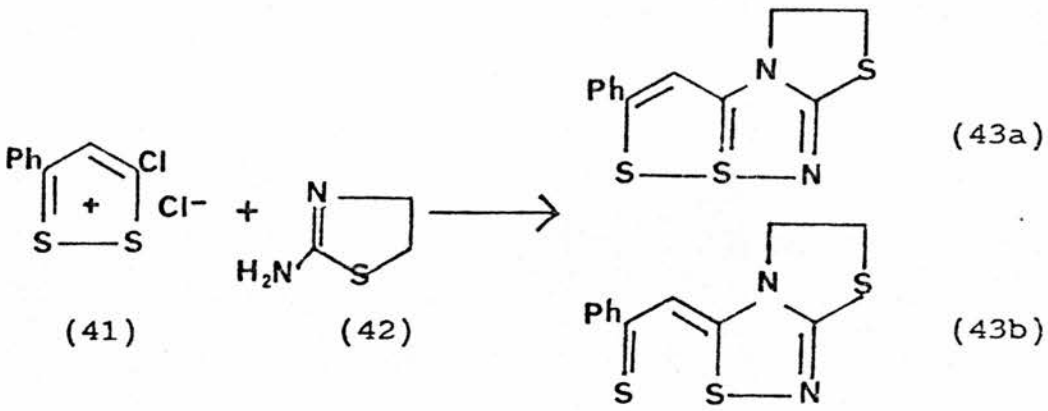
(36) (37)

In (36) Y and Z may be regarded as possessing singly occupied P_Z orbitals. In (37) X, Y and Z may be considered to have singly occupied P_Z orbitals available for π-bonding. Thus if in (36) Z=N, and in (37) X and Z = N, these triheterapentalenes would be novel in that the three-centre bonded sequence would contain pyridine type nitrogen atoms. For the triheterapentalene system as a whole to continue to have a delocalised 10π-electron system in structures (36) and (37), atoms capable of donating two electrons to the π-system are required at position (3) in (36), and at positions (3) and (4) in (37); eg structures (38) and (39).



(38) (39) (40)

Compounds with structure (38) may also be formulated as the monocyclic species (40). Distinction between structures (38) and (40) has required the use of X-ray crystallography in some cases. For example, Mitchell and Reid[84] obtained a yellow product and, in low yield, an orange product (43), from the reaction of 3-chloro-5-phenyl-1,2- dithiolylium chloride (41) with 2-amino-Δ^2-thiazoline (42). This product could be represented either by structure (43a) (*cf* 38) or (43b) (*cf* 40).

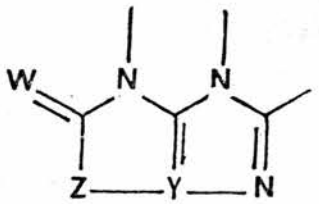


(41) (42) (43a) (43b)

An X-ray crystallographic structure determination[85] showed that the product has the open structure (43b).

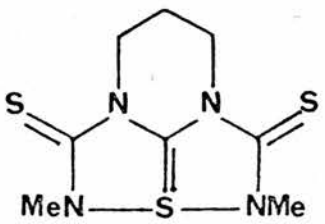
No authentic examples of compounds containing elements (36 or 37) have been reported hitherto, although it has been suggested that compounds containing these units are intermediates in several reactions.

Structure (44), of type (36), containing an exocyclic double bond, shows another possible variation of the basic triheterapentalene structure.

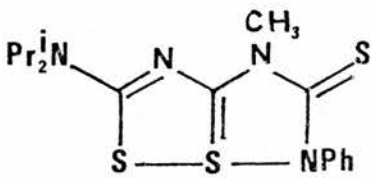


(44)

Several other examples of triheterapentalenes containing exocyclic double bonds are known, eg compounds (45)[2] and (19)[46].

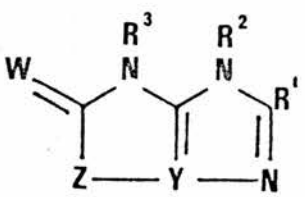


(45)



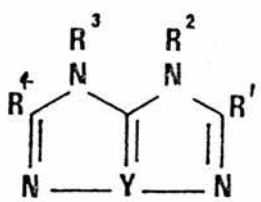
(19)

These compounds have been described as derivatives of hypothetical tetrahydro- and dihydro- 1,6,6a λ^4-triheterapentalenes[86]. One of the aims of the work described in this thesis was to devise syntheses of the new triheterapentalene types (39) and (44), containing pyridine-type nitrogen atoms in the three-centre bonded sequence.



(44)

Y= S; W, Z= Se, S, O, NR



(39)

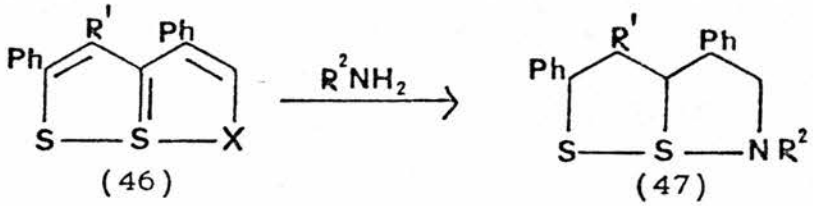
Y= S

2 Synthesis of 1,6,6aλ^4-Triheterapentalenes

As the work described in this thesis is concerned with the synthesis of nitrogen-containing triheterapentalenes some of the more important synthetic routes to these compounds are described here.

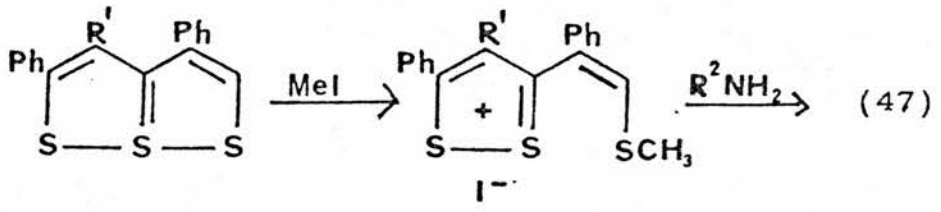
(a) Synthesis of Triheterapentalenes Containing One or Two Nitrogen Atoms.

Azapentalenes are frequently prepared from other triheterapentalenes. They can be formed either directly by reaction of trithiapentalenes with primary aliphatic amines, and by the reaction of oxadithiapentalenes with primary aromatic amines, eg compounds (46, X = O, S) forming 1,6aλ^4-dithia-6-azapentalenes (47)[94,76]. Azapentalenes can also be formed indirectly from other triheterapentalenes by alkylation, followed



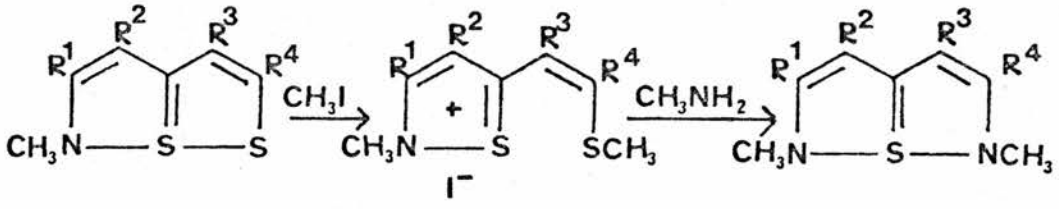
(46) (47)

by treatment with primary amines for instance trithiapentalenes (48, R^1 = H, Ph) react with iodomethane giving the dithiolium salts (49), which form 1,6aλ^4-dithia-6-azapentalenes (47) on treatment with primary amines[94].



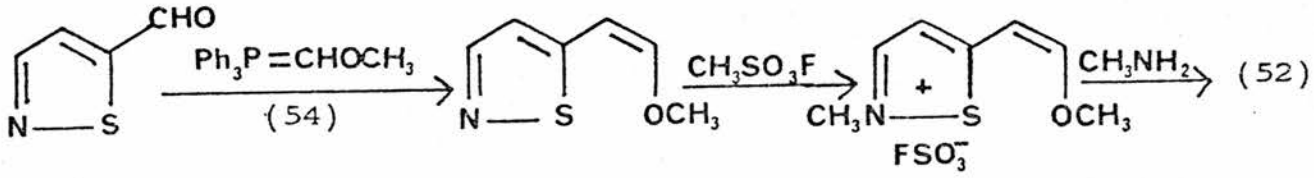
(48) (49)

6a λ^4-thia-1,6-diazapentalenes (52) can be synthesised in a similar manner. Methylation of the dithiaazapentalenes (50) gives the isothiazolium salts (51), which yield 6a λ^4-thia-1,6-diazapentalenes (52) on reaction with methylamine[56].



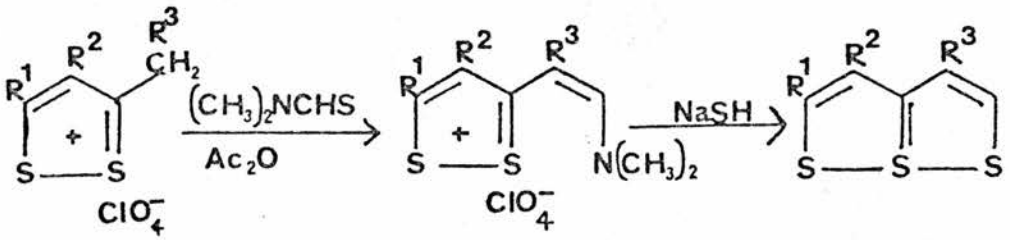
(50) (51) (52)

Alternatively thiadiazapentalene (52) can be formed from 5-formylisothiazole (53). Treatment of compound (53) with the phosphonium ylid (54) gives the 5-(2-methoxyvinyl)isothiazole (55) which is N-methylated by methyl fluorosulphonate to give the salt (56). Treatment of this salt with aqueous methylamine gives the thiadiazapentalene (52, $R^1 = R^2 = R^3 = R^4 = H$).



(53) (55) cis and trans (56)

As has been mentioned, many azapentalenes can be obtained from other triheterapentalenes eg trithiapentalenes. One general synthesis of trithiapentalenes involves the formation of "Vilsmeier" salts (58) from 1,2-dithiolium salts (57). Treatment of the Vilsmeier salts with sodium hydrogen sulphide

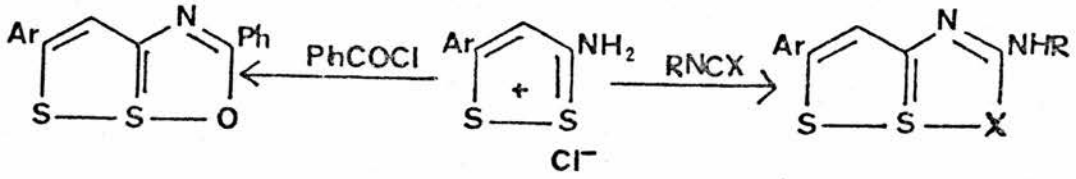


(57) (58) (59)

leads to the 1,6,6a λ^4-trithiapentalenes (59)[50]. The Vilsmeier salts (58) can however also react with methylamine to give the 1,6a λ^4-dithia- 6-azapentalenes (60), or with arenediazonium tetrafluorobarates to give 6,6a λ^4-dithia-1,2-diazapentalenes (61)[95].

(60) (61)

1,6,6a λ^4-Triheterapentalenes containing nitrogen atoms at positions 2,3,4 or 5 can be formed in a variety of ways. The 1,2-dithiolium salts (62) react with benzoyl chloride to give the 1-oxa-6,6a λ^4-dithia- 3-azapentalenes (63)[96]. On treatment with alkyl iso(thio)cyanates

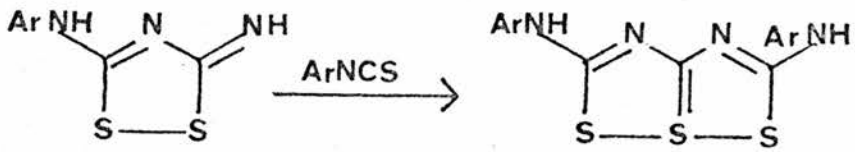


(63) (62) (64; X=O, S)

and aryl iso(thio)cyanates, the salts (62) give compounds (64; X = O, S)[96].

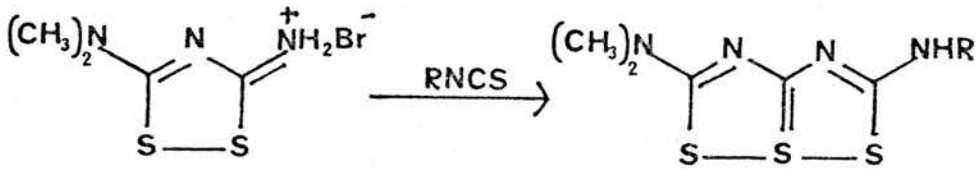
Aryl isothiocyanates react on being heated with the

5-imino-1,2,4- dithiazole (65) to give the 3,4-diazatrithiapentalenes (66)[97].



(65) C (66)

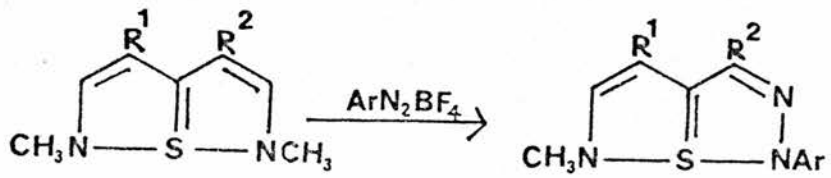
Similar compounds (68) can be synthesised by the reaction of the hydrobromide (67) with isothiocyanates[6].



(67) (68)

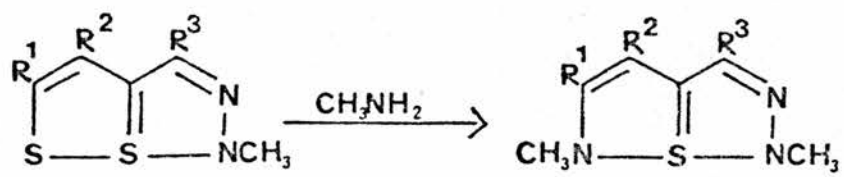
(b) Triheterapentalenes Containing Three Nitrogen Atoms or More.

The 1,6-diaza-6a λ^4-thiapentalenes (69) couple with arenediazonium tetrafluoroborates to give the 1,2,6-triaza compounds (70)[98].



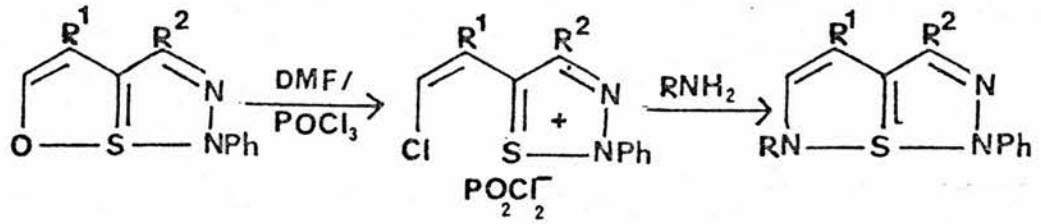
(69) (70)

Analogous compounds (72) can be formed by treating the 6,6aλ^4-dithia-1,2-diazapentalenes (71) with methylamine[98].



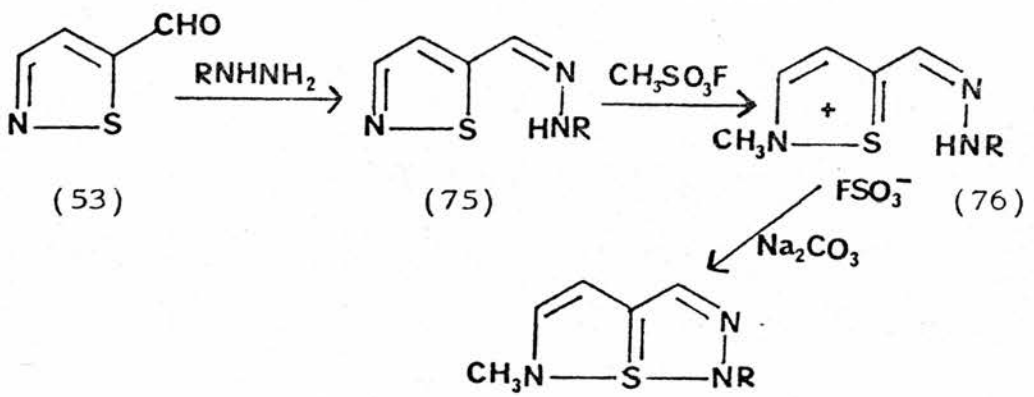
(71) (72)

Recently Reid and Czyzewski have developed two general syntheses of 6a λ^4- thia- 1,2,6- triazapentalenes from oxathiaazapentalenes (73)[99] via the 5- (2-chlorovinyl)- 1,2,3- thiadiazolium salts (74), and



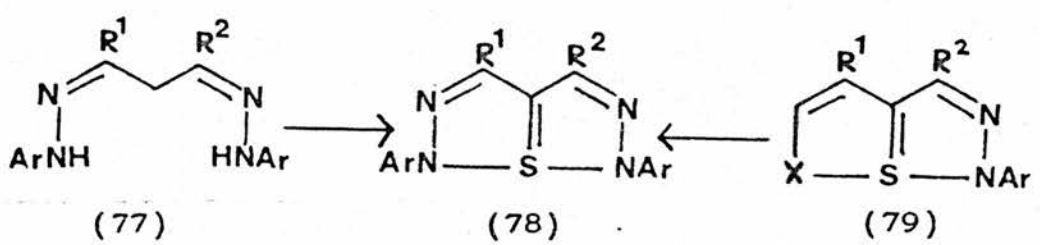
(73) (74)

from 5-formylisothiazole (53)[100] via the hydrazone (75) and the salt (76).



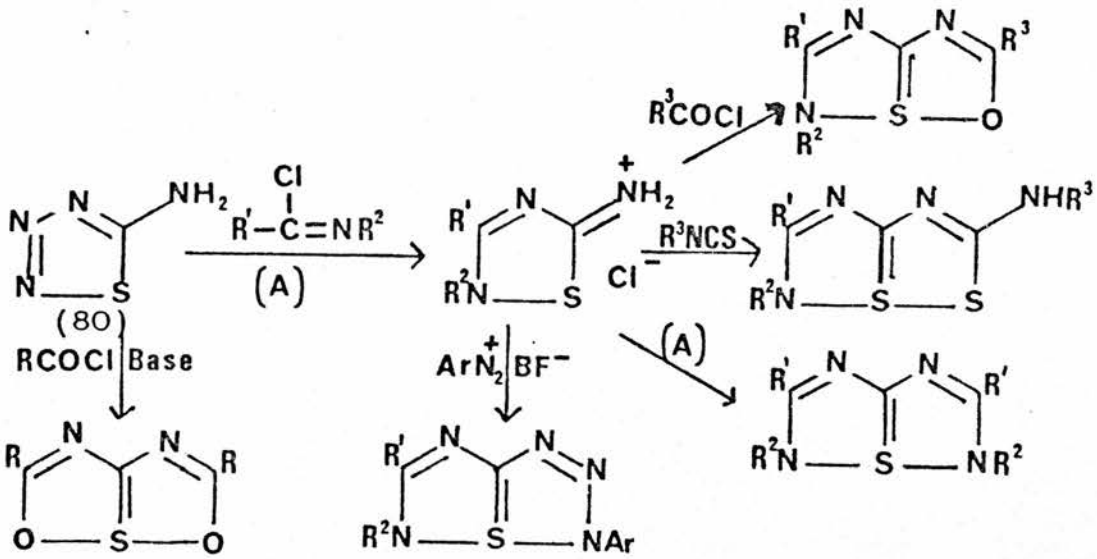
(53) (75) (76)

6a λ^4-Thia-1,2,5,6-tetraazapentalenes (78) have been prepared by the action of sulphur di-or monochloride on the bis-phenylhydrazones (77)[101]. Another recently developed synthesis involves the reaction of arenediazonium tetrafluoroborates with compounds (79; X=O, NMe)[52,98].



(77) (78) (79)

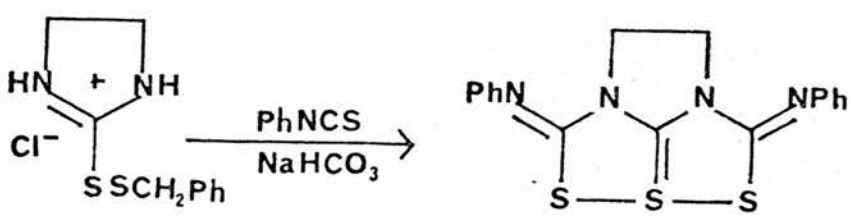
A new general route to polyazatriheterapentalenes, starting from 5-amino-1,2,3,4-thiatriazole (80), has been developed by L'abbé and co-workers. The results are summarised in scheme 1[102,103].



Scheme 1

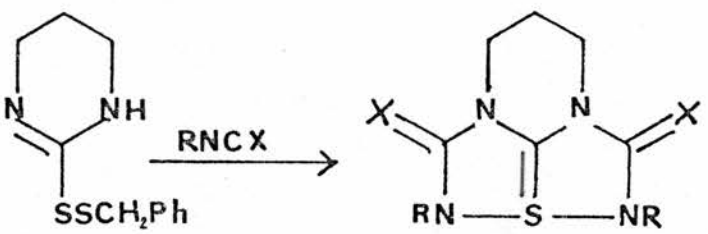
(c) Triheterapentalenes Containing Exocyclic Double Bonds.

Beer and co-workers found that treatment of compound (81) with phenyl isothiocyanate and sodium hydrogen carbonate gave the 2,3,4,5-tetrahydro- 2,5-bis (phenylimino)-3,4-ethano-1,6,6a λ^4-trithia-3,4-diazapentalene (82)[2]. However an analogous reaction



(81) (82)

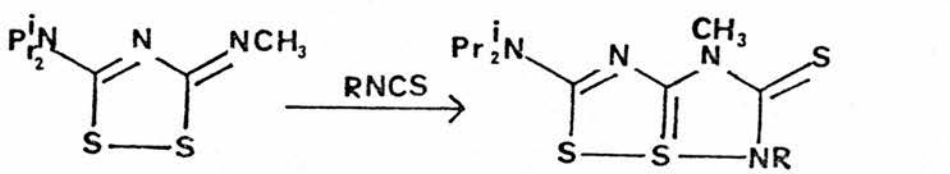
carried out on the disulphide (83) gave the 6a λ^4-thia-1,3,4,6-tetraazapentalene (84)[2].



(83) (84)

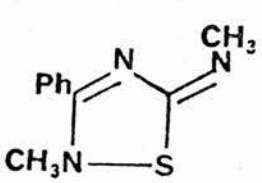
R=Me, Ph
X=O, S

X-ray crystal structure determinations of the isothiocyanate adducts of compound (85) have shown that the products are the 4,5- dihydro-1,6a λ^4-dithia-3,4,6-triazapentalenes (18)[45] and (19)[46]. The S-S bond lengths were found to be 2.494 Å and 2.447 Å in compounds (18) and (19) respectively, while the S-N bond lengths were 1.814 Å and 1.863 Å.

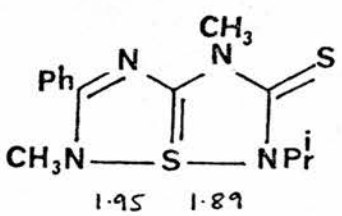


(85) (18; R=Me 19; R=Ph)

Similarly the isopropyl isothiocyanate adduct of compound (86a) has been shown to have the triheterapentalene structure (89a)[104].



(86a)

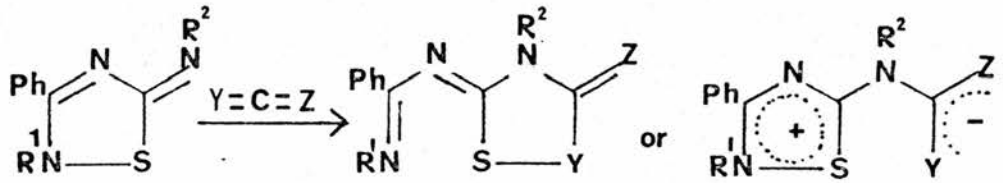


(89a)

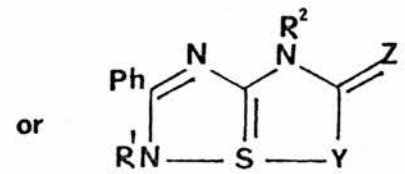
(d) Possible Analogues of 1,6,6aλ^4-Triheteropentalenes.

A number of compounds which have been reported in the literature as monocyclic ("open") structures may be reformulated as triheteropentalenes.

Goerdeler[104] has studied the reaction of the 5-(substituted) imino-1,2,4-thiadiazoles (86) with a selection of heterocumulenes. The products may be formulated as neutral monocyclic species (87), as dipolar structures (88), or as triheteropentalenes (89) containing exocyclic double bonds

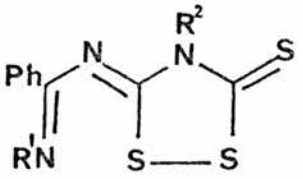


(86) (87) (88)

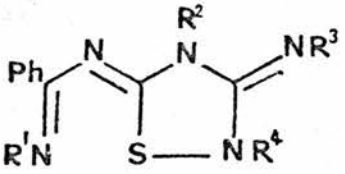


(89)

As has been mentioned the structure in the solid state of the isopropyl isothiocyanate adduct of compound (86) has been shown to be (89a). However the structure of other adducts from (86), eg the adduct with carbon disulphide formulated as (90), or with carbodiimides (91) is still an open question.

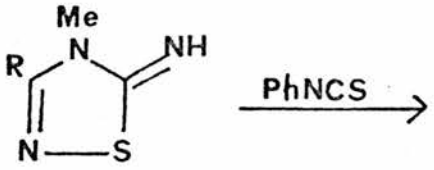


(90)

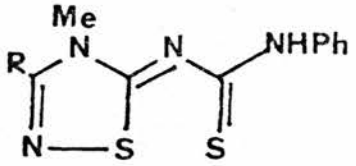


(91)

Several workers have studied the reactions of the 5-imino-1,2,4- thiadiazoles (92)[5] and (93)[105] with phenyl isothiocyanate, which give products formulated as (94).

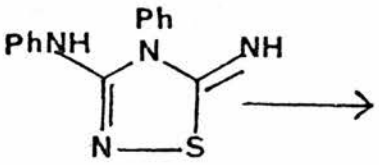


(92; R=H 93; R=Me)

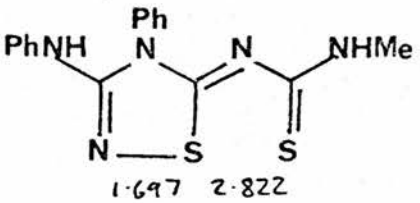


(94; R=H, Me)

The methyl isothiocyanate adduct of "Hector's Base" (95) is known from an X-ray crystal structure determination to have structure (96)[106] the S-N bond length being 1.697 Å with an S-S distance of 2.822 Å.

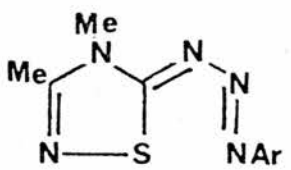


(95)

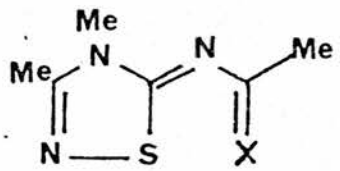


(96)

Compound (93) reacts with arenediazonium tetrafluoroborates[105] to give a product formulated as (97) on the grounds of its proton nmr spectrum. On treatment with boiling acetic anhydride compound (93)



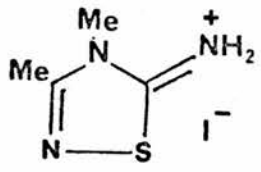
(97)



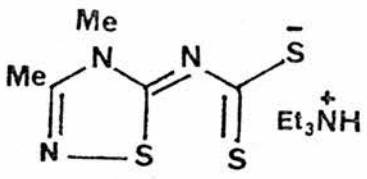
(98a; X=O 98b; X=S)

forms compound (98a), which on thionation with phosphorus decasulphide gives compound (98b)[105].

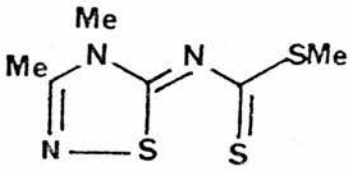
The salt (99) reacted with triethylamine followed by carbon disulphide to give the dithiocarbamate (100), which formed compound (101) on treatment with iodomethane[105].



(99)



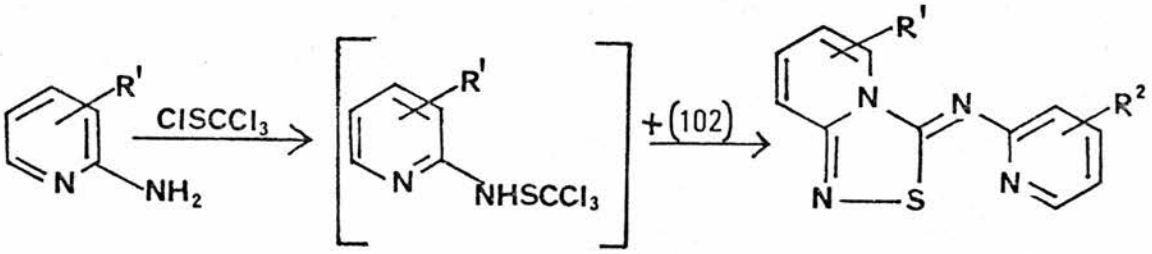
(100)



(101)

The foregoing products(90,91,94,96,97,98,101) have been formulated as monocyclic species for simplicity alone.

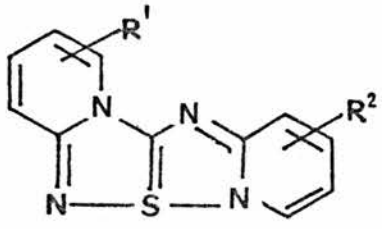
A series of compounds formulated as 3-(2-pyridylimino)-3H-[1,2,4] thiadiazolo [4,3-a] pyridines (104) have been prepared by Potts and Armbruster from the reaction of 2-aminopyridines (102) with perchloromethyl mercaptan in the presence of base[107,108].



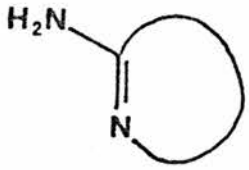
(102) (103) (104)

The product (104) may be reformulated as the triheterapentalene (105), although this structure requires the loss of the

aromaticity of the pyridine ring.

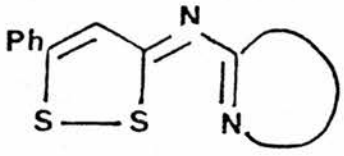


(105)

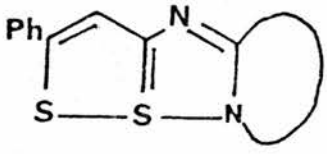


(106)

The reaction of 2-amino-N-heterocycles (106) with 3-chloro-5-phenyl- 1,2-dithiolylium chloride (41) leads to products which can be formulated as triheterapentalenes[84]. Reaction at the ring nitrogen atom of (106) gives orange products analogous to compound (43), (see page 15). However reaction also occurs at the amino substituent of compound (106) and results in the formation of yellow products which can be formulated as (107) or (108).

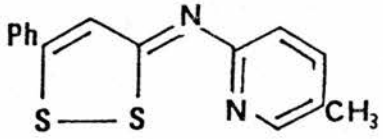


(107)

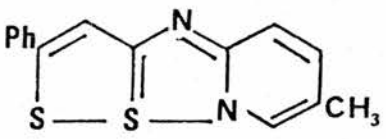


(108)

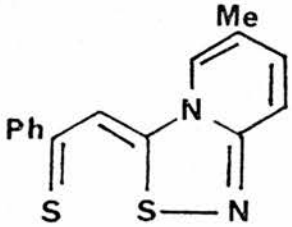
In the reaction of compound (41) with 2-amino-5-methylpyridine as well as an orange product (43c) being formed a yellow product was formed. The structure of the yellow product was shown to be (107a) by X-ray crystallography[109].



(107a)

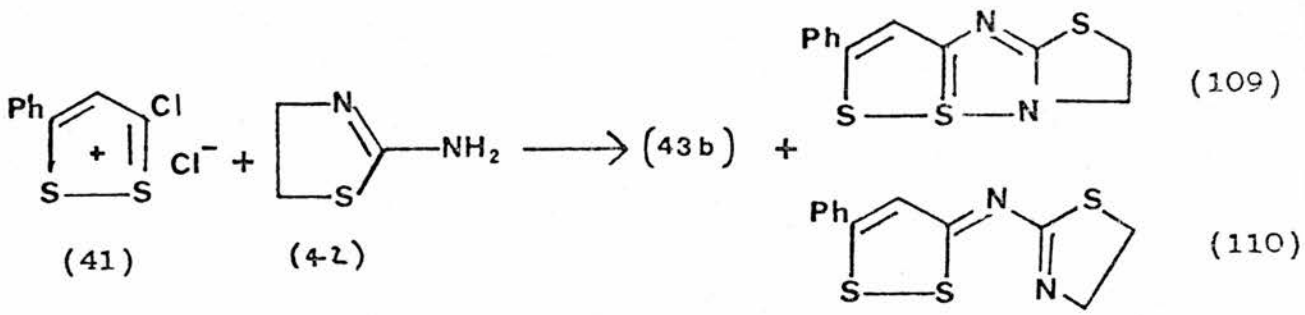


(108a)



(43c)

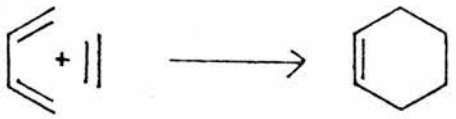
The aromatic stabilisation energy associated with the pyridine ring may be an important factor favouring the structure (107a) over the triheterapentalene structure (108a). If this is the case, Potts and Armbruster were correct in their assignment of the open structures (104) rather than the triheterapentalene structures (105) to the products from the reactions of compound (102) with perchloromethyl mercaptan. On the other hand, in the cases where no loss of aromatic stabilisation energy is involved a triheterapentalene structure might be favoured. For example, in the reaction of compound (41) with 2-amino-Δ^2-thiazoline (42) the yellow product obtained might require to be formulated as structure (109) rather than (110).



(41) (42)

3 Triheterapentalenes and 1,3-Dipolar Cycloadditions

In organic chemistry a cycloaddition reaction is a process in which two or more reactants combine to form a cyclic molecule. The majority of these reactions involve the formation of two new sigma bonds. For example, in the Diels-Alder reaction a cis-1,3- diene combines with an olefin to give a cyclohexene (111).



(111)

Many cycloaddition reactions show the characterisitics of a concerted process but others are stepwise and involve an intermediate which is either a zwitterion or a diradical. There are several theories[12,111,112] as to why some cycloadditions should be concerted and others not. Probably the simplest is the frontier orbital theory of Woodward and Hoffmann[12]. In the concerted cycloaddition of two polyenes, bond formation at each terminus must be developed to some extent in the transition state. Thus orbital overlap must occur simultaneously at both termini. For a low energy concerted process to be possible such simultaneous overlap must be geometrically feasible and must also be potentially bonding.

There are two stereochemically distinct ways in which new bonds can be formed: either to the same face of the π-bond

(suprafacial) or to opposite faces (antarafacial), see Fig 1. Suprafacial,

Fig 1

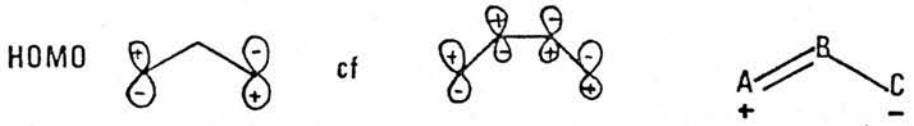
Suprafacial (S,S) approach of two polyenes (Fig 1) is normally sterically suitable for efficient orbital overlap. This type of overlap will only be energetically favourable when the highest occupied molecular orbital (HOMO) of one component and the lowest unoccupied molecular orbital (LUMO) of the other can interact in a bonding fashion at both termini, ie the orbitals are of the correct phase or symmetry. In the Diels-Alder reaction the HOMO and LUMO of each reactant are of the appropriate symmetry so that interaction of these orbitals will result in simultaneous potential bonding character between the terminal atoms (Fig 2).

Fig 2

The symmetries of the HOMO and LUMO of polyenes depend on the number of π-electrons in the polyene. Therefore the initial interaction for a concerted addition also depends on the number of π-electrons provided by each component. The total number of

π-electrons is thus fundamental to whether a concerted reaction is allowed. The rules governing these reactions can be summarised in the following way: concerted s,s or a,a (Fig 1) addition is allowed for a total of $(4n + 2)\pi$-electrons. Concerted s,a addition is allowed for a total of $4n\,\pi$-electrons.

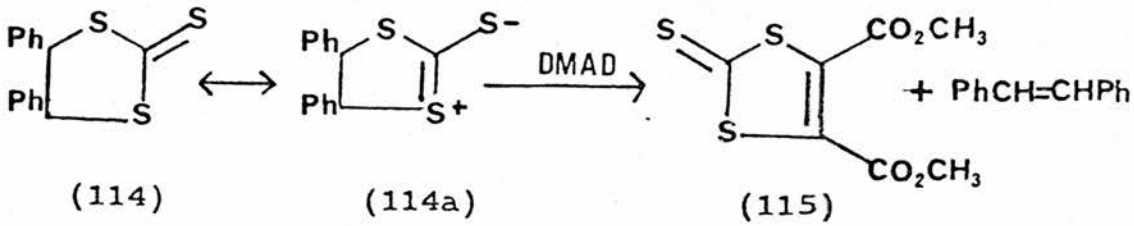
Any component which can supply the same number of electrons as a neutral polyene, in an orbital of the same symmetry, is potentially able to participate in a cycloaddition in place of the polyene. Thus three atom components with four electrons and the symmetry of an allyl anion (112) should be capable of the same types of cycloadditions as dienes. These reactions are referred to as 1,3-dipolar cycloadditions.



allyl anion (112) butadiene 1,3—dipole (113)

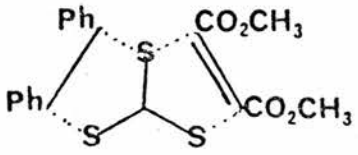
(a) Cycloaddition/Elimination Reactions.

The three atom component with four electrons described above need not be a discrete molecule (eg 113) but can be a mesomeric form of a neutral molecule. For example the reaction of the cis- and trans-4,5-diphenyl-1,3-dithiolan-2-thiones (114)[113] with dimethyl acetylene dicarboxylate (DMAD) results in a concerted cis elimination of an olefin via a bicyclic transition state (116). Further evidence of the concerted mechanism

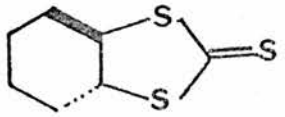


(114) (114a) (115)

of this reaction was shown by the lack or reactivity of the trans- bicyclic thione (117). This did not react with DMAD, as the cis elimination of a concerted pathway would have led to an excessively, strained structure (in this case trans-cyclohexene).

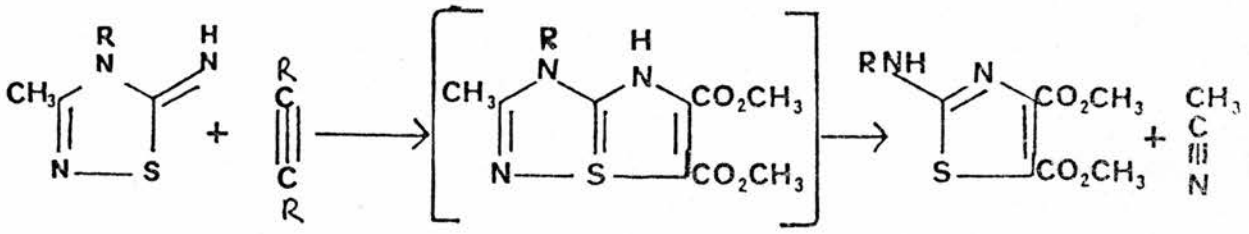


(116)



(117)

Akiba[114] has observed a similar type of reaction on treatment of compound (118) with acetylenes. This gave compounds (119) after loss of acetonitrile.

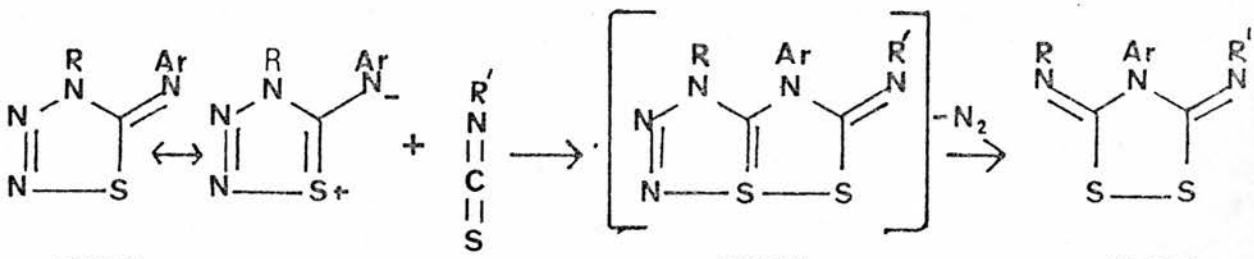


(118) (119)

Many other examples of cycloaddition/elimination reactions like these have been reported in the literature but of particular relevance to the work embodied in this thesis are those rearrangements involving triheterapentalene intermediates.

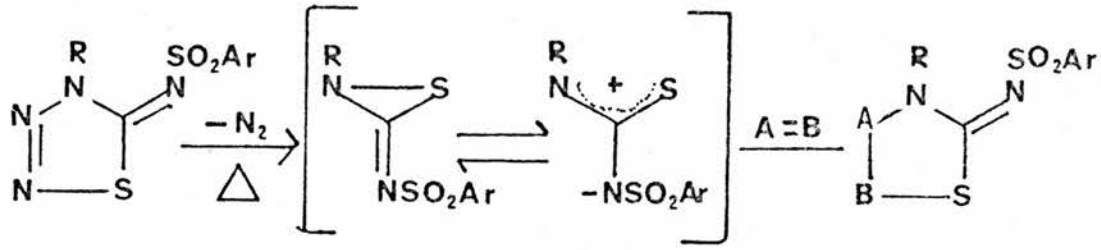
L'abbé[11,115] has studied the reactions of 4-alkyl-5-arylimino- 1,2,3,4-thiatriazolines (120) with various

isothiocyanates to give compounds (122). These reactions were found from kinetic experiments to be bimolecular suggesting the intermediacy of the triheterapentalene (121).



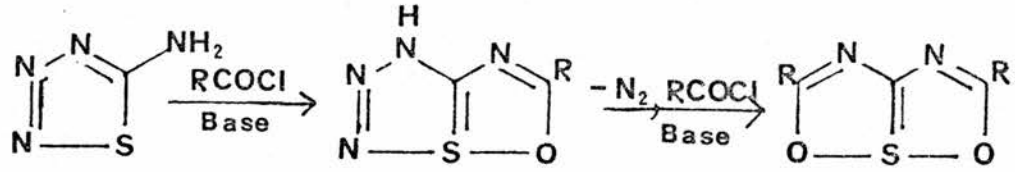
(120) (121) (122)

However when the arylimino group in compound (120) is replaced by an aroylimino group (eg compound 123) the reactions with dipolarophiles (a=b) were found to be unimolecular, consistent with the intermediacy of a thiaziridineimine (124) or its ring-opened dipolar form.



(123) (124)

L'abbé and Beer have independently investigated the acylation reaction of the aminothiatriazole (80) (see page 22).

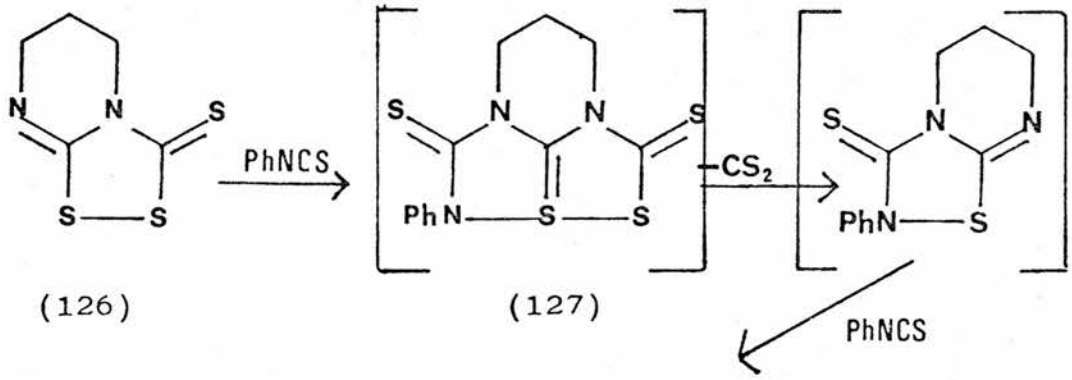


(80) (125)

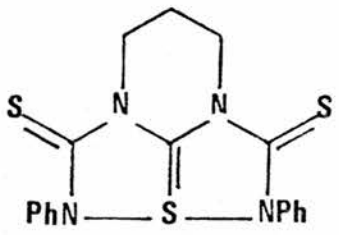
This reaction could occur <u>via</u> the triheterapentalene intermediate

(125). However a thiaziridineimine analogous to (124) may also be considered as an intermediate.

Compound (126) reacts with phenyl isothiocyanate[117] to give the triheterapentalene (128), possibly through the intermediate (127).



(126) (127)



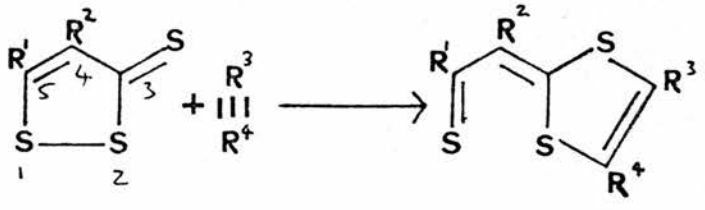
(128)

The reactions of compound (126) with nitriles will be considered later in the Discussion section of this thesis.

(b) Bond Switch Reactions

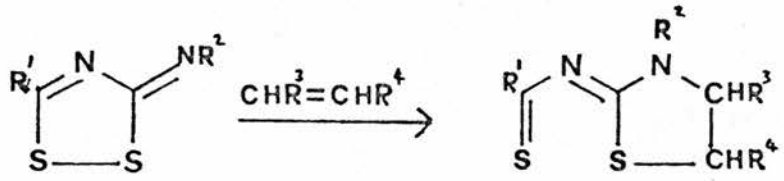
(1) Introduction

Various workers[113,118,119] have studied the cycloaddition of acetylenes to 1,2-dithiole-3-thiones (129). These reactions result in the formation of the 1,3-dithioles (130) by a bond switch in which the sulphur atom from position 2 of the original heterocycle has been incorporated into the newly formed ring.



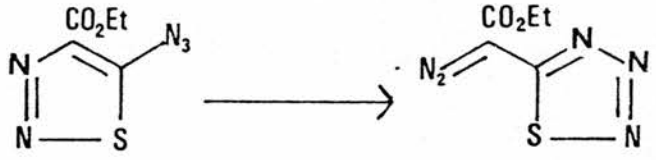
(129) (130)

Goerdeler[120] observed a similar rearrangement in the cycloaddition of olefins to 5-immino-1,2,4-dithiazoles (131).



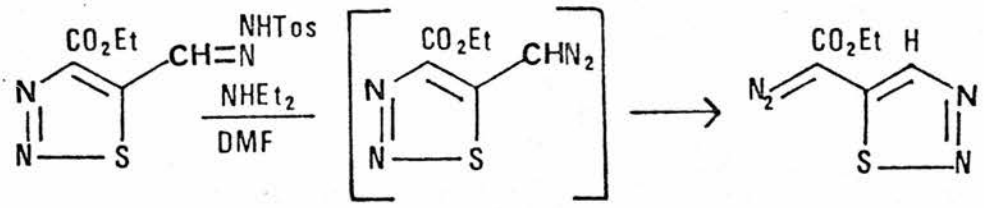
(131)

L'abbé has recently reported two examples of a bond switch involving sulphur as the pivot atom, namely the transformation of 5-azido- 1,2,3- thiadiazole (132) into 5-diazomethyl-1,2,3,4-thiatriazole (133)[125]; and the conversion of the tosylhydrazone (134)



(132) (133)

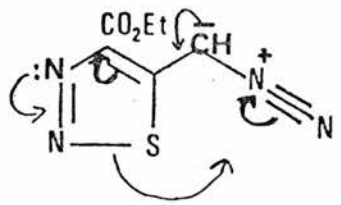
<u>via</u> the thiadiazole (135) into the thiadiazole (136)[126].



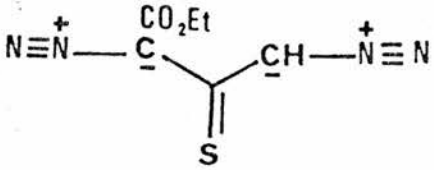
(134) (135) (136)

The observed rearrangement can occur either by a concerted bond switch mechanism, as shown in (137),or <u>via</u> the open-chain

intermediate (138).



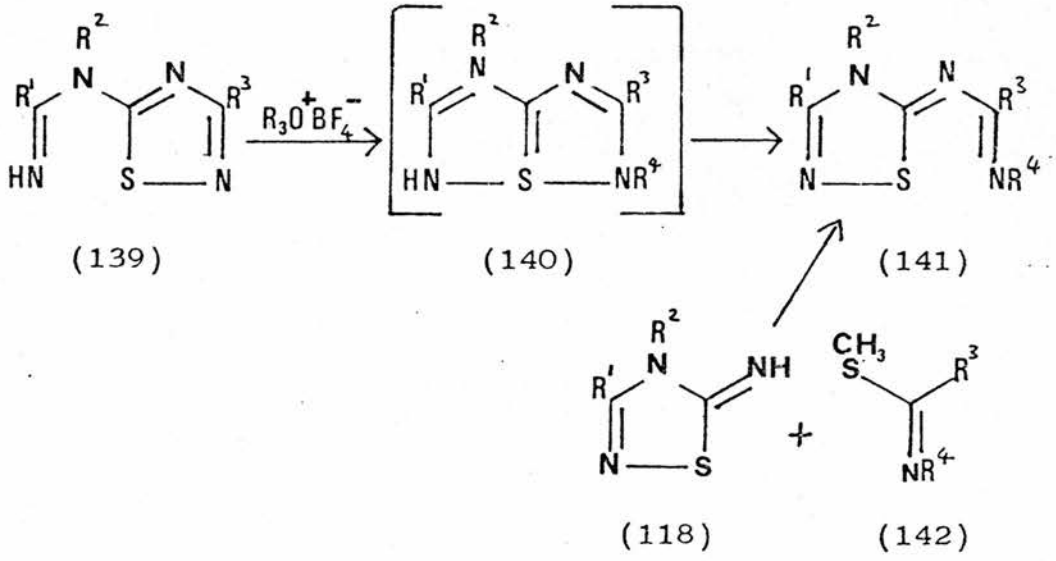
(137)



(138)

(2) Rearrangements Involving Triheterapentalene Intermediates

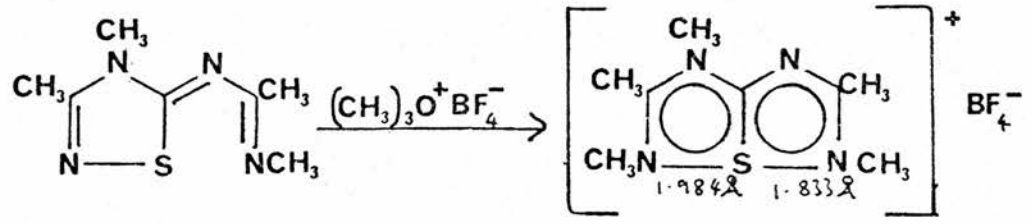
Akiba has found other examples of bond switch reactions, including the alkylation of compound (139) with Meerwein's reagent[121]. This affords compound (141) possibly via an intermediate (140). The structure of the product was confirmed by an unequivocal synthesis from compounds (142) and (118).



(139) (140) (141)

(118) (142)

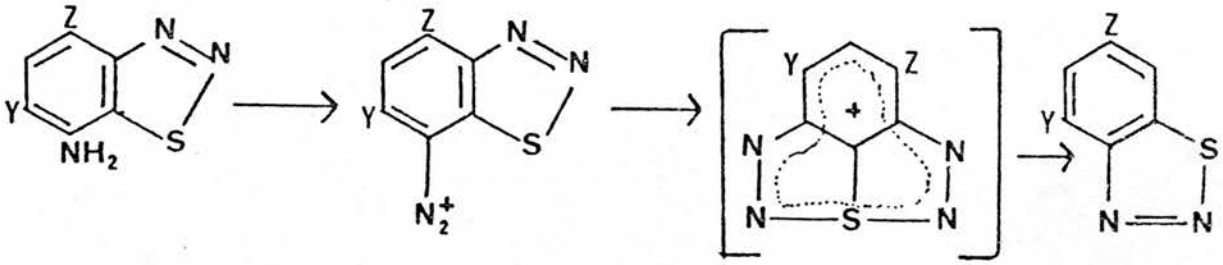
Further alkylation[121] of compound (141, R^1-R^4 = Me) gave a product formulated as (143). X-ray crystallography of the



(141) (143)

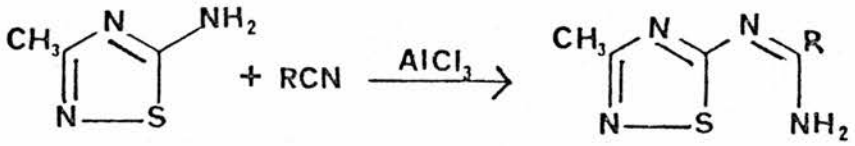
product showed the N-S bond lengths to be 1.984 Å and 1.833 Å, therefore compound (143) may be regarded as a triheterapentalenium salt.

Another bond switch involving a triheterapentalenium intermediate is the rearrangement of the diazonium salts (145), derived from 7-amino- 1,2,3,-benzothiadiazoles (144) into the benzothiadiazoles (146)[127].



(144) (145) (146)

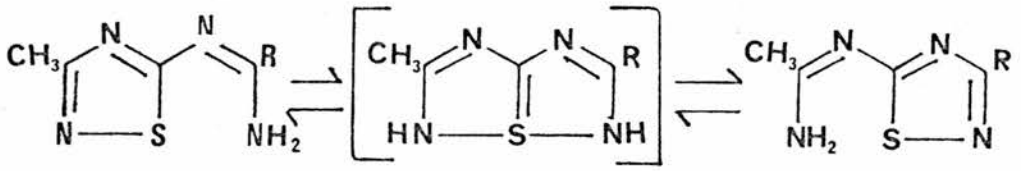
When compound (147) was heated with a nitrile in the presence of aluminium trichloride the 1:1 adduct (148) was obtained[122].



(147) (148)

The ^{1}H nmr of products (148) showed two pairs of signals the ratio of which was found to be temperature dependent. This observation was rationalised by assuming the occurrence of a bond

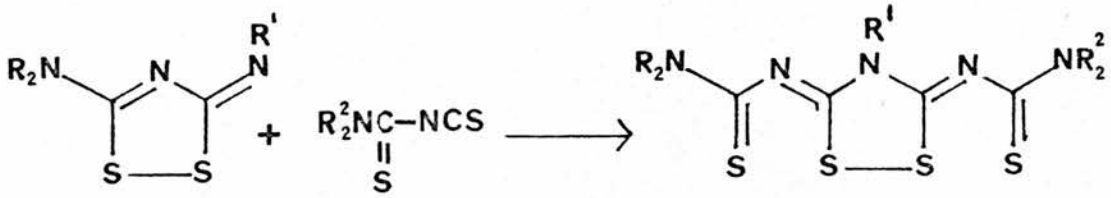
switch between the two forms (a) and (b). The form (148b) is more favoured when



(148a) (148b)

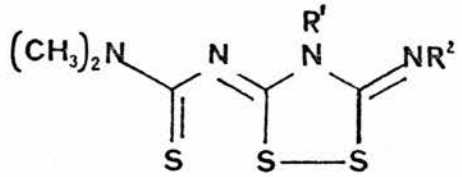
R is a larger alkyl or aryl group with an electron withdrawing substituent, and in solvents with lone pair electrons. The form (148a) is more favoured at higher temperatures.

Oliver[6] and Goerdeler[124] have found that compounds (149) cycloadd across the C-S bond in thiocarbonyl isothiocyanates (150) to give yellow compounds (151).

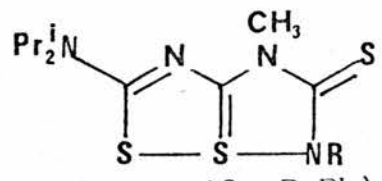


(149) (150) (151)

Oliver also reported that the cycloaddition of other isothiocyanates to compound (149) gave colourless compounds formulated as (152). However



(152)

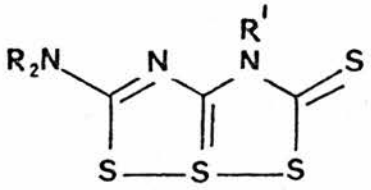


(18; R=Me 19; R=Ph)

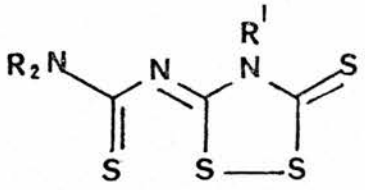
the methyl and phenyl isothiocyanate cycloadducts (18[45] and 19[46]) of compound (149, R = Pr^i, R^1 = Me) are known to have resulted

from addition across the N-C bond of the isothiocyanate, therefore Oliver's adducts should perhaps be reformulated as 1,6a-dithia- 6-azapentalenes, similar to compounds (18) and (19).

Goerdeler[123] and Oliver[6] have found many other examples of cycloadditions of heterocumulenes to compounds (149). For example the carbon disulphide adducts were formulated as the bond switch products (155), presumably having been formed through the triheterapentalene intermediate (154). However in this case the precise structure of the product is not known and could in fact be structure (154).

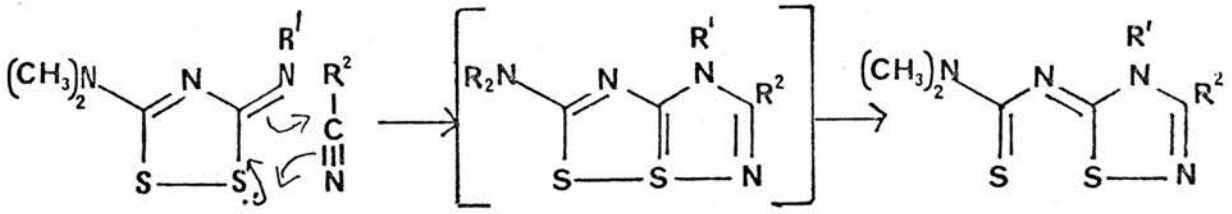


(154)



(155)

A side reaction was observed when alkylations of the imino-1,2,4- dithiazoles (149) in acetonitrile were attempted[110]. 1,3-Dipolar cycloaddition between the iminodithiazole and the nitrile occurred, and the 1,2,4-thiadiazoles (157) were isolated.

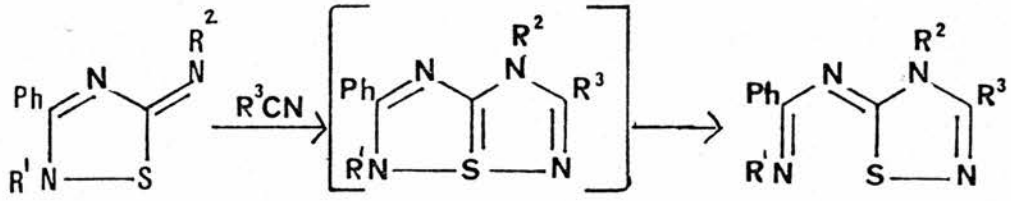


(149; R^1=Me or Ph) (156) (157)

It was proposed that the reaction involved the triheterapentalene

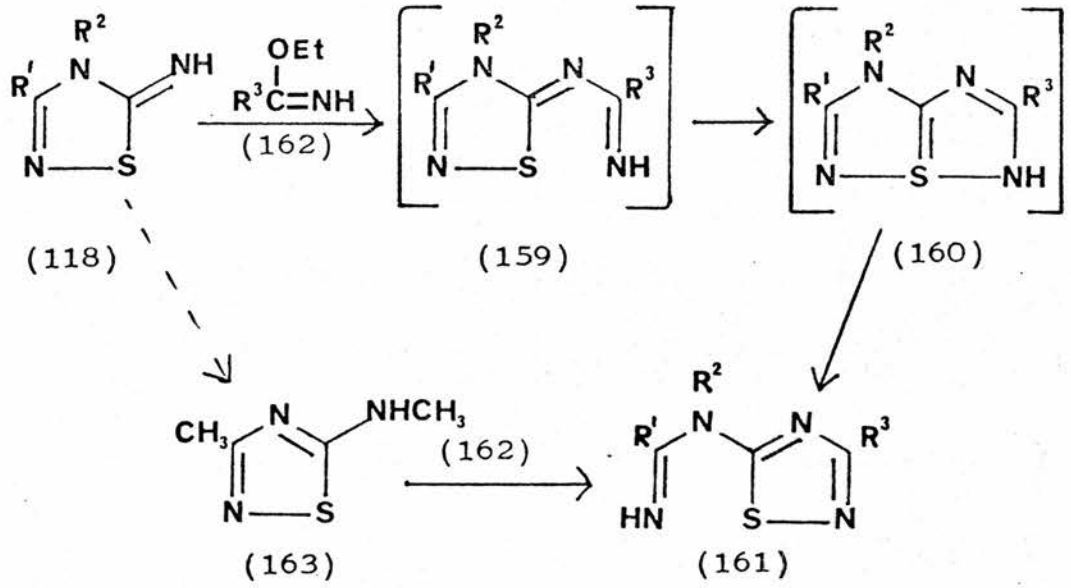
intermediate (156) which contains a pyridine type nitrogen atom in the three-centre bonded S-S-N sequence.

Another reaction that apparently involves a triheterapentalene intermediate containing one pyridine type nitrogen in the three-centre bonded sequence was reported by Goerdeler and Lobac'h[104]. On treatment with nitriles the compounds (86) were converted into compounds (158).



(86) (158)

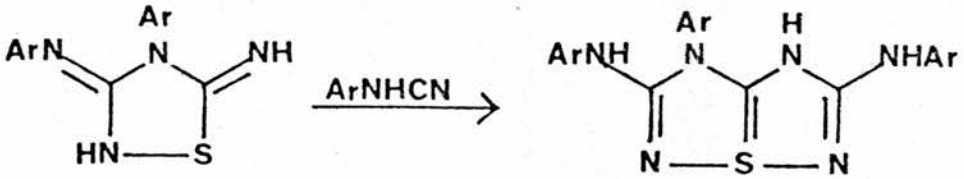
Akiba has studied the reaction of the imino thiadiazoles (118) with the imidates (162)[128]. The expected product (159) was not isolated however, and an X-ray crystal structure analysis showed the product to be compound (161, R^1-R^3 = Me). This transformation was explained by postulating that the product (159) was formed but rearranged by a bond switch to give compound (161), via the triheterapentalene intermediate (160). However it has



(118) (159) (160) (163) (161)

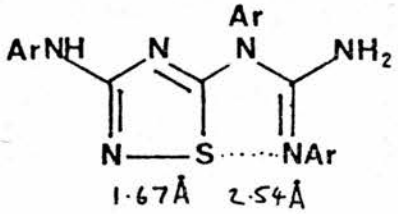
been shown that[129] the imine (118, $R^1 = R^2 = Me$) rearranges, albeit on prolonged heating and in low yield, to give compound (163). It is also known that compound (163) can react with the imidate (162) to give (161), without a bond switch occurring. Thus the transformation of compound (118) to compound (161) observed by Akiba need not have occurred by a bond switch.

Akiba has reported that the reaction of Hector's base, represented by him as (164), with aryl cyanamides gave the triheterapentalene derivatives (165)[130]. The product could have arisen from a bond switch followed by prototropy. His conclusion was based on



(164) (165)

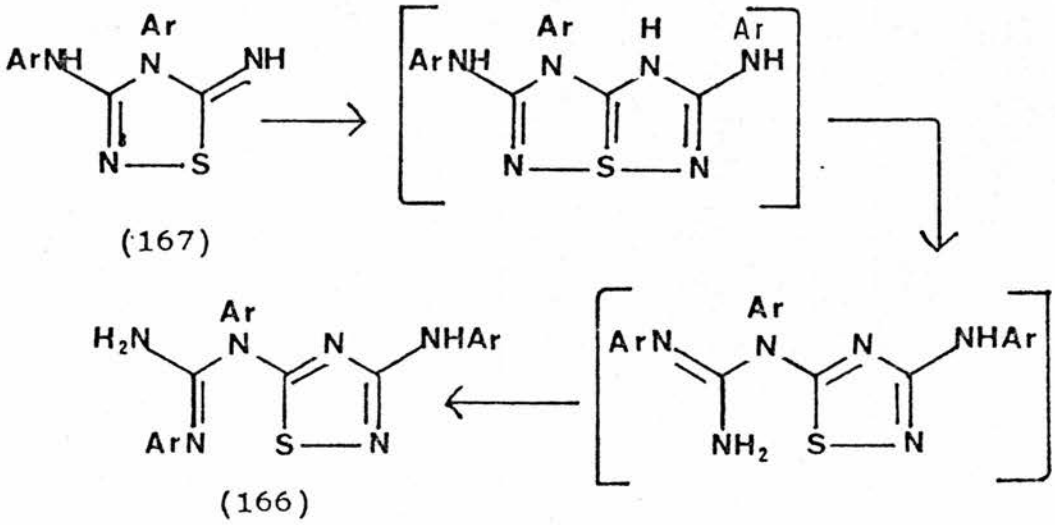
the comparison of ultraviolet and infra-red spectral properties with other heterocyclic systems, and from the mass spectra of the products (165). An X-ray structure determination of compound (165, Ar = p - Br C_6H_4) has shown that the correct structure of the product is (166)[131]. The molecule is approximately planar with S-N



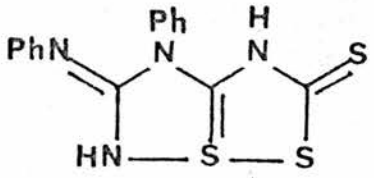
(166)

distances of 1.670 Å and 2.538 Å. Akiba regards these interatomic distances as indicative of a significant intramolecular S.....N interaction. However, Glemser *et al*[132] have presented a correlation of S-N distance with S-N bond order which suggests that the S-N bond order becomes zero at an interatomic distance of *ca* 2.0 Å.

Hector's base has been shown[133] to have structure (167), rather than the structure (164). Its structures in the solid state[133] and in solution[134] are identical. Therefore the formation of compound (166) can be explained in terms of a bond switch, followed by prototropy, and subsequent bond rotation:

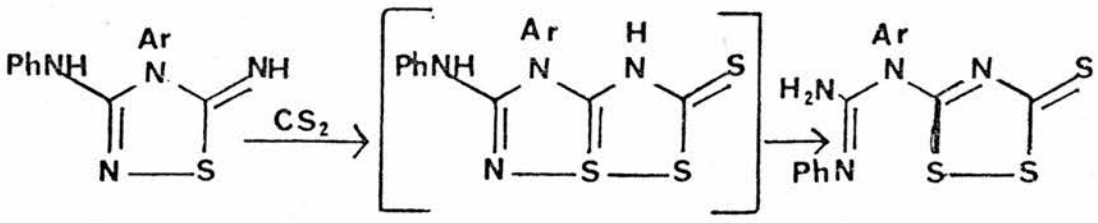


Hector's base forms an adduct with carbon disulphide[135], Butler[136] formulated this compound as the triheterapentalene derivative (168).



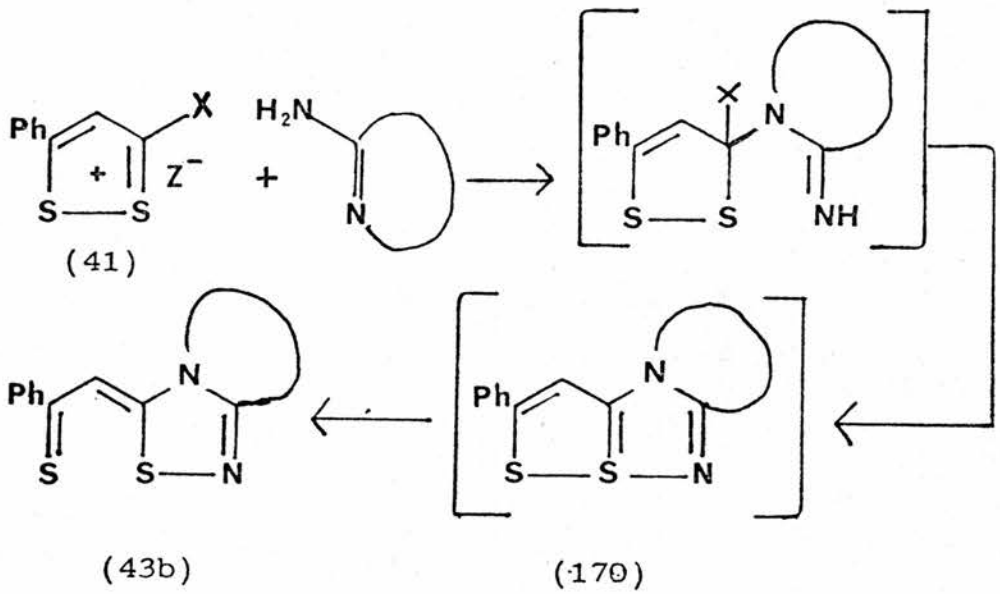
(168)

However Glidewell[137] has shown the correct structure to be (169), and its formation clearly involves a bond switch similar to that described above for the reaction (167)→→(166).



(167) (169)

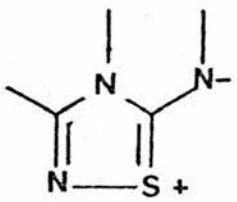
Reid and Mitchell[84] have found another example of a bond switch. In the reaction of the 1,2-dithiolylium salts (41) with 2-amino-N-heterocycles (106), mentioned earlier, the formation of the products (43b) could involve a triheterapentalene intermediate of structure (170).



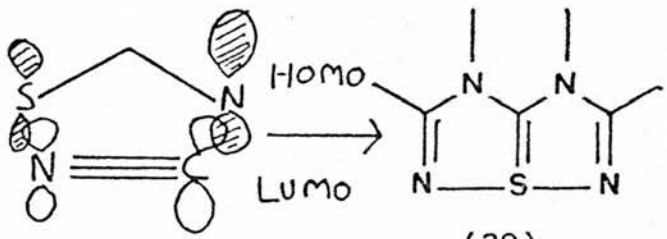
(41) (43b) (170)

1,3-Dipolar cycloadditions form an extensive, and expanding area of heterocyclic chemistry, of great synthetic potential. It was the aim of much of the work described in this thesis to utilise 1,3-dipolar cycloadditions as a means of obtaining new types of triheterapentalenes.

As all 1,3-dipoles, with the exception of nitrile ylides and symmetrical species, have a larger coefficient at the anionic terminus of the HOMO and at the neutral terminus in the LUMO[138], it was envisaged that nitriles which have the highest coefficient on the carbon atom in the LUMO, could cycloadd to the masked 1,3-dipolar form of 5-imino-1,2,4-thiadiazoles (170a) to give a triheterapentalene product of the type (39).

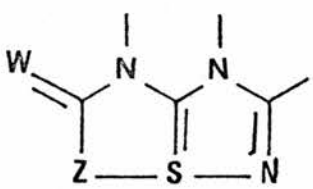


(170a)



(39)

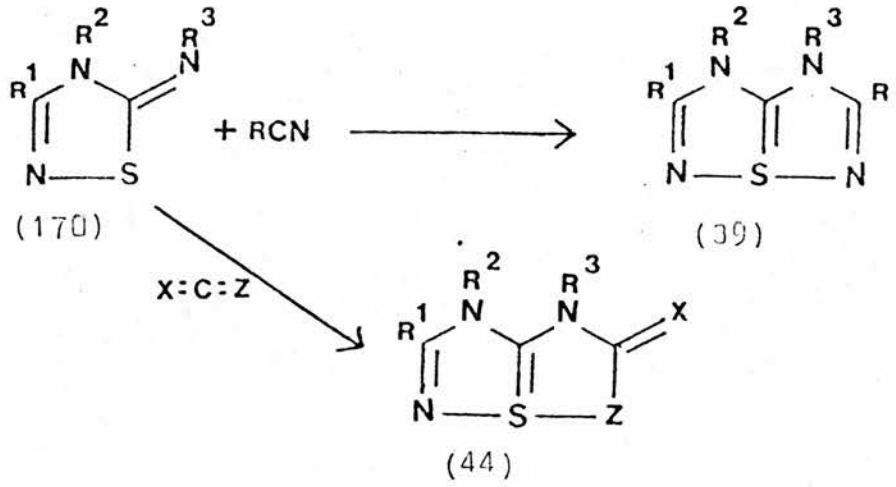
Similarly heterocumulenes (W=C=Z) could react to give triheterapentalenes of type (44). Thus it was hoped to



(44)

synthesise the substituted imino-thiadiazole (170) and to bring about its reaction with nitriles to produce the

triheterapentalenes (39) and with heterocumulenes to give compounds (44).



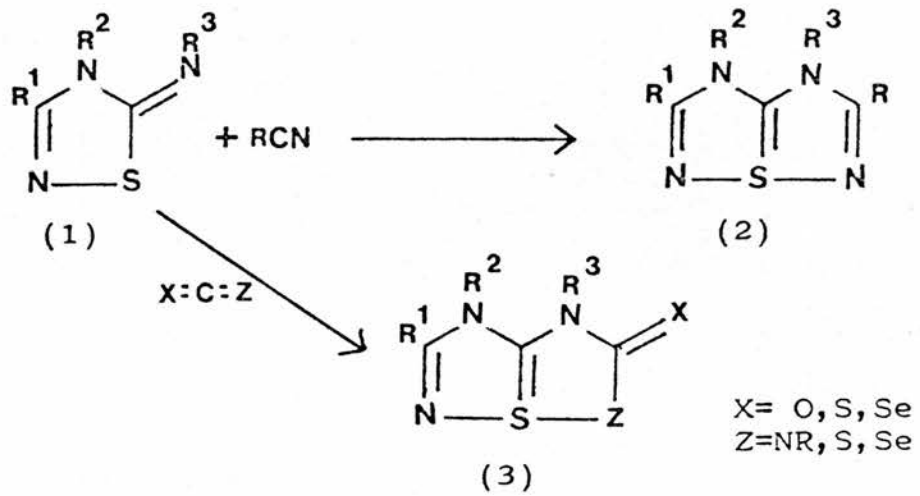
(170) (39) (44)

Part B

DISCUSSION

1 Attempted Synthesis of 4,5-Dihydro- 3,4- dimethyl- 5-methylimino- 1,2,4-thiadiazole

As has already been mentioned one important aim of this work was to synthesise novel 1,6,6a λ^4-triheterapentalene structures containing either one or two pyridine-type nitrogen atoms in the 3-centre bonded sequence. In particular the objective was to synthesise a 4,5-dihydro- 3,4-dialkyl- 5-alkylimino- 1,2,4-thiadiazole (1) as a model compound and then to study its reactions with various nitriles in an attempt to form the novel triheterapentalene structure (2), which has two pyridine-type nitrogen atoms in the 3-centre bonded sequence .



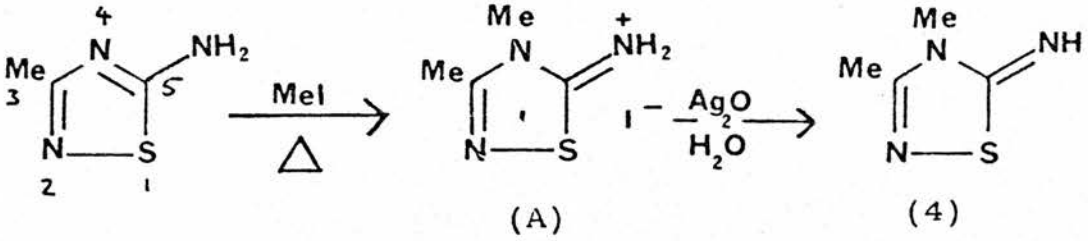
(1) (2) (3)

It was also hoped to react compound (1) with heterocumulenes (X=C=Z) to give compounds of structure (3), which contain one pyridine-type nitrogen in the 3-centre bond and an exocyclic double bond.

(a) Synthesis and Reactions of 5-Amino- 3-methyl- 1,2,4-thiadiazole.

Firstly we proposed to synthesise (1, R^1=R^2=R^3=Me) from 5-amino- 3-methyl- 1,2,4-thiadiazole by successive methylations

and deprotonations. This compound was chosen for our studies because the simplicity of its structure would facilitate ^{1}H nmr spectral studies, and because the starting material, 5-amino-3-methyl- 1,2,4-thiadiazole, is readily available[1]. It is known from the literature[5] that 5-amino- 3-methyl- 1,2,4-thiadiazole is methylated at position 4, this yields 4,5-dihydro- 5-imino-3,4-dimethyl- 1,2,4-thiadiazole (4) after deprotonation of the salt (A). The imine (4) was reacted with iodomethane in methyl or ethyl alcohol to give a product which was shown to be a complex mixture on examination by ^{1}H nmr spectroscopy.



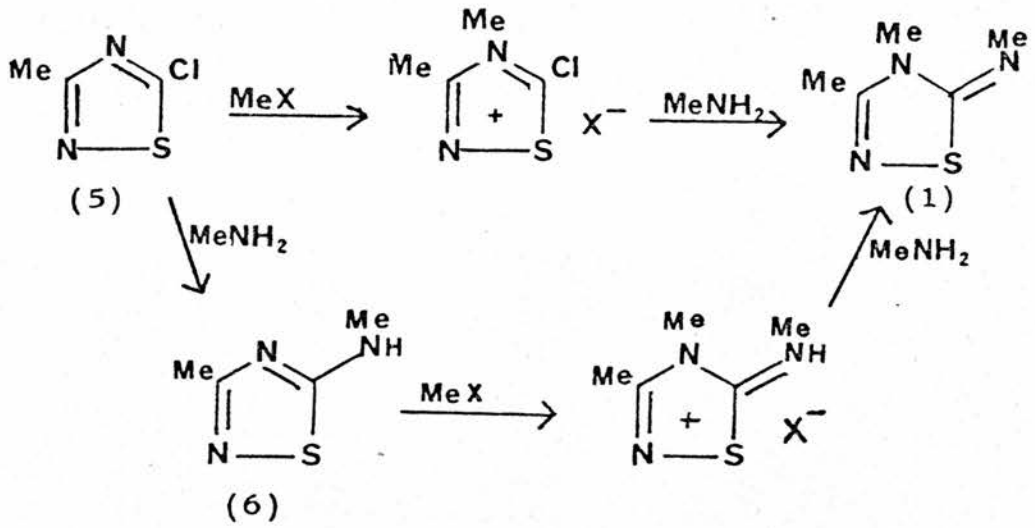
(A) (4)

On treatment with methyl fluorosulphonate in dichloromethane the imine (4) gave a white precipitate which also contained a mixture of products similar to that obtained from reaction of (4) with iodomethane. As both reactions gave mixtures of products which were difficult to separate neither was useful as a synthetic route to the desired thiadiazole (1, $R^1=R^2=R^3=$ Me).

(b) Synthesis and Reactions of 5-Chloro- 3-methyl-1,2,4-thiadiazole.

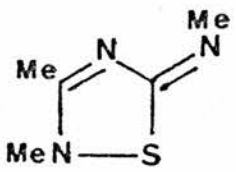
An alternative route to (1) was envisaged starting from another readily available[3] thiadiazole, 5-chloro- 3-methyl-1,2,4- thiadiazole (5), which is obtained from the reaction of

acetamidine hydrochloride with perchloromethyl mercaptan. Either methylation of compound (5) followed by reaction with methylamine, or alternatively the reaction of compound (5) with methylamine first to give 5-methylamino- 3- methyl- 1,2,4-thiadiazole (6) followed by the methylation and deprotonation of the resulting salt could also give (1, $R^1=R^2=R^3=Me$).

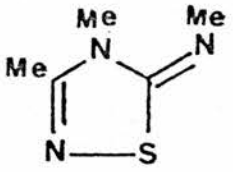


The chlorothiadiazole (5) reacted smoothly with a solution of methylamine in ethanol to give 5-(N-methylamino)- 3-methyl- 1,2,4- thiadiazole (6) in high yield[3]. A solution of compound (6) in dichloromethane reacted with methyl fluorosulphonate to give a white precipitate which was found to be a mixture of salts by ^1H nmr spectroscopy. Deprotonation of the salt mixture with methylamine gave a colourless oil which after distillation gave a t.l.c. pure, low-melting white solid in moderate yield (42%). A ^1H nmr spectrum of the product in chloroform-D showed three signals of equal integral at δ 2.288, δ 3.002 and δ 3.310, and the mass spectrum of the product showed a molecular ion peak at m/e

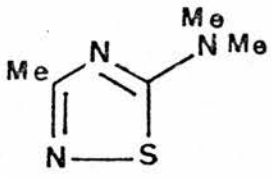
143, indicating that mono-methylation of compound (6) had occurred. There are three possible products of mono-methylation of compound (6) namely (7), (8) and (9), corresponding to alkylation at the three different nitrogen atoms.



(7)



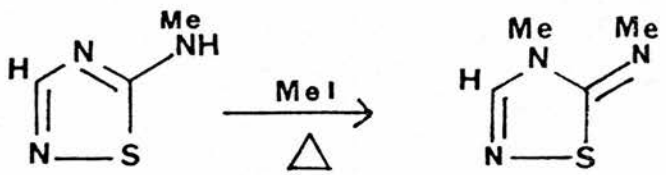
(8)



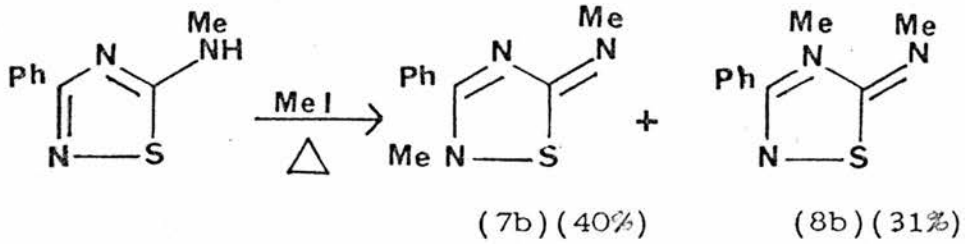
(9)

Compound (9), a colourless oil, was synthesised unambiguously, in good yield, by the reaction of the chlorothiadiazole (5) with an excess of dimethylamine in ethanol.

The ^{1}H nmr spectrum of compound (9) in chloroform-D showed two signals in the ratio of 2:1 at δ 3.15 [6H, $N(Me)_2$] and δ 2.425 (3H, 3-Me), confirming that methylation of (6) does not occur on the exocyclic nitrogen atom. Indeed Goerdeler found[5] that methylation of 5-methylamino- 1,2,4-thiadiazole by iodomethane in a sealed-tube gave 4,5-dihydro- 4-methyl- 5-methylimino- 1,2,4-thiadiazole (8a) in 62% yield. On the other hand, methylation of 5-methylamino- 3- phenyl- 1,2,4-thiadiazole under similar conditions had given a mixture of 2-methyl- 3-phenyl- thiadiazole (7b) (40%) and 4-methyl- 3-phenyl- thiadiazole (8b) (31%).

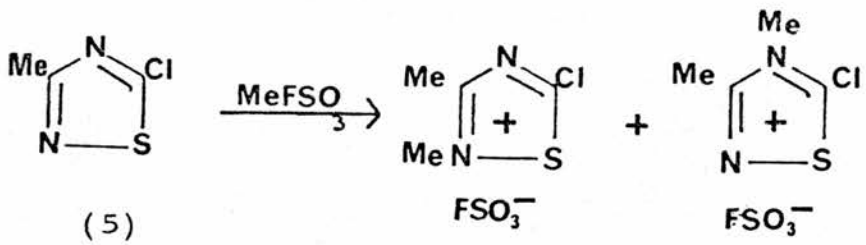


(8a)



(7b)(40%) (8b)(31%)

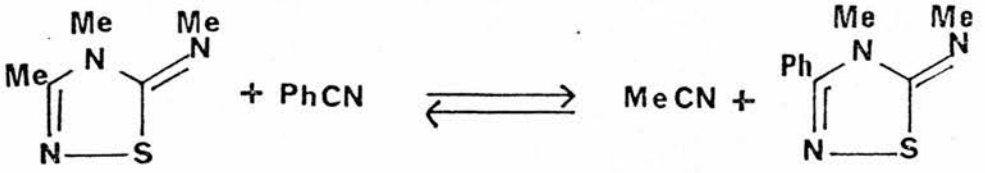
Methylation of compound (5) in dichloromethane with methyl fluorosulphonate gave a product which a ^{1}H nmr spectrum showed to be a mixture of isomers in the approximate ratio of 9:1 indicating that methylation had occurred at both ring positions 2 and 4.



(5)

Reaction of the product mixture with an excess of ethanolic methylamine solution gave a white solid in good yield (65%). This product was found to be identical to the product from the methylation of compound (6), confirming that the product could not have structure (9). A definite differentiation between isomers (7) and (8) on the basis of ^{1}H nmr spectral shifts is impossible as the environments of the methyl groups at N(2) and N(4) are too similar [see Table (E)]. A tentative formulation of the product as the 2,3-dimethyl isomer (7) can however be made on the evidence of the mass spectrum of the product [see Table

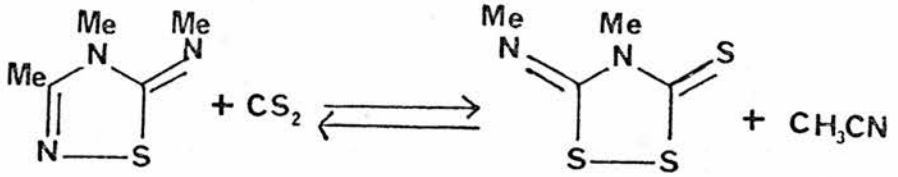
(G)]. The base peak in the spectrum occurs at m/e 61 which corresponds to a CH_3NS fragment which could not be formed in a simple manner from the breakdown of compound (8). All other peaks in the mass spectrum however could have arisen from the breakdown of either (7) or (8). A more definite formulation of the product as structure (7) can be made on the basis of the results of its behaviour with nitriles and heterocumulenes. First, the product did not react with benzonitrile even on prolonged (9.5 hours) refluxing in toluene, and was recovered from the reaction mixture in high yield. From a comparison with the reaction of 5,6-dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (17) with nitriles described in detail in Section 3(a) (page 62), it can be predicted that 3,4-dimethyl- 5-methylimino - 1,2,4-thiadiazole (8) would have reacted with benzonitrile to give 4-methyl- 3-phenyl- 5-methylimino- 1,2,4-thiadiazole (10) with the elimination of acetonitrile.



(8) (10)

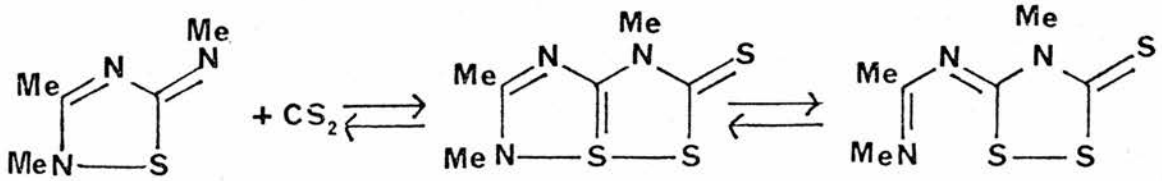
Second, the product (7 or 8) failed to react with carbon disulphide in dichloromethane solution at room temperature and after refluxing for one hour. On evaporation of the reaction mixture the thiadiazole (7 or 8) was recovered quantitatively. It will be shown (Section 6(a), page 88) that compound (17) readily reacted with carbon disulphide to give a 1:1 adduct. Thus compound (8) would also have been expected to react rapidly

at room temperature with carbon disulphide to give a 1:1 adduct, or slowly in refluxing dichloromethane to give 4,5-dihydro-4-methyl- 5-methylimino- 3H- 1,2,4-dithiazole-3-thione (11).



(8) (11)

The fact that the 2,5-dihydro- 2,3-dimethyl- 5-methylimino-1,2,4- thiadiazole (7) did not react with carbon disulphide is perhaps a little surprising in that a similar 1:1 adduct formation could have been envisaged leading to the novel triheterapentalene (12) or further through a bond-switch reaction, similar to those observed by Oliver[6] (see Introduction, page 39) in the reaction of dithiazoles with carbon disulphide or by Goerdeler[123] in the reaction of imino isothiazoles with carbon disulphide, leading to the dithiazole-3-thione (13).



(7) (12) (13)

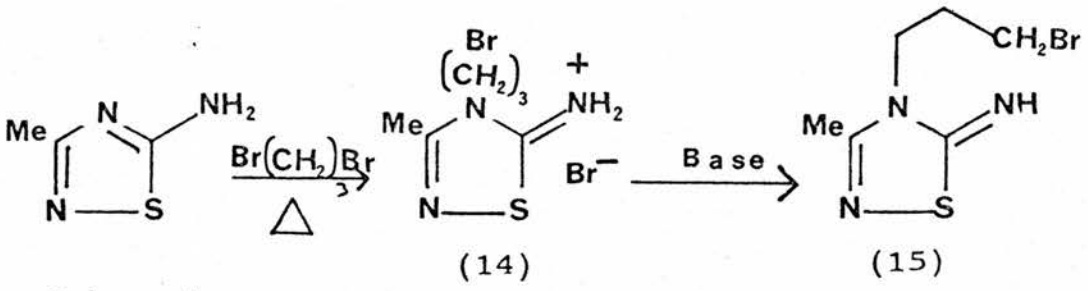
In conclusion, the desired product 4,5-dihydro- 3,4-dimethyl- 5-methylimino- 1,2,4-thiadiazole (1, R^1=R^2=R^3= Me) could not be synthesised efficiently either by the methylation of 4,5-dihydro- 5-imino- 3,4-dimethyl- 1,2,4- thiadiazole (4) which

gave a mixture of products, or from 5-chloro- 3-methyl-1,2,4-thiadiazole (5) by reactions which gave predominantly the 2,5-dihydro- 2,3-dimethyl- 5-methylimino- 1,2,4-thiadiazole (7).

2 Synthesis of 5,6-Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazoles

As the synthesis of the thiadiazole (8) proved unsuccessful an alternative model compound was chosen for our studies. The main problem in the methylation reactions of the 5-amino- 3-methyl- 1,2,4-thiadiazole had been that, although the first methylation occurred selectively at position 4 in the ring to give the 5-imino- 3,4- dimethyl- 1,2,4-thiadiazole (4), the second methylation was not selective and occurred at position 2 in the ring as well as at the desired exocyclic nitrogen atom. A possible way around this problem would be to allow the first alkylation to occur at nitrogen 4 and to constrain the molecule in such a way that the second alkylation could only occur at the exocyclic nitrogen atom. This could be achieved by using an α,ω-dihaloalkane, thus introducing a bridge between the nitrogen atom at position 4 in the ring and the exocyclic nitrogen atom.

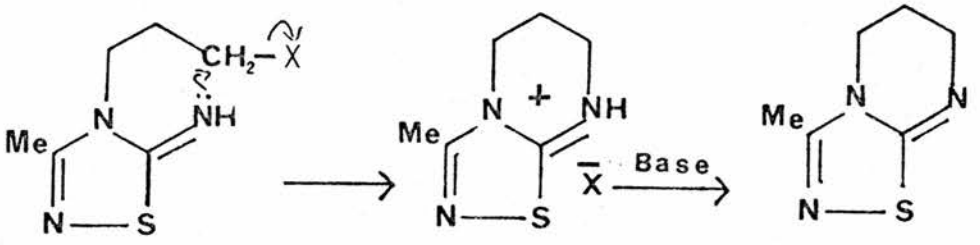
By allowing 5-amino- 3-methyl- 1,2,4-thiadiazole to react with, for example, 1,3-dibromopropane the salt (14) could be formed. Deprotonation of (14) would lead to the 5-imino-thiadiazole (15).



(14) (15)

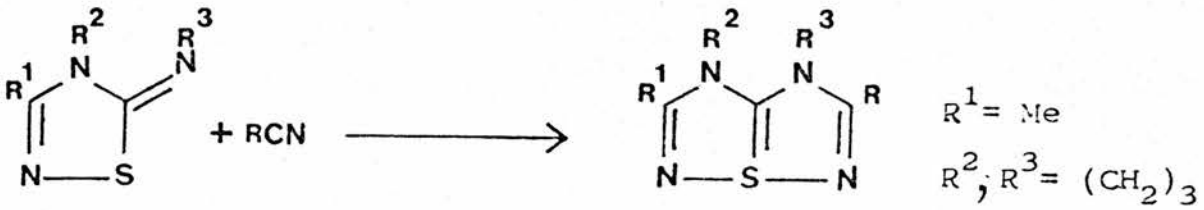
Scheme 1

Compound (15) could then cyclise on being heated to give the hydrobromide (16) which, on deprotonation would give 5,6-dihydro-3-methyl- 4H-pyrimido [1,2,-d] [1,2,4] thiadiazole (17).



(15) (16a = Br) (16b = I) (17)

The pyrimido thiadiazole (17) can be reformulated as [1,R^1= Me, R^2, R^3 =$(CH_2)_3$] and therefore, in principle at least, has the necessary structural features required for reaction with nitriles to give the novel triheterapentalene structure (2).



(1) (2)

(a) Synthesis of 5,6-Dihydro- 3-methyl- 4H- pyrimido [1,2,-d] [1,2,4] thiadiazole.

The reaction of 5-amino- 3-methyl- 1,2,4-thiadiazole with 1,3- dibromopropane was investigated under a variety of conditions. When 5-amino- 3-methyl- 1,2,4-thiadiazole was allowed to react with a 5:1 molar excess of 1,3-dibromopropane in dimethylformamide at a moderate temperature (130 ^{o}C) for 30 minutes, straw coloured needles crystallised from the cold

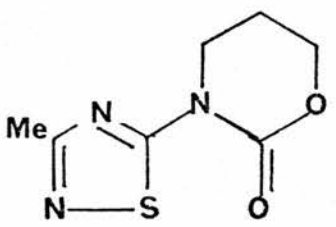
reaction mixture. On being analysed, these crystals were found to be the 5,6-dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium bromide (16a), rather than the expected 5-amino- 3-methyl- 4-(3-bromopropyl)- 1,2,4-thiadiazolium bromide (14). This result suggests that the 5-amino- 3-methyl- 1,2,4-thiadiazole is basic enough to act as a proton scavenger in a dipolar aprotic solvent. This means, however, that the possible yield of the desired pyrimidothiadiazole (17) is necessarily reduced, as half of the original amino thiadiazole goes to form 5-amino- 3-methyl- 1,2,4- thiadiazolium bromide. Deprotonation of the hydrobromide (16a) with aqueous sodium hydroxide followed by extraction with dichloromethane gave the pyrimidothiadiazole (17) as a white crystalline solid in 20% overall yield, after recrystallisation from cyclohexane/ether. Addition of a catalytic amount of sodium iodide to the reaction mixture did not improve the yield significantly. Refluxing the reaction mixture also failed to improve the yield of (17) and produced more side products.

An analogous reaction performed under identical reaction conditions was also carried out using 1,3-diiodopropane in place of the 1,3-dibromopropane. This gave the impure hydroiodide (16b), and after deprotonation of the salt (16b) and sublimation, the pyrimidothiadiazole (17) was obtained in 23% overall yield.

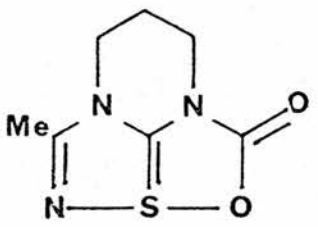
In an attempt to improve the yield of the pyrimidothiadiazole (17) the reaction of 5-amino- 3-methyl- 1,2,4-thiadiazole with 1,3- dibromopropane was carried out in the presence of an excess of solid potassium carbonate. Rather than acting solely as a proton scavenger however the potassium

carbonate was found to react with dibromopropane. The aminothiadiazole, dibromopropane and potassium carbonate were reacted at 120 °C for 20 minutes and without heating for a further 10 minutes before being diluted with water and extracted with benzene. T.l.c. of the benzene extracts showed a mixture of at least eight components including 1,3-dibromopropane, three fast-running compounds, pyrimidothiadiazole (17) and very slow running material.

One of the t.l.c. fast-running components was obtained by chromatography as a highly crystalline white solid. A ^1H nmr spectrum of this product in chloroform-D [see Table (E)] showed peaks at δ 2.275 (quintet), δ 2.55, δ 4.25 (t), δ 4.525 (t), a similar pattern of peaks to that of the pyrimidothiadiazole (17) but shifted downfield, suggesting that the product contained a trimethylene bridge. The mass spectrum of the product showed a molecular ion peak at m/e 199, implying that a unit of CO_2 had also been incorporated into the product. Two possible structures for the product are (i) the cyclic urethane (18), and (ii) the triheterapentalene (19), which has a structure corresponding to one of the types containing one pyridine- type nitrogen atom in the 3-centre bonded sequence.



(18)



(19)

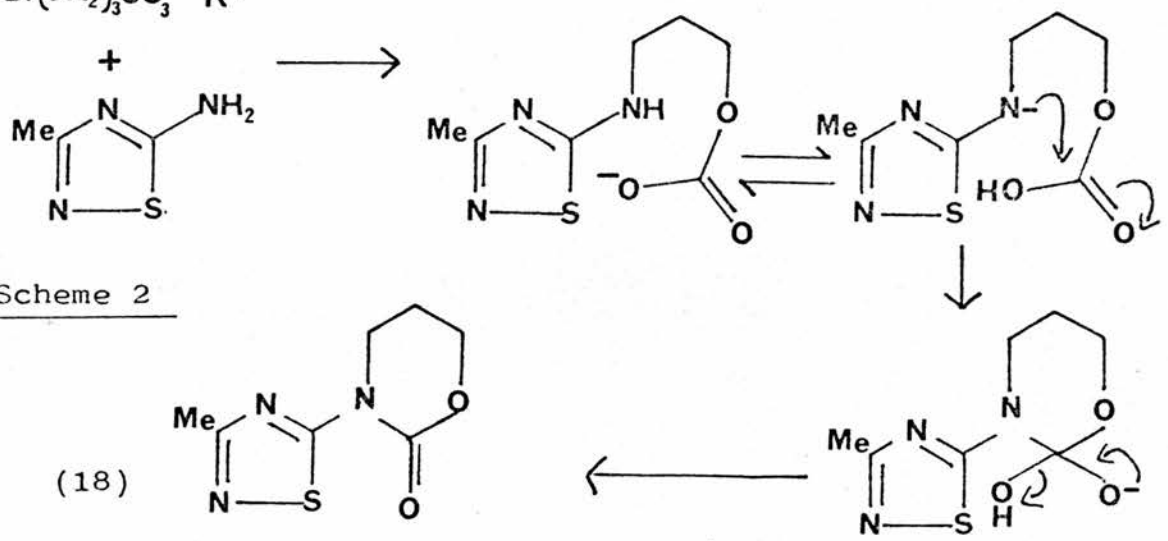
The infra-red spectra of these two compounds would be very

different. Urethanes R-O-CO-N absorb strongly in the region 1740 cm^{-1}-1690 cm^{-1} whereas υ_{CO} in the triheterapentalene (19) would be expected at higher frequency, namely between 1750 cm^{-1} and 1730 cm^{-1}. The product was found to absorb strongly at 1711 cm^{-1} and 1691 cm^{-1}, suggesting that it has the cyclic-urethane structure (18).

A possible mechanism for the formation of the cyclic urethane (18) is shown in scheme 2.

(a) $Br(CH_2)_3Br + K_2CO_3 \longrightarrow Br(CH_2)_3CO_3^- K^+ + KBr$

(b) $Br(CH_2)_3CO_3^- K^+$ +

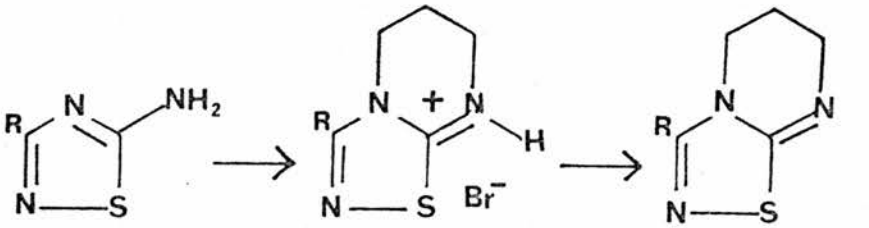


Scheme 2

(18)

(b) Synthesis of 5,6-Dihydro- 4H-pyrimido [1,2,-d] [1,2,4] thiadiazole and 5,6-Dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole.

To test the generality of the reaction of 1,3-dibromopropane with aminothiadiazoles it was decided to synthesise 5,6-dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (22) and the 3-phenyl analogue (23) from the corresponding aminothiadiazoles.



(20;R=H)
(21;R=Ph)

(24;R=H)
(25;R=Ph)

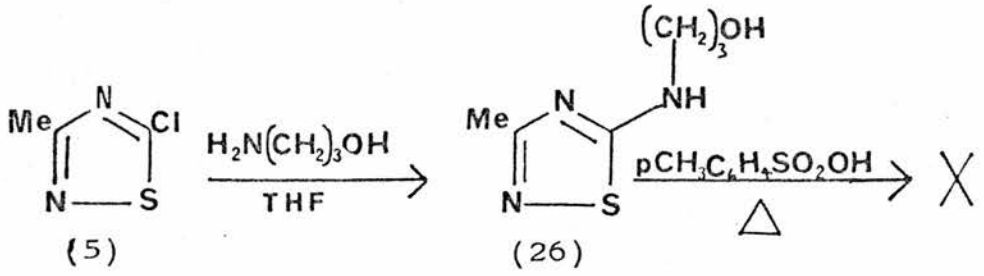
(22;R=H)
(23;R=Ph)

The 5-aminothiadiazole (20) was refluxed for 15 minutes with an excess of 1,3-dibromopropane in dimethylformamide, and cooled to give a tacky brown solid, which afforded the hydrobromide (24) on recrystallisation from propanol. On deprotonation and careful workup under mild conditions the pyrimidothiadiazole (22) was obtained in 22% overall yield. The 5-amino- 3-phenyl- thiadiazole (21) reacted analogously to amine (20) but longer refluxing (1.5 hours) was necessary to produce the hydrobromide (25), which gave the 3-phenyl-pyrimidothiadiazole (23) in 17% overall yield after deprotonation and workup.

(c) Attempted Synthesis of 5,6-Dihydro-3-methyl-4H-pyrimido [1,2-d] [1,2,4] thiadiazole by Other Routes.

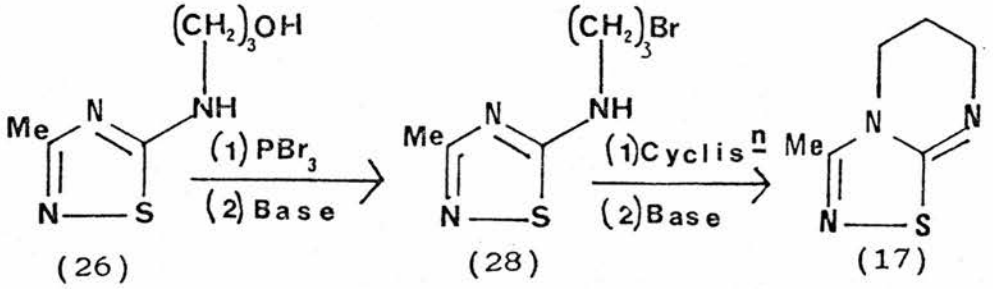
Several syntheses of the pyrimidothiadiazole (17) were attempted, starting from 5-chloro- 3-methyl- 1,2,4-thiadiazole (5).

(1) The chlorothiadiazole (5) in tetrahydrofuran solvent reacted readily with an excess of 3-amino-propan-1-ol to give 5-(3-hydroxypropylamino)- 3-methyl- 1,2,4-thiadiazole (26) in good yield.



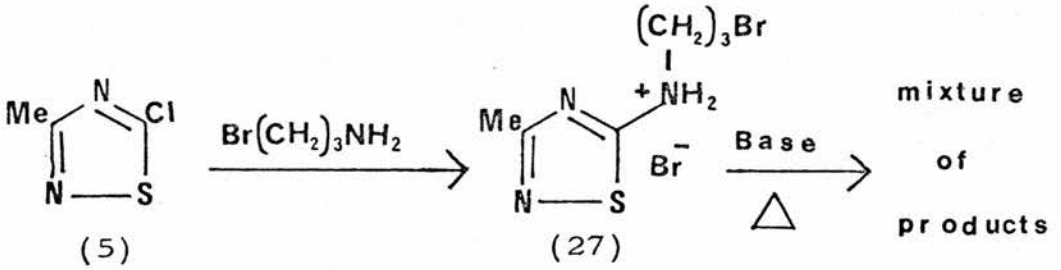
Thermal cyclisation of compound (26) in toluene was attempted in the presence of a catalytic amount of p-toluene sulphonic acid. However no cyclisation product (17) was observed on t.l.c. of the reaction mixture after three hours refluxing.

(2) The hydroxypropylamino thiadiazole (26) reacted with phosphorus tribromide in dichloromethane at room temperature to give a mixture of products. The reaction mixture was deprotonated with aqueous sodium carbonate and extracted with ether and dichloromethane. The organic extracts were found by t.l.c. to contain some pyrimidothiadiazole (17) and slower running material, as well as starting material (26) and the desired bromopropyl compound (28). The organic extracts were evaporated and a solution of the residue in toluene was refluxed for 30 minutes. After deprotonation and chromatography the pyrimidothiadiazole (17) was obtained in 13% yield.



(3) An alternative route to the 5-(3-bromopropylamino)-3-methyl- 1,2,4- thiadiazole (28) involving the reaction of

bromopropylamine with the chlorothiadiazole (5) was investigated. Reaction of the chlorothiadiazole (5) with bromopropylamine gave the salt (27) which was not isolated. However on deprotonation and attempted thermal cyclisation in toluene a mixture of products resulted, which included the desired cyclisation



(5) (27)

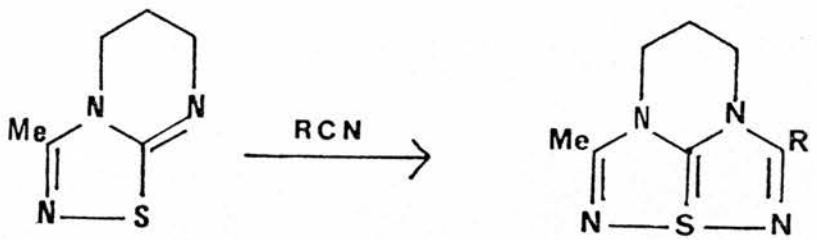
product (17) as well as very polar material. The reaction was therefore abandoned at this point.

Thus although 5,6-dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (17) can be prepared by these reactions the yields were low and the product was not as clean as that obtained from the reaction of dibromopropane with aminothiadiazole, probably due to competition from intermolecular coupling reactions of compound (28). Therefore it was decided to use the synthesis starting from 5-amino- 3-methyl- 1,2,4-thiadiazole and proceeding via compound (16) for the preparation of compound (17) to be used as starting material in subsequent work.

3 Reactions of 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazoles with Nitriles

(a) The Reactions of 5,6-Dihydro- 3-methyl-4H-pyrimido [1,2 -d] [1,2,4] thiadiazole .

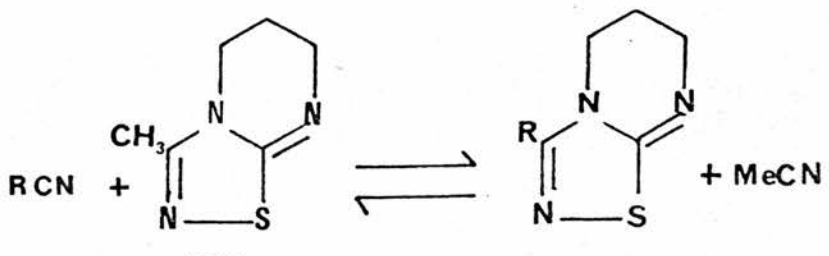
The reaction of 5,6-dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazoles with nitriles is exemplified by the reactions of 5,6-dihydro- 3- methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (17). It was anticipated that the reaction of compound (17) with nitriles could lead to the novel triheterapentalene structure (29), if not as a stable



(17) (29)

product then as a higher energy intermediate or transition state with similar geometry to that of the triheterapentalene.

The reaction of compound (17) with a variety of nitriles was investigated. In general these reactions resulted in the replacement of CH_3CN by the reactant nitrile. These reactions occurred under



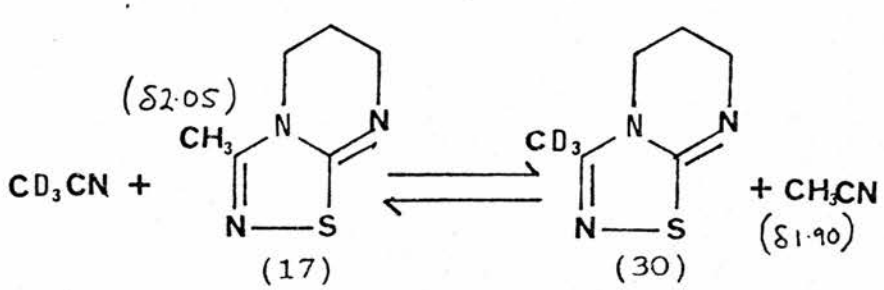
(17)

	R=	%Yield
(23)	Ph	55
(30)	CD_3	84
(31)	$CNCH{=}CH$	65
(33)	$MeOCH_2$	62
(34)	Py	82
(35)	$pNO_2C_6H_4$	50

a variety of conditions.

The reaction of pyrimidothiadiazole (17) with nitriles was shown to be reversible in the case of deuterated acetonitrile (CD_3CN). The pyrimidothiadiazole (17) reacted slowly in refluxing acetonitrile-D_3 to give the 3-(trisdeuteriomethyl)-pyrimidothiadiazole (30) in good yield (84%). The reversible nature of this conversion was illustrated by the reaction of (30) with acetonitrile to give back compound (17) in high yield (86%). The reaction of acetonitrile-D_3 with (17) was followed by ^1H nmr spectroscopy. A 0.5 M solution of compound (17) in acetonitrile-D_3 (ca 36:1 molar excess of nitrile) was left to stand at room temperature and the ^1H nmr spectrum subsequently recorded at various time intervals. The progress of the reaction could be followed from the relative integrals of the signals due to the methyl group of the product (CH_3CN) at δ 1.90 and, corresponding to the methyl group in the unreacted starting material (17) at δ 2.05 [see graph, page 166]

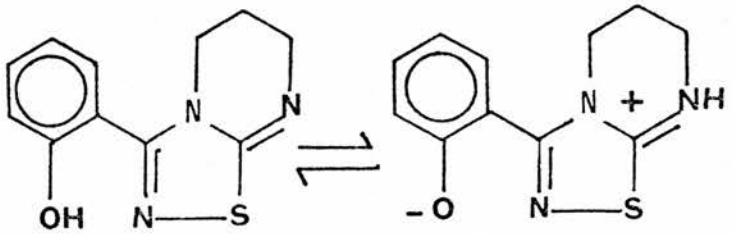
It can be seen from the graph that equilibrium is reached after approximately 30 days. The equilibrium ratio for the reaction, calculated at t_∞ (after ca 50 days) gave a value of 2.75 i.e. a 73% conversion of compound (17) to compound (30).



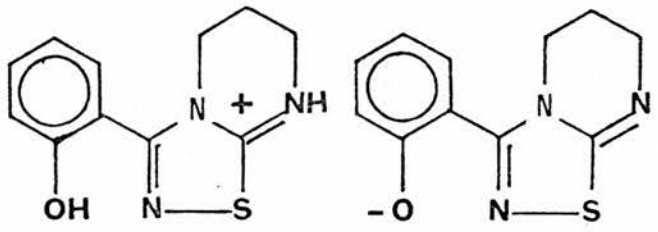
The reaction of the pyrimidothiadiazole (17) with nitriles occurred under a variety of conditions, slowly at room temperature, more quickly in boiling toluene solution or in the boiling reactant nitrile alone. As in the case of the reaction of compound (17) with acetonitrile-D_3 these reactions were, in principle at least, reversible.

As has already been shown compound (17) reacted with acetonitrile- D_3 to give compound (30), either slowly at room temperature or more quickly in refluxing solution. Compound (17) also reacted rapidly in boiling benzonitrile to give 3-phenyl-pyrimidothiadiazole (23) in modest yield.

The pyrimidothiadiazole (17) reacted with methoxyacetonitrile, pyridine- 4-carbonitrile and p-nitrobenzonitrile in boiling toluene to give compounds (33), (34) and (35) respectively. Compound (17) reacted with an excess of 2-cyanophenol in boiling toluene to give a white precipitate, which on recyrstallisation from ethanol afforded 3-(2-hydroxyphenyl)- pyrimidothiadiazole (36) as off-white spars. The product (36) had a very high melting point [228-229 °C (with decomposition)] and was only sparingly soluble in polar organic solvents at room temperature. This insolubility and melting behaviour suggests that the product does not have the simple structure (36a) but could perhaps have a salt-like structure (36b), in which the acidic phenolic proton has transferred to the basic nitrogen atom at position 7. Further evidence for the



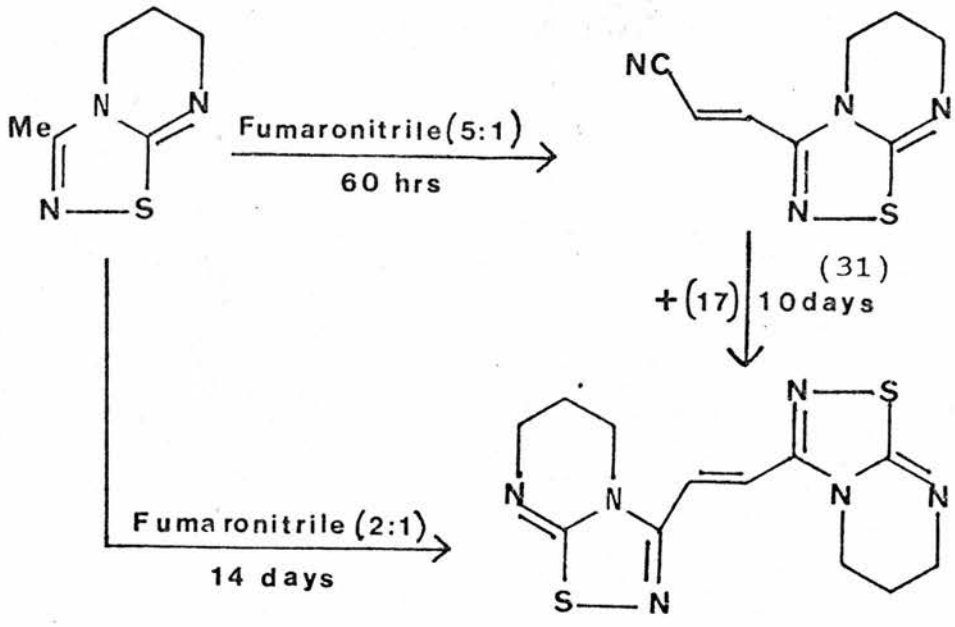
(36a) (36b) I



(36b) II

salt-like character of (36) is seen in the infra-red spectrum which has a broad absorption at 2560 cm^{-1} due to $\overset{+}{N}$-H; however this is not conclusive as hydrogen bonded O-H groups absorb in the region 3200-2500 cm^{-1}.

When solutions of fumaronitrile (10 mmol) and the pyrimidothiadiazole (17) (5 mmol) in toluene were mixed at room temperature a deep yellow colour appeared almost immediately. This colour arose mainly from the expected product compound (31). However t.l.c. of the reaction mixture after two hours revealed the presence of a second, very slow- running, yellow product. This product, 1,2-di {5,6-dihydro-4H- pyrimido [1,2-d] [1,2,4] thiadiazole-3-yl} ethene (32), was obtained in 79% yield as a yellow solid by filtration of the reaction mixture after 14 days. Using a 5:1 molar excess of fumaronitrile



(32)

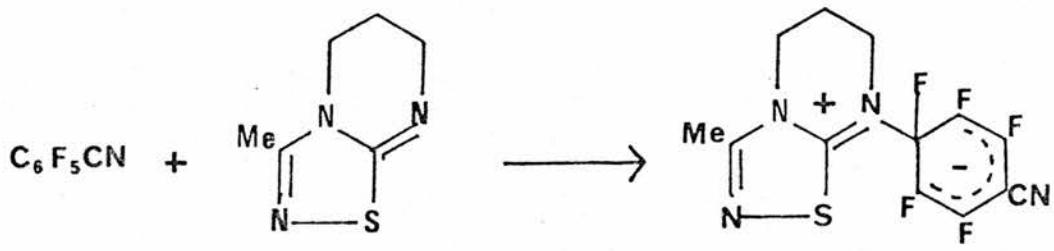
and leaving the reaction for only 60 hours at room temperature, the 3-cyanovinyl pyrimidothiadiazole (31) was obtained in 65% yield after chromatography. However, compound (31) readily disproportionates to give compound (32) and fumaronitrile, and was converted into compound (32), in moderate yield, by reaction with one equivalent of compound (17) in toluene.

Some of the reactions of nitriles with compound (17) were atypical and did not result in straight forward replacement of CH_3CN by the reactant nitrile.

Compound (17) did not react with trimethylacetonitrile even after being refluxed for two hours in an excess of the nitrile. This lack of reactivity is probably due to steric hindrance of the carbon atom of the attacking nitrile.

On addition of compound (17) to pentafluorobenzonitrile a deep red precipitate was formed. This red precipitate was probably a Meisenheimer complex formed by nucleophilic attack of

the imino-nitrogen of compound (17) on the aromatic ring.



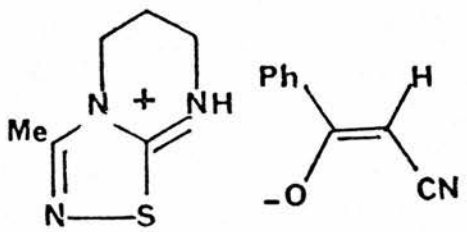
A solution of equimolar quantities of compound (17) and cyanomethyltriphenylphosphorane in refluxing chloroform gave triphenylphosphine oxide in 55% yield; compound (17) was recovered in 82% yield. Rather than acting as a 1,3-dipolaraphile the cyanomethyltriphenylphosphorane may have undergone base catalysed hydrolysis by traces of water in the solvent.

$$Ph_3\overset{+}{P}-\overset{-}{C}HCN \xrightarrow[Base]{H_2O} Ph_3PO + CH_3CN$$

The reactions of compound (17) with nitriles containing an activated methylene group next to the nitrile function were different again.

A white precipitate was formed rapidly on mixing solutions of benzoylacetonitrile and compound (17) in toluene. Elemental analysis of the precipitate indicated that a 1:1 adduct of the nitrile and (17) had been formed in 84% yield. A mass spectrum of the product however did not show a molecular ion peak at m/e 300, but only the spectra of the starting materials. The adduct dissolved in dimethyl sulphoxide-D_6 gave only the spectra of the pyrimidothiadiazole (17) and benzoylacetonitrile, indicating that

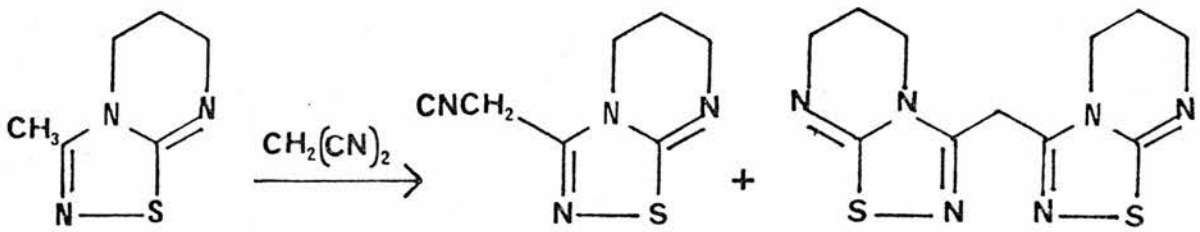
the product had dissociated in the polar solvent. The infra-red spectrum (KBr disc) of the product showed a very broad absorption at 2700 cm^{-1}-2400 cm^{-1} due to $\upsilon \overset{+}{N}$-H, and a strong absorption at 2150 cm^{-1} due to υ(C≡N). This is a shift to lower frequency of the υ(C≡N) [υ(C≡N) in benzoylacetonitrile occurs at 2258 cm^{-1}] indicative of C=C=N type character resulting from a negative charge conjugated with a nitrile. There is also no peak at 1690 cm^{-1} in the product, whereas υ C=O in benzoylacetonitrile occurs at 1690 cm^{-1}, suggesting that the adduct is an enolate salt of structure (37), and results from reaction of the basic nitrogen atom in the pyrimidothiadiazole (17) with the weakly acidic hydrogens of the benzoylacetonitrile.



(37)

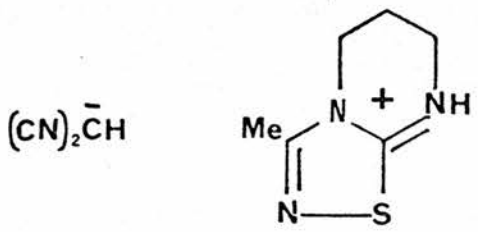
Similarly, soon after mixing solutions of compound (17) and malononitrile in toluene at room temperature, a yellow colour appeared and a precipitate formed slowly. T.l.c. of the precipitate in methanol showed three spots: a fast-running yellow compound (r_f 0.7), pyrimidothiadiazole (17) (r_f 0.25) and a slow-running yellow compound (r_f 0.1). From a comparison with the reaction of compound (17) with fumaronitrile, the fast-running product was probably 3-(cyanomethyl)-pyrimidothiadiazole (38) and the slow-running yellow product was probably di-{5,6-dihydro- 4H- pyrimido [1,2-d] [1,2,4]

thiadiazole-3-yl} methane (39).



(17) (38) (39)

As in the reaction of benzoylacetonitrile with compound (17) however, the products (38) and (39) contain an acidic methylene group and a basic imino nitrogen. The insolubility of the products in toluene could therefore be due to there being either inter- or intra-molecular salt formation [eg (40)]. Dissolution of salt (40) in methanol could cause dissociation to give back malononitrile and compound (17), which was observed on t.l.c. of the precipitate from the toluene reaction mixture.

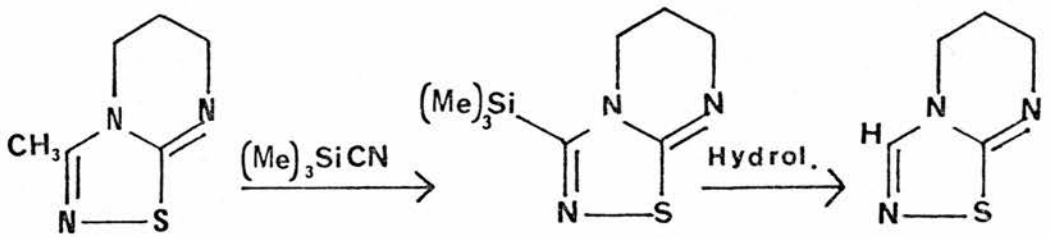


(40)

A ^{1}H nmr spectrum of a sample of the precipitate in dimethyl sulphoxide-D_6 showed the major reaction product to be compound (38) and a mass spectrum [see Table (D)] was consistent with this.

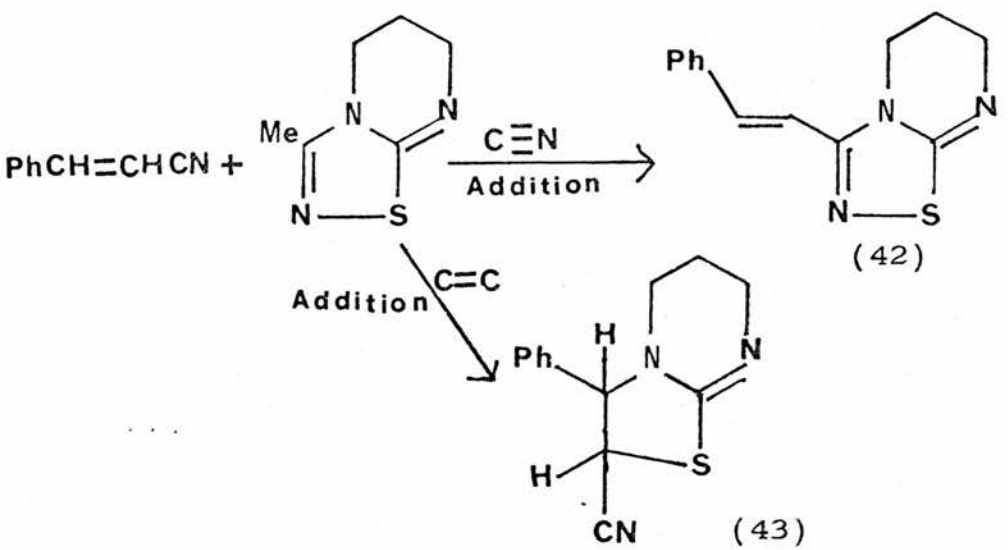
In an attempt to find an alternative synthesis of the pyrimidothiadiazole (22) the reaction of compound (17) with trimethylsilyl cyanide was carried out under a variety of

conditions, both in trimethylsilyl cyanide alone and also in hydrocarbon solvents. The aim of the reaction was to synthesise the 3-trimethylsilyl- pyrimidothiadiazole (41) which on hydrolysis would yield the pyrimidothiadiazole (22). However, a mixture of products resulted from both reactions and decomposed during workup.



(17) (41) (22)

As compound (17) reacted smoothly with benzonitrile to give 3-phenyl-pyrimidothiadiazole (23) it was decided to investigate the reaction of (17) with trans-cinnamonitrile, a vinylogue of benzonitrile. Two possible reactions were envisaged (a) addition across the carbon-nitrogen triple-bond leading to 3-styryl pyrimidothiadiazole (42), (b) addition across the carbon-carbon double-bond leading to 2-cyano- 3-phenyl-pyrimidothiadiazole (43) (or the 3-cyano-2-phenyl-isomer).



(42) (43)

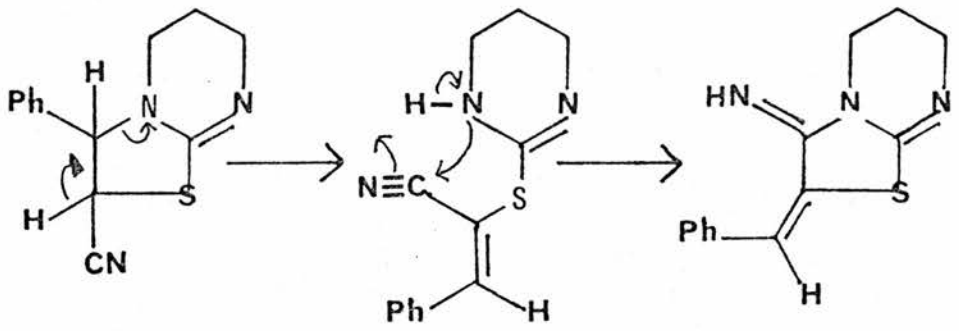
After refluxing a solution of trans-cinnamonitrile and pyrimidothiadiazole (17) in toluene for seven hours t.l.c. showed two overlapping spots at r_f 0.65, with traces of several slower running compounds. The reaction mixture was chromatographed on silica to remove the excess of cinnamonitrile and then rechromatographed to separate the two fast-running products. The faster-running of the two products was obtained as white needles in 11% yield after recrystallisation from cyclohexane. The mass spectrum of this product showed a molecular ion peak at m/e 243 (41%), and microanalysis agreed with the composition of $C_{13}H_{13}N_3S$, as expected for compounds (42) and (43). The infra-red spectrum of the product in a KBr disc showed a weak absorption at 2245 cm^{-1} due to υ C≡N, while a carbon tetrachloride solution showed a very weak absorption at 2250 cm^{-1}, suggesting the product had a structure (43) rather than (42). The ^1H nmr spectrum of the product however, was solvent dependent [see Table (E)]. In chloroform-D two triplets (each 2H) were seen at δ 3.1 and δ3.5 respectively, and two doublets (each 1H) at δ4.0 and δ4.8. The coupling constant $J_{2,3}$ for the doublets was 6.1 Hz which implies an axial-equatorial arrangement as would be expected for the hydrogen atoms at C(2) and C(3) in structure (43). The spectrum obtained in dimethyl sulphoxide-D_6 however was significantly different and showed a broad multiplet from δ 2.8-3.4 (4H), instead of two triplets, and two doublets at δ4.6 and δ5.1, $J_{2,3}$ 3.9 Hz. The spectrum in acetonitrile-D_3 was different again, having a multiplet at δ3.0

(2H) and a triplet at δ 3.4 (2H); the two doublets are much closer together at δ 4.6 and δ 4.9 (each 1H) with $J_{2,3}$ 4.7 Hz. These results suggest that a conformational change was occurring in the molecules but it is difficult to see exactly what sort of change could account for such large differences in chemical shift and coupling constant between solvents.

The slower-running of the two products on t.l.c. was obtained as a cream powder in 23% yield after recrystallisation from cyclohexane. Microanalysis again was consistent with a composition of $C_{13}H_{13}N_3S$ but the mass spectrum showed only a small molecular ion peak at m/e 243 (4%) with a more intense peak at m/e 242 (14%), M^+-H. There were also large peaks at m/e 134 (21%) $[PhCH{=}C{=}S]^+$, m/e 129 (9%) $[PhCH{=}CHCN]^+$, m/e 44 (100%) $[CS]^+$. The ^{1}H nmr spectrum of this product was not solvent dependent and showed [Table (C)] a quintet (δ1.9, 2H), two triplets (δ3.5 andδ3.7, 2H), an aromatic multiplet (δ7.5, 5H), a singlet (δ7.75, 1H) and a broad signal (δ9.0, 1H) which was exchangeable in D_2O. Therefore the slower-running product does not have structure (42) (which contains no exchangeable hydrogens). The infra-red spectrum of the product, both in the solid state and solution, showed a strong absorption at 3340 cm^{-1}-3320 cm^{-1} due to υ N-H; no peak was visible around 2260-2200 cm^{-1} suggesting that the product did not contain a nitrile function, although this can not be taken as altogether conclusive as some unconjugated cyanides, eg cyanohydrins[17] show no C≡N absorption.

A possible structure (44) for the slower-running of the two products, consistent with the spectral and analytical data, is

shown below with a possible mechanism for its formation.

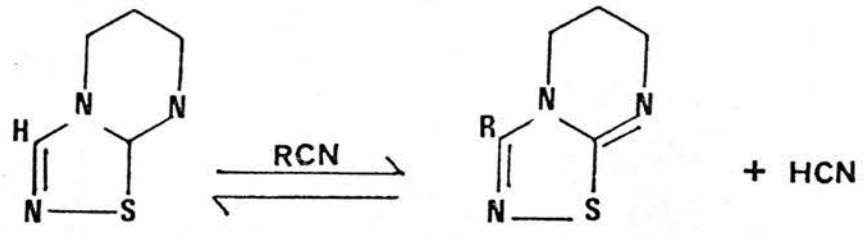


(43) (43a) (44)

The products (43) and (44) seem to decompose on chromatography and are therefore difficult to separate in this way. Although no C-N addition product (42) was observed, a small amount may have been present but decomposed during prolonged chromatography.

(b) The Reaction of 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazole with Nitriles.

The results of the reactions of pyrimidothiadiazole (22) with nitriles parallel those of compound (17). Compound (22) reacted slowly with refluxing acetonitrile to give pyrimidothiadiazole (17) in 46% yield, and with benzonitrile in refluxing toluene to give compound (23) in 59% yield.



(22) (17; R=Me) (23; R=Ph)

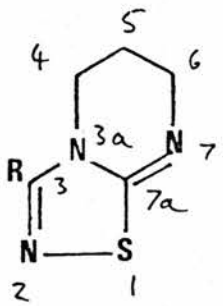
(c) Spectral Properties of the 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles.

(1) ^{1}H nmr Spectra [Table (A)]

The ^{1}H nmr spectra of the pyrimidothiadiazoles show a multiplet (seen as a quintet) around δ 1.8 due to 5-CH_2, two triplets, sometimes overlapping, between δ 3.2 and δ 4.0 due to 4-CH_2 and 6-CH_2, and signals due to the substituent at position 3.

(2) ^{13}C nmr Spectra [Table (B)]

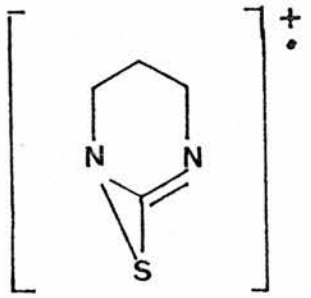
The pyrimido [1,2-d] [1,2,4] thiadiazole system generally exhibits three triplets and two singlets [a doublet and a singlet in the case of compound (22)] in the ^{13}C nmr spectrum. A triplet at approximately δ 19 due to C(5), J_{CH} 130-131 Hz; two overlapping triplets between δ 42 and δ 47 due to C(4) and C(6). The coupling constant J_{CH} for the highfield triplet is larger than that of the lowfield triplet although both occur in the region of 138-146 Hz. The coupling constant J_{CH} of the methylene group C(4) and C(6) is known to be related to the degree of charge localisation on the nitrogen atoms[8,9] 3a and 7, therefore a tentative assignment of the highfield triplet as C(4) and the lowfield triplet as C(6) can be made. The two very lowfield

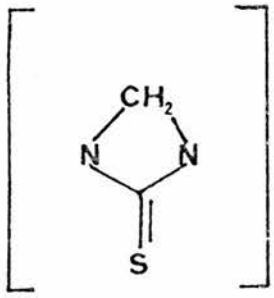


signals can be assigned conclusively in the case of compound (22, R=H) as C(3) appears as a doublet at δ 147 (J_{CH} 205.8 Hz), and C(7a) as a singlet at δ 161. Thus the singlets observed at δ160-163 in other pyrimidothiadiazoles can be assigned as C(7a) and the singlet found between δ 154 and δ 158 as C(3). These assignments parallel those of other 5-(substituted amino)-3,4-disubstituted- 1,2,4-thiadiazoles[9].

(3) Mass Spectra [Table (D)]

The mass spectra of the pyrimidothiadiazoles are characterised by (i) an $M^{+\cdot}$ peak, usually intense and often the base peak, (ii) a peak of low intensity at m/e 114 corresponding to $M^{+\cdot}$-RCN (45), (iii) peaks

(45) 

(46) 

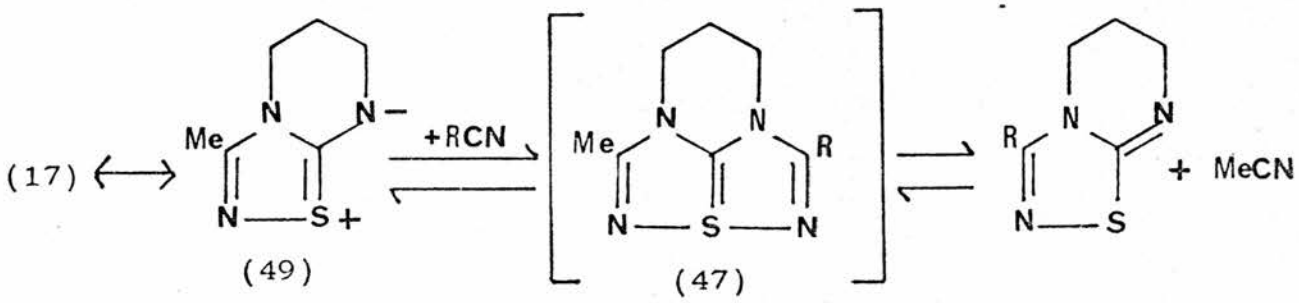
due to the nitrile sulphide $[RCNS]^{+\cdot}$ (intense and sometimes the base peak) resulting from scission of the C(3)-N(3a) and S(1)-C(7a) bonds (cf the thermal fragmentation of 1,3,4-dithiazole-2-ones giving nitrilesulphides[10]), and (iv) smaller peaks due to the nitriles $[RCN]^{+\cdot}$. All spectra also exhibit a peak of variable intensity at m/e 86 corresponding to a $[CH_2NCSN]^{+\cdot}$ fragment (46) or some isomer. The salts of the pyrimidothiadiazoles do not exhibit $M^{+\cdot}$ peaks but do show the spectra of the free bases and the counter ion.

4 Mechanism of the Reaction of 5,6-Dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole with Nitriles

Two mechanisms can be considered for the formation of the cycloadducts from (17); (a) concerted cycloaddition of the nitrile onto (17) followed by elimination of acetonitrile, (b) elimination of acetonitrile generating a thiaziridine-imine *in situ* followed by addition of the reactant nitrile.

(a) Addition-Elimination Mechanism.

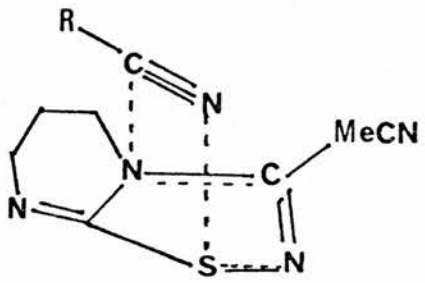
This mechanism is a bimolecular reaction involving first the addition of the reactant nitrile to give a triheterapentalene structure (47), with the arrangement of double bonds at the ends of the three-centre bond which we had set out to make, either as a high energy Intermediate or a Transition State with the same geometrical arrangement as the triheterapentalene, followed by elimination of MeCN to give the observed product (or elimination of RCN to give back the starting materials).



In this mechanism compound (17) is acting as a masked-1,3-dipole toward nitriles. The 1,3-dipolar structure (49) is isoelectronic with the allyl anion, and is therefore allowed to undergo a concerted reaction with 2π- electronic systems in a suprafacial

manner[12], although a stepwise mechanism for the addition of the nitrile is not excluded[13].

An alternative intermediate (48) can be proposed in this mechanism but as the pyrimidothiadiazole (17) is symmetrically substituted at N(3a) and N(7), and the reactions are reversible, it is indistinguishable practically from (47).

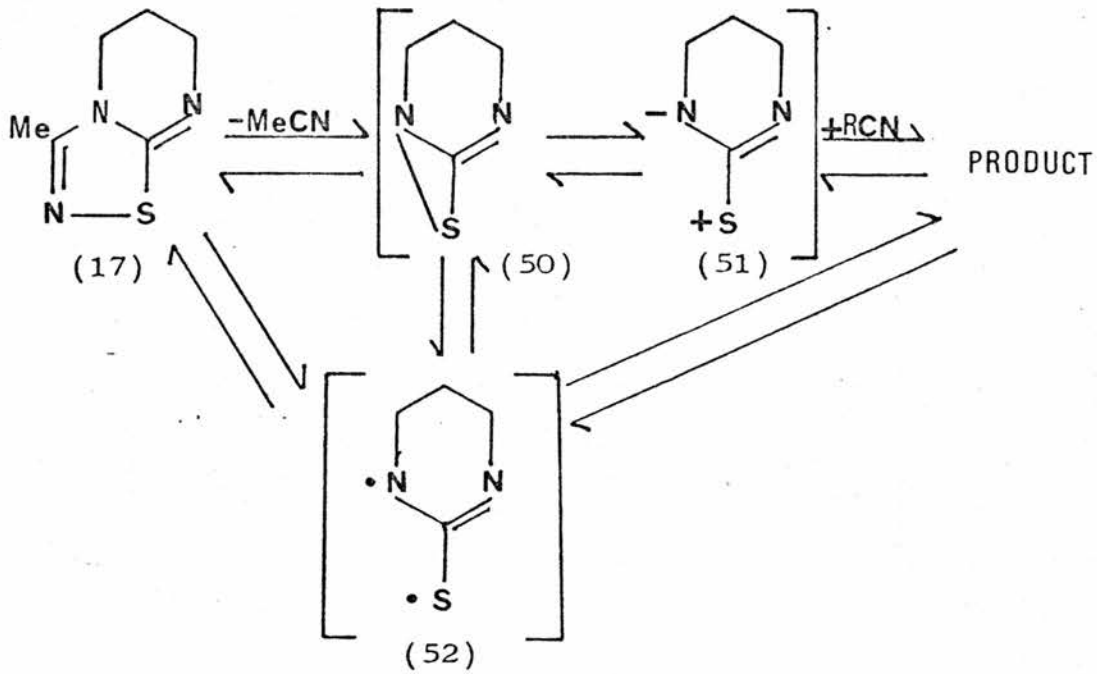


(48)

This mechanism was proposed by L'abbé *et al*[11] in the reactions of 4-alkyl- 5-(alkylimino)- 1,2,3,4-thiatriazoles with various heterocumulenes.

(b) Elimination-Addition Mechanism.

This is a two-step process involving firstly a unimolecular decomposition (retrocycloaddition) with loss of MeCN from compound (17) to give a thiaziridineimine (50), or its ring-opened dipolar form (51), or a singlet diradical species (52) [which could be formed either from compound (17) or from compound (50)], followed by addition of RCN to give the observed products.



A two-step unimolecular mechanism of this type was proposed by L'abbé[14] to explain the reactions of 4-alkyl-5-sulphonylimino- 1,2,3,4-thiatriazoles with enamines.

Distinguishing between the above mechanisms for the reaction of (17) with nitriles is not without problems. The close structural similarity of the reactants and products makes following the reaction by U.V. spectroscopy difficult, although the major drawback of this method is that at the low concentrations required for U.V. spectroscopy the reactions are extremely slow. ^{1}H nmr spectroscopy can be used to follow the progress of the reaction for example of compound (17) with acetonitrile-D_3, but as even small changes in the concentration of the reactant nitrile or compound (17) could significantly alter the dielectric constant of the reaction mixture, and hence the mechanism, kinetically meaningful information cannot be obtained by this technique.

Although quantitative kinetic information cannot be obtained for the reactions some qualitative conclusions may be

drawn from the fact that compound (17) reacts smoothly with CD_3CN and fumaronitrile at room-temperature, at which compound (17) is quite stable. This would tend to favour a bimolecular mechanism, although the reactions carried out in refluxing toluene and at higher temperatures could be occurring by either or both mechanisms.

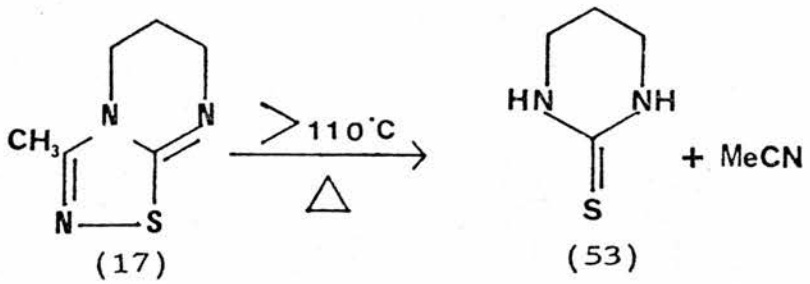
5 Thermolysis Reactions of 5,6-Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazoles

In connection with the possibility of a diradical species being an intermediate in the reaction of the pyrimidothiadiazoles with nitriles it was decided to examine the behaviour of the pyrimidothiadiazoles on heating.

(a) The Thermolysis of 5,6-Dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole in Various Solvents.

Solvents with abstractable hydrogen atoms were used which, it was hoped, would reduce any radical intermediates formed on thermolysis of the pyrimidothiadiazole (17).

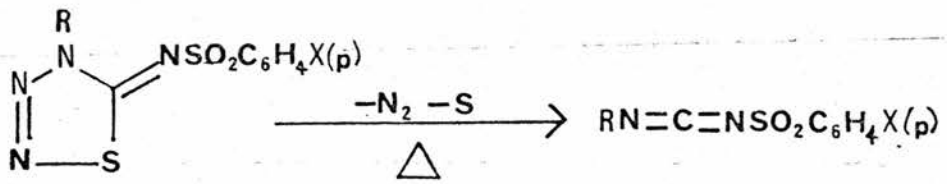
The pyrimidothiadiazole (17) was found to decompose slowly in refluxing 1,2,3,4-tetrahydronaphthalene (tetralin) (bp 207 °C) to give hexahydropyrimidine-2-thione (53) in 65% yield. This is a minimum yield of the thiourea as it is the yield after sublimation of the crude reaction product. Compound (17) also decomposed to give the thiourea (53) in refluxing 1-methyl-4-isopropylbenzene (p-cymene) (bp 178 °C), and in boiling tert-butylbenzene (bp 160 °C) although in this case there was extensive charring.



(17) (53)

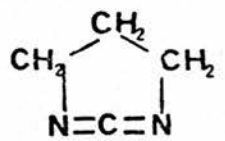
Two interesting features of this conversion are of note.

First, the pyrimidothiadiazole (17) decomposes at quite high temperatures to give another stable heterocycle without loss of sulphur. This contrasts with the behaviour of 4-alkyl-5-sulphonylimino- 1,2,3,4-thiatriazoles (54) which afforded sulphonylcarbodiimides (55) on thermolysis[14].



(54) (55)

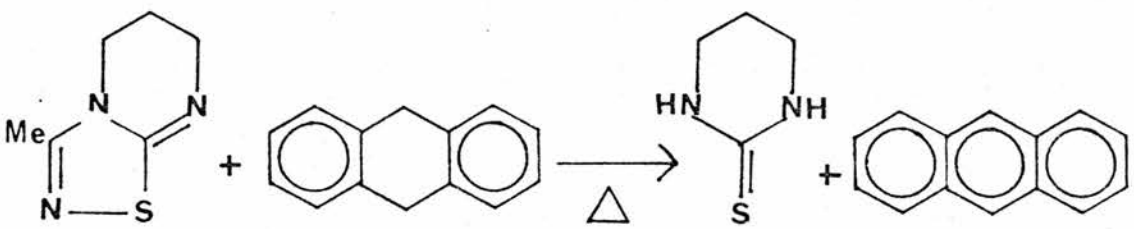
A possible explanation for the retention of sulphur in the decomposition of compound (17) is that the formation of a carbodiimide would lead to a very strained ring system (56).



(56)

The second feature is that the thiourea (53) formed in the thermolysis of compound (17) in hydrocarbon solvents is a reduction product. This suggests that at high temperature compound (17) does decompose to give a radical intermediate which can abstract hydrogen from the reaction mixture. There are two sources of abstractable hydrogen present in the system, namely the benzylic protons of the tetralin solvent (for benzylic protons D=88 kcal mol^{-1})[18], and the acetonitrile by-product (D $NCCH_2$-H=93 kcal mol^{-1})[19]. To identify the source of the hydrogen in the product (53) the thermolysis of compound (17) was carried out in the presence of one equivalent of 9,10-dihydroanthracene

(57), which has two readily abstractable benzylic hydrogens (D C-H=76.6± 1.5 kcal mol^{-1})[18], in an inert high-boiling solvent, o-dichlorobenzene. This gave the hexahydropyrimidine-2-thione (53) in 80% yield and anthracene (58) in 58% yield after workup.

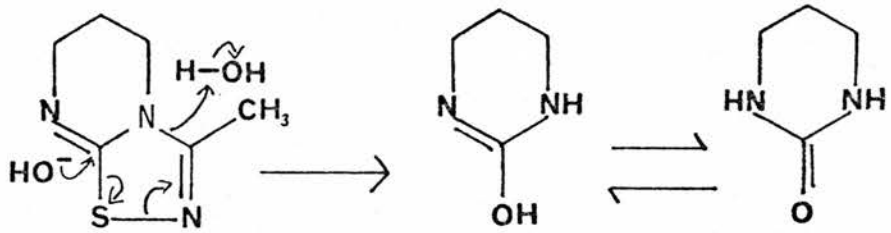


(17) (57) (53) (58)

However on prolonged refluxing in toluene, which also contains abstractable hydrogens (D $C_6H_5CH_2$-H = 85 kcal mol^{-1})[18], compound (17) was found to be stable. Only a trace of the thiourea (53) was observed by t.l.c. of the reaction mixture after refluxing for 72 hours, and the pyrimidothiadiazole (17) was recovered in good yield. This indicates that at low temperatures (below 110 °C) the pyrimidothiadiazole (17) does not decompose to give a diradical intermediate, and therefore it is unlikely that the reactions of compound (17) with nitriles which occur in refluxing toluene or at lower temperatures are taking place via the diradical intermediate (52).

On the other hand, when compound (17) was refluxed in a mixture of butan-1-ol and water (bp 110-120 °C) for 72 hours a mixture of hexahydropyrimidine- 2-thione (53, 32%) and hexahydropyrimidin- 2-one (59, 21%) was obtained. This reaction must be taking place by a different mechanism from the radical-abstraction reactions mentioned above. A possible

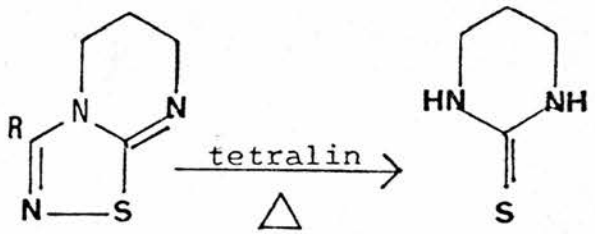
mechanism for the formation of the urea (59) is shown below.



(59)

(b) The Thermolysis of 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole and 5,6-Dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole in Tetralin.

The pyrimidothiadiazoles (22) and (23) decomposed to give hexahydropyrimidine- 2-thione (53) on boiling in tetralin, although compound (22) gave only a low yield of the thiourea (53).



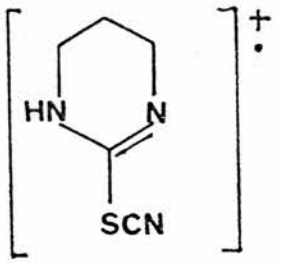
(22 ; R=H)
(23 ; R=Ph)

(53)

(c) The Thermolysis of 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazole in Toluene.

Whereas the 3-methyl-pyrimidothiadiazole (17) was stable in refluxing toluene, the pyrimidothiadiazole (22) decomposed slowly to give in high yield a white solid which was very slow-running on t.l.c. (silica, eluting with methanol). Elemental analysis was consistent with a molecular formula of $C_9H_{13}N_5S_2$ and this

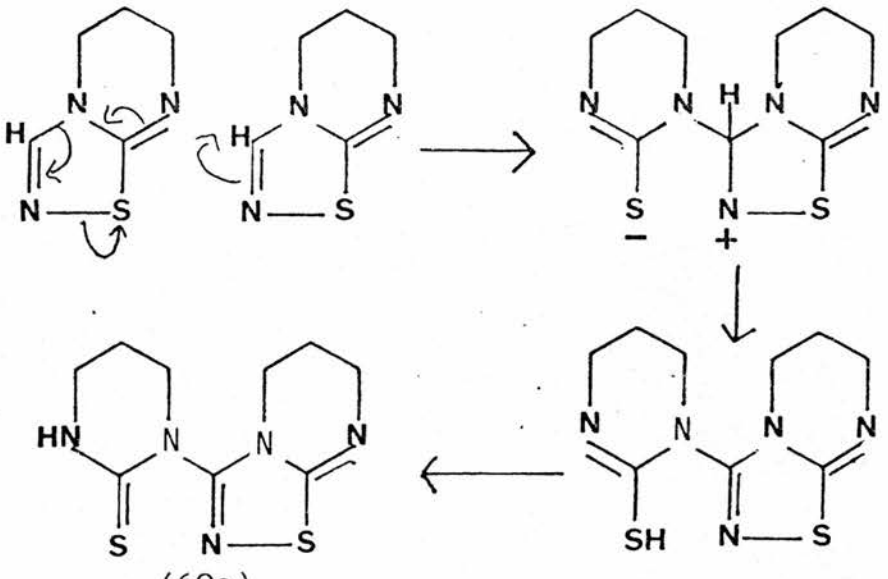
agreed with the mass spectrum which showed an intense molecular ion peak at m/e 255 (70%). The mass spectrum of the product also showed intense peaks at m/e 116 (100%) due to the thiourea (53) and 141 (74%) due to either compound (22) or perhaps the 2-thiocyanato-tetrahydropyrimidinium ion (X).



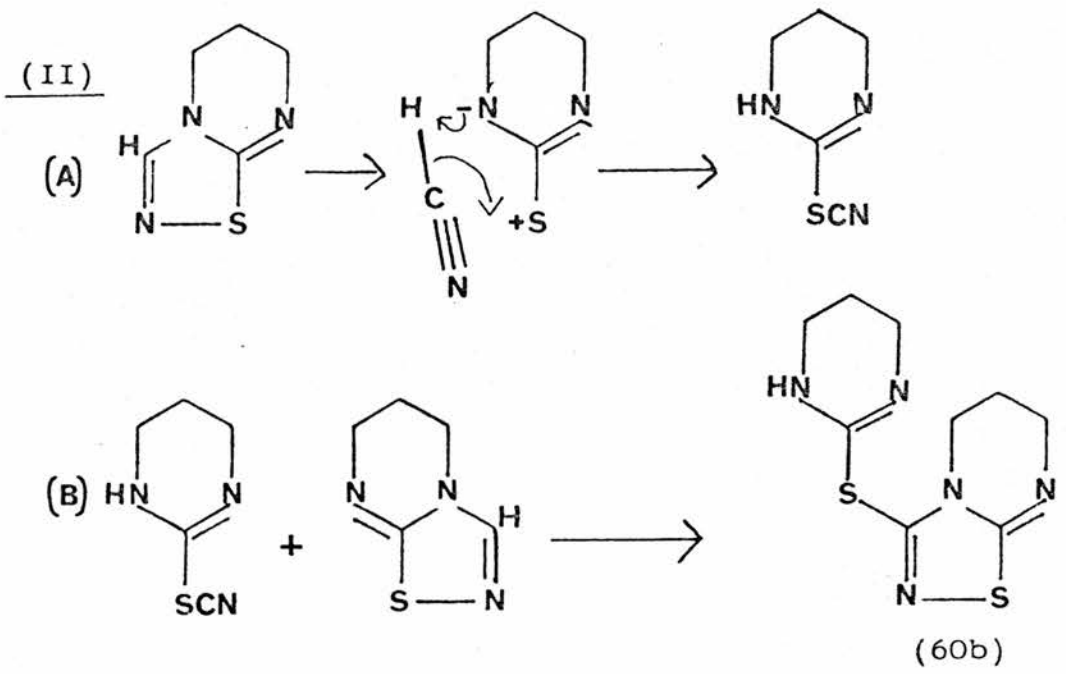
(X)

The proton nmr spectrum of the product in dimethyl sulphoxide -D_6 was complex [Table (E)], showing multiplets (2 x quintet) at δ1.67-2.00 (4H) and (4 x triplet) δ 2.48-3.77 (8H), and a broad exchangeable signal at δ 8.98 (NH). These data suggest that two molecules of the starting material have combined with loss of HCN. Two possible structures of the product are (60a) and (60b). Possible mechanisms for their formation are also shown.

(I)

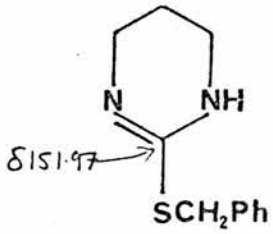


(60a)

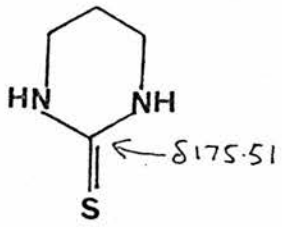


The ^{13}C nmr spectrum of the product was also complex [Table (F)] but showed three quaternary carbon atoms. From a comparison with the spectra of the pyrimidothiadiazoles [Table (B)], the signal at δ 150.76 could be due to C(3), δ 158.51 due to C(7a) and δ176.62 due to the thiocarbonyl carbon. The ^{13}C chemical shift of the thiocarbonyl carbon in thioureas lies in the range δ175-194[20], and the thiocarbonyl carbon in the thiourea (53) occurs at δ 175.51. This evidence thus favours structure (60a). The i.r. spectrum is consistent with this assignment in that there are medium intensity peaks in the fingerprint region at 1187 cm^{-1} and 1172 cm^{-1}, which could be due to the thiocarbonyl stretching frequency [ν_{str} C=S in the thiourea (53) occurs at 1210 cm^{-1}]. The ^{13}C nmr spectrum of compound (61) shows the imino carbon at δ 151.97[21] which suggests that the product does

not have structure (60b).

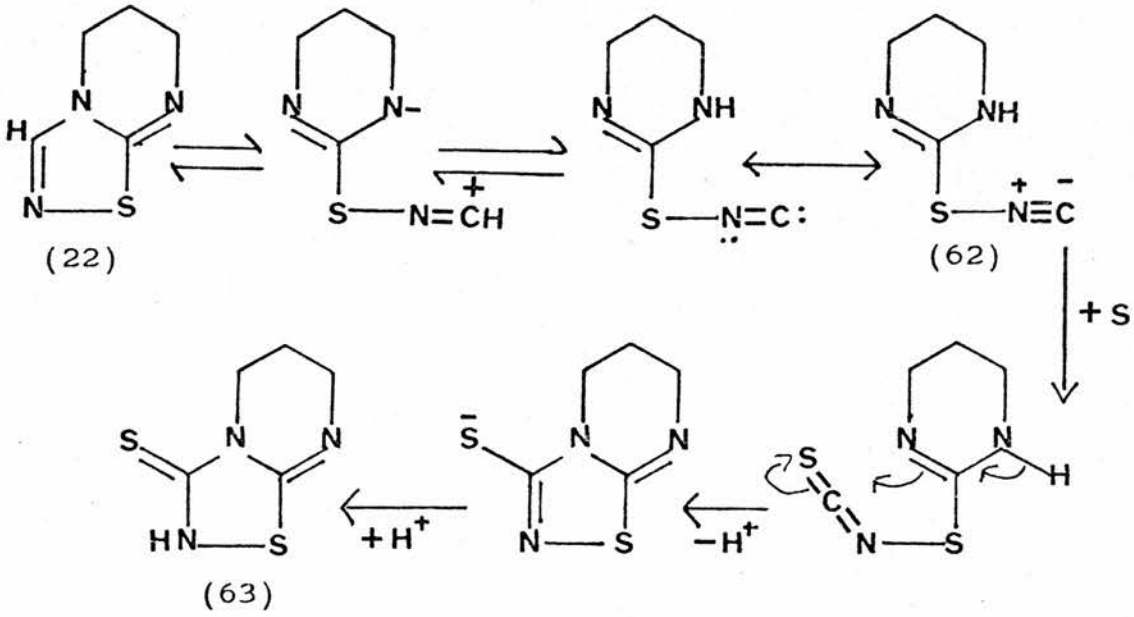


(61)



(53)

The thermolysis of the pyrimidothiadiazole (22) in toluene was also carried out in the presence of a 7-fold excess of sulphur. It had been hoped that sulphur would trap a dipolar intermediate, eg structure (62), if present, leading to the formation of compound (63). However the reaction gave only compound (60) in low yield after workup.



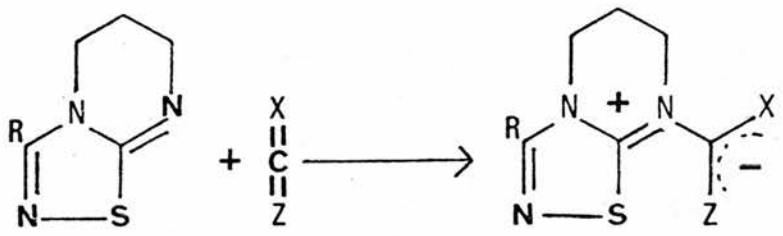
Conclusion:

The data do not allow a conclusive differentiation between the unimolecular (decomposition) mechanism and the bimolecular

(triheterapentalene intermediate) mechanism for the reactions of the pyrimidothiadiazole (17) with nitriles. However from the results of the thermolysis reactions of compound (17) it seems most likely that the reactions of compound (17) with nitriles are in fact bimolecular. The pyrimidothiadiazole (17) must be in equilibrium with acetonitrile and the thiaziridine imine (50) [or its ring opened forms (51) or (52)], for the reactions of compound (17) with nitriles at room temperature to be unimolecular. If this equilibrium occurs at room temperature it seems likely that over an extended period of time in refluxing toluene, at least some of the acetonitrile would be lost from the reaction mixture and that the imine (50) [or its ring opened forms (51) or (52)] would react with traces of water in the reaction mixture, or with atmospheric oxygen, or with the toluene solvent itself to give some decomposition products. These decomposition products are, however, not observed; the pyrimidothiadiazoles (17) having been found to be stable in refluxing toluene, with only a trace of the thiourea (53) being seen on t.l.c. after 72 hours.

6 The Reaction of 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazoles with Heterocumulenes

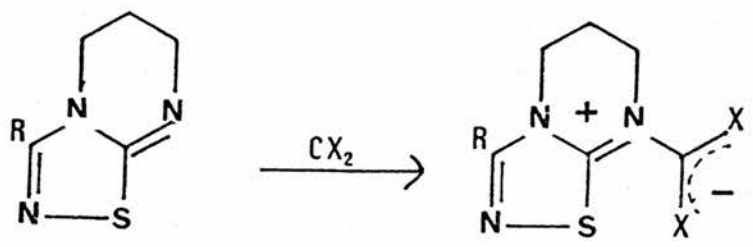
So far the reactions of the 5,6-dihydro-4H-pyrimido [1,2,-d] [1,2,4] thiadiazoles with nitriles have been discussed. These reactions were designed to form the triheterapentalenes with two pyridine-type nitrogens in the three-centre bonded heteroatom sequence. The reaction of the pyrimidothiadiazole (64) with heterocumulenes (X=C=Z) could also lead to novel triheterapentalenes (65), containing one pyridine-type nitrogen in the three-centre bond, and are therefore of relevance to the aims of the work in this thesis.



(64) (65) X and Z=O,S,Se,NR

(a) Reactions with Heterocumulenes.

Solutions of the pyrimidothiadiazoles (66a-c) in chloroform reacted at room temperature on the addition of carbon disulphide to give 1:1 adducts in 90-97% yield, as brightly coloured precipitates and are formulated as structures (67)-(69).



(66 a; R=H)
(b; R=Me)
(c; R=Ph)

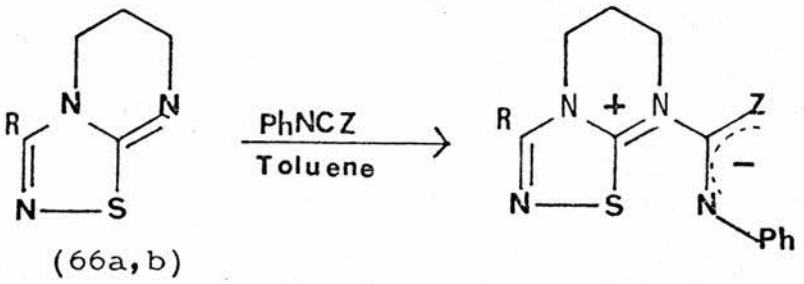
	R	X
(67	H	S)
(68	Me	S)
(69	Ph	S)
(70	H	Se)
(71	Me	Se)

These products were characterised by microanalysis, mp and mass spectrum, but were insufficiently soluble for ^{1}H nmr spectral examination.

Solutions of the pyrimidothiadiazoles (66a) and (66b) in toluene also reacted at room temperature with carbon diselenide to give the bright green 1:1 adducts formulated as (70) and (71) in greater than 96% yield. These products were characterised by microanalysis, mp and mass spectrum but like compounds (67-69) were too insoluble for ^{1}H nmr spectral examination.

In further attempts to synthesise triheterapentalenes with one pyridine-type nitrogen atom in the three-centre bond the reactions of the pyrimidothiadiazoles with methyl and phenyl iso(thio)cyanates were investigated.

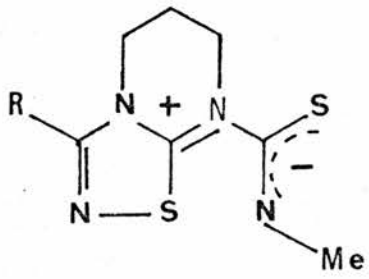
Phenyl iso(thio)cyanate reacted on mixing at room temperature with solutions of (66a) and (66b) in toluene to give the colourless 1:1 adducts (72-75) as white precipitates in almost quantitative yield.



(66a,b)

	R	Z
(72	H	O)
(73	Me	O)
(74	H	S)
(75	Me	S)

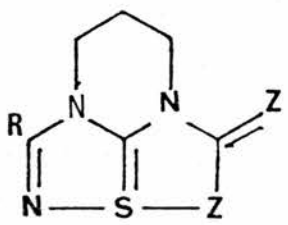
Methyl isothiocyanate reacted analogously with (66a) and (66b) to give (76) and (77) in high yield as white precipitates from toluene.



(76;R=H)
(77;R=Me)

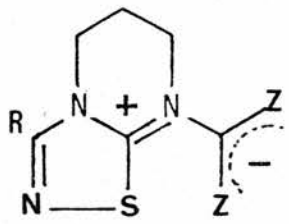
(b) Structure of the Heterocumulene Adducts.

There are two possible structures for the carbon disulphide and carbon diselenide adducts of (66), either the triheterapentalene (78) or the zwitterionic structure (79).



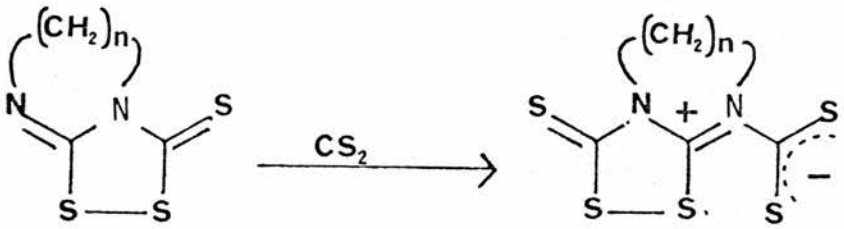
(78)

Z = S or Se



(79)

It is interesting to note that the structure (79, X=S) is similar to that proposed by Beer[2] for the CS_2 adduct (81a) of the dithiazole-3-thione (80a).



(80 a;n=2)
(b;n=3)

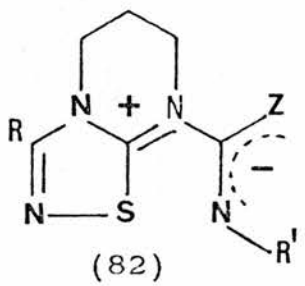
(81 a;n=2)
(b;n=3)

However, no such adduct (81b) was found by Beer for the six-membered ring compound (80b)[2] although Glidewell and

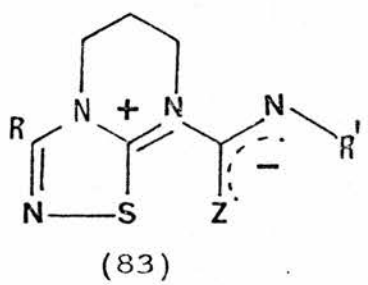
Pogorzelec have calculated[15] that (81b) is only slightly less likely to be formed than (81a), ($\Delta H_f^{\ominus}$/kJ mol^{-1} for (81a) and (81b) from (80a) and (80b) are +10.3 and +11.7 respectively).

The adducts from our reactions are formulated as the zwitterionic structures (79) on the basis of their high insolubility, even in polar organic solvents, and because no molecular ion is seen in their mass spectra. Breakdown occurs and only peaks due to the pyrimidothiadiazole (66) and the carbon disulphide or carbon diselenide are present.

The situation in the case of the iso(thio)cyanate adducts is more complicated as four structures (82), (83), (84) and (85) are possible.



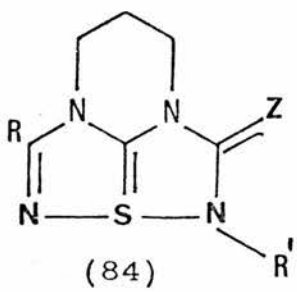
(82)



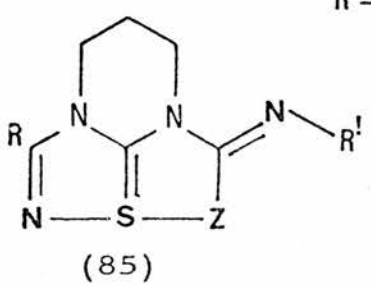
(83)

Z = O or S

R' = Me or Ph



(84)



(85)

The mass spectra of the adducts are characterised by the absence of a molecular ion peak, as was observed with the carbon disulphide and carbon diselenide adducts. The ^{1}H nmr spectra of the adducts [Table (C)] showed a positively charged

pyrimidothiadiazole nucleus thus favouring structures (82) and (83). Structure (85) can be ruled out on the grounds that all the adducts show either carbonyl absorptions at approximately 1660 cm^{-1} or thiocarbonyl absorptions in the region 1166-1146 cm^{-1}. To differentiate conclusively between structures (82), (83) and (84), an X-ray crystal structure analysis was obtained for compound (75)[16], this showed (Figure 1) the framework of the heterocycle to be essentially planar.

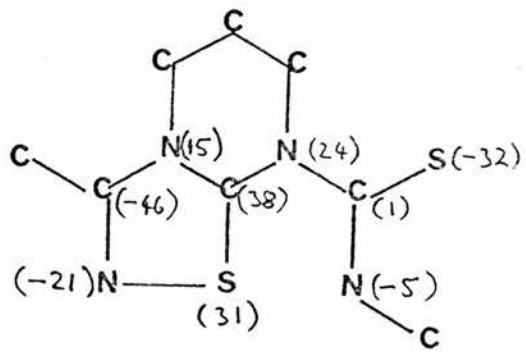


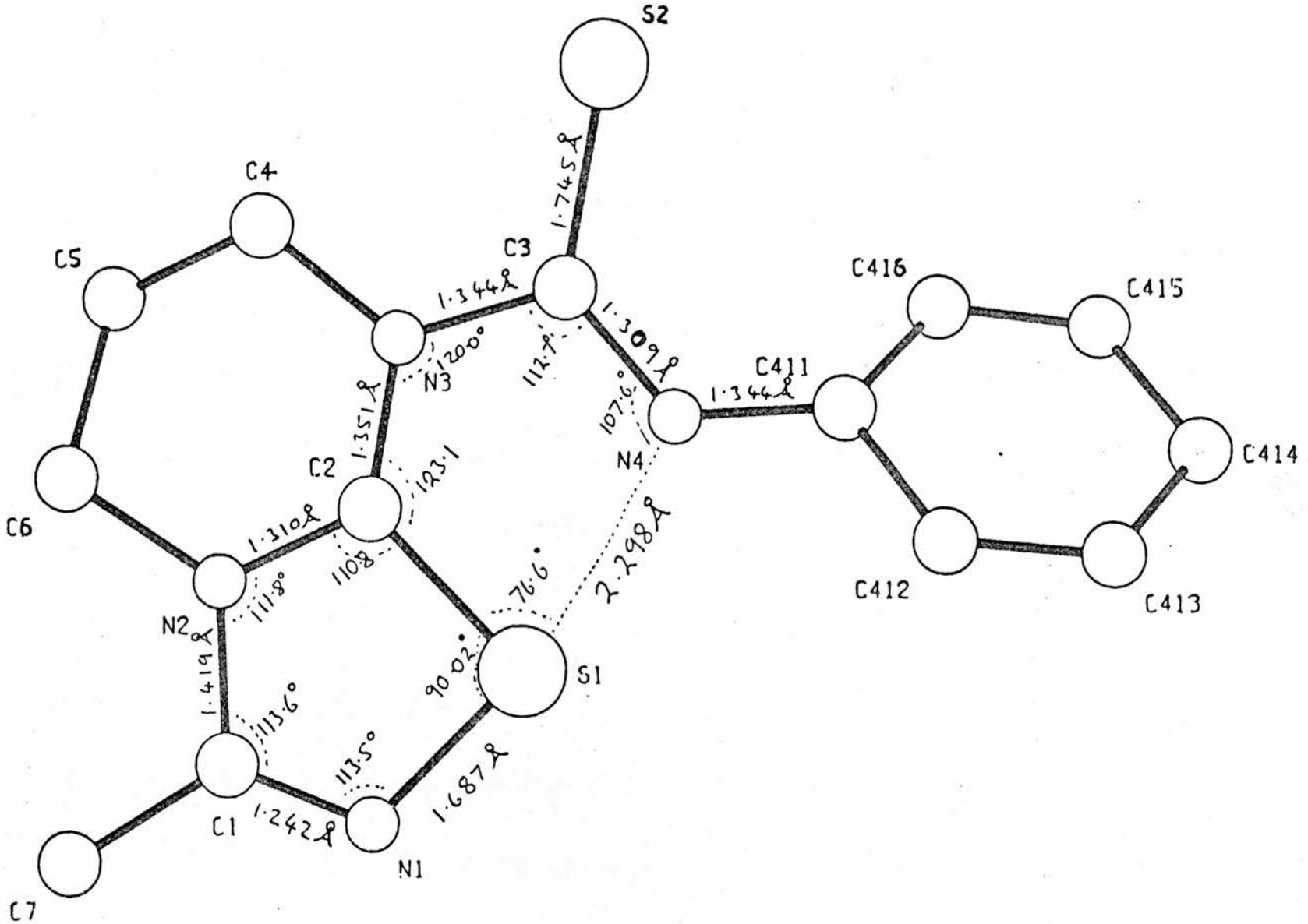
Figure 1 (Deviations from the mean plane in $Å \times 10^{-2}$)

with the thiocarbamate moiety arranged as in structures (82) and (84) rather than (83). The bond lengths (page 94) clearly indicate that the adduct has the open structure (82, R^1=Ph, X=S) rather than (84), as the distances S(1)-N(1) (1.687 Å) and S(1)-N(4) (2.298 Å) are, respectively, much shorter and much longer than the S-N bond lengths in 1,6,6a λ^4-triheterapentalenes (see Introduction page 6).

Conclusion:

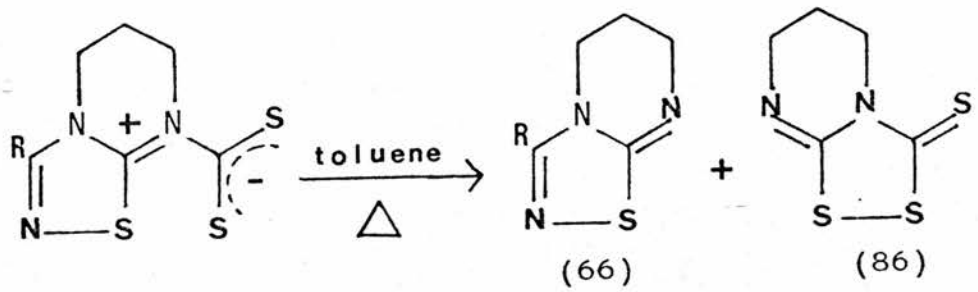
The structure of the phenyl isothiocyanate adduct of pyrimido thiadiazole (17), compound (75), has been shown to be the zwitterionic, open structure (82, R^1=Ph, X=S). As the other phenyl and methyl iso(thio)cyanate adducts, compounds (72)-(77),

have similar physical and spectral (^{1}H nmr, i.r. and mass spectrum) properties to those of compound (75) it seems likely that they too will have open structures (82). Similarly the physical and spectral properties of the carbon disulphide and carbon diselenide adducts of the pyrimidothiadiazoles (66), compounds (67)-(71), suggest that these compounds have the zwitterionic structures (79) rather than triheterapentalene structures (78).

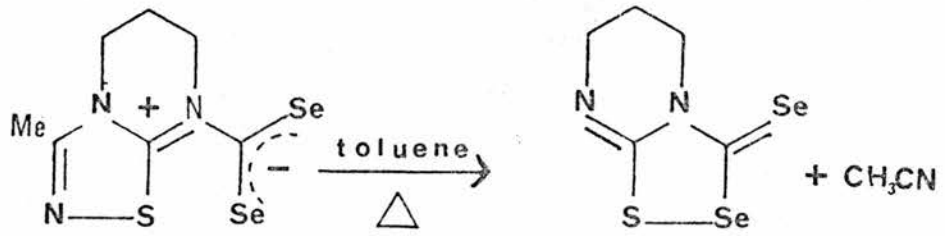

S2
1·745 Å
C4
C5
C3
1·344 Å
C416
C415
1·309 Å
C411
1·344 Å
N3
120·0°
112·7°
107·6°
C2
1·351 Å
N4
C414
123·1
C6
1·310 Å
2·298 Å
110·8°
76·6°
111·8°
N2
C412
C413
1·419 Å
90·02°
S1
113·6°
113·5°
1·687 Å
C1
1·242 Å
N1
C7

(c) Thermolysis Reactions of the Heterocumulene Adducts.

The carbon disulphide adducts (67)-(69) dissociated in boiling toluene to give the starting pyrimidothiadiazole (66) in approximately 70% yield and a small amount (<10%) of 5,6-dihydro-4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)-thione (86). Adduct (67) gave a rather higher yield (11%) of the thione (86) together with the decomposition products of (66, R=H) which were identical to those obtained from the thermolysis of (22) alone in toluene.



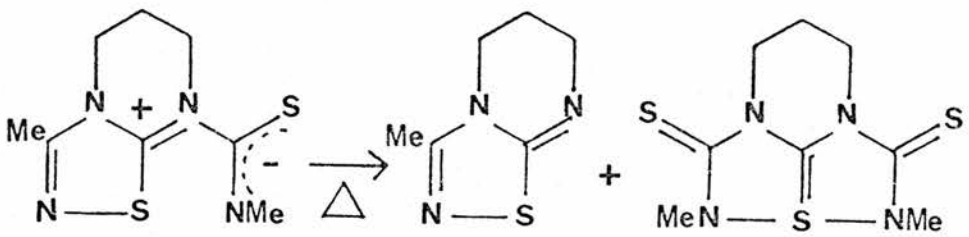
A solution of the carbon diselenide adduct (71) in boiling toluene was deep orange. On cooling 5,6-dihydro-4H-pyrimido [2,1-c] [2,1,4] thiaselenazole- 3(3H) -selenone (87) crystallised as orange needles. Chromatography of the mother liquors afforded a further crop of compound (87). As far as is known compound (87) is the first example of a heterocycle containing sulphur, selenium and nitrogen atoms in the same ring, fused to another heterocyclic ring. It is a reasonably stable compound at room temperature in the dark and keeps well when stored under refrigeration.



(71) (87)

The high yield (72.5%) of compound (87) in this reaction as compared with the very low yield of the dithiazole (86) from the thermolysis of the CS_2 adducts could be due, at least in part, to carbon diselenide being less volatile than carbon disulphide and acetonitrile, and therefore it is not lost from the reaction mixture to the same extent.

Whereas the phenyl isothiocyanate adduct (75) could be recrystallised unchanged from acetonitrile, it was found that the methyl isothiocyanate adducts rearranged on warming in solution. On attempted recrystallisation from boiling toluene compound (77) disproportionated to give the triheterapentalene (88) and the pyrimidothiadiazole (17) in high yield. Compound (88) is a rare example of a triheterapentalene containing exocyclic double bonds.



(77) (17) (88)

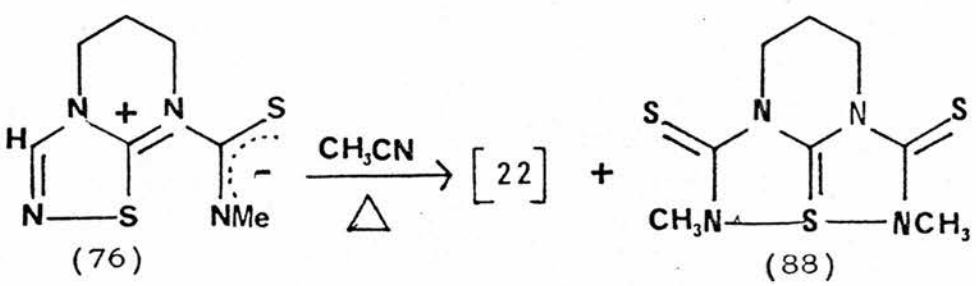
Repetition of the reaction in acetonitrile solvent gave the same products in similarly high yield. Two features of this reaction are of particular note. First, the isolation of the

triheterapentalene (88), in almost quantitative yield, rather than the bicyclic species (89) is interesting.

(89)

This result complements Beer's[2] findings that all attempts to isolate the intermediate (89) from his reactions between compound (86) and isothiocyanates were unsuccessful. Second, compound (88) is still formed in high yield when acetonitrile is used as a solvent for the reaction. This suggests that the intermediate (89) reacts rapidly with low concentrations of methyl isothiocyanate, however (89) does not react with even a large excess of acetonitrile.

Thermolysis of the adduct (76) in acetonitrile also gave the triheterapentalene (88), but the yield was not as high as in the thermolysis of compound (77) and the other product of the reaction- pyrimidothiadiazole (22) was found to have decomposed under the reaction conditions.

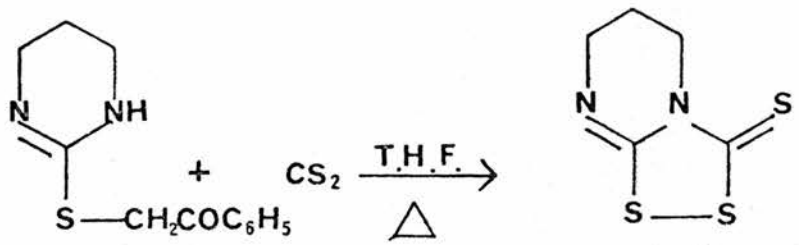


(76) (88)

(d) Synthesis of 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles from Hexahydropyrimidine-2-thione.

Since it had been found that pyrimidothiadiazoles could be converted, in low yield, into 5,6-dihydro-4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)-thione (86) by reaction with carbon disulphide followed by thermolysis in an inert solvent, it was decided to investigate the possibility of using the reverse reaction of (86) with nitriles as a potential route to the pyrimidothiadiazoles.

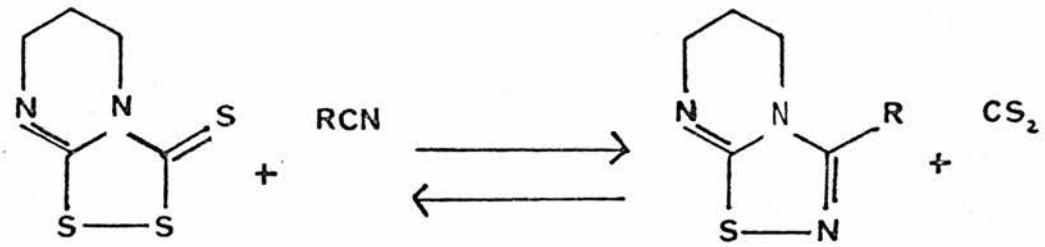
The dithiazole-3-thione (86) was readily prepared in modest yield from 2-phenacylthio- 3,4,5,6-tetrahydropyrimidine (90) by a modification of Beer's method. The 2-phenacylthiopyrimidine (90)



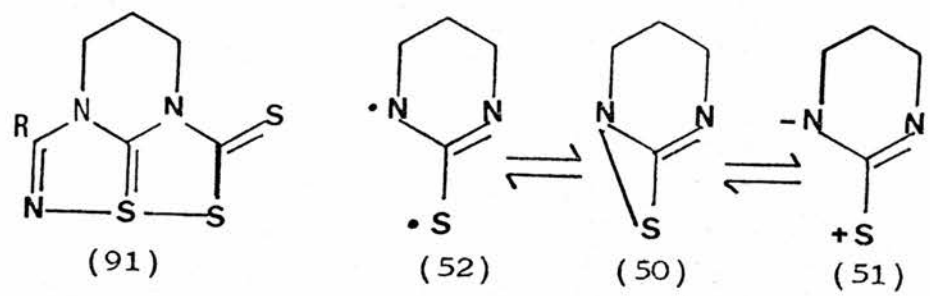
(90) (86)

had been prepared in high yield from hexahydropyrimidine-2-thione by a modification of Shadbolt's method. The dithiazole-3-thione (86) reacted slowly with benzonitrile and pyridine-4-carbonitrile in refluxing toluene to give the pyrimidothiadiazoles (23) and (34) in good yield. However the reaction of (86) with acetonitrile in refluxing xylene was very slow and t.l.c. of the

reaction mixture after 30 hours showed some pyrimido thiadiazole (17) to be present, as well as considerable amounts of hexahydropyrimidine- 2-thione (53) and unreacted dithiazole-3-thione (86). Therefore this reaction was not pursued further.



It is clear from the foregoing that some pyrimidothiadiazoles can be prepared in good yield by the reaction of nitriles with 5,6-dihydro-4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)-thione. Although as in the reaction of nitriles with the pyrimidothiadiazoles, these reactions could be occurring by two routes, either via a triheterapentalene intermediate (or transition state with the geometry of a triheterapentalene) (91) or through a decomposition intermediate (50), (51) or (52). Thus



(91) (52) (50) (51)

the large amount of hexahydropyrimidine-2-thione (53) formed in

the reaction of compound (86) with acetonitrile in refluxing xylene could have arisen from the decomposition of the starting thione (86) before it had time to react with the acetonitrile or from slow decomposition of the product (17).

Similarly, little can be stated conclusively about the mechanism of the thermolyses of the carbon disulphide adducts as the effect of heat on the adducts could be to promote the formation of the intermediate (91) which could then lose CS_2 or CH_3CN to give the observed products. The first step might also be the loss of CS_2 from the adduct to give the pyrimidothiadiazole which could then decompose further with loss of CH_3CN to give (50), (51) or (52) which could react with carbon disulphide still dissolved in the reaction mixture, thus forming the thione (86).

It is obvious that both above mechanisms could account for the formation of the selenone (87) in high yield from the thermolysis of the carbon diselenide adduct (71).

Part C

EXPERIMENTAL

EXPERIMENTAL

Introductory Notes

Melting points were obtained on a Kofler hot-stage apparatus. Yields refer to recrystallised t.l.c. pure material, unless otherwise stated.

Ultraviolet and visible spectra were measured using a Unicam SP800 spectrometer. Infra-red spectra were recorded with a Perkin Elmer 1330 spectrometer, and refer to solids dispersed in KBr discs, unless otherwise stated. Mass spectra and accurate mass determinations were carried out using an AEI MS920 instrument.

Nmr spectra were executed by Mrs M. Smith, Department of Chemistry, University of St Andrews. ^{1}H nmr spectra were recorded at ambient temperature, unless otherwise stated, using a Bruker WP80 operating at 80 MHz. Solutions in chloroform-D, acetonitrile-D_3 (CD_3CN), dimethylsulphoxide-D_6 [$(CD_3)_2SO$] and trifluoroacetic acid-D were 0.4 M. When this concentration could not be attained, saturated solution were employed. Chemical shifts (δ) are given in p.p.m. downfield from tetramethylsilane as internal reference, except in high temperature studies, where hexamethyldisiloxane was used. J values were obtained from the digital printout of the spectrum. Unless otherwise stated (d= doublet, t= triplet, q= quartet, qi= quintet, m= multiplet and b= broad peak), chemical shift values refer to singlet absorptions.

^{13}C Nmr spectra were recorded at ambient temperature using a Varian CFT20 operating at 20 MHz. Saturated solutions in chloroform-D and dimethylsulphoxide were employed. Chemical

shifts are given in p.p.m. downfield from tetramethylsilane as internal reference.

Carbon, hydrogen and nitrogen elementary microanalyses were executed by Mrs S. Smith, Department of Chemistry, University of St Andrews.

Procedures Criteria used in the identification of products included melting points (mp), t.l.c. behaviour and nmr and mass spectra.

Thin layer chromatography (t.l.c.) was carried out with silica (MN Kieselgel-G) coated plates (ca 0.25 mm thick). Column chromatography was performed using Sorbsil Silica Gel M60. Solvent mixtures are described in ratios by volume.

Solutions were dried over anhydrous sodium or magnesium sulphate and solvents were evaporated at reduced pressure with a Buchi rotary film evaporator. Solids were dried in vacuo over phosphoric anhydride.

Materials "Petroleum" refers to petroleum ether of boiling range 40-60 ^{o}C and "ether" refers to diethyl ether. Acetone, cyclohexane, methanol, ethanol, propan-1-ol, butan-1-ol, n-hexane, o-dichlorobenzene, benzene and toluene were all redistilled commercial solvents. Benzene, ether, toluene were refluxed over sodium wire for one hour and then redistilled to give the dry solvents. These solvents were stored over sodium wire. The crude ether was pre-dried over calcium chloride for ca 24 hours before refluxing and distilling. This was the ether used for chromatography.

Acetonitrile was refluxed over sodium hydride (50% dispersion in oil, 2 g per litre) for 30 minutes, distilled then

refluxed over phosphoric anhydride for one hour and redistilled twice.

Dimethylformamide was dried for *ca* one week over powdered calcium hydride and then distilled at 15 mm of Hg.

Dichloromethane (methylene chloride) and chloroform were refluxed over phosphoric anhydride for one hour and distilled twice.

1,2,3,4-Tetrahydronaphthalene (tetralin), 1-methyl-4-isopropyl- benzene (*p*-cymene) and t-butyl benzene were refluxed over lithium aluminium hydride (*ca* 2g/l) for 30 minutes and distilled.

Perchloromethyl mercaptan, phenyl iso(thio)cyanate, methyl isothiocyante and iodomethane (methyl iodide) were distilled commercial reagents. Methyl fluorosulphonate was a distilled commercial reagent and was stored under refrigeration in a polythene bottle. Carbon disulphide was Analar grade. Carbon diselenide, 1,3-dibromopropane and 1,3-diiodopropane were commercial reagents.

The nitriles used were commercial reagents. The solids purified by recrystallisation while the liquids were redistilled.

Tables of nmr (^{1}H and ^{13}C) and mass spectral data are to be found at the end of the experimental section.

1 Attempted Synthesis of 4,5-Dihydro- 3,4-dimethyl- 5-methylimino-1,2,4-thiadiazole.

(a) Methylation of 4,5-Dihydro-5-imino- 3,4-dimethyl- 1,2,4-thiadiazole

(1) With Iodomethane

Iodomethane (2.14 g, 0.94 ml, 15.10 mmol) was added to a stirred solution of the iminothiadiazole (4) (0.643 g, 4.98 mmol) in ethanol (5 ml). The resulting solution was refluxed (oil bath) for 8 hours during which time a green colouration was formed in the solution and a dark-green solid precipitated. After cooling in an ice bath to 0 ^{o}C the reaction mixture was filtered and the precipitate was washed with ether/acetone (1:1) (15 ml). The ethanol filtrate was added to an equal volume of ether and cooled in an ice-bath before being filtered. The green precipitates were combined and amounted to 0.813 g. A sample of the product, in dimethyl sulphoxide-D_6, was examined by ^{1}H nmr, this showed singlets at 2.50 and 3.625 due to the hydroiodide of the starting iminothiadiazole, also smaller peaks at 2.70, 3.09, 3.19, 3.45, 3.87 and a broad peak at 9.98 due probably to isomers of the methylation product; 5-amino- 2,3,4- trimethyl- 1,2,4-thiadiazolium iodide and 3,4-dimethyl- 5-methylimino- 1,2,4-thiadiazole.

Carrying the reaction out in methanol rather than ethanol solvent gave a similar mixture of products.

(2) With Methyl fluorosulphonate

A solution of methyl fluorosulphonate (0.6848 g, 0.485 ml, 5.97 mmol) in benzene (5 ml) was added to a solution of the iminothiadiazole (4) (0.6606 g, 5.11 mmol) in benzene (15 ml) and the resulting mixture left to stand for one hour at room temperature. The benzene solvent was then decanted off and the white precipitate washed with benzene (10 ml) and ether (10 ml). A ^{1}H nmr of a sample of the precipitate in dimethyl sulphoxide-D_6 showed a complex mixture of products similar to that obtained from the reaction of compound (4) with iodomethane. The white precipitate was dissolved in water and deprotonated with aqueous sodium hydroxide and the products extracted with ether (2 x 100 ml) and dichloromethane (100 ml). The combined extracts were dried and evaporated to give a yellow oil (0.6654 g). ^{1}H Nmr examination of a sample of this oil in dimethyl sulphoxide-D_6 showed a complex mixture of products, and therefore the reaction was not pursued further.

(b) Synthesis and Reaction of 5-Chloro- 3-methyl- 1,2,4-thiadiazole

5-Chloro- 3-methyl- 1,2,4-thiadiazole was synthesised by the method of Goerdeler[3].

(1) Reaction of 5-Chloro- 3-methyl- 1,2,4-thiadiazole with Methylamine followed by reaction with Methyl fluorosulphonate.

5-(N-methylamino)- 3-methyl- 1,2,4-thiadiazole was synthesised from 5-chloro- 3-methyl- 1,2,4-thiadiazole and

methylamine by the method of Goerdeler[3].

Methyl fluorosulphonate (2.71 g, 1.92 ml, 23.76 mmol) was added to a stirred solution of 5-(N-methylamino)- 3-methyl-1,2,4-thiadiazole (2.5826 g, 20.00 mmol) in dichloromethane (20 ml) and the resulting mixture left to stand for two hours at room temperature. After this time, ether (20 ml) was added and the mixture left for a further two hours to precipitate the product salt completely, before being filtered. The white, slightly sticky powder thus obtained was dissolved in ethanol (15 ml) and added to ethanolic methylamine solution (33% w/v) (25 ml). This mixture was then evaporated and the residue extracted with ether (4 x 50 ml). The combined ether extracts were evaporated and the resulting colourless oil block-distilled to give 2,3-dimethyl-5-methylimino- 1,2,4-thiadiazole (7) as colourless flakes (1.2010 g, 42%), bp 85-90 °C at 0.2 mm of Hg, mp 40-42 °C.

A satisfactory microanalysis of this product could not be obtained due to its hygroscopic nature.

Accurate Mass Found: 143.051265

$C_5H_9N_3S$ Requires: .051716

Mass Spectrum, see Table (G)

^1H nmr, see Table (E)

(2) Formation of 5-N,N-Dimethylamino- 3-methyl-1,2,4-thiadiazole

Ethanolic dimethylamine (30% w/v) (25 ml, approx. 160 mmol) was added to a solution of 5-chloro- 3-methyl- 1,2,4- thiadiazole (2.71 g, 2.00 ml, 20.13 mmol) in ethanol (5ml) with cooling in an ice-water bath. The reaction mixture was left to stand at room temperature for two hours before being evaporated to dryness and

the residue extracted with ether (3 x 25 ml). The combined ether extracts were evaporated and the resulting yellow oil block-distilled to give 5-(N,N-Dimethylamino)- 3- methyl- 1,2,4-thiadiazole (9) as a colourless oil (2.59 g, 91%), bp 90-95 °C at 0.1 mm of Hg.

Found: 41.49 %C; 5.87 %H; 29.19 %N

$C_5H_9N_3S$ Requires: 41.94 %C; 6.33 %H; 29.34 %N

Accurate Mass Found: 143.052706

$C_5H_9N_3S$ Requires: .051716

Mass Spectrum, see Table (G)

^1H nmr, see Table (E)

(3) Reaction of 5-Chloro- 3-methyl- 1,2,4-thiadiazole with Methyl fluorosulphonate followed by reaction with Methylamine

Methyl fluorosulphonate (2.71 g, 1.92 ml, 23.76 mmol) was added to a solution of the chlorothiadiazole (2.71 g, 2.00 ml, 20.13 mmol) in dichloromethane (10 ml) and the resulting mixture left to stand overnight at room temperature. The white precipitate which had formed was filtered off and washed with ether (15 ml) and amounted to 4.6473 g. Examination of the precipitate in dimethyl sulphoxide-D_6 by ^1H nmr showed singlets at δ 2.35 (C-CH_3) and δ 3.28 (N-CH_3) however there were also smaller singlets, approximately one tenth the integral of the larger peaks, at δ 2.49 (C-CH_3) and δ 3.62 (N-CH_3) indicating that both nitrogen atoms had been methylated. There was also a peak at δ 10.5 which was possibly due to an hydrolysis product of the chlorothiadiazole.

The impure white precipitate (4.6473 g) was added to a stirred ethanolic solution of methylamine (33% w/v) (25 ml), with

cooling in an ice bath and the resulting mixture left to stand for two hours at room temperature. The reaction mixture was then evaporated to dryness and extracted with ether (4 x 25 ml). The combined ether extracts were evaporated and block-distilled (bp 80-85 °C at 0.2 mm of Hg) to give 2,5-dihydro- 2,3-dimethyl- 5-methylimino- 1,2,4-thiadiazole (7) as colourless flakes (1.8105 g, 65%), mp 40-42 °C. This product was identical (mp, mixed mp, ^{1}H nmr, t.l.c.) with the product formed by reaction of the chlorothiadiazole with methylamine followed by methyl fluorosulphonate.

(c) The Reactions of 2,5-Dihydro- 2,3-dimethyl- 5-methylimino- 1,2,4- thiadiazole

(1) With Benzonitrile

Benzonitrile (2.02 g, 2 ml, 19.6 mmol) was added to a solution of the thiadiazole (7) (0.1455 g, 1.02 mmol) in toluene (5 ml) and the resulting mixture refluxed (oil bath) for 9.5 hours. The cold reaction mixture was chromatographed on silica (10 cm x 2.2 cm) eluting with toluene. The first 125 ml of toluene eluate brought through the unreacted benzonitrile and was discarded. The next 750 ml of methanol eluates brought through the thiadiazole and were combined and evaporated to give a colourless oil which was block-distilled (bp 80-90 °C at 0.3 mm of Hg) to give the starting thiadiazole back as a colourless low melting solid (0.1161 g, 80 %).

(2) With Carbon disulphide

Analar carbon disulphide (12.63 g, 10 ml, 166 mmol) was added to a solution of the thiadiazole (7) (0.1440 g 1.01 mmol)

in dichloromethane (5 ml). As there was no immediate reaction visible the reaction mixture was refluxed for one hour. T.l.c. of the cold reaction mixture showed only starting thiadiazole to be present. On evaporation the reaction mixture gave the thiadiazole back as a colourless solid (0.1438 g, 100%). The recovered material was checked by ^{1}H nmr and found to be identical to the starting material.

2 Synthesis of 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles

Preparation of Starting Materials:

5-Amino- 3-methyl- 1,2,4- thiadiazole and 5-amino-3-phenyl-1,2,4-thiadiazole were prepared by the methods of Goerdeler[1].

(a) Syntheses of 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles from 5-Amino-1,2,4-thiadiazoles.

5-Amino-1,2,4-thiadiazole was prepared by the following modification of Goerdeler's method.[1]

Sodium (45 g, 1.96 mol) was dissolved in methanol (500 ml). Bromine (64 g, 20.51 ml, 0.4 mol) and the sodium methoxide solution (approx. 200 ml) were simultaneously added dropwise over 30 minutes to a stirred solution of potassium thiocyanate (38.86 g, 0.4 mol) and formamidinium acetate (41.65 g, 0.4 mol) in methanol (500 ml), with cooling in an acetone/CO_2 bath at -10 °C. After the bromine and sodium methoxide had been added the mixture was stirred at 0 °C for 2.5 hours. Glacial acetic acid (12.59 g, 12 ml, 210 mmol) was then added, followed by enough aqueous sodium sulphide (saturated solution) to remove any excess of bromine (yellow colour discharged). The mixture was filtered and the filtrate was evaporated to dryness, giving a creamy yellow solid, which was extracted with ether (4 x 200 ml). The ether extracts were filtered and dried over magnesium sulphate before being reduced in volume to approx. 500 ml. Hydrogen chloride gas was bubbled through the solution to

precipitate the hydrochloride of the product.

The resulting white precipitate was dissolved in water (500 ml). Saturated aqueous sodium hydrogen carbonate solution (250 ml) was added, and the mixture was extracted with ethyl acetate (4 x 250 ml). The combined ethyl acetate extracts were dried and evaporated, and the residue was recrystallised from chloroform (750 ml). 5-Amino-1,2,4-thiadiazole was obtained as colourless flakes (17.90 g, 0.18 M, 44%), mp 119-20 °C (lit. mp 119-20 °C). (Lit. [1] yield from formamidinium chloride, 45%).

(1) Synthesis of 5,6-Dihydro- 3-methyl-4H-pyrimido [1,2-d] [1,2,4] thiadiazole.

Method (a) 1,3-Dibromopropane (51.714 g, 26 ml, 256.43 mmol) was added to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (5.75 g, 50 mmol) in dimethyl formamide (25 ml) and the resulting solution was heated in an oil bath at 130 °C for 0.5 hours, then allowed to cool spontaneously to room temperature. The mixture was filtered and the resulting brown needles washed with a little ether, and dried to give 2.8034 g of impure brown needles.

To obtain an analytically pure sample the product was recrystallised from methanol (charcoal) to give 5,6-dihydro-3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium bromide (16) as colourless needles, mp 290-292 °C (with decomposition from 284 °C, as seen by a brown colouration on the outside of the crystals).

Found: 30.39 %C; 4.30 %H; 17.79 %N

$C_6H_{10}N_3BrS$ Requires: 30.52 %C; 4.27 %H; 17.79 %N

Mass Spectrum, the product lost HBr to give a spectrum

identical to that of compound (17), see Table (D).

^{1}H nmr, see Table (C)

1M-Aqueous sodium hydroxide (20 ml) was added to a solution of the brown needles (2.8034 g) in water (40 ml). The mixture was extracted with dichloromethane (4 x 150 ml) and the combined extracts were dried and evaporated, with a minimum of heating being used. The resulting red-orange solid residue was recrystallised by extraction into ether/cyclohexane (9:1) (4 x 50 ml) and then evaporation with gentle heating to reduce the total volume to approximately 50 ml. 5,6-Dihydro- 3-methyl-4H-pyrimido [1,2-d] [1,2,4] thiadiazole (17) was obtained as cream needles (1.5657 g, 20%), mp 72-74 °C, sublimes 125-130 °C (0.7 mm of Hg).

Found: 46.28 %C; 5.54 %H; 27.01 %N

$C_6H_9N_3S$ Requires: 46.43 %C; 5.84 %H; 27.07 %N

Accurate Mass Found: 155.050786

$C_6H_9N_3S$ Requires: .051716

Mass Spectrum, see Table (D)

^{1}H nmr, see Table (A)

^{13}C nmr, see Table (B)

U.v. spectrum: (Cyclohexane) λ max (nm) 269.5 (log ε 3.57), 253.5 (3.72), 233.5 (3.65)

Method (b) 1,3-Dibromopropane (19.89 g, 10 ml, 98.51 mmol) was added to a solution of 5-amino- 3-methyl-1,2,4-thiadiazole (2.3 g, 20 mmol) in dimethylformamide (10 ml) and a catalytic amount of sodium iodide. The resulting solution was refluxed for 5 minutes before being allowed to cool spontaneously to room temperature. The impure brown needles that had formed were

filtered off and washed with a little ether, and amounted to 1.1924 g. This brown solid was added slowly to 1M-aqueous sodium hydroxide (10 ml) with cooling in an ice-water bath. The mixture was then extracted with dichloromethane (3 x 100 ml) and the combined extracts were dried and evaporated to give a deep red-orange solid which was sublimed at the oil pump (125-30 °C, 0.7 mm of Hg). 5,6-Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (17) was obtained as a white powder (0.531 g, 17%), this powder was identical (^{1}H nmr, mass spectrum, t.l.c.) to a sample made by method (a).

Method (c) 1,3-Diiodopropane (73.95 g, 29 ml, 250 mmol) was added to a warmed solution of 5-amino- 3-methyl- 1,2,4-thiadiazole (5.75 g, 50 mmol) in dimethylformamide (25 ml) and the resulting mixture was heated, with stirring, in an oil-bath at 130 °C for 0.5 hours, then allowed to cool spontaneously to room temperature. The resulting impure red crystals (3.2107 g) were filtered off and washed with ether (20 ml).

To obtain an analytically pure sample the product was recrystallised from methanol/ethanol (1:1) (Charcoal) to give 5,6-dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium iodide (16b) as colourless needles, mp 164-165 °C (with decomposition)

Found: 25.74 %C; 3.83 %H; 14.78 %N

$C_5H_8N_3SI$ Requires: 25.45 %C; 3.56 %H; 14.84 %N

Mass Spectrum, the product lost HI to give a spectrum identical to that of compound (17), see Table (D).

^{1}H nmr, see Table (C)

1M-Aqueous sodium hydroxide (35 ml) was added to a suspension of the impure hydroiodide (6.9907 g, 25 mmol) in water (70 ml). The mixture was extracted with dichloromethane (4 x 200 ml) and the combined extracts dried and evaporated to give a viscous red oil which was sublimed (150-160 °C, 0.9 mm of Hg) to give (17) as an off-white powder (2.6267 g, 69%). This product was identical (^{1}H nmr, mass spectrum, t.l.c.) to a sample obtained by method (a).

Method (d) Reaction of 5-Amino-3-methyl-1,2,4-thiadiazole with 1,3-Dibromopropane and Potassium Carbonate in Dimethylformamide

1,3-Dibromopropane (19.89 g, 10 ml, 99.5 mmol) was added to a stirred suspension of potassium carbonate (8.3 g, 60 mmol) and a catalytic amount of sodium iodide in a solution of 5-amino-3-methyl- 1,2,4- thiadiazole (2.30 g, 20 mmol) in dimethylformamide (20 ml), and the resulting mixture heated in an oil bath (120 °C) for 20 minutes and then stirred at room temperature for a further 10 minutes until evolution of gas was no longer observed. Water (100 ml) was then added and the mixture extracted with benzene (2 x 400 ml). The combined benzene extracts were then washed with water (6 x 100 ml), dried, and evaporated to give a red-orange oil (9.2304 g). The combined aqueous extracts were extracted with dichloromethane (3 x 250 ml) and afforded a red oil (1.0265 g) after drying and evaporation. T.l.c. of the residue from the benzene extracts showed a mixture of approximately eight components: three fast running spots just behind the solvent front; dibromopropane (R_f 0.87); a spot at R_f 0.8 possibly due to dimethylformamide; three spots close together

at R_f 0.75, 0.7, 0.65; thiadiazole (17) (R_f 0.2); and very polar material. T.l.c. of the residue from the dichloromethane extracts showed three spots at: R_f 0.7; R_f 0.2 [due to thiadiazole (17)]; and very polar material just above the origin.

The residue from the benzene extracts was chromatographed on silica (34 cm x 2.5 cm) eluting with benzene/ether (2:1) collecting 50 ml aliquots. The first 100 ml of eluate brought through the fast running material. The next 500 ml of eluates showed two spots on t.l.c. (R_f 0.8 and R_f 0.7) and afforded a white solid (0.2214 g) on evaporation. The following 50 ml of eluate also showed two spots on t.l.c., the slower one being more intensely stained, and gave a white solid (0.4600 g) on evaporation. Later eluates showed a mixture of products made up of some thiadiazole (17) and slower running material.

The white solid (0.4600 g was recrystallised from cyclohexane/benzene (3:1) to give 5-{3- (2-oxo- 3,4,5,6- tetrahydro- 2H- 1,3-oxazinyl)}- 3- methyl- 1,2,4- thiadiazole (18) as white needles (0.2345 g, 6%), mp 144-5 °C.

Found: 42.41 %C; 4.59 %H; 20.87 %N

$C_7H_9N_3O_2S$ Requires: 42.20 %C; 4.55 %H; 21.09 %N

Accurate Mass Found: 199.040237

$C_7H_9N_3O_2S$ Requires: .041544

Mass spectrum, see Table (G)

^1H nmr, see Table (E)

^{13}C nmr, see Table (F)

I.r. spectrum showed peaks at: 1745 cm^{-1} (m), 1711 cm^{-1} (s), 1696 cm^{-1} (s), 1660 cm^{-1} (m)

(2) Synthesis of other 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles

(a) 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole

1,3-Dibromopropane (19.89 g, 10 ml, 98.5 mmol) was added to a solution of 5-amino-1,2,4-thiadiazole (1.01 g, 10 mmol) in dimethylformamide (2.5 ml) and the resulting solution was refluxed for 15 minutes, then allowed to cool spontaneously to room temperature. The liquid was decanted off and the remaining tacky brown solid was recrystallised from propan-1-ol (3 ml) to give an impure brown powder (1.61 g).

To obtain an analytically pure sample the product was recrystallised from ethanol (Charcoal) and then from ethanol to give 5,6-dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium bromide (24) as straw coloured needles, mp 242-45 °C (with decomposition from 230 °C).

Found: 26.91 %C; 3.56 %H; 18.66 %N

$C_5H_8N_3SBr$ Requires: 27.04 %C; 3.63 %H; 18.92 %N

Mass spectrum, the product lost HBr to give a spectrum identical to that of compound (22), see Table (D)

^1H nmr, see Table (C).

1M-Aqueous sodium hydroxide (10 ml) was added to a solution of this brown powder (1.61 g) in water (25 ml). The mixture was extracted with dichloromethane (4 x 100 ml), and the combined extracts were dried and evaporated, with a minimum of heating being used. The resulting red solid residue was recrystallised by extraction into ether/ cyclohexane (9:1) (2 x 50 ml) followed by evaporation with gentle heating to reduce the total volume to

approximately 30 ml. 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (22) was obtained as colourless flakes (0.31 g, 22%), mp 90-92 °C (with decomposition).

Found: 42.18 %C; 4.95 %H; 29.59 %N

$C_5H_7N_3S$ Requires: 42.53 %C; 5.00 %H; 29.76 %N

Accurate Mass Found: 141.036057

$C_5H_7N_3S$ Requires: .036067

Mass Spectrum, see Table (D)

^1H nmr, see Table (A)

^{13}C nmr, see Table (B)

(b) 5,6-Dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole.

5-Amino-3-phenyl-1,2,4-thiadiazole (1.7728 g, 10.00 mmol) was dissolved in dimethylformamide (6 ml) with slight heating, to this solution 1,3-dibromopropane (19.89 g, 10 ml, 98.5 mmol) was added and the resulting mixture refluxed for 1.5 hours. The cooled mixture was filtered and the cream powder (1.6257 g) washed with ether.

To obtain an analytically pure sample the product was recrystallised from ethanol to give 5,6-dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazolium bromide (25) as colourless needles, mp 295-297 °C (with decomposition from 280 °C. The heating started at 250 °C).

Found: 44.13 %C; 4.02 %H; 13.94 %N

$C_{11}H_{12}N_3SBr$ Requires: 44.30 %C; 4.06 %H; 14.09 %N

Mass spectrum, the product lost HBr to give a spectrum identical to that of compound (23), see Table (D)

^{1}H nmr, see Table (C)

1M-Aqueous sodium hydroxide (15 ml) was added to a suspension of the cream powder (1.6257 g) in water (50 ml). The mixture was extracted with dichloromethane (5 x 100 ml), and the combined extracts were dried and evaporated. The white solid residue which resulted was recrystallised from cyclohexane/ether in a similar manner to that used with compound (22), to give 5,6-dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (23) as colourless needles (0.3782 g, 17%), mp 114-115 °C.

Found: 60.63 %C; 4.86 %H; 19.50 %N

$C_{11}H_{11}N_3S$ Requires: 60.83 %C; 5.10 %H; 19.34 %N

Accurate Mass Found: 217.067256

$C_{11}H_{11}N_3S$ Requires: .06736

Mass Spectrum, see Table (D)

^{1}H nmr, see Table (A)

^{13}C nmr, see Table (B)

U.v. spectrum: (Cyclohexane) λ max (nm) 200 (log ε 4.21), 201.5 (4.21), 227 (4.11), 252.9 (3.82), 312.5 (3.37).

(b) Attempted Synthesis of 5,6-Dihydro- 3-methyl- 4H-pyrimido [1,2-d][1,2,4] thiadiazole by Alternative Routes.

(1) Reaction of 3-Amino propan-1-ol with 5-Chloro- 3-methyl- 1,2,4- thiadiazole.

Chlorothiadiazole (6.775 g, 5.00 ml, 50.33 mmol) in tetrahydrofuran (5 ml) was mixed with 3-amino propanol (7.5614 g, 7.7 ml, 100.67 mmol), with cooling in an ice-bath. The mixture was left to stand at room temperature for one hour before ether (20 ml) was added. The reaction mixture separated into two

layers; an opaque colourless upper layer and a clear slightly yellow lower layer, and was left to stand overnight before the then clear, colourless upper layer was decanted off and evaporated to dryness to give 5-(3- hydroxypropylamino)-3-methyl- 1,2,4 - thiadiazole (26) as colourless flakes (7.4602 g, 86%), mp 67-71 °C.

To obtain an analytically pure sample the product was sublimed (bp 180-185 °C at 0.5 mm of Hg) however a good analysis was not obtained as the product was very hygroscopic.

Found: 41.38 %C; 7.14 %H; 24.25 %N

$C_6H_{11}N_3OS$ Requires: 41.60 %C; 6.40 %H; 24.25 %N

Accurate Mass Found: 173.06213

$C_6H_{11}N_3OS$ Requires: .06226 .

Mass Spectrum, see Table (G)

^1H nmr, see Table (E)

^{13}C nmr, see Table (F)

(2) Attempted Thermal Cyclisation of 5-(3-hydroxypropylamino)- 3-methyl- 1,2,4-thiadiazole.

A solution of the thiadiazole (26) (3.45 g, 19.91 mmol) and p-toluene sulphonic acid (0.20 g, 1.05 mmol) in sodium dried toluene (100 ml) was refluxed in a Dean-Stark apparatus. After three hours refluxing the reaction mixture was examined by t.l.c. however there was no cyclised thiadiazole (17) observed, indicating that the hydroxypropyl aminothiadiazole will not dehydrate to give the desired cyclisation product under these conditions.

(3) Reaction of 5- (3-Hydroxypropylamino)- 3-methyl-1,2,4-thiadiazole with Phosphorus tribromide.

Phosphorus tribromide (2.7072 g, 0.94 ml, 10 mmol) was added slowly to a solution of the thiadiazole (26) (1.57 g, 9.06 mmol) in dichloromethane (100 ml). The mixture became opaque on mixing and was left to stand at room temperature for one hour before being transferred to a separating funnel and neutralised with a solution of sodium carbonate (18 g) in water (100 ml). The resulting mixture was extracted with ether (4 x 100 ml) and dichloromethane (4 x 100 ml). The combined ether extracts were dried and evaporated to give a pale yellow oil (0.78 g), t.l.c. of this oil showed a mixture of 5,6-dihydro- 3-methyl-4H-pyrimido [1,2,d] [1,2,4] thiadiazole (17) and starting hydroxypropylamino thiadiazole. On drying and evaporating the combined dichloromethane extracts gave a yellow oil (0.28 g) which was shown to be a mixture on t.l.c. . The combined products (1.06 g) were dissolved in tetrahydrofuran (20 ml) and the solution refluxed for 0.5 hours, before being evaporated and dissolved in water (25 ml). 1M Aqueous sodium hydroxide (7 ml) was added and the resulting mixture extracted with dichloromethane (3 x 100 ml). The combined extracts were dried and evaporated and the residue chromatographed on silica (20 cm x 2.2 cm) eluting with ether/methanol (19:1) solvent. The first 200 ml of eluate contained fast running material, the following 200 ml of eluate showed no product on t.l.c. and was therefore discarded. The next 500 ml of ether/methanol eluates and 250 ml of methanol eluates which showed slow running material on t.l.c.

were combined and evaporated and the residue recrystallised from cyclohexane/ether (see page113) to give 5,6-dihydro- 3-methyl-4H-pyrimido [1,2-d] [1,2,4] thiadiazole (17) as white needles (0.20 g, 13%). This product was identical (mp, mixed mp, t.l.c.) to an authentic sample of (17).

(4) Reaction of 3-Bromopropylamine with 5-chloro- 3-methyl-1,2,4-thiadiazole.

Sodium ethoxide solution (0.2345 g, 10.2 mmol of sodium in 20 ml of ethanol) was added to a solution of bromopropylamine hydrobromide (2.33g, 10.6 mmol) in ethanol (15 ml), chlorothiadiazole (5) (1.355 g, 1 ml, 10.07 mmol) was then added and the resulting mixture left to stand at room temperature for two hours. The reaction mixture was then evaporated and dissolved in water (35 ml) and 1M aqueous sodium hydroxide added (15 ml). The resulting mixture was extracted with dichloromethane (3 x 100 ml) and the combined extracts dried and evaporated to give a solid which was dissolved in toluene (25 ml). The toluene solution was refluxed (oil bath) for two hours before being cooled and added to 0.3 M aqueous sodium hydroxide (50 ml). The product was extracted with dichloromethane (3 x 150 ml) and the combined extracts dried and evaporated to give a pale orange semi-solid residue (0.79 g). This product however would not redissolve in dichloromethane, suggesting that further reaction had occurred. Examination of the dichloromethane extracts before evaporation showed a mixture of products; some cyclised thiadiazole (17) (R_f 0.25) as well as faster running material (R_f 0.6), possibly 5- (3-bromopropylamino) 3-methyl-1,2,4-thiadiazole (28), and slower running material (R_f 0.1)

possibly the product from inter-molecular coupling of the bromopropylamino thiadiazole.

3 Reaction of 5,6-Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole with Nitriles

(1) With Acetonitrile-D_3

A solution of thiadiazole (17)(0.7764 g, 5.00 mmol) in acetonitrile -D_3 (3.930 g, 5 ml, 89.16 mmol) was refluxed (oil bath) for 7 hours. The solution was then evaporated to dryness and a further 5 ml of acetonitrile -D_3 added and this solution refluxed for 7 hours. The reaction mixture was then evaporated to dryness again and the solid residue recrystallised from ether/cyclohexane to give 5,6-dihydro- 3-(trisdeuteriomethyl)- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (30) as white needles (0.6678 g, 84%), mp 72-4 °C.

Found: 45.15 %C; 5.78 %H; 27.01 %N

$C_6H_6D_3N_3S$ Requires: 45.54 %C; 5.73 %H; 26.55 %N.

Accurate Mass Found: 158.069493

$C_6H_6D_3N_3S$ Requires: .070550

Mass Spectrum, see Table (D)

^1H nmr, see Table (A)

^{13}C nmr, see Table (B)

(2) With Acetonitrile -D_3 followed by Acetonitrile

A solution of thiadiazole (17) (0.7771 g, 5.01 mmol) in acetonitrile -D_3 (3.930 g, 5 ml, 89.16 mmol) was refluxed (oil bath) for 7 hours. The reaction mixture was then evaporated to dryness and a further 5 ml of acetonitrile-D_3 added and refluxed again for 7 hours. A ^1H mnr spectrum of an aliquot of the reaction mixture, diluted with acetonitrile-D_3, showed no ring-methyl signal at δ2.2 (cf 17) indicating that there was no

starting thiadiazole still present. The reaction mixture was evaporated to dryness and the ^1H nmr spectrum of the solid residue obtained in chloroform-D, this was identical to that of compound (30). The solid residue was then dissolved in acetonitrile (3.930 g, 5 ml, 95.74 mmol) and refluxed (oil bath) for 7 hours before being evaporated to dryness and redissolved in fresh acetonitrile (5 ml), to be refluxed for a further 7 hours. The reaction mixture was then evaporated and a ^1H nmr spectrum obtained for a sample of the solid residue. This was identical to the spectrum of the starting methyl-thiadiazole (17). The solid residue was recrystallised as before from cyclohexane/ether to give 5,6-dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole as white spars (0.6712 g, 86%); mp 73-75 °C, mixed mp 73-75 °C.

(3) With Acetonitrile-D_3. ^1H nmr experiment

The pyrimidothiadiazole (17) (0.0388 g, 0.250 mmol) was dissolved in acetonitrile-D_3 (0.3930 g, 0.50 ml, 8.92 mmol) and the resulting solution stored at ambient temperature in a ^1H nmr tube, sealed with a plastic cap. The ^1H nmr spectrum of the solution was recorded at various intervals from the mixing of the reactants. Tetramethylsilane was used as internal standard. The ratio of the integral of the CH_3CN signal at δ 1.90 to the methyl signal of the pyrimido thiadiazole at δ 2.05 was plotted against time (/hour), see graph (page 166).

t(/hour)	CH_3CN/Ring-Me
0.5	0.0324
2.5	0.054
27.5	0.189
51	0.323
123	0.697
167	1.208
216	1.463
289	2.184
336	2.932
383	3.612
480	4.900
624	9.45
1199	9.817

(4) With fumaronitrile - 2:1 molar ratio

A solution of thiadiazole (17)(0.7760 g, 5.00 mmol) and nitrile (0.7800 g, 10.00 mmol) in toluene (35 ml) was left to stand in the dark at room temperature for 14 days. Olive-green rosettes were visible on the wall of the reaction flask after this time. The yellow mother liquors were decanted off and the product crushed up in some fresh toluene (15 ml) and then filtered and dried to give 1,2-di-{5,6-dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole-3-yl} ethene (32) as an homogeneous (t.l.c.) yellow powder (0.6055 g 79%). The yellow powder was recrystallised from ethanol to give dark yellow needles (0.1338 g) however there was extensive decomposition, mp 194-198 °C (with decomposition from approximately 165 °C).

Found: 46.92 %C; 4.65 %H; 27.21 %N

$C_{12}H_{14}N_6S_2$ Requires: 47.04 %C; 4.61 %H; 27.43 %N

Mass Spectrum, see Table (D)

^1H nmr, see Table (A)

(5) With Fumaronitrile - 5:1 molar ratio

Filtered solutions of thiadiazole (17)(0.7756 g, 5.00 mmol) in toluene (25 ml) and fumaronitrile (1.9549 g, 25.04 mmol) in toluene (60 ml) were mixed and a yellow colouration appeared

after a few seconds. The solution was left to stand at room temperature for 60 hours. The deep yellow coloured solution was then chromatographed on silica (37 cm x 2.2 cm) eluting with . The first 1 L of toluene eluate (toluene) brought through the excess of nitrile, and the succeeding 1 L of eluates (toluene/ether) (4:1) showed neither nitrile nor product on t.l.c. and were discarded. The next 500 ml of toluene/ether (1:1) followed by 300 ml ether, and 2.8 l ether/methanol (19:1) were homogeneous (t.l.c.) and brought through the faster running of the two yellow products. These fractions were combined and gave 5,6-dihydro- 3-(2-cyanovinyl)- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (31) as a yellow powder (0.6211 g, 65%). However t.l.c. of this powder showed a trace of the slower running (32) which was formed by disproportionation of (31) to (32) and fumaronitrile. Therefore a microanalysis of (31) could not be obtained.

Accurate Mass Found: 192.045246

$C_8H_8N_4S$ Requires: .046966

Mass Spectrum, see Table (D)

^1H nmr, see Table (A)

The final 2 L of methanol eluates brought through the slower running yellow product (32) and amounted to 0.1625 g (11%).

Compound (31) was converted into (32) in the following manner. The yellow powder (31) (0.6211 g, 3.23 mmol) was dissolved in toluene (25 ml) and thiadiazole (0.5019 g, 3.23 mmol) added. This solution was left to stand for 10 days at room temperature before being filtered to remove the yellow

precipitate (0.3427 g). The solution was then left for a further 10 days and filtered again to give 0.2153 g of yellow powder. The combined yield of (31) was 0.5580 g (36.5% from the original methyl thiadiazole). This product was identical (mp, mixed mp, ^{1}H nmr, t.l.c.) to a sample formed directly from the reaction of 5,6-dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole and fumaronitrile.

(6) With Methoxyacetonitrile

A solution of thiadiazole (17)(0.7740 g, 4.99 mmol) and nitrile (1.6252 g, 1.7 ml, 22.9 mmol) in toluene (3 ml) was refluxed (oil bath) for 4 hours. The cooled solution was chromatographed on silica (40 cm x 2.2 cm) eluting with methanol/ether (1:4). The first 250 ml of eluates containing toluene and the excess of nitrile was discarded. The succeeding 2.5 L of eluates containing the product and a trace of starting thiadiazole were evaporated to yield a yellow oil which was purified by distillation. 5,6-Dihydro- 3-methoxymethyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (33) was obtained as a colourless oil (0.5730 g, 62%), bp 150-160 °C (0.7 mm of Hg).

Found: 45.22 %C; 6.21 %H; 22.35 %N

$C_7H_{11}N_3OS$ Requires: 45.38 %C; 5.98 %H; 22.68 %N

Accurate Mass Found: 185.0612

$C_7H_{11}N_3OS$ Requires: .0622

Mass Spectrum, see Table (D)

^{1}H nmr, see Table (A)

^{13}C nmr, see Table (B)

(7) With Pyridine-4-carbonitrile

A solution of thiadiazole (17)(0.7770 g, 5.00 mmol) and

nitrile (5.2058 g 50.00 mmol) in toluene (100 ml) was refluxed (oil bath) for 30 hours. The cooled solution was then chromatographed on silica (28 cm x 2.2 cm), with ether/methanol (2.125:1) for elution. The first 200 ml of eluate containing toluene and the excess of nitrile was discarded. The following 3.15 L of ether/methanol and 1.5 L of methanol eluates were homogeneous (t.l.c.) and were combined and evaporated to give a reddish oil which solidified slowly on addition of cyclohexane/ether (1:9). The solid was recrystallised by extraction into cyclohexane/ether (1:9) (5 x 50 ml) and then the solution was concentrated by distillation on a water bath to a volume of 100 ml, and gave 5,6-dihydro- 3-(4-pyridyl)-4H-pyrimido [1,2-d] [1,2,4] thiadiazole (34) as off-white granules (0.90 g, 82.4%), mp 143-5 °C.

Found: 55.22 %C; 4.67 %H; 25.97 %N

$C_{10}H_{10}N_4S$ Requires: 55.02 %C; 4.62 %H; 25.67 %N

Accurate Mass Found: 218.06188

$C_{10}H_{10}N_4S$ Requires: .06261

Mass Spectrum, see Table (D)

^1H nmr, see Table (A)

^{13}C nmr, see Table (B)

(8) With 4-Nitrobenzonitrile

A solution of the thiadiazole (17)(0.7764 g, 5.00 mmol) and nitrile (0.7401 g, 5.00 mmol) in toluene (15 ml) was refluxed (oil bath) for 4 hours. The cooled solution was chromatographed on silica (41 cm x 2.7 cm) eluting with methanol/ether (3:2). The first 250 ml of eluates brought through the unreacted nitrile and were discarded. The succeeding 900 ml of eluates, which were

homogeneous (t.l.c.), brought through the product and gave 0.8347g of yellow crystalline solid on evaporation. The final 500 ml of eluates contained a mixture of product and starting thiadiazole and amounted to 0.1389 g of yellow oil on evaporation. The yellow product was recrystallised from cyclohexane/dichloromethane (4:1) to give 5,6-dihydro-3-(4-nitrophenyl)- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (35) as yellow spars, (0.6485 g, 50%), mp 172-174 °C.

Found: 50.72 %C; 3.67 %H; 21.42 %N

$C_{11}H_{10}N_4O_2S$ Requires: 50.37 %C; 3.84 %H; 21.36 %N

Accurate Mass Found: 262.053166

$C_{11}H_{10}N_4O_2S$ Requires: .052438

Mass Spectrum, see Table (D)

^1H nmr, see Table (A)

^{13}C nmr, see Table (B)

(9) With 2-Cyanophenol

A solution of thiadiazole (17)(0.7783 g, 5.01 mmol) and nitrile (1.1933 g, 10.02 mmol) in toluene (36 ml) was refluxed (oil bath) for 6.5 hours. The white solid which formed slowly was hot filtered, washed with boiling toluene (25 ml), and dried (0.4640 g). The combined toluene filtrates were evaporated to give a yellow oil which yielded a yellow powder on the addition of methanol. The solid was filtered and dried, and amounted to 0.2163 g.

Recrystallisation of the combined solids from ethanol gave 5,6-dihydro- 3-(2-hydroxybenzene)- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (36) as off-white spars (0.6230 g, 54%), mp 228-9 °C (with decomposition from 225 °C).

Found: 56.84 %C; 4.82 %H; 18.32 %N

$C_{11}H_{11}N_3SO$ Requires: 56.63 %C; 4.75 %H; 18.01 %N

Accurate Mass Found: 233.06333

$C_{11}H_{11}N_3SO$ Requires: .06227

Mass Spectrum, see Table (D)

I.r. Data: Broad peak at approximately 2561 cm^{-1} due to N-H, several strong peaks around 1591 cm^{-1} due to υ C=C/C=N , multiple peaks below 1000 cm^{-1} due to phenol ring.

^1H nmr, see Table (A)

(10) With Trimethylacetonitrile

A solution of the pyrimidothiadiazole (17) (0.1554 g, 1.00 mmol) in trimethylacetonitrile (0.752 g, 1 ml, 9.05 mmol) was refluxed (heating mantle) for 2 hours after which time t.l.c. showed only starting materials to be present. The cooled solution was chromatographed on silica (9 cm x 2.2 cm) eluting with ether to remove the nitrile and then 400 ml of methanol/ether (1:1) to bring off the homogeneous (t.l.c.) thiadiazole. This thiadiazole (0.1146 g, 74%) was recrystallised from cyclohexane with a small amount of ether to give (17) as white needles (0.0732 g, 47%) which were identical (mp, mixed mp, ^1H nmr) to an authentic sample of (17).

(11) With Pentafluorobenzonitrile

A deep red precipitate formed on the addition of the pyrimidothiadiazole to pentafluorobenzonitrile. The precipitate was insoluble in excess pentafluorobenzonitrile, but did dissolve in methanol to give a deep red coloured solution. The red colouration was thought to be due to a Meisenheimer complex and therefore the reaction was not pursued further.

(12) With Cyanomethyltriphenylphosphine

Filtered solutions of the thiadiazole (17) (0.1562 g, 1.00 mmol) in chloroform (3 ml) and cyanomethyltriphenylphosphine (0.3623 g, 1.00 mmol) in chloroform (6 ml) were mixed and the resulting solution refluxed (oil bath) for 8 hours. The cold reaction mixture was then chromatographed on silica (13 cm x 2.2 cm) eluting with benzene. The first 50 ml of benzene eluate followed by 400 ml of benzene/ether (1:1) and 100 ml of ether eluates were discarded. The next 1 L of eluates (ether) were homogeneous (t.l.c.) and gave triphenyl phosphine oxide as a white solid (0.1665 g, 55%), mp 155-6 °C (Lit 153-5 °C); m/e 278 (M^+).

The following 1 L of eluates (methanol) brought off the unreacted starting thiadiazole (0.1288 g, 82%), homogeneous by t.l.c. and ^1H nmr, mp 72-4 °C, mixed mp 72-4 °C.

(13) With Benzoylacetonitrile

Benzoylacetonitrile (0.7268 g, 5.00 mmol) was dissolved in toluene (5 ml) with sight heating and added to a solution of pyrimidothiadiazole (17) (0.7760 g, 5.00 mmol) in toluene (10 ml), and washed in with toluene (2 ml). A white precipitate formed rapidly and the mixture was left to stand at room temperature for 48 hours. The white solid was filtered off and washed with toluene (10 ml) and then with a little ether before being dried. T.l.c. of the mother liquors showed only unreacted starting material. 5,6-Dihydro- 3-methyl- 4H-pyrimido [1,,2-d] [1,2,4] thiadiazolium benzoylacetonitrile enolate (37) was obtained as white rhombuses (1.2547 g, 84%), mp 90.5-92.5 °C.

Found: 59.98 %C; 5.37 %H; 18.86 %N

$C_{15}H_{17}N_4OS$ Requires: 59.98 %C; 5.37 %H; 18.65 %N

Mass spectrum, no M^+ peak was observed at m/e 300 only the spectra of the starting thiadiazole and the benzoylacetonitrile.

^1H nmr, the product dissolved in DMSO-D_6 to give only the spectra of the starting thiadiazole and the nitrile, indicating that the product was dissociating in solution.

I.r. Data: Very broad peak between 2400 cm^{-1}-2700 cm^{-1} due to υ N-H; strong peak at 2150 cm^{-1} υ CN. There is no peak at approximately 1690 cm^{-1} where the C=O bond in benzoylacetonitrile absorbs however there is a strong broad peak at approximately 1600 cm^{-1} due to υ C=N and υ C=C.

(14) With Malononitrile

Filtered solutions of the thiadiazole (17) (0.1554 g, 1.00 mmol) in toluene (5 ml) and malononitrile (0.3298 g, 4.99 mmol) in toluene (15 ml) were mixed and the resulting solution left to stand at room temperature for 36 hours. The reaction mixture became yellow coloured soon after mixing and a slight opacity was visible as a precipitate was deposited on the walls of the reaction flask. After 36 hours the yellow toluene mother liquors were decanted off and the yellow solid residue (0.108 g) dissolved in methanol. Examination of this methanol solution by t.l.c. showed a fast running yellow product (R_f 0.7), starting thiadiazole (R_f 0.25) and a slow running yellow product (R_f 0.1). From a comparison with the reaction of the thiadiazole (17) with fumaronitrile the fast running product was probably 5,6-dihydro- 3-(cyanomethyl)- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (38), or a salt thereof (either inter- or intramolecular) (cf benzoyl acetonitrile reaction), while the

slower running material was probably di-(5,6-dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole-3-yl)- methane (39). As some starting thiadiazole was also found in the solid precipitate some 5,6-dihydro- 3-methyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazolium malononitrile anion (40) had been formed but had dissociated in the methanol solvent to give malononitrile and starting thiadiazole [cf benzoyl acetonitrile adduct in $(CD_3)_2SO$]. A ^1H nmr of a sample of the precipitate was obtained [see Table (A)] confirming that the major product has a structure (38) in solution. A mass spectrum of a sample of the precipitate was also obtained [see Table (D)].

Accurate Mass Found: 180.04609

$C_7H_8N_4S$ Requires: .04695

An acceptable microanalysis of compound (38) was not obtained.

(15) With Trimethylsilylcyanide

The reaction of the thiadiazole and trimethylsilylcyanide was attempted under various conditions both neat and in hydrocarbon solvents (benzene and toluene), however on each occasion a mixture of products resulted which decomposed on workup.

(a) Reaction in trimethylsilylcyanide

A solution of thiadiazole (17) (0.1549 g, 1.00 mmol) in nitrile (0.9672 g, 1.3 ml, 9.75 mmol) was heated in an oil bath at 130 °C for 4 hours. The reaction mixture had turned dark brown-black by this time. The mixture was dissolved in dichloromethane (100 ml) and to this aqueous sodium hydroxide solution (100 ml of 0.25 M) was added. The aqueous layer was

extracted with more dichloromethane (2 x 150 ml) and the combined organic fractions dried over magnesium sulphate before being evaporated to give a brown power (0.1090 g). T.l.c. of this product showed several products, with streaking.

(b) Reaction in benzene

A solution of thiadiazole (17)(0.1573 g, 1.01 mmol) in benzene (1 ml) and nitrile (0.9672 g, 1.3 ml, 9.75 mmol) was refluxed (oil bath) for 4 hours. The reaction mixture had become a pale yellow-brown colour by this time and the work up was as above in (a). The resulting fawn powder (0.1198 g) was dissolved in chloroform-D and the ^{1}H nmr spectrum obtained: this showed the starting thiadiazole to be present however the integral for the methyl signal at δ 2.2 was less (approximately, 90%) than expected indicating that some 5,6-dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (22) could be present.

(c) Reaction in toluene

Procedure was as above; thiadiazole (1 mmol) in toluene (5 ml) and nitrile (1.3 ml) was refluxed for 1.5 hours and gave a product which decomposed during workup.

(16) With trans-Cinnamonitrile

trans-Cinnamonitrile (10.28 g, 10 ml, 79.59 mmol) was added to a solution of the thiadiazole (1.5532 g, 10.01 mmol) in toluene (50 ml) and the resulting mixture refluxed (oil bath) for 7 hours. The cold solution was then chromatographed on silica (37 cm x 1.4 cm) eluting with toluene. The first 650 ml of eluate brought through the excess of cinnamonitrile and was discarded. The next 500 ml of eluates (toluene/ether) (1:1) and 2 L of ether eluates showed two overlapping spots on t.l.c. and

were combined and evaporated to give a yellow solid. The column was cleaned with 750 ml of methanol which, on evaporation, gave a brown waxy solid (0.8993 g).

The yellow solid residue, obtained from the ether/toluene and ether fractions, was rechromatographed on silica (34 cm x 2.2 cm) eluting with ether. The first 250 ml of ether eluate was discarded, the following 2.75 L of ether eluates were homogeneous (t.l.c.) and were combined and evaporated to give a yellowish solid which was recrystallised from cyclohexane to give 2,3,5,6-tetrahydro- 2-cyano- 3-phenyl- 4H- pyrimido [1,2-d] [1,3] thiazole (43) as white needles (0.2598 g, 11%), mp 143.5-145 °C.

Found: 64.37 %C; 5.38 %H; 17.33 %N

$C_{13}H_{13}N_3S$ Requires: 64.17 %C; 5.38 %H; 17.27 %N

Accurate Mass Found: 243.080489

$C_{13}H_{13}N_3S$ Requires: .083011

A mass spectrum showed speaks at m/e 114 (base peak) due to $[C_4N_2S]^{+\cdot}$, 129 (50%) $PhCH{=}CHCN^{+\cdot}$, 102 (48%) $PhC{\equiv}CH^{+\cdot}$, 243 (41%) $M^{+\cdot}$

^1H nmr, see Table (E)

I.r. data: (a) KBr disc. peaks at 1630 cm^{-1} (s) due to ν C=N/C=C; 2245 cm^{-1} (w) ν C=N.

(b) CCl_4 solution (0.2 molar) 1646 cm^{-1} (s) due to ν C=N/C=C; 2250 cm^{-1} (very weak) ν C≡N.

The next 750 ml of eluates (ether/methanol) (19:1) and 250 ml of methanol eluates were combined with the methanol fractions from the first column and evaporated to give a yellow solid that was recrystallised from cyclohexane to give 2,3,5,6-tetrahydro- 3-imino- 2-(benzylidine)- 4H-pyrimido [1,2-d] [1,3] thiazole (44)

as a cream powder (0.5598 g, 23%) mp 134-136 °C.

Found: 64.60 %C; 5.39 %H; 17.19 %N

$C_{13}H_{13}N_3S$ Requires: 64.17 %C; 5.38 %H; 17.27 %N

Accurate Mass Found: 243.084196

$C_{13}H_{13}N_3S$ Requires: .083011

A mass spectrum showed peaks at m/e 44 (base peak) due to $CS^{+\cdot}$, 134 (21%) $PhCH{=}C{=}S^{+\cdot}$, 242 (14%) $M^{+\cdot}-H$, 129 (9%) $PhCH{=}CHCN^{+\cdot}$, 77 (8%) Ph^{+}, 243 (4%) $M^{+\cdot}$.

^1H nmr, see Table (E)

I.r. data (a) KBr disc. peaks at 3332 cm^{-1} (m) υ N-H; 1595-1650 cm^{-1} (m) υ C=N/C=C; 1415 cm^{-1} (m); 1170 cm^{-1} (m)

(b) CCl_4 solution (0.2 molar), 3320 cm^{-1} (s) N-H; 1660 cm^{-1}, 1630 cm^{-1}, 1608 cm^{-1} (s) υ C=N/C=C; 1410 cm^{-1} (s).

Note The products (43) and (44) seem to decompose slightly on chromatography and are therefore difficult to separate in this way.

(17) With Benzonitrile

A solution of thiadiazole (17) (0.7771g, 5.01mmol) in benzonitrile (2.52g, 2.5ml, 24.5mmol) was refluxed for 0.5 hours. The cold solution was then chromatographed on silica (41 cm x 2.5 cm) eluting with ether. The first 200 ml of eluate brought through the excess of nitrile, the succeeding 1.5 L of eluates (methanol/ether) (1:9) were homogenous and on evaporation and recrystallisation from cyclohexane /benzene (1:1) afforded 5,6-dihydro- 3-phenyl- 4H- pyrimido [1,2-d][1,2,4] thiadiazole (23) as a white powder (0.5939g, 55%). The product was identical (mp, mixed mp, nmr) with an authentic sample of compound (23).

4 Reaction of 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole with Nitriles.

(1) With Acetonitrile

A solution of the thiadiazole (22) (0.7103g, 5.03 mmol) in acetonitrile (19.65 g, 25 ml, 478.68 mmol) was refluxed for 14 hours. The cooled solution was evaporated to dryness and the solid residue sublimed (140 °C, at 0.1 mm of Hg) to give a white solid 0.4178 g. This solid was recrystallised from cyclohexane/ether to give 5,6-dihydro- 3-methy- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (17) as white needles (0.3594 g, 46%). This product was identical (mp, mixed mp, t.l.c., ^{1}H nmr) with an authentic sample.

(2) With Benzonitrile

Benzonitrile (5.151 g, 5.1 ml, 49.95 mmol) was added to a solution of the thiadiazole (22) (0.7066 g, 5.00 mmol) in toluene (20 ml) and the resulting mixture refluxed (oil bath) for 8.5 hours. The cooled solution was then chromatographed on silica (43 cm x 2.5 cm) eluting with ether/methanol (20:1). The first 700 ml of eluate brought through the excess of benzonitrile and fast running material and was discarded. The following 1 L of ether/methanol and 1 L of methanol eluates brought through the product and the unreacted starting thiadiazole. These fractions were combined and evaporated before being recrystallised from benzene/cyclohexane (1:1) to give 5,6-dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (23) as off-white granules (0.6403 g, 59%). This product was identical (mp, mixed mp, t.l.c., ^{1}H nmr) with an authentic sample.

5 Thermolysis reactions of 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles

(a) Thermolysis Reactions of 5,6-Dihydro- 3-methyl-4H-pyrimido- [1,2-d] [1,2,4] thiadiazole in Various Solvents

(1) In Tetralin (1,2,3,4-Tetrahydronaphthalene)

A solution of the thiadiazole (17) (0.7764 g, 5.00 mmol) in tetralin (50 ml) was refluxed (bp 207 °C) for 4 hours under a steady flow of argon. The reaction mixture was allowed to cool overnight and then filtered. The resulting pale brown needles were washed with cyclohexane (15 ml) before being sublimed (190-200 °C at 0.3 mm of Hg), to give hexahydropyrimidine-2-thione (53) as a homogeneous (t.l.c.) cream powder (0.3768 g, 65%). This product was recrystallised from ethanol to give colourless needles, mp 210-211 °C, mixed mp 210-211 °C.

(2) In Toluene

A solution of the thiadiazole (17) (0.7775 g, 5.01 mmol) in toluene (20 ml) was refluxed (oil bath) for 72 hours under a steady flow of argon. The cooled reaction mixture was examined by t.l.c. and found to contain starting thiadiazole and a trace of hexahydropyrimidine- 2-thione (53). The mixture was chromatographed on silica (9 cm x 2.2 cm) eluting with ether. The first 200 ml of ether eluate was shown to contain hexahydropyrimidine- 2-thione by t.l.c. however on evaporation a negligible yield was obtained. The next 500 ml of eluates (ether/methanol) (19:1) and 2.5 L of methanol eluates were homogeneous (t.l.c.) and were combined and evaporated. The solid residue was recystallised from cyclohexane/ether, in the manner

described on page 113, to give the starting thiadiazole (17) as white needles (0.5800 g, 75%), mp 72-74°C, mixed mp 72-74°C.

(3) In tert-Butylbenzene

A solution of the thiadiazole (17)(0.1469g, 0.95 mmol) in tert-butylbenzene was heated in an oil bath at approximately 160 °C, under a steady flow of argon. After 4 hours the reaction mixture was examined by t.l.c. and showed little decomposition. After a further 4 hours of heating quite a large amount of charring was visible on the walls of the reaction vessel. T.l.c. of the mother liquor showed starting thiadiazole and hexahydropyrimidine- 2-thione to be present. The reaction mixture was not processed further.

(4) In 1-Methyl-4-isopropyl-benzene (p-Cymene)

A solution of the thiadiazole (17) (0.0791 g, 0.51 mmol) in p-cymene (5 ml) was refluxed (bp 176-178 °C) in a heating mantle. After heating for one hour the reaction mixture was examined by t.l.c. and this showed a small amount of hexahydropyrimidine- 2-thione as well as starting material. The reaction mixture was reheated for a further one hour and again examined by t.l.c.; this showed starting thiadiazole, (R_f 0.2), hexahydropyrimidine- 2-thione (R_f 0.6) and a yellow coloured product at the solvent front . There was some charring visible in the reaction vessel. After refluxing for a further 2.5 hours extensive charring was visible in the reaction vessel and t.l.c. showed only a small amount of starting thiadiazole to be present as well as several faster running products.

(5) In Butanol/Water

A solution of the thiadiazole (17) (0.7773 g, 5.01 mmol) in

a mixture of butan-1-ol (35 ml), water (35 ml) and ethanol (2.5 ml) was refluxed for 72 hours (approximately 110-120 °C), before being allowed to cool spontaneously. Chromatography of the cold reaction mixture was carried out on silica (35 cm x 2.2 cm), eluting with either. The first 100 ml of ether eluate brought through the alcohol-water solvent mixture and was discarded, the next 1.5 L of eluates (methanol/ether) (1:19) gave hexahydropyrimidine- 2-thione (53) as a white powder (0.1855 g, 32%) which showed one spot on the t.l.c., mp and mixed mp 209-210°C. The next 500 ml of eluates (methanol/ether) (1:9) were mixed and therefore discarded, the following 750 ml of methanol/ether (1:9) eluates afforded hexahydropyrimidine-2-one (59) as a white powder on evaporation (0.1055 g, 21%), mp and mixed mp 254-6 °C.

Found: 47.89 %C; 8.11 %H; 27.98 %N.

$C_4H_8N_2O$ Requires: 47.99 %C; 8.05 %H; 27.80 %N.

(6) (i) In o-Dichlorobenzene and 9,10-Dihydroanthracene

The thiadiazole (17) (0.7772 g, 5.0 mmol) was added to a solution of 9,10-dihydroanthracene (0.9063 g, 5.03 mmol) in o-dichlorobenzene (25 ml) and the resulting mixture refluxed under a slow stream of argon for 6 hours, before being allowed to cool spontaneously overnight. The cold reaction mixture was filtered to remove a mixture of fluorescent pale brown flakes and non-fluorescent brown needles. The brown precipitate (0.5997 g) was extracted with petrol (5 x 50 ml) to remove anthracene and then sublimed (200-210 °C, 0.5 mm of Hg) to give hexahydropyrimidine- 2-thione (53) as a white powder (0.4640 g, 80%). This product was identical (t.l.c., mp, mixed mp) with an

authentic sample of (53).

Evaporation of the petrol extracts afforded 0.1145 g of anthracene as a white powder, mp 214-216 °C.

The dichlorobenzene mother liquors were chromatographed on silica (25 cm x 2.2 cm) to separate the fast-running dichlorobenzene, dihydroanthracene and anthracene from the slower running hexahydropyrimidine- 2-thione and unreacted thiadiazole. A negligible quantity of hexahydropyrimidine- 2-thione and thiadiazole was obtained from this chromatography. However the fast-running fractions were combined and evaporated before being rechromatographed on alumina (Beckmann type I, pH neutral, 100-250 mesh) (53 cm x 2.2 cm)eluting with petrol. The first 150 ml of eluate brought through the o-dichlorobenzene solvent, the following 2 L of petrol eluates brought through the dihydroanthracene and anthracene together, and on evaporation gave 0.4146 g of white powder. G.l.c. analysis of this powder (Pye Unicam PU4500 chromatograph with an L.D.C. 308 Computing Integrator) showed it to contain 98% anthracene and 2% dihydroanthracene. Thus the overall yield of anthracene from the reaction was 0.5218 g (58%) with 1% of 9,10-dihydroanthracene recovered.

(ii) Thermolysis of 9,10-Dihydroanthracene in o-Dichlorobenzene.

A solution of 9,10-Dihydroanthracene (0.8990 g, 4.99 mmol) in o-dichlorobenzene (25 ml) was refluxed under a slow stream of argon for 6 hours before being allowed to cool to room temperature. The cold reaction mixture was chromatographed on alumina (Beckmann type I) (40 cm x 2.2 cm) eluting with petrol.

The first 200 ml of eluate brought through the o-dichlorobenzene solvent, and the following 1.5 L of petrol brought through the dihydroanthracene and anthracene together and amounted to 0.5808 g of white powder. G.l.c. of this powder under the same conditions as above [(6)(i) showed it to comprise of 96% 9,10-dihydroanthracene and 4% of anthracene; that is a 62% yield of dihydroanthracene and a 3% yield of anthracene.

(b) Thermolysis of 5,6-Dihydro-3-phenyl-4H-pyrimido [1,2-d] [1,2,4] thiadiazole in Tetralin

A solution of the thiadiazole (23) (1.0880g, 5.01 mmol) in tetralin (50 ml) was refluxed for 6 hours under a slow stream of argon. As the reaction mixture was originally heated to the boil it became slightly opaque and some deposition occurred on the walls of the reaction vessel, however as the mixture began to boil the precipitate redissolved and the mixture became clear. After 6 hours the reaction mixture was a clear dark red-brown solution, with a little charring visible on the walls of the reaction flask. The mixture was cooled overnight and then filtered to remove the light-fawn coloured needles (0.4744 g) which had formed and these were sublimed (200-210 ^{o}C at 0.1 mm of Hg) to give a pale yellow powder (0.4308 g). On recrystallisation from ethanol hexahydropyrimidine- 2-thione (53) was obtained as colourless needles (0.2970 g, 51 %). This product was identical (mp, mixed mp, t.l.c., ^{1}H nmr) with an authentic sample. T.l.c. of the ethanol mother liquors showed hexahydropyrimidine- 2-thione and also some starting thiadiazole. Therefore the above yield of 51% is a minimum yield.

(c) Thermolysis of 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazole in Hydrocarbon Solvents.

(1) In Tetralin

The thiadiazole (22) (0.7153 g, 5.07 mmol) was dissolved in tetralin (80 ml) with gentle warming. The solution was then refluxed for one hour under a slow stream of argon, and then left to cool spontaneously to room temperature. There was extensive charring and solid visible on the walls of the reaction vessel. A little methanol (10 ml) was added to the reaction mixture and the resulting solution was passed down a short silica column (10 cm x 2.2 cm) eluting with methanol/ether (1:19) to separate the hexahydropyrimidine- 2-thione from slower running material. The product from this column was sublimed (210 ^{o}C, 0.1 mm of Hg) to give hexahydropyrimidine- 2-thione (53) as a straw coloured powder (0.1100 g, 19%). A sample of this product was recrystallised from ethanol and a melting point, mixed melting point and ^{1}H nmr obtained. These showed the product to be identical to an authentic sample of (53). Mp of colourless needles 210 ^{o}C, mixed mp 209-210 ^{o}C.

(2) In Toluene

As the thiadiazole (22) could only be synthesised on a small scale the following procedure was adopted to obtain an adequate quantity for the reaction. Four lots of thiadiazole (22), 3 x 10 mmol each in 50 ml of toluene and 1 x 5 mmol in 25 ml of toluene, were refluxed (oil bath) for 3.5 hours after which time a white precipitate had been formed. The reaction mixtures were allowed to cool spontaneously to room temperature and the toluene mother liquors were decanted off and combined

before being evaporated to give an off-white solid. This solid residue was found by ^{1}H nmr to contain mainly starting thiadiazole and was therefore redissolved in toluene (50 ml) and refluxed for a further 6 hours to give more white precipitate. The cold toluene mother liquors were found by t.l.c. to contain some starting thiadiazole and hexahydropyrimidine- 2-thione as well as traces of other products.

The combined white precipitates from the first 3.5 hour refluxes were extracted with hot (100 °C) dimethylformamide (25 ml) and the resulting solution hot-filtered through a sinter before being allowed to cool. The cold mixture was then filtered and the fawn powder washed with ether (10 ml) and dried to give 1.1776 g of product. The dimethylformamide filtrate was then reheated to 100 °C and used to extract the precipitate from the 6 hour reflux. A further 1.1043 g of fawn powder was obtained from the cold solution. The dimethylformamide mother liquors were reduced in volume and gave a further 0.8775 g of product. All the products that showed a single spot on t.l.c. (R_f 0.2) were combined to give 5,6-dihydro- 3-{1-(2-thioxo hexahydropyrimidinyl)}- 4H-pyrimido [1,2,-d] [1,2,4] thiadiazole (60a) as a fawn powder (3.1594 g, 71%).

To obtain an analytically pure sample the product was recrystallised from ethanol (charcoal) to give colourless needles, mp 220-221 °C (with decomposition from 215 °C).

Found: 42.38 %C; 5.18 %H; 27.48 %N

$C_9H_{13}N_5S_2$ Requires: 42.33 %C; 5.13 %H; 27.43 %N

Accurate Mass Found: 255.060216

$C_9H_{13}N_5S_2$ Requires: .06122

Mass Spectrum, see Table (G)

^{1}H nmr, see Table (E)

^{13}C nmr, see Table (F)

I.r. Data: medium intensity peaks around 3100 cm^{-1} possibly υ NH, and around 2900cm^{-1} and 3000 cm^{-1} due to υ CH, strong peak at 1635 cm^{-1} due to υ C=N, strong peaks between 1531-1566 cm^{-1}, strong peaks at 1415 cm^{-1} and 1275 cm^{-1}, medium peaks at 1172 cm^{-1} and 1187 cm^{-1} (υ C=S), many medium-small peaks below 1000 cm^{-1}.

(3) In Toluene with Sulphur present

The thiadiazole (22) (0.1420 g, 1.01 mmol) was dissolved in a boiling solution of sulphur (0.2283 g, 7.13 mmol) in toluene (10 ml) and the resulting mixture refluxed for 7 hours. After this time a white precipitate was visible in the reaction mixture and this was hot filtered and the white solid recrystallised from ethanol to give compound (60) as a white powder (0.0825 g, 32%). This product was identical (t.l.c., mp, mixed mp) with a sample previously obtained. T.l.c. of the toluene mother liquors showed sulphur and some unreacted thiadiazole as well as a trace of hexahydropyrimidine- 2-thione.

6 Reaction of 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazoles with Heterocumulenes

I (a) Reaction with Carbon disulphide

General Method:

Analar carbon disulphide (31.65 g, 25 ml, 416 mmol) was added, with stirring, to a filtered solution of the thiadiazole (5.00 mmol) in chloroform (10 ml). A coloured precipitate was formed immediately on mixing. The reaction mixture was left to stand at room temperature for 0.5 hours then filtered and the precipitate washed with ether before being dried.

(1) 5,6- Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (0.7060 g, 5.00 mmol) was used. 5,6-Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazolium-7- dithiocarboxylate (67) was obtained as a very pale orange powder (1.0399g, 96%), mp 93-95 °C (with decomposition from 88 °C. Mp of the starting thiadiazole 90-92 °C).

Found: 33.02 %C; 3.22 %H; 19.47 %N

$C_6H_7N_3S_3$ Requires: 33.16 %C; 3.25 %H; 19.34 %N

Mass spectrum, showed no M^+ peak at m/e 217, only the spectra of starting thiadiazole and carbon disulphide.

^1H nmr, a spectrum could not be obtained due to the product's low solubility.

(2) 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (0.7760 g, 5.00 mmol) was used. 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-dithiocarboxylate (68) was obtained as a pink powder (1.1181 g, 97%), mp 91-94 °C (with decomposition from 90 °C). The product

was recrystallised from acetonitrile/carbon disulphide (1:1) to give pink spars which melted above 90 °C (with decomposition from 85 °C).

Found: 36.63 %C; 4.12 %H; 18.37 %N

$C_7H_9N_3S_3$ Requires: 36.34 %C; 3.92 %H; 18.16 %N

Mass spectrum, showed no $M^{+\cdot}$ peak at m/e 231, only the spectra of starting thiadiazole and carbon disulphide.

^1H nmr, a spectrum could not be obtained due to the product's low solubility.

(3) 5,6-Dihydro- 3-phenyl- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole (1.0865 g, 5.00 mmol) was used. 5,6- Dihydro- 3-phenyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-dithiocarboxylate (69) was obtained as a tangerine powder (1.3292 g, 91 %). The product did not melt but decomposed above 100 °C (as seen by colour disappearing) to give the starting thiadiazole back which melted, as normal, at 114-115 °C.

Found: 48.91 %C; 3.72 %H; 14.52 %N

$C_{12}H_{11}N_3S_3$ Requires: 49.12 %C; 3.78 %H; 14.32 %N

Mass spectrum, showed no $M^{+\cdot}$ peak at m/e 293, only the spectra of starting thiadiazole and carbon disulphide.

^1H nmr, a spectrum of the product could not be obtained due to its low solubility.

(b) Reaction with Carbon diselenide

(1) Reaction of 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2,d] [1,2,4] thiadiazole

Carbon diselenide (0.8512 g, 0.32 ml, 5.01 mmol) was added to a filtered solution of thiadiazole (0.7768 g, 5.00 mmol) in toluene (25 ml). The green precipitate which formed immediately

on mixing was filtered off and washed with toluene (50 ml), and ether (25 ml) before being dried. 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-diselenacarboxylate (71) was obtained as a green powder (1.6046 g, 99%), mp 155-156 °C (with decomposition from 152 °C).

Found: 26.06 %C; 2.77 %H; 12.93 %N

$C_7H_9N_3SSe_2$ Requires: 25.86 %C; 2.79 %H; 12.92 %N

Mass spectrum, showed no M^+ peak at M/e 325, only the spectra of starting thiadiazole and carbon diselenide.

^1H nmr, a spectrum could not be obtained due to the product's low solubility.

(2) Reaction of 5,6-Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole.

Carbon diselenide (0.1702 g, 0.064 ml, 1.00 mmol) was added to a filtered solution of the thiadiazole (0.1418 g, 1.00 mmol) in toluene (5 ml). The green precipitate which formed immediately on mixing was filtered off and washed with toluene (10 ml) followed by ether (15 ml) before being dried. 5,6- Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-diselenacarboxylate (70) was obtained as a green powder (0.3004 g, 96%), mp 150-155 °C (with decomposition, preheated block to 120 °C).

Found: 23.29 %C; 2.26 %H; 13.37 %N

$C_6H_7N_3SSe_2$ Requires: 23.16 %C; 2.27 %H; 13.51 %N

Mass spectrum, showed no M^+ peak at m/e 311, only the spectra of the starting thiadiazole and carbon diselenide.

^1H nmr, a spectrum could not be obtained due to the product's low solubility.

(c) Reaction with Phenyl isocyanate

(1) Reaction of 5,6- Dihydro- 4H-pyrimido [1,2-d] [1,2,4] thiadiazole with Phenyl isocyanate.

Phenyl isocyanate (4.7128 g, 4.30 ml, 39.56 mmol) was added to a filtered solution of the thiadiazole (0.7060 g, 5.00 mmol) in toluene (25 ml). The white precipitate which was formed immediately on mixing was filtered off and washed with toluene (25 ml) followed by ether (25 ml) before being dried. 5,6- Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-(phenylcarbamate) (72) was obtained as a white powder (1.2564 g, 97%), mp 144-145 °C.

Found: 55.44 %C; 4.67 %H; 21.51 %N

$C_{12}H_{12}N_4OS$ Requires: 55.37 %C; 4.65 %H; 21.52 %N

Mass spectrum, no M^{+} peak was observed at m/e 260, only the spectra of the starting thiadiazole and phenyl isocyanate.

^1H nmr, see Table (C)

I.r. Data, strong peak at 1660 cm^{-1} due to $\nu C=O$, strong peak at 1589 cm^{-1} due to $\nu C=C/C=N$. Note, no peak between 2275-2250 cm^{-1} due to $\nu N=C=O$.

(2) Reaction of 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole with Phenyl isocyanate.

Phenyl isocyanate (4.7128 g, 4.30 ml, 39.56 mmol) was added to a filtered solution of the thiadiazole (0.7763 g, 5.00 mmol) in toluene (25 ml). The white precipitate which formed immediately on mixing was filtered off after a few minutes and washed with toluene (50 ml) followed by ether (50 ml) before being dried. 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-(phenylcarbamate) (73) was obtained as a

white powder (1.2945 g, 94%), mp 137-139 °C.

Found: 56.61 %C; 5.21 %H; 20.22 %N

$C_{13}H_{14}N_4OS$ Requires: 56.92 %C; 5.14 %H; 20.42 %N

Mass spectrum, no $M^{+\cdot}$ peak was observed at m/e 274, only the spectra of the starting thiadiazole and phenyl isocyanate.

^1H nmr, see Table (C)

I.r. Data, a strong peak at 1661 cm^{-1} due to νC=O, strong peak at 1590 cm^{-1} due to νC=C/C=N.

(d) Reaction with Phenyl isothiocyanate

(1) Reaction of 5,6- Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole with Phenyl isothiocyanate.

Phenyl isothiocyanate (5.4240 g, 4.8 ml, 40.12 mmol) was added to a filtered solution of the thiadiazole (0.7065 g, 5.00 mmol) in toluene (25 ml). The white precipitate which formed immediately on mixing was filtered off and washed with toluene (25 ml) followed by ether (25 ml) before being dried. 5,6-Dihydro- 4H pyrimido [1,2-d] [1,2,4] thiadiazolium-7-(phenylthiocarbamate) (74) was obtained as a white powder (1.3677 g, 99%), mp 169-171 °C (with decomposition).

Found: 52.45 %C; 4.44 %H; 19.97 %N

$C_{12}H_{12}N_4S_2$ Requires: 52.15 %C; 4.38 %H; 20.27 %N

Mass spectrum, no $M^{+\cdot}$ peak was observed at m/e 276, only the spectra of the starting thiadiazole and phenyl isothiocyanate.

^1H nmr, see Table (C)

I.r. Data, strong peaks between 1550-1580 cm^{-1} due to νC=C/C=N. Strong peak at 1154 cm^{-1} due to νC=S . No peak between 2140-1990 cm^{-1} due to νN=C=S.

(2) Reaction of 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole with Phenyl isothiocyanate.

Phenyl isothiocyanate (5.4240 g, 4.8 ml, 40.12 mmol) was added to a filtered solution of the thiadiazole (0.7763 g, 5.00 mmol) in toluene (25 ml). The thick white precipitate which formed immediately on mixing was filtered off after a few minutes and washed with toluene (35 ml) followed by ether (30 ml) before being dried. 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2,-d] [1,2,4] thiadiazolium- 7-(phenylthiocarbamate) (75) was obtained as a white powder from toluene (1.4230 g, 98%), mp 153-155 °C (with decomposition from 148 °C) or as colourless plates from acetonitrile, mp 153-155 °C. (with decomposition from 148 °C).

Found: 53.93 %C; 4.92 %H; 19.11 %N

$C_{13}H_{14}N_4S_2$ Requires: 53.77 %C; 4.86 %H; 19.29 %N

Mass spectrum, no M^+ peak was observed at m/e 290, only the spectra of the starting thiadiazole and phenyl isothiocyanate.

^1H nmr, see Table (C)

I.r. Data, strong peaks between 1500-1600 cm^{-1} due to $\nu C=C/C=N$. Strong peak at 1152 cm^{-1} due to $\nu C=S$.

X-ray crystal analysis, see page (94)

(e) Reaction with Methyl Isothiocyanate

(1) Reaction of 5,6- Dihydro- 4H-pyrimido [1,2,-d] [1,2,4] thiadiazole with Methyl isothiocyanate.

Methyl isothiocyanate (3.6881 g, 3.45 ml, 50.44 mmol) was added to a filtered solution of the thiadiazole (0.7060 g, 5.00 mmol) in toluene (25 ml). The white precipitate which formed immediately on mixing was filtered off and washed with toluene (25 ml) followed by ether (25 ml) before being dried. 5,6-

Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium-7-(methylthiocarbamate) (76) was obtained as a colourless powder (1.0288 g, 96%), mp 122-125 °C (with decomposition from 115 °C).

Found: 39.10 %C; 4.63 %H; 25.76 %N

$C_7H_{10}N_4S_2$ Requires: 39.23 %C; 4.70 %H; 26.14 %N

Mass spectrum, no $M^{+\cdot}$ peak was observed at m/e 214 only the spectra of the starting thiadiazole and methyl isothiocyanate.

^1H nmr, see Table (C)

I.r. Data, strong peaks between 1564-1590 cm^{-1} due to $\upsilon C=C/C=N$. Strong peak at 1146 cm^{-1} due to $\upsilon C=S$.

(2) Reaction of 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2,-d] [1,2,4] thiadiazole with methyl isothiocyanate.

Methyl isothiocyanate (3.7415 g, 3.50 ml, 51.17 mmol) was added to a filtered solution of the thiadiazole (0.7775 g, 5.01 mmol) in toluene (25 ml). A white precipitate was formed almost immediately and the mixture was left to stand for 10 minutes, before being filtered. The precipitate was washed with toluene (25 ml) and ether (30 ml) then dried to give 5,6-dihydro-3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-(methylthiocarbamate) (77) as a white powder (1.1109 g, 97%), the product decomposed above 135 °C to give a white residue.

Found: 42.36 %C; 5.27 %H; 24.18 %N

$C_8H_{12}N_4S_2$ Requires: 42.08 %C; 5.30 %H; 24.54 %N

Mass spectrum, no $M^{+\cdot}$ peak was observed at m/e 228, only the spectra of the starting thiadiazole and methyl isothiocyanate.

^1H nmr, the product was very insoluble in dimethylsulphoxide - D_6 and therefore a satisfactory spectrum

could not be obtained.

I.r. Data, strong peaks at 1597 cm^{-1} and 1565 cm^{-1} due to υ C=N and υ C=C. Strong peak at 1166 cm^{-1} due to υ C=S.

II Thermolysis Reactions of the Heterocumulene Adducts

(a) Thermolysis of 5,6- Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7- dithiocarboxylates in toluene.

(1) Reaction of 5,6- Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-dithiocarboxylate.

The dithiocarboxylate (67) (1.0873 g, 5.00 mmol) was suspended in toluene (25 ml) and the resulting mixture refluxed (oil bath) for one hour, after which time the reaction mixture was seen (t.l.c.) to contain some 5,6- dihydro-4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)-thione and several slower running products as well as some charring on the walls of the reaction flask. The reaction mixture was then refluxed for a further 2.5 hours. The cooled toluene solution was chromatographed on silica (15 cm x 2.2 cm) eluting with toluene. The first 50 ml of toluene eluate was discarded and the following 250 ml of eluates (toluene/ether) (1:1) and 500 ml of ether eluates were homogeneous (t.l.c.) and were combined and evaporated to give a yellow powder (0.1316 g) which was recrystallised from cyclohexane/dichloromethane (3:1). 5,6-Dihydro-4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)- thione (86) was obtained as yellow needles (0.1043 g, 11%). This product was identical (mp, mixed mp, t.l.c., ^{1}H nmr) with an authentic sample synthesised from the reaction of carbon disulphide and 2-(phenacylthio)- 3,4,5,6-tetrahydropyrimidine.[2]

The charred residue in the reaction flask was shown to contain a mixture of products including hexahydropyrimidine-2-thione (53) and compound (60).

(2) Reaction of 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-dithiocarboxylate.

Method (i): A suspension of the dithiocarboxylate (68) (1.1567 g 5.00 mmol) in toluene (25 ml) was refluxed (oil bath) for four hours. The cooled solution was then chromatographed on silica (15 cm x 2.2 cm) eluting with toluene. The first 50 ml of toluene eluate was discarded, the next 250 ml of eluates (toluene/ether) (1:1) and 1 L of ether eluates were homogeneous (t.l.c.) and were combined and evaporated to give a pale-yellow powder (0.0776 g) which was recrystallised from cyclohexane/dichloromethane (3:1) to give 5,6-dihydro-4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)- thione (86) as yellow needles (0.0622 g, 6.5 %), mp 154-155 °C, mixed mp 154-155 °C. [^{1}H nmr and t.l.c. behaviour was also identical to an authentic sample of (86)].

The next 1.5 L of eluates (methanol) were evaporated and recrystallised from cyclohexane/ether to give 5,6- dihydro-3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (17) as white needles (0.5634 g, 72.6 %). This product was identical (t.l.c., mp, mixed mp, ^{1}H nmr) with an authentic sample.

Method (ii): A suspension of the dithiocarboxylate (68) (1.1580 g, 5.005 mmol) in toluene (25 ml) was refluxed (oil bath) for three hours, however on cooling carbon disulphide was found to be still present, therefore the mixture was reheated and the toluene solvent was distilled off and fresh toluene (25 ml) added. This process was repeated three times over two hours. After this time the reaction mixture was cooled and then, as there was no precipitate of the starting dithiocarboxylate,

evaporated to dryness at the water pump and then at the oil pump to give a straw coloured solid (0.7760 g) which was recrystallised from cyclohexane/ether to give 5,6- dihydro-3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (17) as white needles (0.6767 g, 87%). This product was identical (mp, mixed mp, t.l.c.) with an authentic sample.

(3) Reaction of 5,6- Dihydro- 3-phenyl- 4H-pyrimido [1,2,-d] [1,2,4] thiadiazolium- 7-dithiocarboxylate.

A suspension of the dithiocarboxylate (69) (1.4685 g, 5.005 mmol) in toluene (25 ml) was refluxed (oil bath) for two hours. The cooled mixture was then chromatographed on silica (15 cm x 2.2 cm) eluting with toluene. The first 200 ml of toluene eluate brought through the benzonitrile side-product and was discarded. The next 200 ml of eluates (ether) were homogeneous (t.l.c.) and brought through the thione (86). The thione fractions were combined and evaporated to give an orange solid which was recrystallised from cyclohexane/dichloromethane (3:1) to give 5,6- dihydro-4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)-thione (86) as orange needles (0.0753 g, 7.9%), mp 154-155 °C, mixed mp 153-155 °C. The following 500 ml of ether eluates were heterogeneous (t.l.c) and were discarded. The next 250 ml of eluates (methanol/ether) (1:19), 1 L of methanol/ether (1:1) and 750 ml of methanol were homogeneous (t.l.c.) and were combined and evaporated to give an off-white solid which was recrystallised from cyclohexane/ether, in the manner described previously. 5,6-Dihydro- 3-phenyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (23) was obtained as white needles (0.7498 g, 69 %), mp 114-115 °C, mixed mp 114-115 °C.

(b) Reaction of 5,6- Dihydro- 3-methyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-diselenacarboxylate in refluxing toluene.

A suspension of the diselenacarboxylate (70) (1.6272 g, 5.00 mmol) in toluene (50 ml) was refluxed (oil bath) for 30 minutes. The reaction mixture was hot filtered to remove any selenium precipitate and then left to cool overnight. The orange needles which had formed were filtered off and washed with a little toluene (10 ml) and dried to give a homogeneous (t.l.c.) orange solid (0.7220 g). The mother liquors from the reaction mixture were then chromatographed on silica (37 cm x 1.4 cm) eluting with toluene. The first 500 ml of toluene eluate brought through carbon diselenide, the next 200 ml of eluates (ether/toluene) (1:19) were homogeneous (t.l.c.) and were evaporated to give an orange solid residue which was recrystallised from cyclohexane (50 ml) to give orange needles (0.3094 g). 5,6- Dihydro-4H-pyrimido [2,1-c] [2,1,4] thiaselenazole- 3(3H)-selenone (87) was obtained as orange crystals (1.0314 g, 72.5%), mp 144-146 °C (with decomposition).

Found: 21.25 %C; 2.08 %H; 9.69 %N

$C_5H_6N_2SSe_2$ Requires: 21.14 %C; 2.13 %H; 9.86 %N

Accurate mass Found: 285.856583

$C_5H_6N_2SSe_2$ Requires: .858219

Mass spectrum, see Table (G)

^1H nmr, see Table (E)

^{13}C nmr, a spectrum was unobtainable due to the product's low solubility and instability.

I.r. Data, strong peaks at 1610 cm^{-1} ($\upsilon C=N$), 1373 cm^{-1},

1165 cm^{-1}. Medium peaks at 1034 cm^{-1} and 900 cm^{-1}.

(c) Reactions of 5,6- Dihydro- 4H- pyrimido [1,2-d] [1,2,4] thiadiazolium- 7-(methylthiocarbamate).

(1) In Toluene

A suspension of the thiadiazolium thiocarbamate (77) (1.1421 g, 5.00 mmol) in toluene (25 ml) was heated to the boil (at which temperature the reaction mixture was clear and colourless) and then left to cool spontaneously. The white crystalline product was filtered off and washed with toluene (25 ml) and ether (10 ml) before being dried. 2,3,4,5- Tetrahydro- 1,6- dimethyl- 3,4-propano- 6a λ^4-thia- 1,3,4,6- tetra- azapentalene- 2,5-dithione (88) was obtained as white needles (0.6472 g, 49.7%). This product was identical (mp, mixed mp, t.l.c., ^1H nmr) with an authentic sample obtained from the reaction of methyl isothiocyanate with 5,6- dihydro-4H-pyrimido- [2,1-c] [1,2,4] dithiazole- 3(3H)-thione[2].

The toluene mother liquors were evaporated to dryness and the white solid residue sublimed (120-130 °C at 0.4 mm of Hg) to give the pyrimidothiadiazole (17) as a white powder (0.2938 g, 37.8%). This product was identical (mp, mixed mp, t.l.c.) with an authentic sample.

(2) In Acetonitrile.

A suspension of the thiadiazolium thiocarbamate (77) (1.1410 g, 5.00 mmol) in acetonitrile (25 ml) was boiled for approximately three minutes until the reaction mixture was clear and colourless and then allowed to cool spontaneously. The white crystalline product was filtered off and washed with acetonitrile (20 ml) before being dried. T.l.c. of this white solid showed

two spots therefore it was recrystallised from acetonitrile (40 ml) to give 2,3,4,5- tetrahydro- 1,6-dimethyl- 3,4-propano-6aλ^4-thia- 1,3,4,6- tetra- azapentalene- 2,5- dithione (88) as white needles (0.5423 g), showing a single spot on t.l.c., mp 204-205 °C, mixed mp 203-205 °C.

The combined acetonitrile mother liquors were chromatographed on silica (15 cm x 2.2 cm) eluting with methanol/ether (1:19). The first 200 ml of eluate was evaporated to give 0.0477g of the thiapentalene (88) which was combined with the product from recrystallisation giving a total of 0.5900 g (45%). The next 250 ml of eluate was discarded and the following 350 ml of methanol/ether and 1 L of methanol eluates were combined and evaporated to give the pyrimidothiadiazole (17) as a white powder (0.2502 g, 32%). This product was identical (mp, mixed mp, t.l.c.) with an authentic sample.

(2) The Thermolysis of 5,6-Dihydro- 4H-pyrimido [1,2,-d] [1,2,4] thiadiazolium- 7-(methylthiocarbamate) in Acetonitrile.

The thiadiazolium thiocarbamate (76) was dissolved in acetonitrile (25 ml) by boiling the mixture for 2-3 minutes. The solution was then left to cool spontaneously to room temperature before being filtered to remove the white needles which had formed. The process was repeated twice to give 2,3,4,5- tetrahydro- 1,6-dimethyl- 3,4-propano-6aλ^4-thia- 1,3,4,6- tetra-azapentalene- 2,5-dithione (88) as white needles (0.3647 g, 28%). This product was identical (mp, mixed mp, t.l.c.) with an authentic sample. The acetonitrile mother liquors were evaporated to dryness to give a pale brown solid (0.4206 g) which showed various products on t.l.c.: some hexahydropyrimidine-

2-thione (53) (R_f 0.6), a spot at R_f 0.4 possibly compound (17), pyrimidothiadiazole compound (22) (R_f 0.3), and compound (60) (R_f 0.1), and material at the origin.

III Synthesis and Reactions of 5,6- Dihydro- 4H- pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)thione.

(a) Synthesis of 2-(Phenacylthio)- 3,4,5,6- tetrahydropyrimidine.

The (phenacylthio)- tetrahydropyrimidine was prepared by the following modification of Shadbolt's method[4].

A solution of α-bromoacetophenone (20.16 g, 101.28 mmol) in acetone (100 ml) was added to a stirred solution of hexahydropyrimidine- 2-thione (11.62 g, 100.01 mmol) in dimethylformamide (270 ml). The resulting mixture was left to stand at room temperature for 1.5 hours before being filtered and the precipitate washed with acetone (50 ml) and dried. Ether (100 ml) was added to the dimethylformamide filtrate and the mixture filtered again and dried. 2-Phenacylthio- 3,4,5,6- tetrahydropyrimidine hydrobromide was obtained as a white powder (29.63 g, 94%), mp 261-263 ^{o}C (Lit. 263-4 ^{o}C).

The hydrobromide (29.63 g) was deprotonated in two approximately equal lots. The hydrobromide was dissolved in water 750 ml and excess concentrated aqueous ammonia added, the resulting mixture was left to stand for 0.5 hours before being filtered and the precipitate dried. 2-Phenacylthio- 3,4,5,6- tetrahydropyrimidine (90) was obtained as a white power (15.74 g, 67%) mp 138-40 ^{o}C.

(b) Synthesis of 5,6-Dihydro-4H-pyrimido- [2,1-c] [1,2,4] dithiazole- 3(3H)-thione.

The dithiazole-3-thione was prepared by the following modification of Beer's method [2].

Carbon disulphide (253.2 g, 200 ml, 3.32 M) was added to a solution of 2-phenacylthio- 3,4,5,6- tetrahydropyrimidine (90) (9.36 g, 40 mmol) in tetrahydrofuran (150 ml) and the resulting mixture refluxed for two hours before being evaporated to dryness and the orange solid residue recrystallised from cyclohexane/chloroform (2:1) (approx. 500 ml). 5,6-Dihydro-4H-pyrimido- [2,1-c] [1,2,4] dithiazole- 3(3H)-thione (86) was obtained as yellow/orange needles (4.3086 g,57%), mp 155-156 °C, Lit. 154-156°C).

(c) Reaction of 5,6-Dihydro-4H-pyrimido [2,1-c] [1,2,4] dithiazole- 3(3H)- thione with Nitriles.

(1) With Benzonitrile

Benzonitrile (5.151 g, 5.1 ml, 49.95 mmol) was added to a solution of the dithiazole (86) (0.9503 g, 5.00 mmol) in toluene (25 ml) and the resulting mixture was refluxed for 15 hours. The cooled mixture was then chromatographed on silica (15 cm x 2.2 cm) eluting with ether. The first 750 ml of ether eluate brought through the unreacted dithiazole and mixed fractions. The next 200 ml of ether eluates followed by 2 L of methanol/ether (1:5) and 500 ml of methanol eluates were homogeneous (t.l.c) and were combined and evaporated to give a red-brown oil which was recrystallised from cyclohexane/ether (approx. 50 ml). 5,6-Dihydro- 3-phenyl- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (23) was obtained as colourless needles (0.7887 g, 73%). This product was identical (mp, mixed mp, t.l.c.) with an authentic sample.

(2) With Pyridine-4-carbonitrile

Filtered solutions of the dithiazole (86) (0.9501 g, 5.00

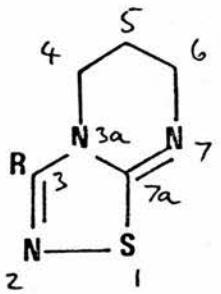
mmol) in toluene (35 ml) and pyridine- 4-carbonitrile (1.5610 g, 15.00 mmol) in toluene (30 ml) were mixed and the resulting solution refluxed (oil bath) for 26.5 hours before being allowed to cool . The cold mixture was filtered to give hexahydropyrimidine- 2-thione (53) as off-white needles (0.0181 g, 3%) which were identical (mp, mixed mp, t.l.c.) with an authentic sample. The filtrate was chromatographed on silica (22 cm x 2.2 cm) eluting with toluene. The first 200 ml of toluene eluate followed by 250 ml of toluene/ether (1:1), 250 ml of ether and 250 ml of methanol/ether (1:19) eluates brought through the excess of pyridine- 4-carbonitrile and the unreacted dithiazole. The next 250 ml of eluates (methanol/ether) (1:9) showed no spot on t.l.c. and were discarded. The final 1.5 L of eluates (methanol) were homogeneous (t.l.c.) and afforded 5,6-dihydro-3-(4-pyridyl)- 4H- pyrimido [1,2-d] [1,2,4] thiadiazole (34) as white granules after recrystallisation from approximately 150 ml of cyclohexane/ether (1:9) (0.7959 g, 73%). This product was identical (mp, mixed mp, t.l.c.) with a sample prepared from the reaction of thiadiazole (17) with pyridine- 4-carbonitrile.

(3) With Acetonitrile.

Acetonitrile (15.72 g, 20.00 ml, 28.29 mmol) was added to a solution of the dithiazole (86) (0.1900 g, 1.00 mmol) in sodium dried xylene (10 ml) and the resulting mixture refluxed for 30 hours. T.l.c. of the reaction mixture after this time showed some thiadiazole (17) to be present however there were also considerable amounts of hexahydropyrimidine- 2-thione and unreacted dithiazole (86) visible. The reaction was therefore not processed further.

Tables (A)-(F)

Introduction



List of nmr solvents

(a) = $CDCl_3$, (b) = $(CD_3)_2SO$, (c) = CD_3CN,

(d) = C_6D_5Br, (e) = $C_6D_5NO_2$,

(f) = CF_3CO_2D.

Key to Tables

Table (A)

1 = signal overlaps with solvent peak

2 = overlapping triplet and singlet

3 = temperature 373 K, HMDS standard, $(CD_3)_2SO$ solvent

4 = signal overlaps with water signal

5 = dilute solution in $CDCl_3$, insoluble in $(CD_3)_2SO$

6 = acidic protons exchangeable in D_2O

Table (B)

Solutions are saturated solutions in $CDCl_3$ (approx. 0.4 M)

* = There is no signal seen for the CD_3 - carbon atom in the noise decoupled spectrum, however a multiplet is seen beteen 14 and 16 ppm in the undecoupled spectrum; J is approximately 20 Hz

1 = overlapping triplets

Table (C)

1 = overlaps with water signal

2 = only weakly soluble

3 = overlapping triplets

4 = no N-H signal observed

Table (E)

* = overlapping signals

+ = overlaps with water signal

Table (F)

1 = two peaks under the solvent plus two other peaks, multiplicity unseen as signals overlap.

Table (A)

Chemical shifts in the 80 MHz ^{1}H nmr spectra of the 5,6-dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles.

(δ in ppm, J in Hz)

Compound No	Solv	5-CH_2	4-/6-CH_2	3-(R)	
(22)	(a)	1.903 (qi)	3.542 (t), 3.892 (t)	7.322[1] (H)	
	(b)	1.742	3.362, 3.889	7.797	
	(d)	1.378	3.218, 3.294	6.873[1]	
	(e)	1.876	3.575, 3.953	7.535[1]	
(17)	(a)	1.906 (qi)	3.490 (t), 3.798 (t)	2.187 (CH_3)	
	(b)	1.75	3.32, 3.82	2.18	
	(c)	1.806	3.355, 3.770	2.108	
(30)	(a)	1.973 (qi)	3.490 (t), 3.798 (t)		
	(c)	1.806	3.355, 3.770		
(23)	(a)	1.824 (qi)	3.535 (t), 3.831 (t)	7.508 (m) (Ph)	
	(b)	1.717	3.368, 3.825	7.578	
(35)	(a)	1.90 (qi)	3.575 (t) 3.90 (t)	8.10 (dd) (p-NO_2-C_6H_4)	
	(b)	1.75	3.40, 3.88	8.175	
(33)	(a)	1.88 (qi)	3.53 (t), 3.93 (t)	4.275 (CH_2)	3.40 (CH_3)
	(b)	1.76	3.27[2], 3.87	4.20	3.27[2]
(34)	(a)	1.864 (qi)	3.551 (t), 3.880 (t)	7.475 (dd) (H's ortho to ring)	8.778 (dd) (H's meta to ring)
	(b)	1.735	3.386, 3.877	7.652,	8.766
(36)	(b)[3]	1.662 (qi)	3.313 (t), 3.569 (t)	6.75-7.40 (m) (aromatic H's)	5.5-6.0 (bs) (NH or OH-)
(31)	(a)	1.928 (qi)	3.520 (t), 3.880 (t)	6.452 (d)(CHCN), J_{transH}16.11	6.970 (d) J_{transH}16.11
	(b)	1.772	3.3[4] 3.944	6.623 (d)(CHCN), J_{transH}16.11	7.492 (d) J_{transH}16.11
(32)	(a)[5]	1.931 (qi)	3.532 (t), 3.932 (t)	7.193 (H)	
(38)	(b)	1.754 (qi)	3.337 (t)[4], 3.789 (t)	4.179[6] (CH_2)	

Table (B)

Chemical shifts in the 20 MHz ^{13}C nmr spectra of the 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles (J in Hz)

Carbon signals (δ in ppm)

Compound No	Solv	5-CH_2 (t)	4-,6-CH_2 (t)	3-C	7a-C	R	
(22)	(a)	19.36 J 130.9	42.96, 46.17 J 142.4 J 140.1	147.12 (d) J 205.8	161.26		
(17)	(a)	19.10 J 130.4	43.11, 44.94 J 142.1 J 139.9	154.84	162.46	16.11 (q) (Me) J 130.1	
	(b)	18.63 J 130.7	42.51, 44.41 J 146.2 J 138.6	156.23	160.56	15.67 (q) J 129.9	
(30)	(a)	19.12 J 130.7	43.11 44.96 J 141.4 J 140.0	154.87	162.5	(*)	
(23)	(a)	19.47 J 130.8	45.29, 45.60[1] J 140.5 (approx)	157.36	162.79	128-130 (m) (Ph)	
(35)	(a)	19.34 J 131.2	45.20, 45.76[1]	155.14	162.03	135.12 (C-3[1]), 149.10 (C-NO_2) 124.03 (d), 129.50 (d) J 175.4 J 167.5	
(33)	(a)	19.16 J 130.7	43.16, 45.31 J 142.5 J 140.4	154.59	162.40	68.16 (t) (CH_2), 58.47 (q)(Me) J 148.1 J 142.4	
(34)	(a)	19.26 J 131.1	45.17, 45.55[1] J 142 (approx)	154.87	162.02	136.62, 122.23 (d), 150.54 (d) J 166.5 ortho to ring J 177.3 ortho to N	

Table (C)

Chemical shifts in the 80 MHz ^{1}H nmr spectra of (a) the 5,6-dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazolium salts and (b) the 5,6-dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazolium-7-substituted Zwitterions.

Compound No	Solv	5-CH_2 (qi)	4-,6-CH_2 (t)	3-(R)	7-(R)
(a)					
(24)	(a)	2.166	3.645, 4.274	8.618 (H)	10.6 (b, N-H)
(16a)	(a)	2.08	3.575, 4.125	2.45 (Me)	
	(f)	2.41	3.85 , 4.34	2.64	4
(16b)	(a)	2.15	3.63 , 4.20	2.50	
(25)	(a)	2.044	3.563[1], 4.058	7.597 (m) (Ph)	8.43 (b, NH)
(b)					
(72)	(a)	2.184	3.895, 4.219	8.521 (H)	6.7-7.5 (m) (Ph)
(74)	(a)[2]	2.303	4.3 , 4.5[3]	8.624 (H)	7.03-7.43 (m) (Ph)
(76)	(a)	2.227	4.271, 4.341	8.511 (H)	3.059 (Me)
(73)	(a)[2]	2.25	3.886, 4.109	2.397 (Me)	6.9-7.6 (m) (Ph)
(75)	(a)	2.303	4.185, 4.417	2.449 (Me)	7.0-7.5 (m) (Ph)

Table (D)

Mass Spectral Data of the 5,6-Dihydro-4H-pyrimido [1,2-d] [1,2,4] thiadiazoles m/e (height as % of Base peak)

Compound No	$M^{+\cdot}$	$M^{+\cdot}$-RCN	$RCNS^{+}$	$RCN^{+\cdot}$	Other peaks
(22)	141 (41)	114 (28)	59 (100)	-	86 (100)
(17)	155 (29)	114 (5)	73 (56)	41 (23)	86 (58) 28 (100)
(30)	158 (67)	114 (17)	76 (100)	44 (13)	86 (93)
(23)	217 (100)	114 (8)	135 (90)	103 (30)	86 (47) 77 (30)
(35)	262 (50)	114 (7)	180 (29)	148 (18)	86 (16) 44 (100)
(33)	185 (100)	114 (10)	103 (4)	-	86 (27) 170 (72) 72 (55)
(34)	218 (54)	114 (10)	136 (100)	104 (62)	86 (40) 78 (35)
(36)	233 (100)	114 (13)	151 (67)	119 (33)	86 (6) 216 (20)
(31)	192 (100)	114 (9)	110 (81)	78 (30)	86 (79) 72 (28)
(32)	306 (27)	-	-	192 (80)	86 (73) 72 (100) 110 (67) 116 (71)
(38)	180 (50)	114 (6)	98 (37)	66 (18)	86 (100) 152 (20)

Table (E)

^{1}H nmr spectra (δ in ppm, J in Hz)

Compound No	Solv	
(7)	(a)	2.288 (3H, 3-CH_3), 3.002 (3H, 5-NCH_3), 3.310 (3H, 2-CH_3)
	(b)	2.266 (3H, 3-CH_3), 2.876 (3H, 5-NCH_3), 3.243 (3H, 2-CH_3)
(4)	(a)	2.29 (3H, 3-CH_3), 3.325 (4-CH_3),
	(b)	2.23 (3H, 3-CH_3), 3.20 (4-CH_3)
(9)	(a)	2.425 (3H, 3-CH_3), 3.15 (6H, N-CH_3)
(18)	(a)	2.275 (qi, 2H, 6^1-CH_2), 2.55 (3H, 3-CH_3), 4.24 (t, 2H$_3$ 4^1-CH_2), 4.525 (t, 2H, 6^1-CH_2)
(26)	(a)	1.875 (qi, 2H, -CHz-), 2.40 (3H, 3-CH_3), 3.475 (t, 2H, N-CH_2-), 3.80 (t, 2H, O-CH_2-)*, 4.05 (b, 1H, O-H)*, 7.10 (b, 1H, N-H)
	(b)	1.725 (qi, 2H, -CH_2-), 2.27 (3H, 3-CH_3), 3.175 (t, 2H, N-CH_2-)*, 3.525 (t, 2H, O-CH_2)*, 4.55 (t, 1H, OH), 8.375 (t, 1H, N-H)
(43)	(a)	1.857 (qi, 2H, 5-CH_2), 3.066, 3.496 (t, 2H, 4- and 6-CH_2-), 4.028 (d, 1H, 3-H, $J_{2,3}$ 6.104 H), (d, 1H, 2-H), 7.422 (m, 5H, 3-Ph)
	(b)	1.806 (qi, 2H, 5-CH_2), 2.85-3.40 (m, 4H, 4- and 6-CH_2), 4.655 (d, 1H, 3-H, $J_{2,3}$ 3.906 Hz), 5.128 (d, 1H, 2-H), 7.425 (m, 5H, 3-Ph)
	(c)	1.790 (qi, 2H, 5-CH_2), 3.032 (m, 2H, 4-CH_2), 3.386 (t, 2H, 6-CH_2), 4.639 (d, 1H, 3-H, $J_{2,3}$ 4.761 Hz), 4.883 (d, 1H, 2-H), 7.431 (m, 5H, 3-Ph)
(44)	(a)	1.973 (qi, 2H, 5-CH_2), 3.633 and 3.786* (t, 4H, 4- and 6-CH_2) 7.267 (1H, 8-H), 7.453 (m, 5H, Ph).
	(b)	1.861 (qi, 2H, 5-CH_2), 3.493 and 3.700 (t, 4H, 4- and 6-CH_2), 7.486 (m, 5H, Ph), 7.752 (1H, H), 9.0 (b, 1H, exchangeable in D_2O, N-H)
(60a)	(b)	1.67-2.00 (m (2 x qi), 4H, 2 x CH_2), 2.48-3.77 (m (4 x t)$^+$, 8H, 4 x CH_2), 8.981 (b, 1H, exchangeable in D_2O, N-H)
(87)	(a)	1.922 (qi 2H, 5-CH_2), 3.499 (t, 2H, 6-CH_2), 4.143 (t, 2H, 4-CH_2)
	(b)	1.821 (qi, 2H, 5-CH_2), 3.362 (t, 2H, 6-CH_2), 4.057 (t, 2H, 4-CH_2)

Table (F)

^{13}C nmr spectra (δ in ppm, J in Hz)

Compound No	Solv	
(18)	(a)	18.94 (q, Me), J 128.7; 21.09 (t, 5^1-C), J 131.2; 46.17 (t, 4^1-C) J 146.2; 67.61 (t, 6^1-C), J 152.; 151.16 (3-C), 167.69 (5-C), 177.76 (2^1-C)
(26)	(a)	18.91 (q, Me), J 128.7; 31.51 (t, C-CH_2), J 126.4; 44.03 (t, N-CH_2), J 135.8; 59.78 (t, O-CH_2) J 141.3; 170.05 (3-C), 184.45 (5-C)
(60b)	(b)	18.29 (t), 20.00 (t), 44.75 and 47.43[1], 150.76, 158.51, 176.62.

Table (G)

Mass Spectra - m/e (% height)

(7) 143 (42) $M^{+\cdot}$, 128 (6) $M^{+\cdot}-CH_3$, 114 (4) $M^{+\cdot}-NCH_3$, 102 (11) $M^{+\cdot}-CH_3CN$, 101 (7), 74 (18), 73 (58) $CH_3CNS^{+\cdot}$, 61 (100) $CH_3NS^{+\cdot}$, 56 (97) $CH_3CNCH_3^{+}$

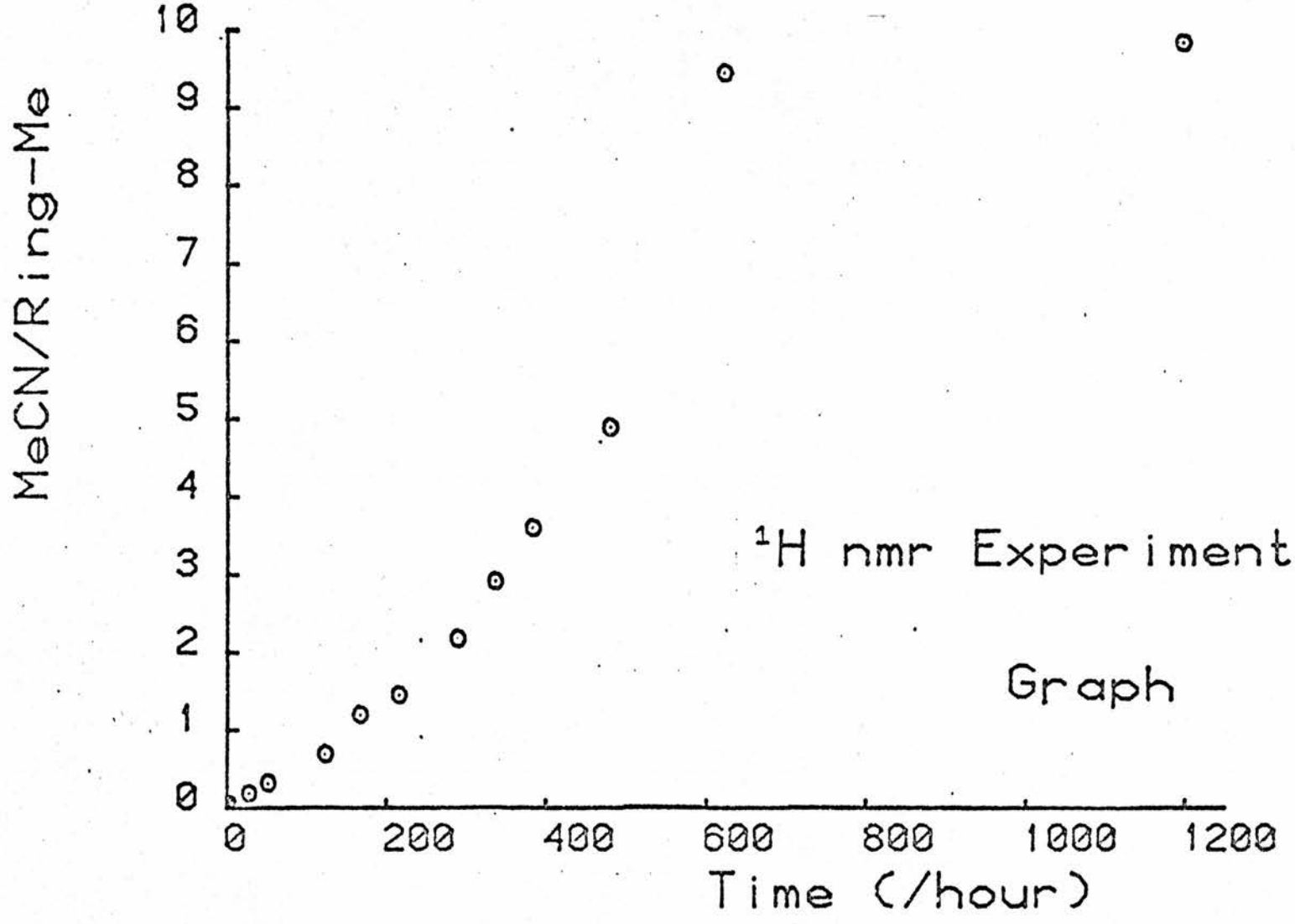
(9) 143 (54) $M^{+\cdot}$, 128 (6) $M^{+\cdot}-CH_3$, 114 (46) $M^{+\cdot}-NCH_3$ or $-(CH_3\ CH_2)$, 102 (100) $M^{+\cdot}-CH_3CN$ 87 (63) $M^{+\cdot}-(Me_2NC)$, 73 (81) $CH_3CNS^{+\cdot}$, 46 (44) SN^{+}, 42 (50)

(18) 199 (76) $M^{+\cdot}$, 128 (20) $C_4H_6N_3S^{+}$, 114 (74) $C_3H_4N_3S^{+}$, 86 (23) $(CH_2)_3\ CO_2^{+\cdot}$, 73 (100) $MeCNS^{+\cdot}$, 44 (65) $CO_2^{+\cdot}$, 41 (41) $MeCN^{+\cdot}$

(26) 173 (12) $M^{+\cdot}$, 142 (98) $M^{+\cdot}-CH_2OH$, 132 (22) $M^{+\cdot}-MeCN$, 129 (40) $M^{+\cdot}-CH_2CH_2O$ 128 (37) $M^{+\cdot}-CH_2CH_2OH$, 115 (12) $M^{+\cdot}-(CH_2)_2CH_2O$, 87 (28) $M^{+\cdot}-NH(CH_2)_3OH$, 74 (65) $NH(CH_2)_3OH^{+}$, 73 (100) $MeCNS^{+\cdot}$, 55 (25) $C_2H_3N_2^{+}$, 41 (23) $MeCN^{+\cdot}$

(6-b) 255 (70), 200 (28), 170 (37), 169 (34), 141 (74), 116 (100), 114 (28), 99 (22), 97 (34), 73 (56), 71 (44), 62 (72), 59 (53)

(87) 286 (4) and 284 (3) $M^{+\cdot}$, 206 (14) and 204 (10) $M^{+\cdot}-Se$, 172 and 170 (24) $CSe_2^{+\cdot}$, 158 (34), 126 (100) $M^{+\cdot}-Se_2$, 124 (41) $CSSe^{+\cdot}$, 99 (5)


MeCN/Ring-Me
10
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2
1
0
0
200
400
600
800
1000
1200
Time (/hour)
^{1}H nmr Experiment
Graph

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