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

and Related Compounds

being a Thesis presented by

Jane Blacas Rhodes, B.Sc.

to the

University of St Andrews

in application for

the Degree of Doctor of Philosophy

To my parents

Declaration

I declare that this thesis is based on 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.

Jane B. Rhodes

September 1985

Certificate

I hereby certify that Jane Blacas Rhodes, B.Sc. has spent ten terms at research work under my 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 1978, and subsequently graduated with First Class Honours in Chemistry in July 1982.

In October 1982 I was awarded a Research Studentship by the Science and Engineering Research Council, and from then until June 1985, 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 should like to express my gratitude to Professor D. H. Reid for his advice, guidance and continued interest in my work.

I should also like to thank Professor Lord Tedder and Professor Wyatt for making available the laboratory facilities in the Department of Chemistry, University of St Andrews. In addition, I should like to thank Dr R. K. Mackie for his interest in my work. Thanks are also due to the technical staff for their invaluable assistance.

Furthermore, I am indebted to Mrs P. Cooper, Miss E. M. Cullen, Mr P. Pogorzelec and Mr R. Speirs for their help in preparing the typescript of this thesis.

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

Explanatory Note

This thesis is divided into three sections Parts A, B and C. These parts are further divided into a number of principal sections prefixed by a Roman numeral.

Part A consists of a review of the relevant background literature, Part B consists of a discussion of the experimental results obtained, and Part C is complementary to Part B and comprises the experimental details of the results discussed in Part B.

Reference made to the chemical literature is indicated by a number in superscript, a key to which can be found in the bibliography in appendix III.

The structural formulae which have been reproduced for illustrative purposes have been assigned Arabic numerals corresponding to those which have been given to the relevant compounds in the text.

CONTENTS

PART A: INTRODUCTION

PAGE

PART B: DISCUSSION

PAGE

PART C: EXPERIMENTAL

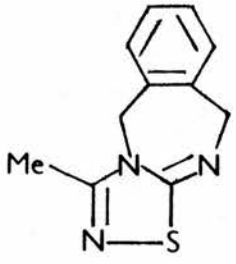
SUMMARY

The main aim of this project was to study new types of 1,6,6aλ^4-triheterapentalenes.

5-Amino-3-methyl-1,2,4-thiadiazole reacted with α,α'-dibromo-o-xylene to give compound (1).

Compound (2) was prepared from 5-amino-3-methyl-1,2,4-thiadiazole and 1,3-dibromopropane.

5-Amino-2-methyl-1,2,4-thiadiazole reacted with 1,3-dibromopropane to give compound (3).



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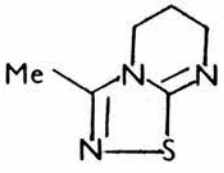

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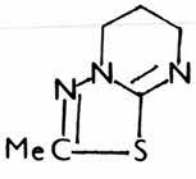
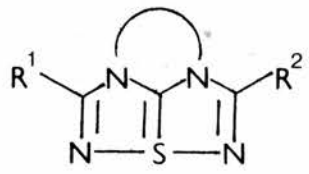


(3)

The reaction of (1) with nitriles was studied as a possible route to compounds of type (4). However, the products attained were in fact of type (5).



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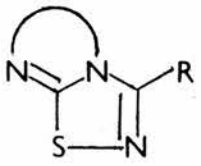
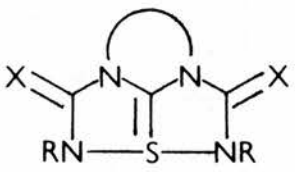


(5)

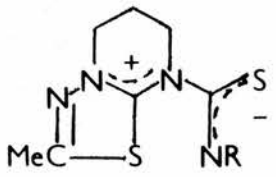
The reactions of (1) and (2) with heterocumulenes were investigated as possible routes to aza analogues of 1,6,6aλ^4-triheterapentalenes (6). The products (6) were obtained for reaction with a variety of iso(thio)cyanates, [X = O,S].



(6)

Two possible mechanisms for the reaction of (1) and (2) with nitriles and heterocumulenes are discussed. Although absolutely conclusive differentiation between these two mechanisms is nc possible from the available data, the results attained sugges a bimolecular mechanism is operating.

Compound (3) was found not to react with nitriles, and to form zwitterions of type (7) on reaction with isothiocyanates rather than the structure (6) formed by (1) and (2).



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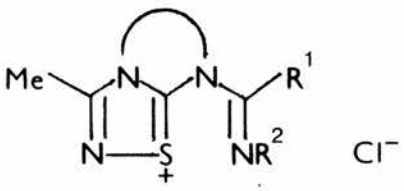
The reactions of (1) and (2) with imidoyl chlorides are discussed. These appear to form 1:1 adducts (8), however, there is evidence to suggest that these salts may have the closed triheterapentalenium structure (9).



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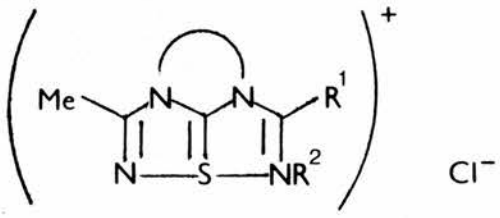

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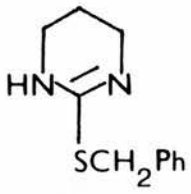
Compounds (10) and (11) were synthesised from benzyl bromide and the corresponding cyclic thioureas, (12) and (13) respectively.



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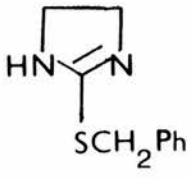

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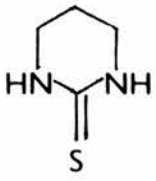

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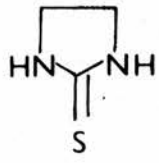
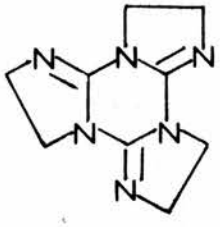


(13)

The thermolysis reactions of (10) and (11) in both isopropyl benzene and 1,2,3,4-tetrahydronaphthalene were investigated. Compound (10) gave the cyclic thiourea (12) in both cases. Compound (11) gave a product in isopropyl benzene tentatively formulated as (14), while in 1,2,3,4-tetrahydronaphthalene it resulted in a mixture of products (13) and (14).



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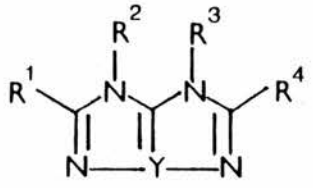
FOREWORD

The main aim of this research project was to synthesise new nitrogen-containing triheterapentalenes, especially compounds based on the structure (1).



(1)

Existing triheterapentalenes possess a 10π-electron system, to which heteroatoms 1 and 6 each contribute a pair of electrons. Consideration of structure (1), however, shows that the lateral nitrogen atoms in the three-centre bond are capable of donating only one electron each to the π-system. Hence, compounds of structure (1) would be novel in that their three-centre bonded sequences would contain pyridine-type nitrogens.

Reviews of the chemistry of triheterapentalenes have been written by Lozac'h[1], Klingsberg[2], Reid[3], Beer[4-6], Leaver[7], Davis[8] and Pedersen[9]. The unusual structure and bonding in these compounds will be discussed more extensively in Part A.

PART A

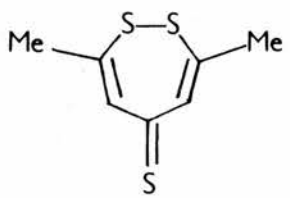
INTRODUCTION

I STRUCTURAL STUDIES OF 1,6,6aλ^4-TRIHETERAPENTALENES

A substantial part of the work described in this thesis is concerned with the chemistry of triheterapentalenes, either as stable compounds or, as transition states or short-lived intermediates. It will therefore be the object of this chapter to review preceding work which has been carried out in this field, and by so doing, to illustrate the type of chemistry involved.

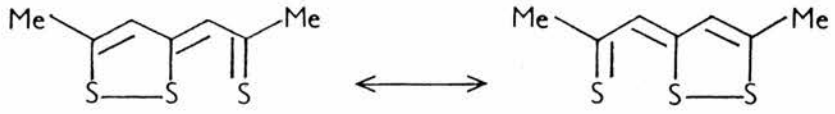
(i) X-Ray Crystallography

In 1925 Arndt, Nachtwey and Pusch[10] isolated a compound from the reaction of 2,4,6-heptanetrione with phosphorus pentasulphide to which they ascribed the structure (1).



(1)

Thirty years later an alternative structure was simultaneously proposed by Guillouzo[11] on the grounds of I.R. spectroscopic studies, and by Bezzi, Mammi and Garbuglio[12] on the basis of X-ray analysis. The new proposal was structure (2).

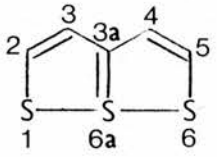


(2)

Valuable supporting evidence for this structure was provided by ^{1}Hnmr[13] spectroscopic studies which showed the expected equivalence of both the methyl and the ring protons. Since then, many compounds of the trithiapentalene type, and their analogues have been synthesised, and their structures in the solid state determined by X-ray crystallography.

An analysis of the parent trithiapentalene system (3) by X-ray crystallography[14] showed that the molecule was planar, possessing C_{2v} symmetry, and that the three sulphur atoms were collinear. The sulphur-sulphur bond distances (2.363Å) are approximately 10% longer than the average distance found for a two-electron, covalent sulphur-sulphur bond[15] (2.10Å), but are considerably shorter than the sum of the Van der Waals radii of the two sulphur atoms (3.70Å)[16]. These observations indicate that there is significant, and indeed equal, bonding interaction between S(6a) and S(6), and between S(6a) and S(1). A comparison of the observed C(2) - S(1) and C(5) - S(6) bond lengths of 1.684Å, and C(3a) - S(6a) of 1.748Å, with those values anticipated for a carbon-sulphur single bond[16] (1.81Å), or a carbon-sulphur double bond[16] (1.61Å) indicates bond orders of greater than unity.

For the remainder of the carbon skeleton, the trithiapentalene system closely resembles that of naphthalene, possessing an analogous 10π-electron system[17].



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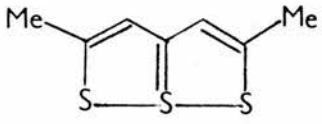

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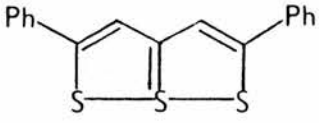

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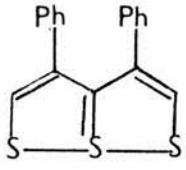

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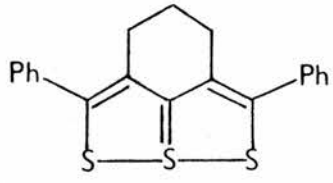

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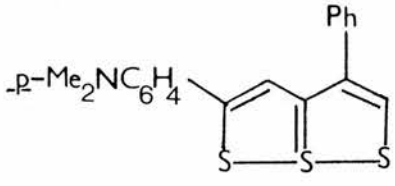

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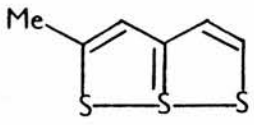

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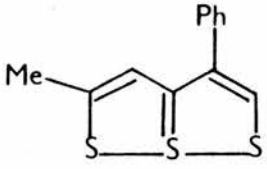

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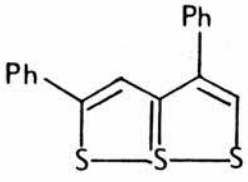

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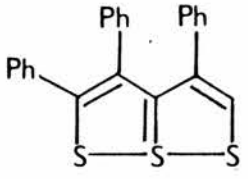

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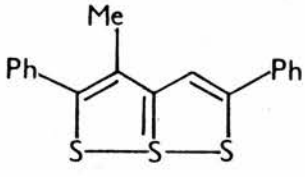

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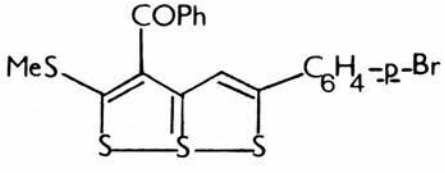

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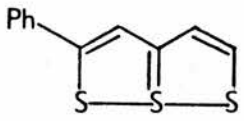

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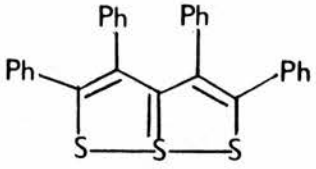

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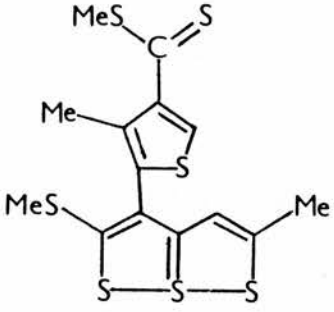

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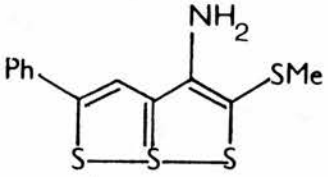

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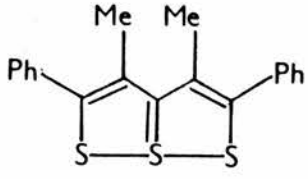

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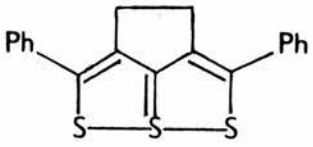


(20)

From a comparison of the trithiapentalene structures (3)-(20)[14,18-34], one notes that the sulphur-sulphur bond lengths lie in the range 2.163Å - 2.561Å, and that equal sulphur-sulphur bond lengths occur in unsymmetrical as well as symmetrical derivatives, [c.f. compounds (3)[14], (4)[18], and (8)[14]]. It should also be noted that not all symmetrically substituted trithiapentalenes have equal sulphur-sulphur bond lengths, [c.f. (6)[19]].

The sum of the sulphur-sulphur bond lengths varies from one derivative to the next, being as small as 4.606Å in compound (19)[20], and as great as 4.743Å in compound (17)[21].

There is no clear indication that the sum of the sulphur-sulphur bond lengths increases when the sulphur-sulphur bonds are of unequal length. Thus, in the unsymmetrical structure (14)[22,23], the sum of the sulphur-sulphur distances is 4.622Å, while in the symmetrical structure (3)[14] it is 4.726Å.

The S(6a) - C(3a) bond length is remarkably constant in different trithiapentalene derivatives. For compounds (3)-(18) the values vary between 1.745Å for (4)[18], and 1.764Å for (16)[24], and none of the values deviate significantly from the value of 1.748Å which was found for the parent compound (3)[14].

The S(1) - C(2) and S(6) - C(5) bond lengths vary more, the former from 1.649Å in (6)[19] to 1.715Å in (18)[25], and the latter from 1.653Å in (6)[19] to 1.727Å in (18)[25]. Thus it seems that the terminal carbon-sulphur bonds are more affected by the substituents than is the central carbon-sulphur bond.

The compounds (19)[20] and (20)[26] are worthy of a separate appraisal as they show deviations from the general trends previously

described.

In the case of compound (19), the central S(6a) - C(3a) bond is 1.779Å which is 0.015Å longer than that of compound (16), and is indeed the longest S(6a) - C(3a) bond which has so far been recorded.

For compound (20), an anomaly of a different kind arises, namely the length of the central S(6a) - C(3a) bond in comparison with the lengths of the lateral S(1) - C(2) and S(6) - C(5) bonds.

In 2,5-diphenyl-3,4-dimethylene-1,6,6aλ^4-trithiapentalene (20), the central carbon-sulphur bond is shorter than the lateral ones. This result is the complete antithesis of what has so far been found in other trithiapentalenes.

In all cases where the trithiapentalene is substituted by phenyl groups, the phenyl substituents are twisted out of the plane of the trithiapentalene system, presumably as a result of weak intermolecular interactions.

Hordvik et al[35] have carried out a CNDO/2 study of the effect of phenyl and methyl substituents on the sulphur-sulphur bonding. The results they obtained were the following:

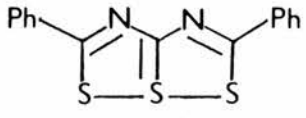
(1) A 2-methyl group causes a lengthening of the S(1) - S(6a) bond, and a 3-methyl group causes a shortening of it.

(2) A 2-phenyl group has a lengthening effect on the S(1) - S(6a) bond which varies with the twist angle of the phenyl group, being negligable at a twist angle of 0°, and most pronounced at 90°.

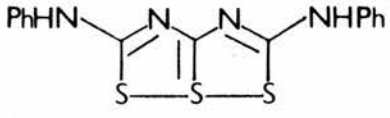
A 3-phenyl group shortens the S(1) - S(6a) bond, but to a small degree only, and in this case the effect is independent of the twist angle of the phenyl group.

Bearing in mind that these results only hold where there is no intramolecular strain which may perturb the bonding, these predictions are thus far in good agreement with the observed effects of methyl and phenyl substituents on the sulphur-sulphur bonding in the trithiapentalene system.

Further experimental evidence of the effect of phenyl substituents on the sulphur-sulphur bonding in trithiapentalenes may be obtained by considering the results attained for the crystal structures of (21)[36] and (22)[37] along with those of compound (5)[30].



(21)



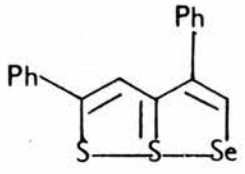
(22)

The sulphur-sulphur bonds are almost equal in length for structure (21), whereas compound (5) is not symmetrical. This is a direct result of less torsion by the phenyl groups in (21), and is in accordance with the CNDO/2 predictions already discussed.

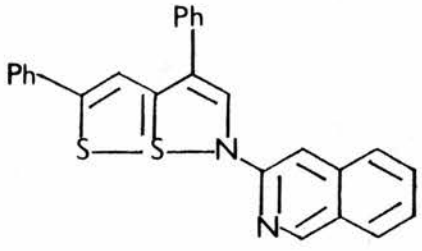
For compound (22), the sulphur-sulphur bond lengths are not equal, but this may be explained in part by intermolecular hydrogen bonding (NH·····N).

Crystal structure determinations of N,S,Se and Te analogues of the trithiapentalenes confirm the planar bicyclic nature of these compounds.

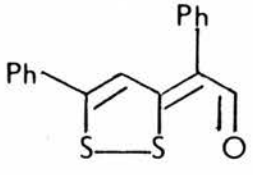
A comparison of (11)[31,34] with structures (23)[38], (24)[39], and (25)[40] serves to illustrate the differences resulting from the replacement of S(6) in (11) by Se, N-R and O respectively.



(23)



(24)



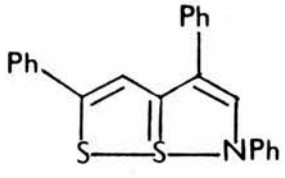
(25)

If one subtracts the difference in covalent radii between selenium and sulphur, 0.12Å, from the S(6a)-Se distance in (23), a value of 2.21Å is obtained which is close to the value found for the S(6a) - S(6) distance in (11) of 2.22Å. Thus, the bonding in the linear three-atom sequence of (11) remains vitually unchanged with the replacement of S(6) by Se.

However, replacement of S(6) by N-R or O, causes a pronounced shortening of the S(1) - S(6a) bond. According to Leung and Nyburg[39], there is a correlation between the difference of electronegativities

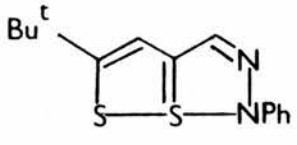
between S and X in the S-S-X system, and the length of the sulphur-sulphur bond; the sulphur-sulphur distance decreases as the difference in electronegativity increases.

It should also be noted that although changing the R-substituent attached to nitrogen appears to have little effect on the geometry of the molecule [c.f. (24) and (26)[41]] substituents elsewhere can have a profound effect on the lengths of the bonds in the S-S-N sequence.

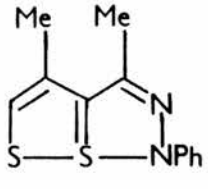


(26)

Comparing structures (27)[42] and (28)[43], the sulphur-sulphur bonds are respectively 2.435Å and 2.493Å, and the sulphur-nitrogen bonds have values of 1.849Å and 1.779Å.



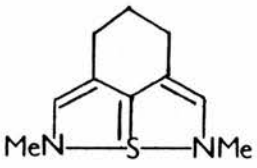
(27)



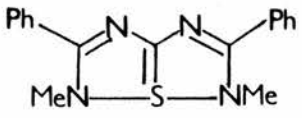
(28)

The sums of the sulphur-sulphur and sulphur-nitrogen bond lengths in (27) (4.272Å) and in (28) (4.284Å) are almost equal, and close to the value of 4.248Å for the sum of the corresponding bond lengths in (24).

Structural studies have also been carried out on (29)[44] and (30)[45].



(29)

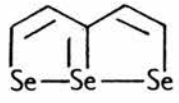


(30)

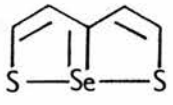
The nitrogen-sulphur bond lengths (1.925Å) in compound (29) are approximately 10% longer than the value expected for a nitrogen-sulphur single bond (1.75Å)[16] as are the nitrogen-sulphur bonds in compound (30).

Compound (29) was not found to be exactly symmetrical and indeed structure (30), reported by Akiba and Iwasaki[45], is the first such example of an N-S-N system with exact C_{2v} symmetry.

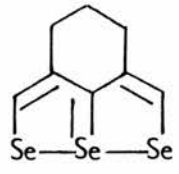
X-ray crystallographic studies of selenium analogues of trithiapentalenes show that they have a marked similarity to the parent trithiapentalene (3).



(31)



(32)

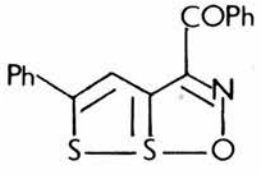


(33)

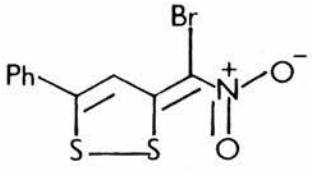
The triselenapentalene (31)[46] is almost C_{2v}-symmetrical. The difference between the selenium-selenium bond length in (31) and the sulphur-sulphur bond length in (3) is 0.22Å, or approximately two times the difference (0.12Å) between the covalent radii of selenium and sulphur[15,16]. Structure (32) exhibits similar trends[47].

Structure (33)[48] was again found to be symmetrical, but a comparison of the selenium-selenium bond lengths with those of (31), showed a significant shortening of the selenium-selenium bonds, and this must be attributed to the presence of the trimethylene bridge. Support for this idea derives from considering the similarly related structures (5) and (7), where structure (7) exhibits an identical shortening of the sulphur-sulphur bonds.

The results of X-ray studies of the oxygen analogues (25)[40], (34)[49] and (35)[50], suggest that the types of bonding in the nitro (35) and carbonyl (25) series are rather similar, while there is definite structural evidence to be found in the sulphur-oxygen distances, and in other dimensions in compound (34), that the sulphur-oxygen bonding is rather stronger in the nitroso compound (34) than in either the nitro or carbonyl compounds. This conclusion is substantiated by the demonstrated preference for co-ordination of sulphur with a nitroso group over either a carbonyl group[49] or a nitro group[49,51].

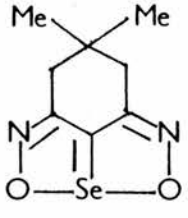


(34)



(35)

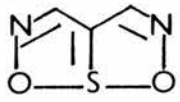
These results suggest that a molecule with two external nitroso groups forming a bicyclic structure should be stable. One such analogue of this type is the structure (36)[52,53].



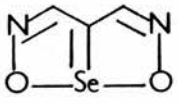
(36)

The results obtained from X-ray crystal analysis clearly favour a bond order of between 0 and 1 for the selenium-oxygen bonds, and are consistent with a structure of the type illustrated.

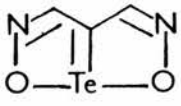
Other similar structures (37), (38) and (39) have also been investigated by X-ray crystallography[54].



(37)



(38)



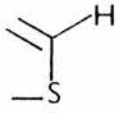
(39)

It is worth mentioning that the lengthening of the O-X(6a) bonds relative to the corresponding sums of the covalent radii are 8.3%, 8.9% and 2.8%, respectively, for the sulphur, selenium and telurium compounds. These increases can be seen to be less than those found for the parent trithiapentalene system.

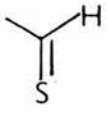
(ii) N.M.R.: Information (or Data)

Lozac'h et al[55] have studied ^{1}Hnmr data of trithiapentalene and related compounds, and have concluded that the aromaticity of trithiapentalene is approximately 65% of that of naphthalene.

Reid and co-workers[56] have also concluded on the basis of ^{1}H chemical shifts that trithiapentalene is an aromatic system. This evidence was adduced by comparing the chemical shift of the 2-H protons in trithiapentalene with that of the thioformyl proton in stable, heterocyclic thioaldehydes[57,58]. The 2-H protons in trithiapentalene were found to resonate at much higher field than does the thioformyl proton, suggesting an environment (40) rather than (41).



(40)



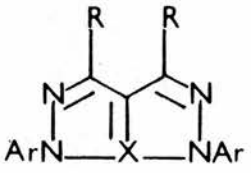
(41)

Symmetrical trithiapentalenes have been found to show magnetic equivalence of the ring protons or identical substituents at the pairs of sites C(2) and C(5), and C(3) and C(4). This illustrates that these compounds, in solution at least, in which intermolecular effects are averaged, possess C_{2v} symmetry[56,59].

However, it should be noted that whereas (6) has been shown to be symmetrical in solution[60] by ^{1}Hnmr spectroscopy, this is in direct

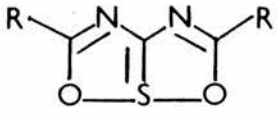
contrast to results obtained from the solid state studies[19].

Many trithiapentalene analogues have also been shown to possess real or time-averaged C_{2v} symmetry in solution [c.f. structures (42) - (47)[61-69]].

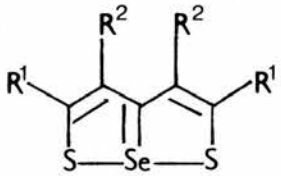


(42)

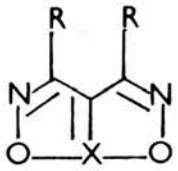
X = S, Se



(43)

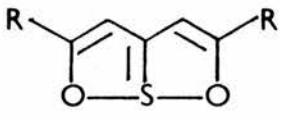


(44)

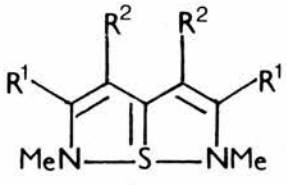


(45)

X = S, Se, Te

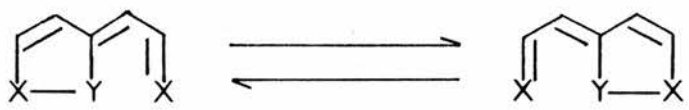


(46)



(47)

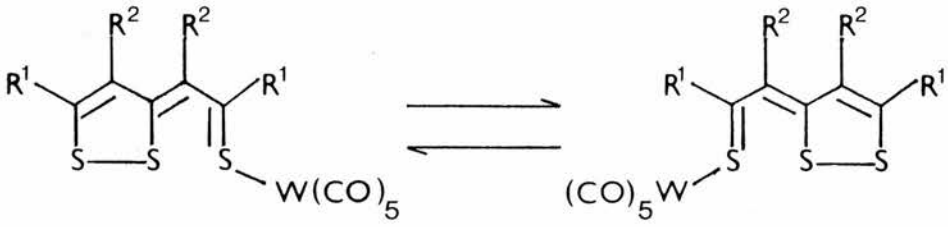
It has been suggested that the observed magnetic equivalence of the ring protons in the trithiapentalenes is simply the result of a rapid interconversion of valence tautomers, viz. (48) and (49)[13].



(48) (49)

However, a number of variable temperature ^{1}Hnmr studies have been carried out at temperatures as low as -90°C, and thus far no departures from C_{2v} symmetry have been observed[68-71].

In contrast to the above, Reid and Pogorzelec[72] recently reported the formation of some pentacarbonyltungsten(0) complexes (50) derived from the corresponding trithiapentalenes.

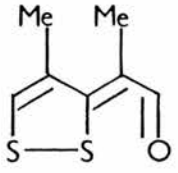


(50)

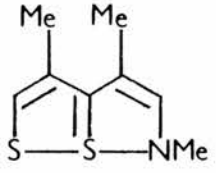
These compounds exhibit fluctional behaviour in solution, and, at temperatures below -10°C, the ring protons (or substituents) show two quite distinct shifts.

The chemical shift values obtained for the ring protons in triheterapentalenes suggest the presence of a ring current due to π-electron delocalisation.

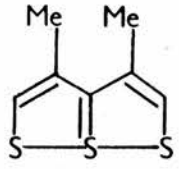
Reid and co-workers[73] carried out an investigation of various 1,6,6aλ^4-trithiapentalenes, 1-oxa-6,6aλ^4-dithiapentalenes and 1,6aλ^4-dithia-6-azapentalenes. The structures (51)[74], (52)[73] and (53)[74] exemplify the general trend observed which was that the progressive increase in deshielding of the ring protons and the substituents along the series (51) → (52) → (53), may be attributed mainly to a corresponding increase in the size of the ring current. It was, therefore, concluded that the extent of the π-electron delocalisation in these systems decreased in the order (53) → (52) → (51).



(51)



(52)



(53)

^{13}Cnmr studies[75,76] have been carried out for various representative trithiapentalenes with varying degrees of substitution by methyl, phenyl and methylthio groups. The results obtained are in good agreement with the theory that symmetrically substituted trithiapentalenes exhibit C_{2v} symmetry in solution.

(iii) Miscellaneous Spectroscopic Techniques

Electron binding energies of the three sulphur atoms in trithiapentalenes should, from first principles, be considered as a good indication of whether or not the trithiapentalene system is symmetrical. In the case of a symmetrical system, two signals in the ratio of 2:1 should be found in the ESCA spectrum, whereas for an unsymmetrical structure three signals in the ratio of 1:1:1 would be expected.

If in fact the system is one of rapidly interconverting valence tautomers, e.g. (48) and (49), it should be possible to detect their presence since the X-ray absorption-photoelectron ejection process occurs in 10^{-14} - 10^{16} s [9].

Clark et al[77,78] have studied various trithiapentalenes in the solid state by means of X-ray photoelectron spectroscopy. The results obtained for the parent compound (3) and the 2,5-dimethyl derivative (4) are consistent with symmetrical structures. By way of contrast, the 3,4-diphenyl derivative (6) was found to be unsymmetrical. These results are in agreement with X-ray crystallographic studies[14,18,19].

It should be noted that a similar investigation carried out by Lindeburg[79] led to the conclusion that structure (4) was not symmetrical. This can be attributed to broad lines in the ESCA spectra which could not be fully resolved. In fact, in a more recent study of (4)[80], this problem was partially overcome, and the results obtained were indicative of a symmetrical structure.

Photoelectron spectra of various analoga of trithiapentalene have also been carried out[81].

Gas phase ESCA spectra have been attained for the 2,5-dimethyl derivative (4)[80], and for 2,5-diaza-1,6-dioxa-6aλ^4-thiapentalene (37), and the selenium (38) and telurium (39) analogues[82]. In all cases the molecules were shown to have C_{2v} symmetry.

Pedersen et al[83] have recorded the microwave spectrum of 1,6-dioxa-6aλ^4-thiapentalene [(46),R^1=H] and its 3,4-dideutero derivative. No evidence for valence tautomerism was found, and all observations were consistent with a planar molecule exhibiting C_{2v} symmetry.

Mass spectrometric studies[84] of 1,6,6aλ^4-trithiapentalene (3) and its derivatives, and also of various selena analogues[85] have been made. The trithiapentalenes behaved as aromatic compounds, giving rise to intense molecular ions. The mass spectra of the analogous selenium containing compounds showed great similarity to those of the trithiapentalenes. The main difference resulted from the more facile loss of selenium compared with sulphur, resulting in the formation of abundant hydrocarbon ions corresponding to the loss of Se_3H.

The redox properties of some 1,6-dioxa-6aλ^4-thia-diazapentalenes [(45), X=S], have been studied by pulse radiolysis and cyclic voltammetry[86]. These heterapentalenes were found to act as photosystem-I electron acceptors at concentrations of the order of 1×10^{-6}M, and to have herbicidal properties similar to those of the bipyridinium herbicides.

II THEORIES OF BONDING

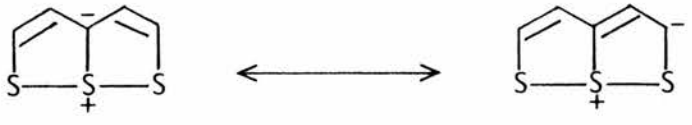
(i) 1,6,6aλ^4-Trithiapentalenes

Classical theory of σ-bonds and π-bonds does not explain all the properties pertaining to trithiapentalenes, and various theoretical explanations have been put forward.

Any theory of bonding in trithiapentalenes must explain their planarity, the approximate collinearity of the three sulphur atoms, and the sulphur-sulphur bond orders of less than unity.

A description of the trithiapentalenes as 'single bond - no bond resonance' compounds has been proposed on numerous occasions[12,87-89]. However, Clark[77] has calculated, by ab initio methods, the total energies for trithiapentalene in both the symmetrical and the unsymmetrical case. On the basis of his results he proposes that the concept of no-bond resonance is incorrect as there is no drastic change in the bonding pattern on distorting a symmetrical system to an unsymmetrical one within the range of sulphur-sulphur distances encountered in trithiapentalenes.

Another interpretation of the bonding invokes a contribution from the 10 π-electron sulphonium ylid structure (54)[90].



(54)

However, this would tend to suggest that electrophilic substitution should take place at position 2, in direct conflict with experimental results[91-93].

Clark and Kilcast[94] have made CNDO/2 calculations on trithiapentalenes concentrating not only on their electronic structure but also on their reactivities. The results obtained suggest that position 3 should be the preferred site of electrophilic attack, which is in accordance with experimental evidence[91-93]. Furthermore, some tendency to react at the lateral sulphur atoms should also be present. This is in agreement with the observation that these sulphur atoms will undergo methylation[70,96]. However, this approach stops short of explaining the rearrangement process which occurs in nitrosation and diazo-coupling reactions of trithiapentalenes. Reid and co-workers[95] have proposed an alternative mechanism which accounts for the various features of the electrophilic substitution of trithiapentalene.

Johnstone and Ward[97] have used a description of the trithiapentalenes which includes the intervention of 3d-orbitals which they consider to be p^2d hybridised, and Maeda[98-100] has also proposed participation of d-orbitals in the sulphur-sulphur σ-bonding.

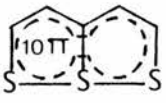
However, more recently, Clark[77], and Palmer and Findley[101], have studied the ground state energies of trithiapentalenes both including and excluding d-orbitals, and have concluded that d-orbital participation does not play an important role.

So far there have been no reports of the isolation of a system with C_{2v} symmetry where the central atom is a first row element. This does not necessarily prove that participation of d-orbitals is

essential, and could, in fact, be a consequence of the inability of the 2p-orbitals of the central atom to overlap sufficiently in order to stabilize the three-centre bond.

The present generally accepted theory was first mooted by Gleiter and Hoffman[102] who treated the trithiapentalene problem as a special case in their analysis of electron-rich three-centre bonds. They consider the three sulphur atoms to be a linear system where three orbitals are occupied by four electrons for σ-bonding and π-bonding is superimposed. The stabilization thus obtained is not expected to be marked since the p_π-p_π overlap is still small when the equilibrium distance for a three-centre bond involving a second-row element is reached. The potential energy of the S(1)-S(6a)-S(6) system as a function of the displacement of S(6a) from an equilibrium position between S(1) and S(6) shows a very flat minimum corresponding to a symmetrical structure when the calculation allows for the inclusion of d-orbitals, and favours an unsymmetrical structure when d-orbitals are excluded. Thus the trithiapentalene system may be formulated according to (55) or (56).

(55)



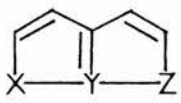
(56)

The concept of electron-rich three-centre bonding is familiar in other areas of chemistry[103], and has been used to describe the bonding in the polyhalide ions e.g. I_3^- [104,105], and also in other hypervalent species e.g. XeF_5^+ [102].

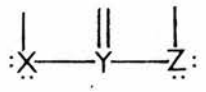
In the linear triiodide ion the bond lengths observed are approximately 9% longer than those found in molecular iodine[104,105], and the bond elongation of around 12% found in trithiapentalenes is not inconsistent with this, being of a similar order of magnitude.

(ii) Variations of the 1,6,6aλ^4-Trithiapentalene System

1,6,6aλ^4-Triheterapentalenes comprise a large number of compounds corresponding to structure (57), in which X and Z are heteroatoms of group V or VI (NR, O, S, Se), and Y is a second or lower row element of group VI (S, Se, Te). The essential structural feature of triheterapentalenes is the heteroatom unit (58) which employs four-electron three-centre bonding.

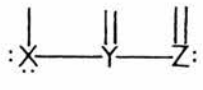


(57)

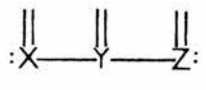


(58)

Variations of the heterapentalene system may be formulated which contain the structural elements (59) or (60).



(59)

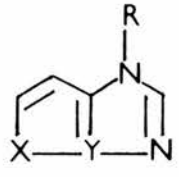


(60)

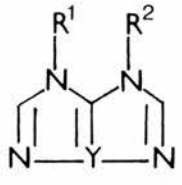
In the former, both Y and Z may be considered to possess a singly occupied p_z-orbital, while X possesses a doubly occupied p_z-orbital. For the latter case, X, Y and Z would all have singly occupied p_z-orbitals.

Authentic examples of compounds containing either of these structural elements have not so far been reported, although several workers have postulated intermediates of these types[106-111].

In order that the triheterapentalene system may retain its delocalised 10π-electron system in structure (59), an atom capable of donating two electrons to the π system is required at position 3. Similarly for structure (60), two such atoms would be required at positions 3 and 4. Possible structures which fulfil this requirement are the aza structures (61) and (62).

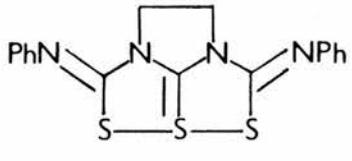


(61)

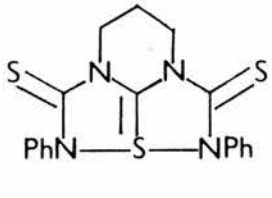


(62)

Another variation of the triheterapentalene structure is provided by structures (63) and (64)[112].

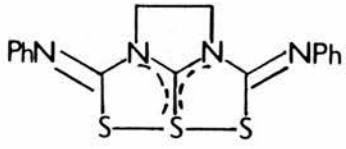


(63)



(64)

An X-ray study[113] carried out on compound (63) suggests that its structure is best represented by (65), with the exocyclic carbon-nitrogen links as pure double bonds, and with relatively little π-overlap between C(2) and N(3), and N(4) and C(5).



(65)

Compounds, (63) and (64), may be regarded as the first, well-defined examples of a new series. p_z-Orbitals are available at all the ring atoms in the bicyclic system. Hence, it is possible for p_π-p_π interaction to take place although this may, of course, be weak.

III SYNTHESIS OF TRIHETERAPENTALENES

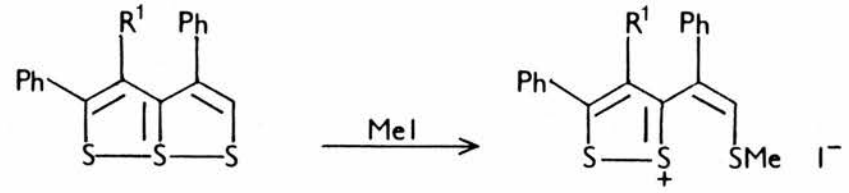
The work embodied in this thesis concerns the formation of nitrogen-containing triheterapentalenes, and hence, a summary of various synthetic routes to such compounds will be provided in this section.

Azapentalenes are frequently prepared from trithiapentalenes. Many general syntheses of trithiapentalenes are documented in the literature[10,56,74,114-118], and hence will not be covered in this section.

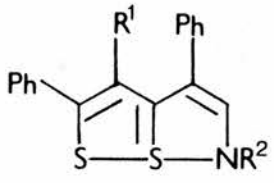
(i) Synthesis of Nitrogen-Containing 1,6,6aλ^4-Triheterapentalenes

(a) Triheterapentalenes Containing One Nitrogen Atom

6-Aza-1,6aλ^4-dithiapentalenes (68) were first prepared by Klingsberg[96]. Trithiapentalenes (66) react with methyl iodide under mild conditions, forming dithiolium salts (67) which, on treatment with primary aromatic amines, give compounds of type (68).



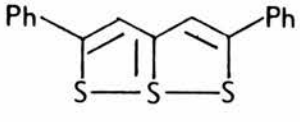
(66) (67)



(68)

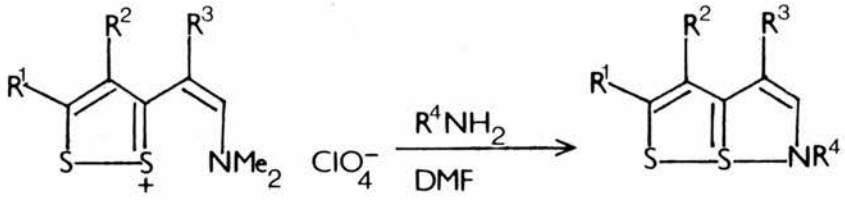
Treatment of the trithiapentalene (66) with sulphur dichloride followed by aniline also yields compounds [(68), R^2=Ph].

S-Alkylation of the symmetrical trithiapentalene (69), rather than the unsymmetrical trithiapentalene (66), proves to be more difficult. This was achieved by using the more powerful alkylating agent triethyloxonium tetrafluoroborate[70]. Thereafter, the synthesis is analogous to that which was described before.



(69)

Another route to 6-aza-1,6aλ^4-dithiapentalenes (71) involves the treatment of the Vilsmeier Salts (70) with primary amines[73,119].



(70) (71)

Direct conversion of 1,6,6aλ^4-trithiapentalenes into the corresponding 6-aza-1,6aλ^4-dithiapentalenes may be achieved by treatment of the trithiapentalene with ethanolic methylamine in acetonitrile[73].

5-Aryl-1,2,4-dithiazole-3-thiones (72) react with phenylacetylene giving aza compounds (73)[120].

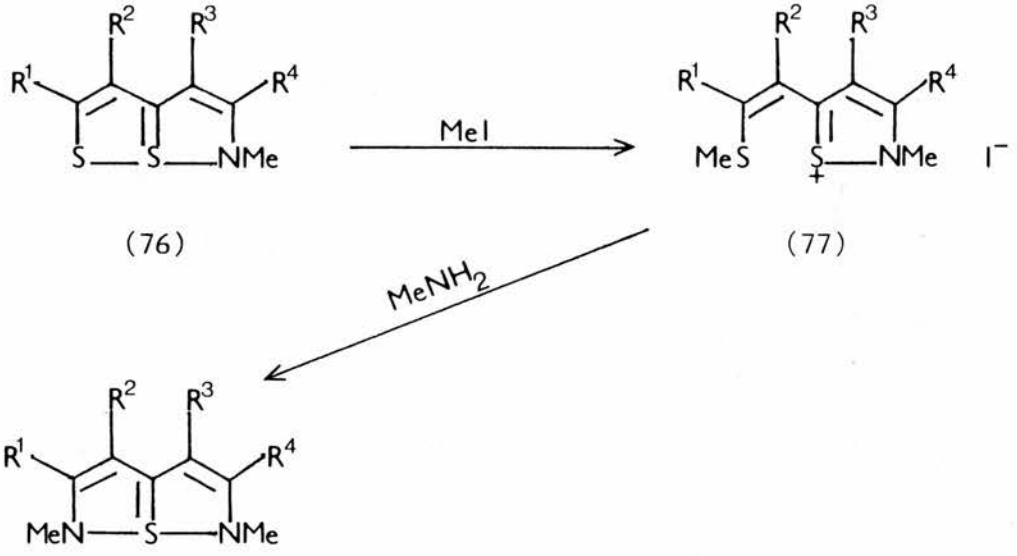
(72) (73)

Alternatively, 3-amino-5-aryl-1,2-dithiolium salts (74) react with isothiocyanate to give related analogues (75)[121].

(74) (75)

(b) Triheterapentalenes Containing Two Nitrogen Atoms

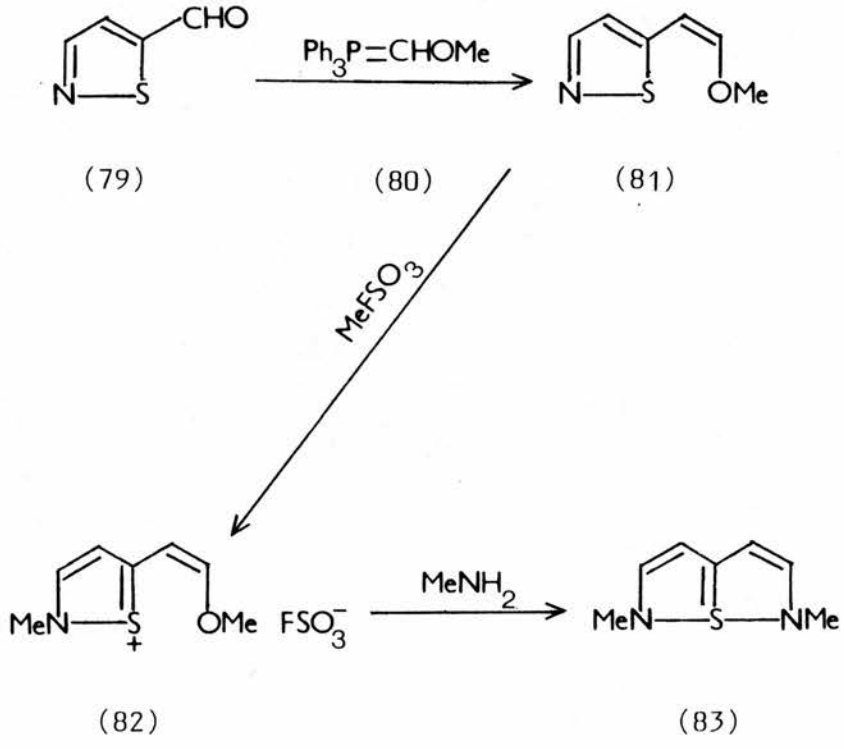
1,6aλ^4-Dithia-6-azapentalenes (76) react rapidly and quantitatively with methyl iodide to give the isothiazolium salts (77). Treatment of these salts with ethanolic methylamine gives the symmetrical 6aλ^4-thia-1,6-diazapentalenes (78)[69].



(76) (77)

(78)

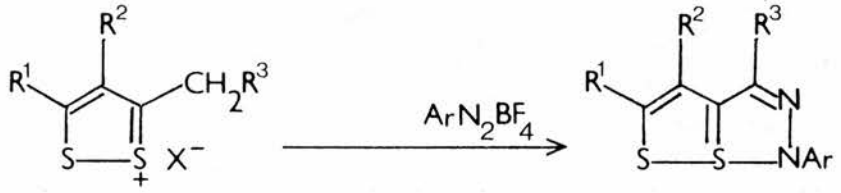
5-Formylisothiazole (79) reacts readily with methoxymethylenetriphenylphosphorane (80) in a Wittig reaction to give compound (81). Methylation of this product with methyl fluorosulphonate results in the crystalline isothiazolium fluorosulphonate (82) which, on treatment with methylamine, gives the thiadiazapentalene (83)[122].



(79) (80) (81)

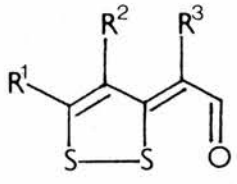
(82) (83)

1,2-Dithiolium salts (84) react smoothly with arenediazonium tetrafluoroborates in aqueous ethanol to give 6,6aλ^4-dithia-1,2-diazapentalenes (85) directly[123].



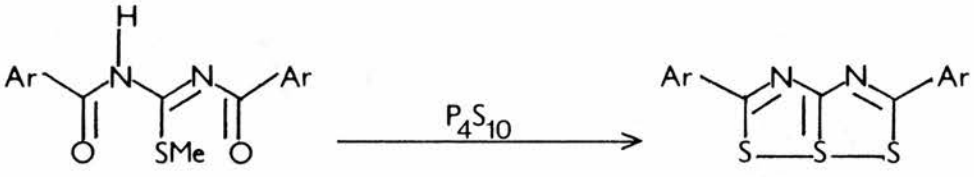
(84) (85)

Compounds of type (85) may also be prepared by treating the dithiolylidene aldehyde (86) with arenediazonium tetrafluoroborate[124].



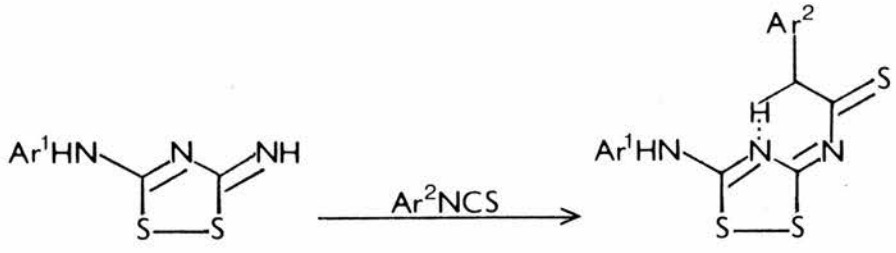
(86)

1,6,6aλ^4-Trithia-3,4-diazapentalenes (88) are obtained in good yields by reacting phosphorus pentasulphide with N,N'-diaroyl-S-methylisothioureas (87)[125].

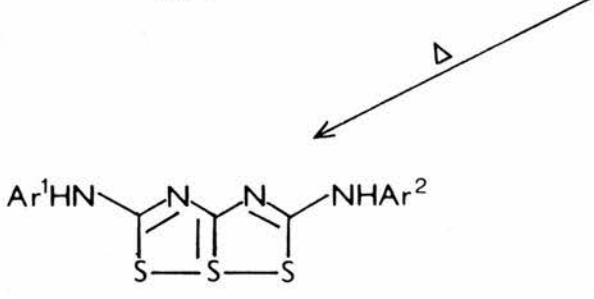


(87) (88)

Arylisothiocyanates react with compound (89) to give trans products (90) which, on heating, are converted into their cis isomers which may be formulated as the 1,6,6aλ^4-trithia-3,4-diazapentalenes (91)[126].



(89) (90)



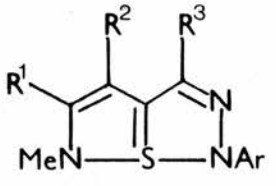
(91)

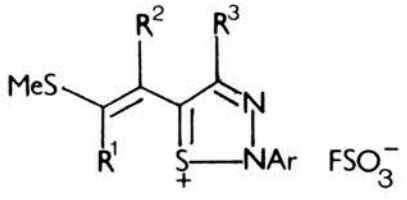
Oliver and Brown[126] have prepared similar compounds (93) by the reaction of the salt (92) with isothiocyanates.

(92) (93)

(c) Triheterapentalenes Containing Three Nitrogen Atoms

6aλ^4-Thia-1,2,6-triazapentalenes (94) may be formed directly from the corresponding 6,6aλ^4-dithia-1,2-diazapentalenes (85) by treatment with ethanolic methylamine[127].

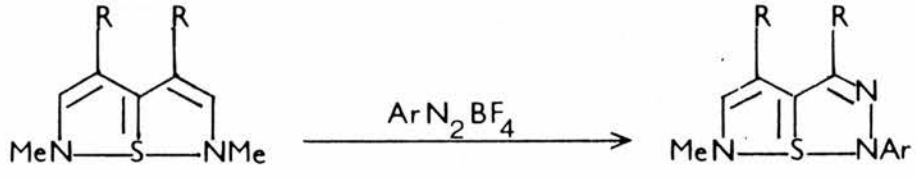




(94) (95)

Alternatively, methylation can be carried out by means of methyl fluorosulphonate. In this case, methylation takes place on sulphur resulting in the 1,2,3-thiadiazolium fluorosulphonates (95) which are subsequently treated with aqueous methylamine to give compounds (94)[127].

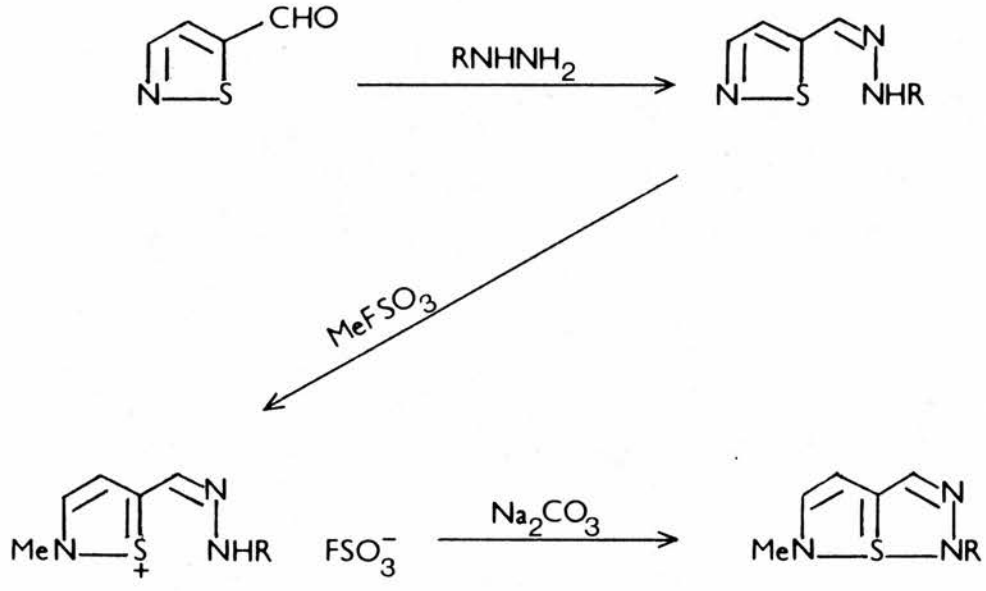
Compounds of type [(94), R^1=H, R^2=R^3] may also be obtained by coupling of 3,4-dialkyl-6aλ^4-thia-1,6-diazapentalenes (96) with arenediazonium tetrafluoroborates[127].



(96) (94)

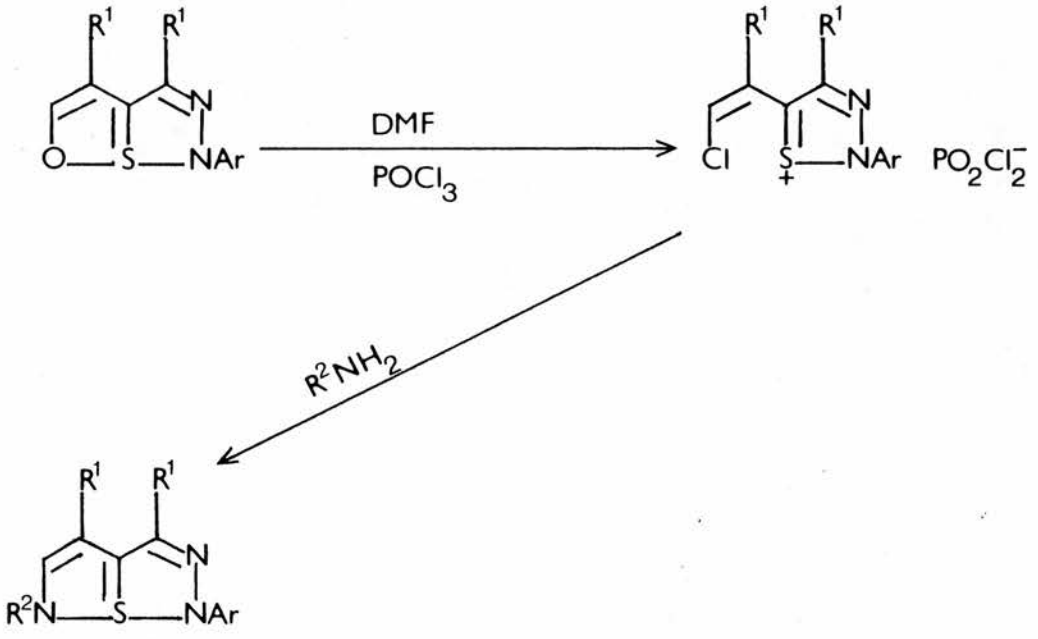
All the above syntheses lead to 1-aryl derivatives. A more versatile synthesis of 6aλ^4-thia-1,2,6-triazapentalenes is shown in scheme 1[122].

Scheme 1



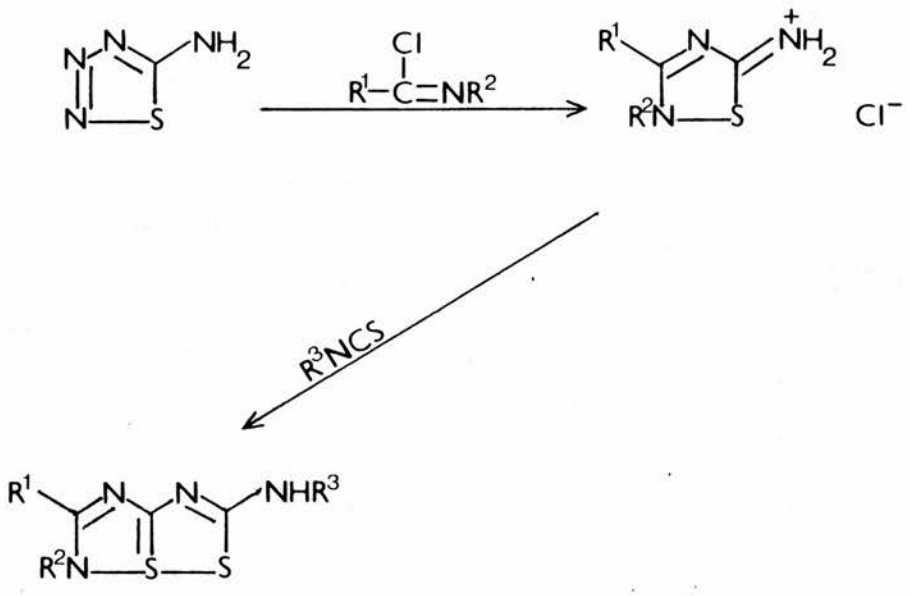
Another general synthesis of 6aλ^4-thia-1,2,6-triazapentalenes is summarised in Scheme 2[128].

Scheme 2



Examples of 1,6aλ^4-dithia-3,4,6-triazapentalenes (97) are provided by the synthesis reported by L'abbé *et al*[109] which is summarised in Scheme 3.

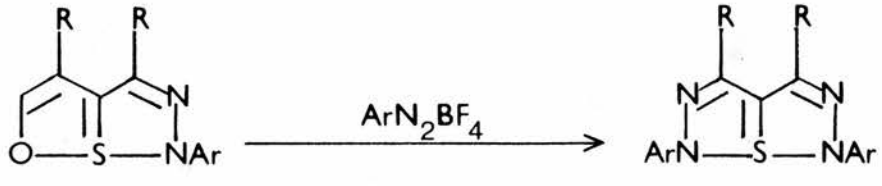
Scheme 3



(97)

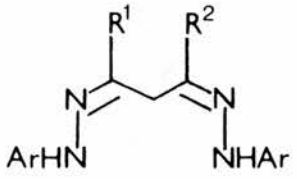
(d) Triheterapentalenes Containing Four Nitrogen Atoms

6aλ^4-Thia-1,2,5,6-tetraazapentalenes (99) can be prepared via compounds (98) by reaction with arenediazonium tetrafluoroborate[61,127].



(98) (99)

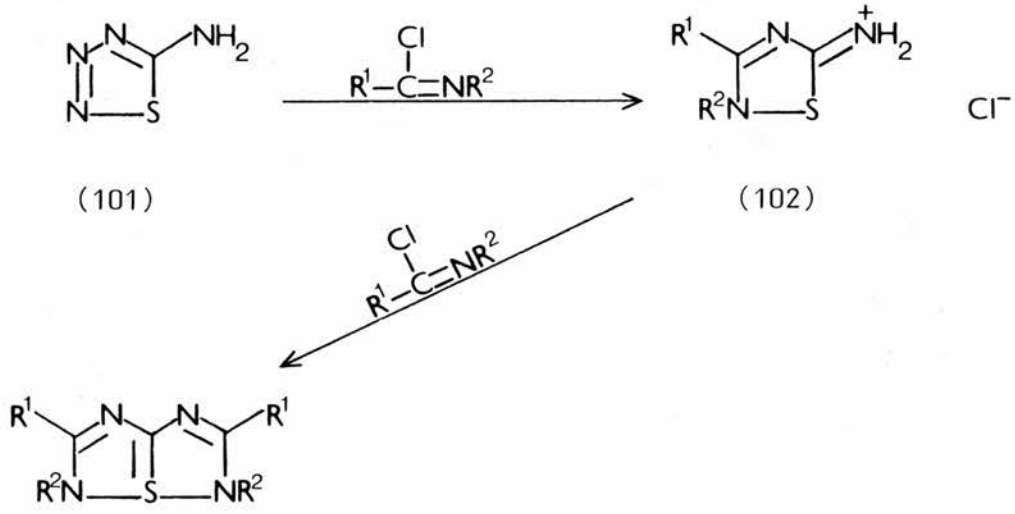
An alternative synthesis proposed by Perrier and Vialle[62], involves treating the bis-arylhydrazones (100) with either sulphur monochloride or sulphur dichloride to give the corresponding tetraazapentalenes.



(100)

6aλ^4-Thia-1,3,4,6-tetraazapentalenes (103) may be synthesised by the method of L'abbé et al[109]. The aminothiatriazole (101) is treated with a two molar equivalent of imidoyl chloride. The reaction proceeds via the 5-imino-1,2,4-thiadiazoline salt (102) as shown in Scheme 4.

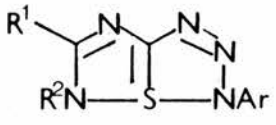
Scheme 4



(101) (102) (103)

(e) Triheterapentalenes Containing Five Nitrogen Atoms

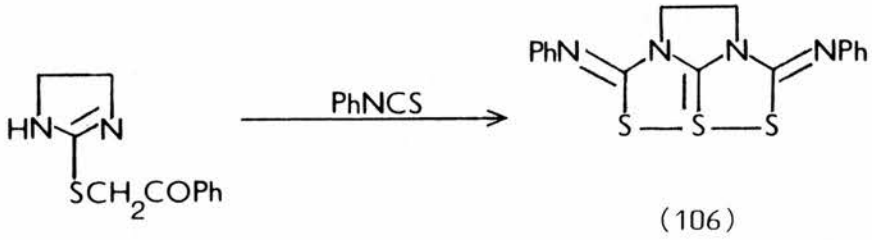
6aλ^4-Thia-1,2,3,4,6-pentaazapentalene (104) is prepared by a similar method to that described in Scheme 4. The initial stage is treatment of (101) with the imidoyl chloride to form (102). This salt is subsequently reacted with arenediazonium tetrafluoroborate to give (104)[129].



(104)

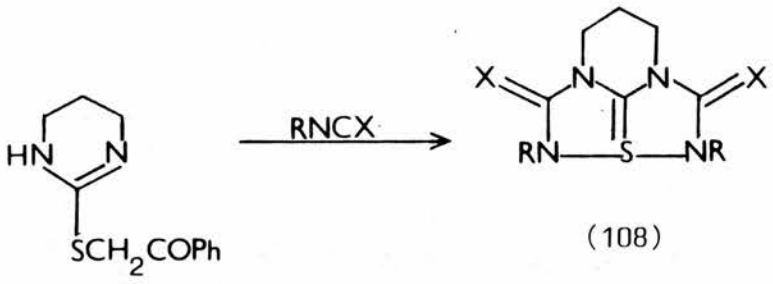
(f) Triheterapentalenes Containing Exocyclic Double Bonds

Beer et al[112] found that treatment of the cyclic isothiourea (105) with phenyl isothiocyanate results in the formation of compound (106).



(105) (106)

In contrast, the cyclic isothiourea (107) when treated with iso(thio)cyanate forms compounds (108).



(107)

(108)

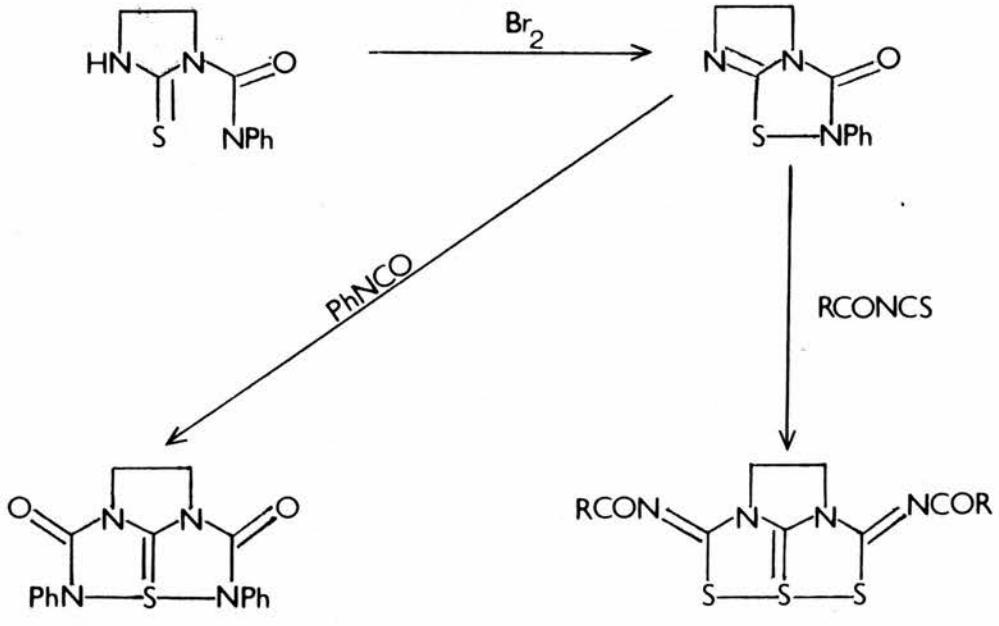
(a) X=O, R=Ph

(b) X=S, R=Ph

(c) X=S, R=Me

In a later communication Beer and co-workers[130] outlined another synthesis to similar compounds (109) and (110). This is summarised in Scheme 5.

Scheme 5



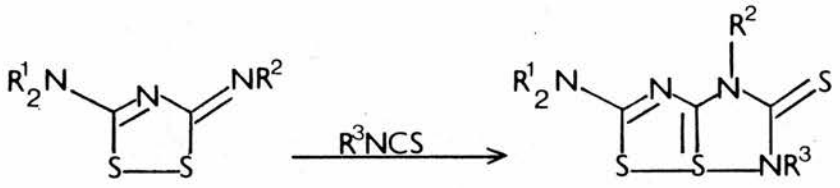
(109)

(110)

R=Ph, EtO

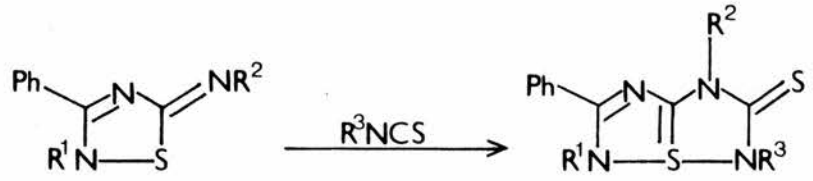
Goerdeler and Ulmen[131] have devised a synthesis of compounds (111) which have been shown to possess a triheterapentalene structure[132,133]. The route to these compounds is illustrated in Scheme 6.

Scheme 6



(111)

Goerdeler and Lobach[134] have similarly synthesised the isothiocyanate adducts (113) of compounds (112) which have also been shown to have triheterapentalene structure.

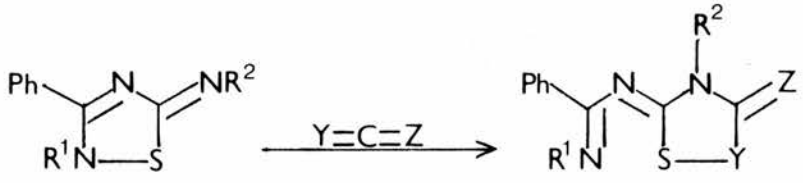


(112) (113)

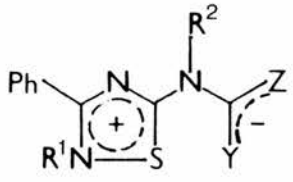
(ii) Analogues of 1,6,6aλ^4-Triheterapentalenes Based on the 1,2,4-Thiadiazole System

A number of compounds which have been reported in the literature as derivatives of the 1,2,4-thiadiazole system could conceivably be formulated as triheterapentalenes. This section describes the routes to such compounds.

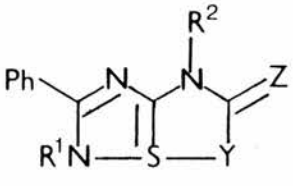
Goerdeler and Lobach[134] have studied the reaction of imino-1,2,4-thiadiazoles (114) with various heterocumulenes. The products obtained may be described as neutral, monocyclic species (115), as zwitterionic species (116), or as triheterapentalenes containing an exocyclic double bond (117).



(114) (115)

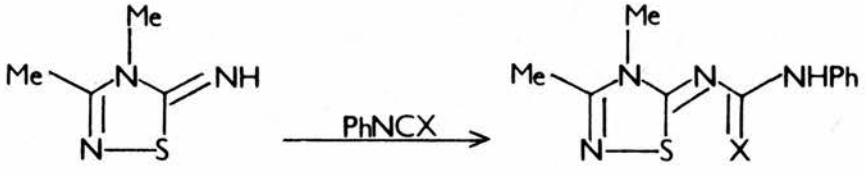


(116)



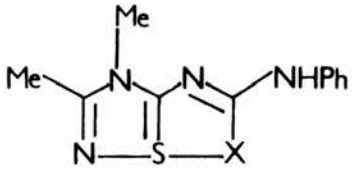
(117)

Mitchell[135] has studied the reactions of 4,5-Dihydro-5-amino-1,2,4-thiadiazoles (118) with phenyl iso(thio)cyanate resulting in the formation of compounds of structure (119), (120) or (121). Similar reactions have also been studied by Goerdeler[136].



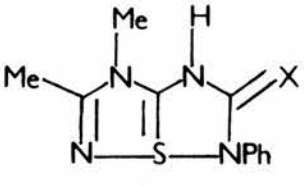
(118) (119)

X=O,S



(120)

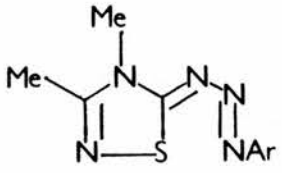
X=O,S



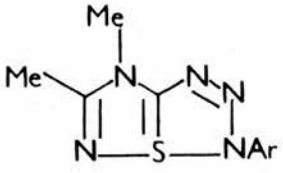
(121)

X=O,S

Compounds of type (118) also react with arenediazonium tetrafluoroborates to give structures which may be formulated as (122) or (123)[135].

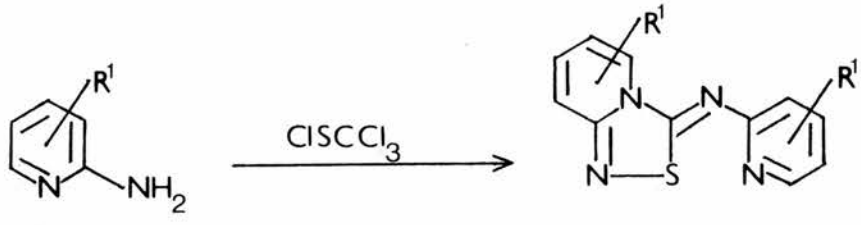


(122)



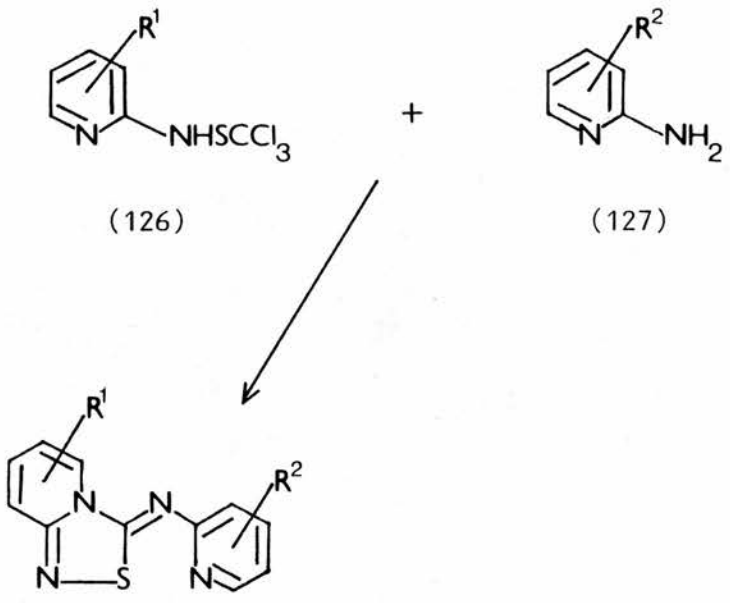
(123)

Potts and Armbruster[137] have prepared a series of compounds which they described as having structure (125), by treating substituted 2-aminopyridines (124) with perchloromethyl mercaptan in the presence of base.



(124) (125)

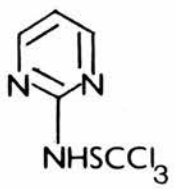
This synthesis was subsequently extended[138] by allowing the intermediate (126)[139] to react with a variety of 2-aminopyridines (127).



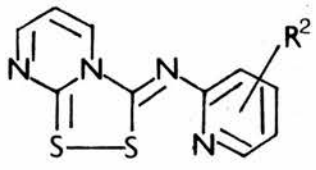
(126) (127)

(128)

Similarly, 2-aminopyrimidine reacts with perchloromethyl mercaptan giving the intermediate (129) which subsequently reacts with 2-aminopyridines (127) to give products of type (130)[140].



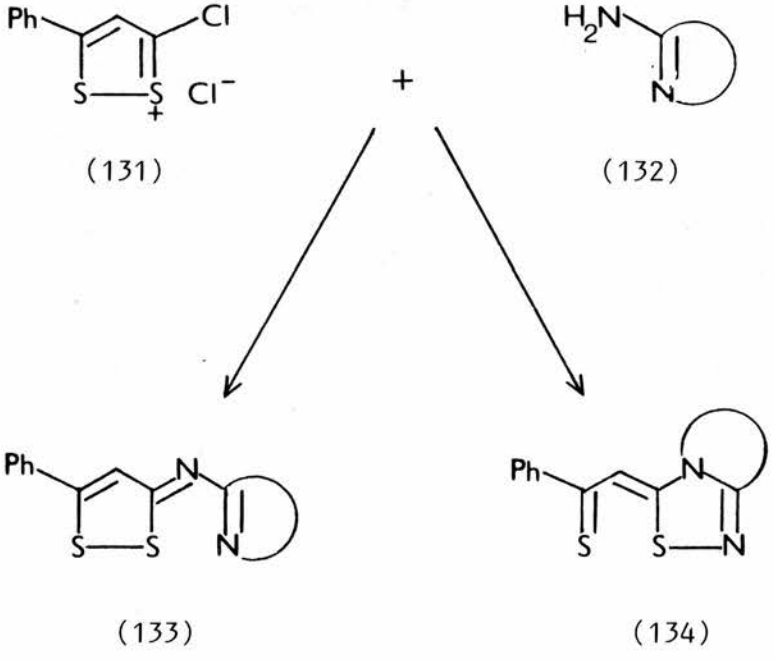
(129)



(130)

The products (125), (128) and (130) could also be formulated as triheterapentalenes.

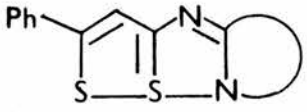
Reid and Mitchell[141] have described condensation reactions of 3-chloro-5-phenyl-1,2-dithiolylium chloride (131) with various 2-amino-N-heterocycles (132) leading to two types of structure (133) and (134) which arise from condensation at the amino substituent or at the ring nitrogen atom, respectively.



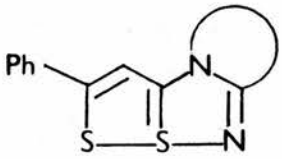
(131) (132)

(133) (134)

Representative products from both series were examined by X-ray crystallography[142,143], and were found to have the open structures (133) and (134) rather than the bicyclic triheterapentalene structures (135) and (136).



(135)



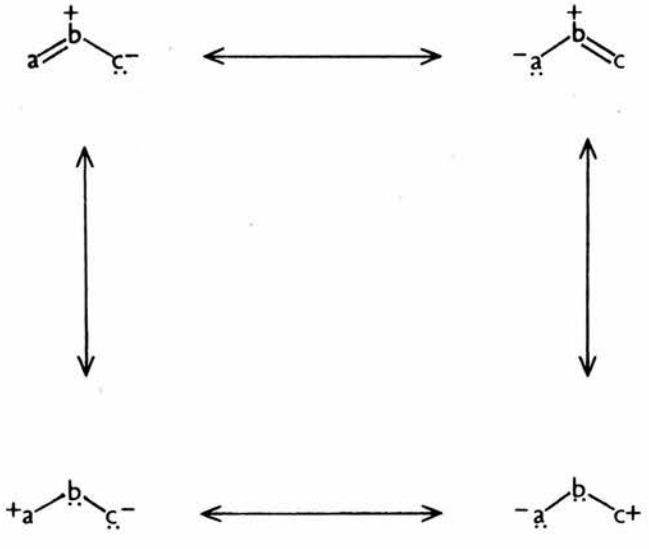
(136)

IV 1,3-DIPOLAR CYCLOADDITIONS

Many of the syntheses described in this thesis involve what are believed to be 1,3-dipolar cycloaddition reactions. Hence, in this section it is proposed to give a brief overview of the necessary constraints in order for 1,3-dipolar cycloaddition to be achieved.

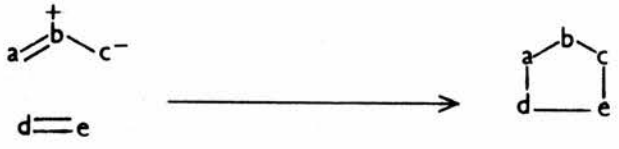
The '1,3-dipole' (137) is defined by Huisgen[144] as a species which is represented by zwitterionic resonance structures (Scheme 7), and which undergoes 1,3-cycloadditions to a multiple bond system, the 'dipolarophile' (138) (Scheme 8).

Scheme 7



(137)

Scheme 8

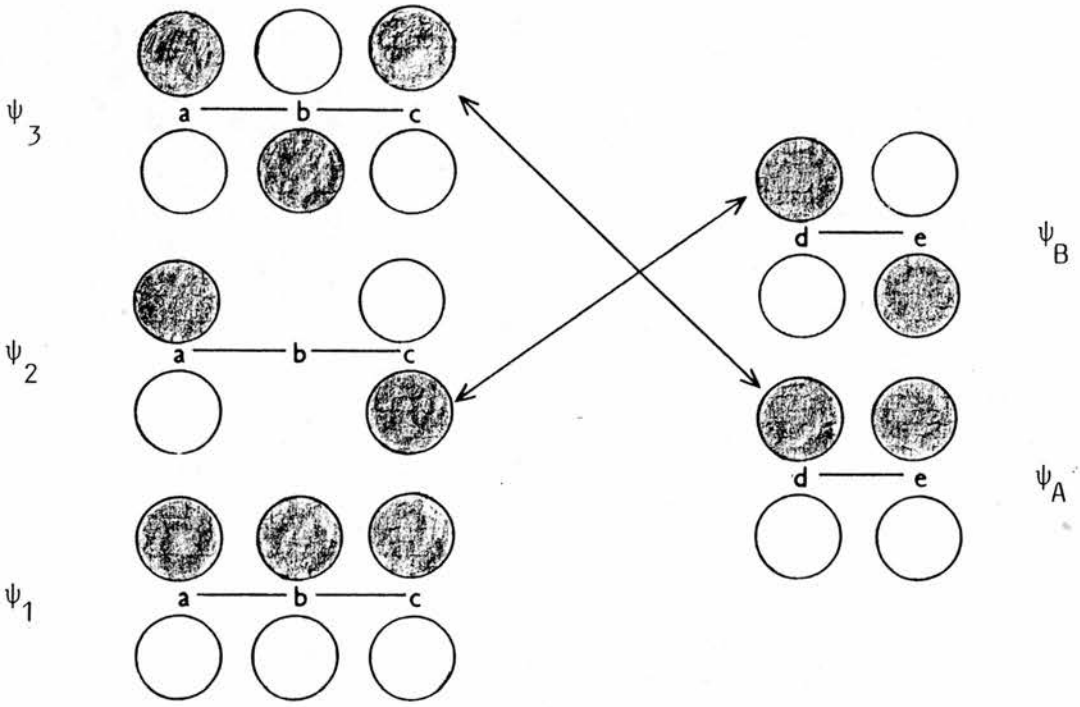


(138)

1,3-Dipoles may be described as heteroallyl anions i.e. as having four electrons in three parallel π-orbitals in an analogous manner to the allyl anion type orbital.

Following the symmetry-allowed scheme[145] $[_{\pi}4_s + _{\pi}2_s]$, 1,3-dipoles undergo only conrotatory cycloadditions of the ring classification 3+2 ——> 5, the 1,3-dipole acting as $_{\pi}4$ reactant and the dipolarophile as $_{\pi}2$. The homo-lumo interactions between the 1,3-dipole and the dipolarophile are shown in Scheme 9.

Scheme 9



The MO symmetry correlation diagram of 1,3-dipolar cycloaddition bears a more than superficial resemblance to that of the well known Diels-Alder reaction.

Many 1,3-dipolar cycloaddition reactions show the characteristics of a concerted process as described. However, others may be said to be stepwise and to involve an intermediate which is either zwitterionic or diradical.

Huisgen[144] has produced a convincing argument refuting the diradical hypothesis, while Woodward and Hoffmann[145] have concluded that there may well be instances of 1,3-dipolar cycloadditions in which the complementary polar character of the reactants is sufficiently extreme as to favour two-step combination proceeding

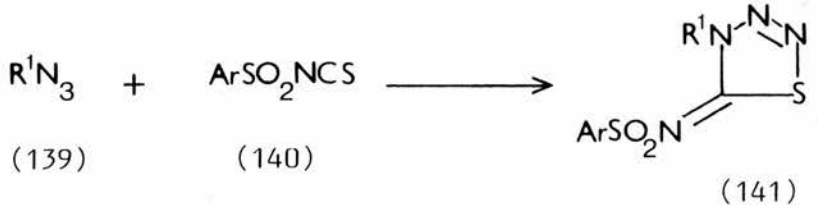
through a relatively stable dipolar intermediate.

Of most relevance to the work reported in this thesis are obviously those cycloaddition reactions which involve triheterapentalene intermediates or final products. However, to ensure completeness, it is proposed to carry out a brief preliminary discussion of those reactions which may be described as elimination/cycloaddition reactions.

(i) Elimination/Cycloaddition Reactions

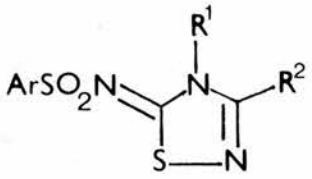
In order to illustrate the general concept of these reactions, the 1,2,3,4-thiatriazolines (141) will serve as a good working model.

Compounds of this type were synthesised by L'abbé et al[146] by the reaction of alkyl azides (139) with arylsulphonyl isothiocyanates (140).

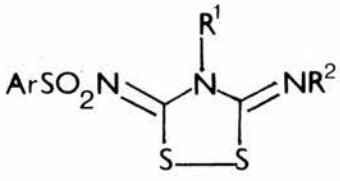


(139) (140) (141)

Several workers[146-150] have investigated the cycloaddition reactions of compounds (141) with a variety of dipolarophiles. L'abbé[147] found that treatment of such compounds (141) with nitriles at 60°C resulted in products with the structure (142).



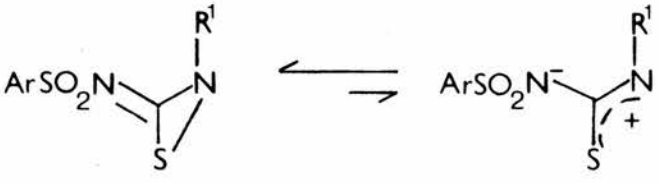
(142)



(143)

Both L'abbé[148] and Neidlein[149] have independently investigated the reactions of 1,2,3,4-thiatriazolines (141) with isothiocyanates which give rise to products of type (143).

Kinetic studies to elucidate the mechanism of these reactions were undertaken by L'abbé[150] with the conclusion that a discrete intermediate was formed by a unimolecular process. The intermediate proposed by both L'abbé and Neidlein was that of a thiaziridineimine (144) or its ring-opened dipolar form (145).

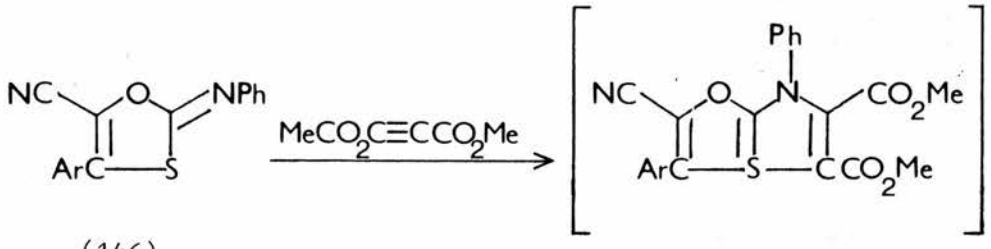


(144) (145)

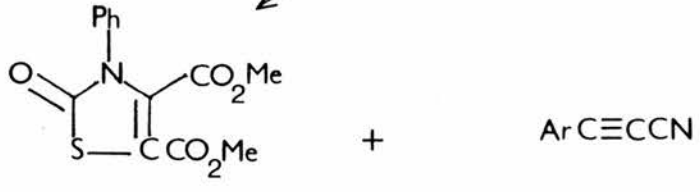
(ii) Cycloaddition Reactions Involving Intermediates with Tetravalent Sulphur

(a) Cycloaddition/Elimination Reactions

Robert and Baudy[151] have studied the addition reactions of dimethyl acetylenedicarboxylate with 2-imino-1,3-oxathioles (146), which result in thiazolones (148), for which they propose the bicyclic intermediates (147). In this reaction, the compounds (146) can be seen to be behaving as masked 1,3-dipoles.



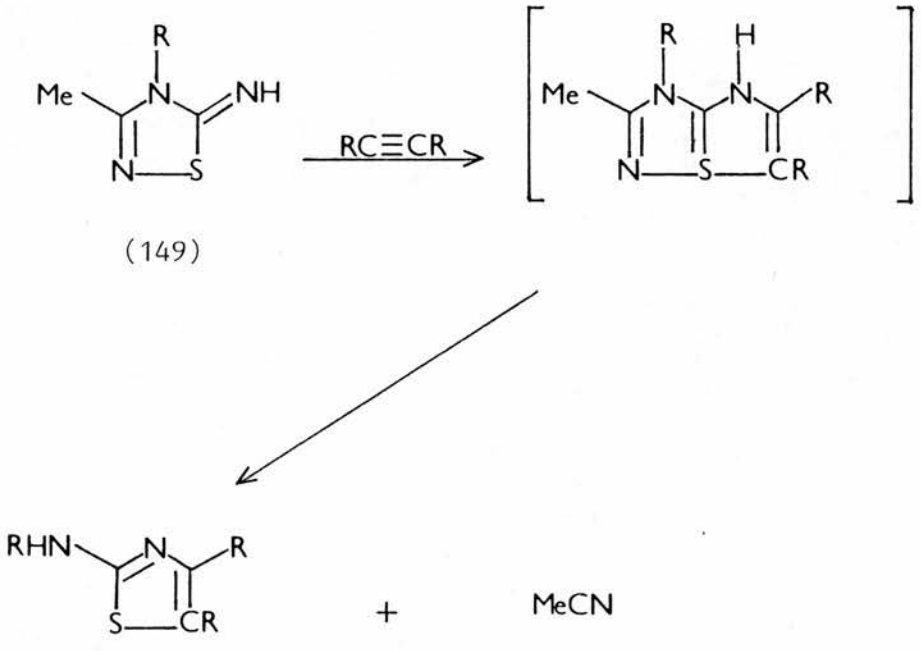
(146) (147)



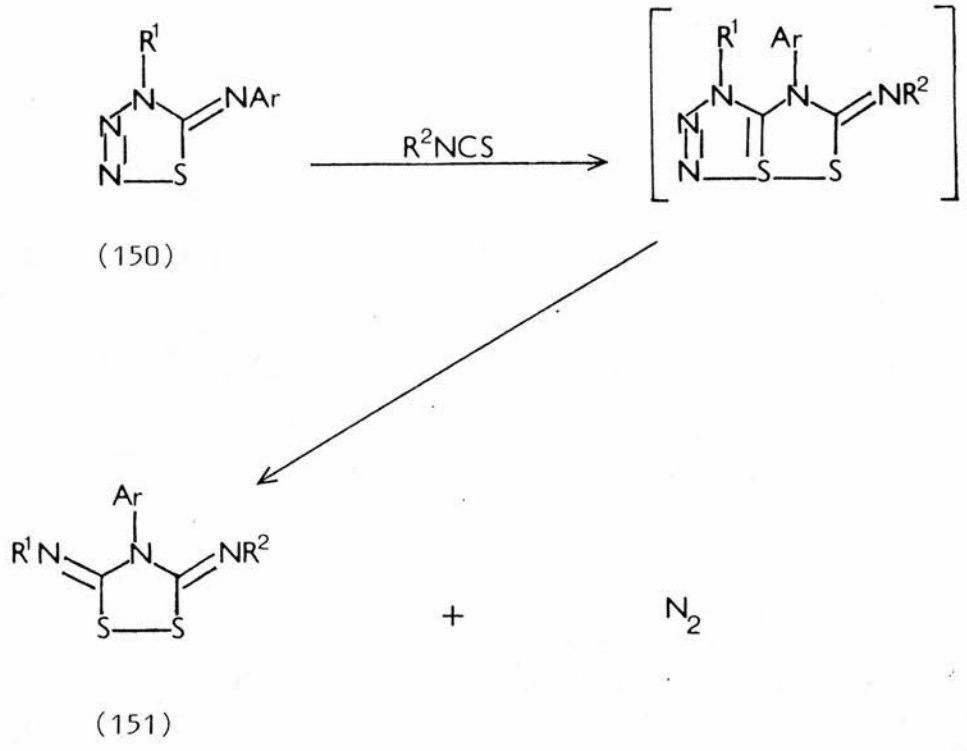
(148)

Akiba[152] has observed similar reactions on treatment of the 1,2,4-thiadiazolines (149) with acetylenes, (Scheme 10).

Scheme 10



L'abbé et al[108,110] have investigated the reactions of 5-arylimino-1,2,3,4-thiatriazolines (150) with a variety of isothiocyanates which lead to the products (151).



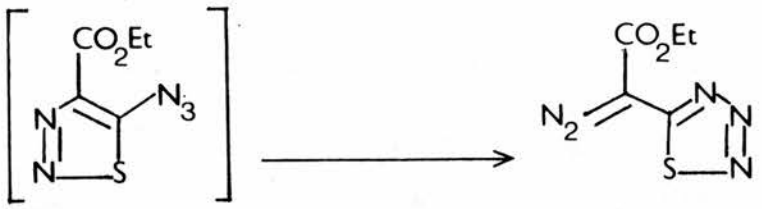
(150)

(151)

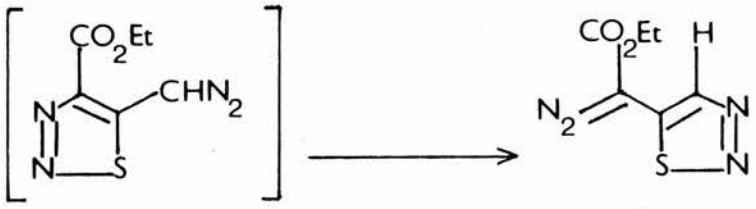
A kinetic study of these reactions indicated that a bimolecular mechanism, which may be that of a triheterapentalene intermediate, was operating. The data collected, however, did not exclude rigorously the alternative stepwise mechanism[153].

(b) Bond Switch Reactions

L'abbé[154,155] has reported two examples of bond switch reactions involving sulphur as the pivot atom. The first is the rearrangement of the 5-azido-1,2,3-thiadiazole (152) to the thiatriazole (153), while the second is a related rearrangement involving the transformation of the 5-diazomethyl-1,2,3-thiadiazole (154) into the thiadiazole (155).

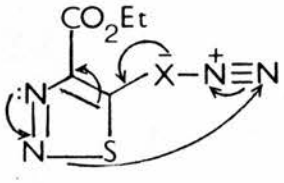


(152) (153)



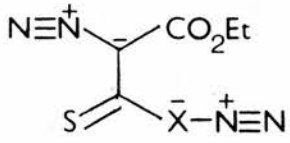
(154) (155)

Mechanistically, the observed rearrangement can occur either by a concerted bond switch mechanism (156), or, via the open-chain intermediate (157).



(156)

X=N, CH

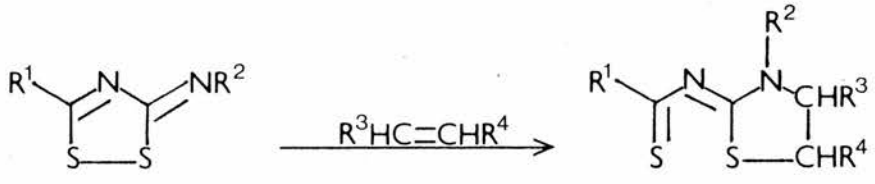


(157)

X=N, CH

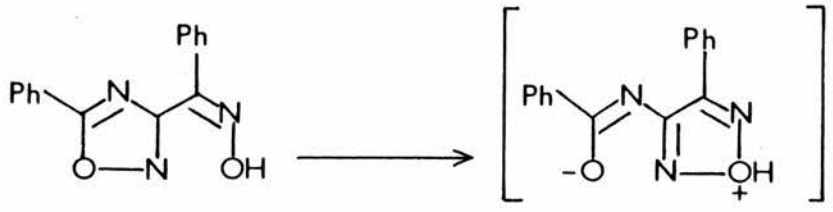
On investigation of the cycloaddition reactions of olefins with 5-imino-1,2,4-thiadiazoles (158), Goerdeler and Linden[156] discovered a similar bond switch mechanism to be operating (Scheme 11).

Scheme 11

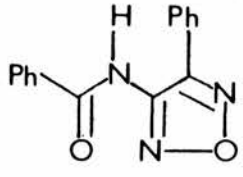


(158)

Vivona et al[157] have recently reported investigations of heterocyclic rearrangements of the Z-isomer of the oximes (159) for which they propose an intermediate (160) involving a bond switch.



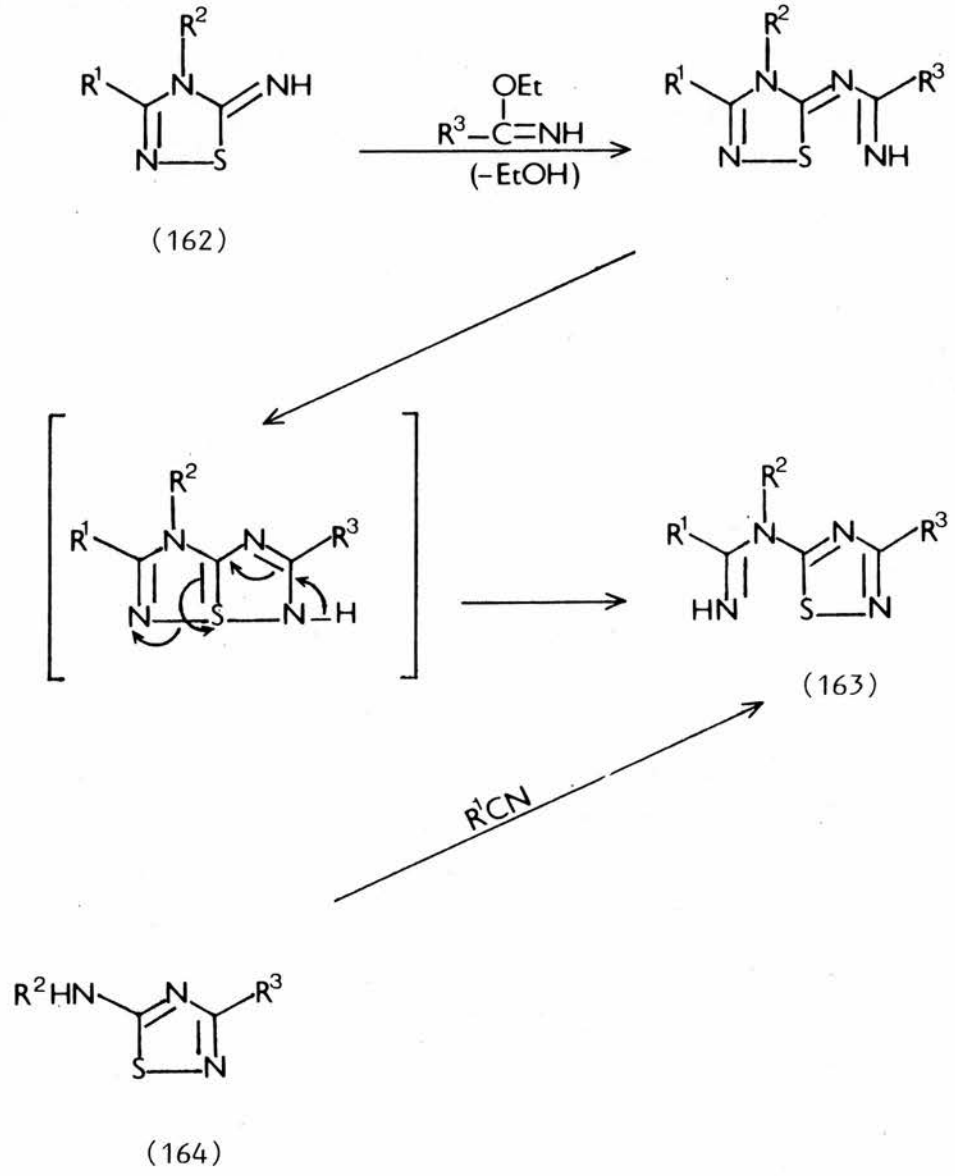
(159) (160)



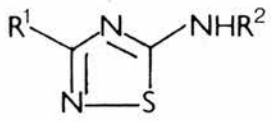
(161)

Akiba[111] has investigated the reactions of the 4,5-dihydro-5-imino-1,2,4-thiadiazoles (162) by means of a bond switch. The structure of these products (163) was confirmed by an unequivocal synthesis from the thiadiazole (164) and nitriles, (Scheme 12).

Scheme 12



Goerdeler[158] has shown that the compound (162) will rearrange to give compound (165).



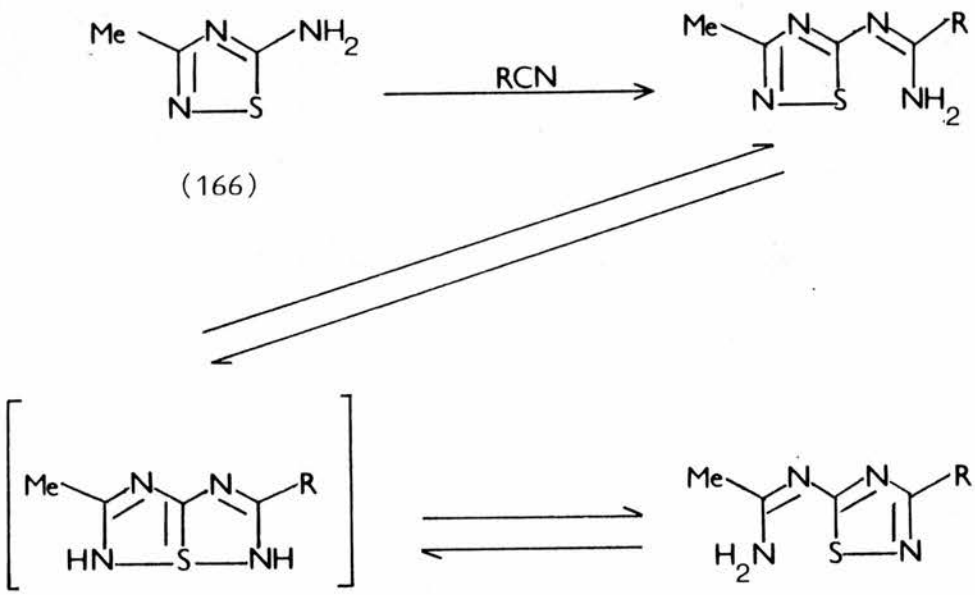
(165)

This being so, the reaction described by Akiba may in fact be the rearrangement of (162) to (165) which subsequently reacts with the imidate to give the final product. This reaction would still, however, involve a bond switch in the latter stage as R^1 and R^3 are not in all cases equivalent.

An X-ray crystal structure determination of the compound [(163), $R^1 = R^2 = R^3 = Me$] showed the molecule to be virtually planar, with S-N and S-NH distances of 1.688Å and 2.500Å respectively. Akiba regarded this S-NH distance as indicative of an intramolecular S·····NH interaction. However, Glemser and co-workers[159] have produced a correlation of S-N distance with S-N bond order which suggests that, at an interatomic distance of approximately 2Å, the S-N bond order becomes zero. If this is in fact correct, the validity of the hypothesis that there is a degree of S·····NH interaction is called into question.

Akiba[160] has reported other examples of bond switch rearrangements. One such rearrangement involves the reaction of the 5-amino-1,2,4-thiadiazole (166) with nitriles (Scheme 13).

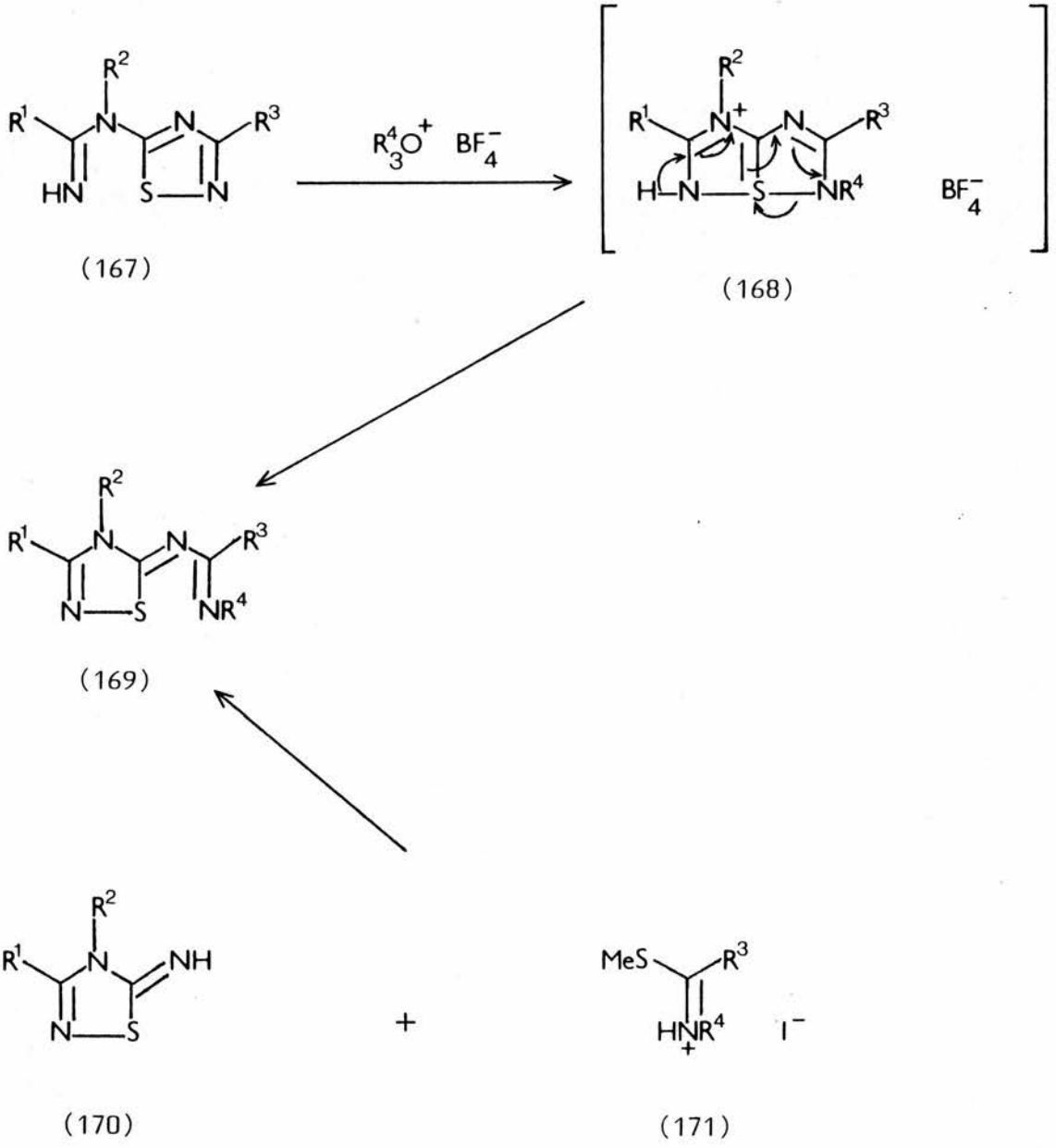
Scheme 13



The ^{1}Hnmr spectra of the 1:1 adducts of (166) with nitriles recorded over a range of temperatures, 34°C-120°C, showed two pairs of signals. Akiba rationalised this observation by assuming the occurrence of ring transformation according to Scheme 13.

The reaction of compounds (167) with Meerwein's reagent[161] via the proposed intermediate (168) affords compound (169). The structure of compound (169) was determined by an independent synthesis from the compounds (170) and (171) (Scheme 14).

Scheme 14



(167)

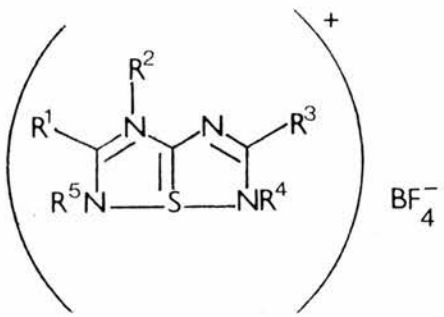
(168)

(169)

(170)

(171)

Further alkylation of (169) with Meerwein's reagent resulted in (172).

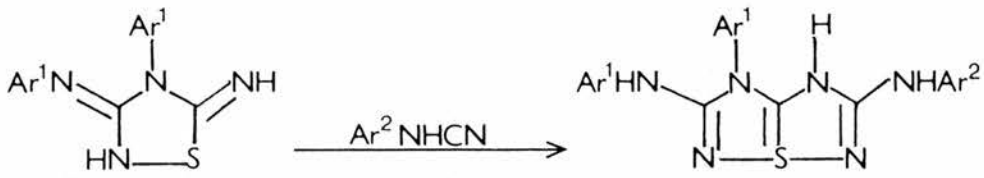


X-ray crystal structure:
R^1 - R^5 = Me.

(172)

An X-ray crystal structure determination of (172)[162] showed the molecule to be almost planar with bond lengths of N(1)-S(6a), and S(6a)-N(6) corresponding to 1.984Å, and 1.833Å respectively. Thus, the structure (172) may be regarded as a triheterapentalenium salt.

Akiba[107] tentatively reported that the reaction products of Hector's base[163], which he formulated as (173), with arylcyanamides were the triheterapentalene derivatives (174). This conclusion was based on comparisons of the ultraviolet and infra-red spectra of the products with those of model compounds, and on mass spectral data for the products.

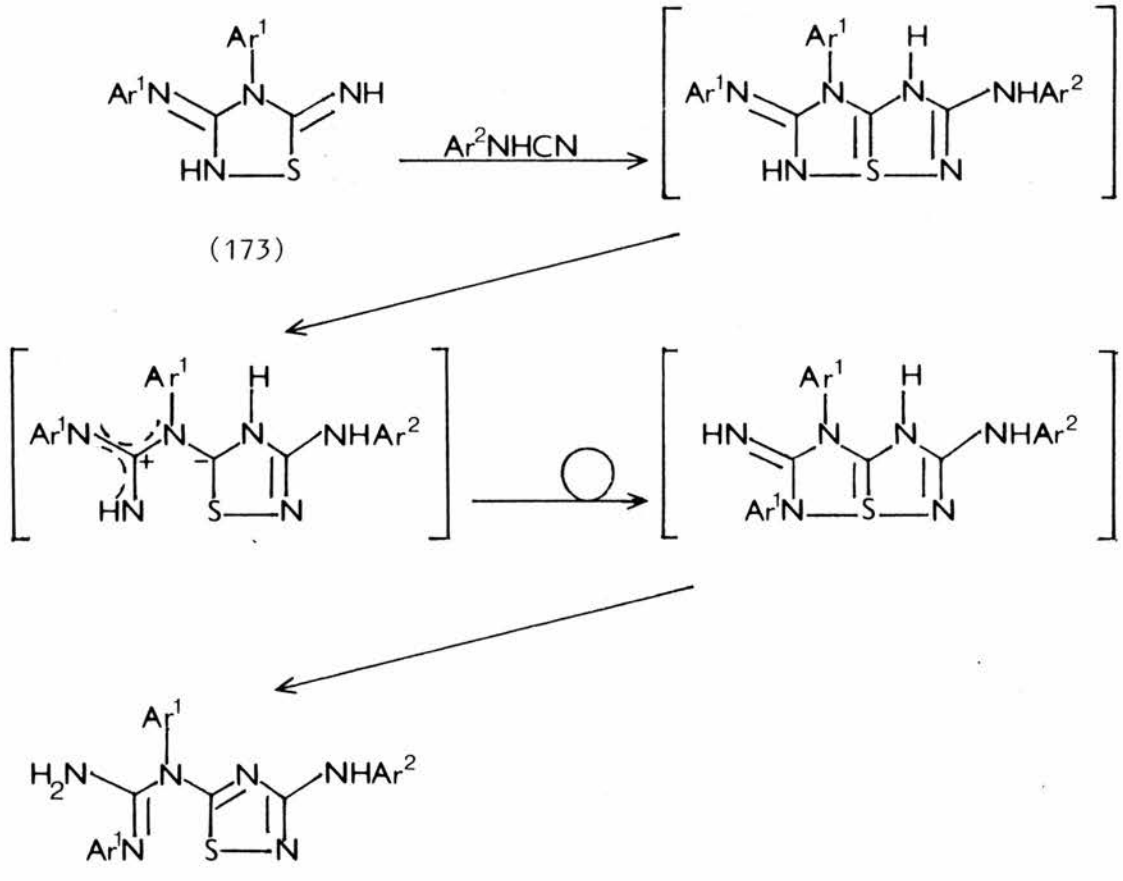


(173) (174)

In a later communication[164], he reported a revised structure for (174) of (175) following a crystal structure determination [(175), Ar=p-BrC_6H_4]. The molecule (175) was found, with the exclusion of the three aryl groups, to be approximately planar with S-N(1) and N(6)-S bond lengths of 2.538Å and 1.670Å respectively. Again, Akiba considers the S-N(1) bond distance to suggest a significant interaction between the corresponding sulphur and nitrogen atoms. As indicated earlier however, this hypothesis is open to question.

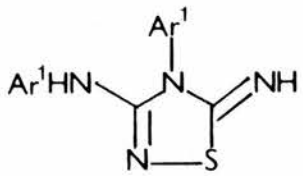
In agreement with the new structure (175), Akiba proposes that the products are formed as set out in Scheme 15.

Scheme 15



(175)

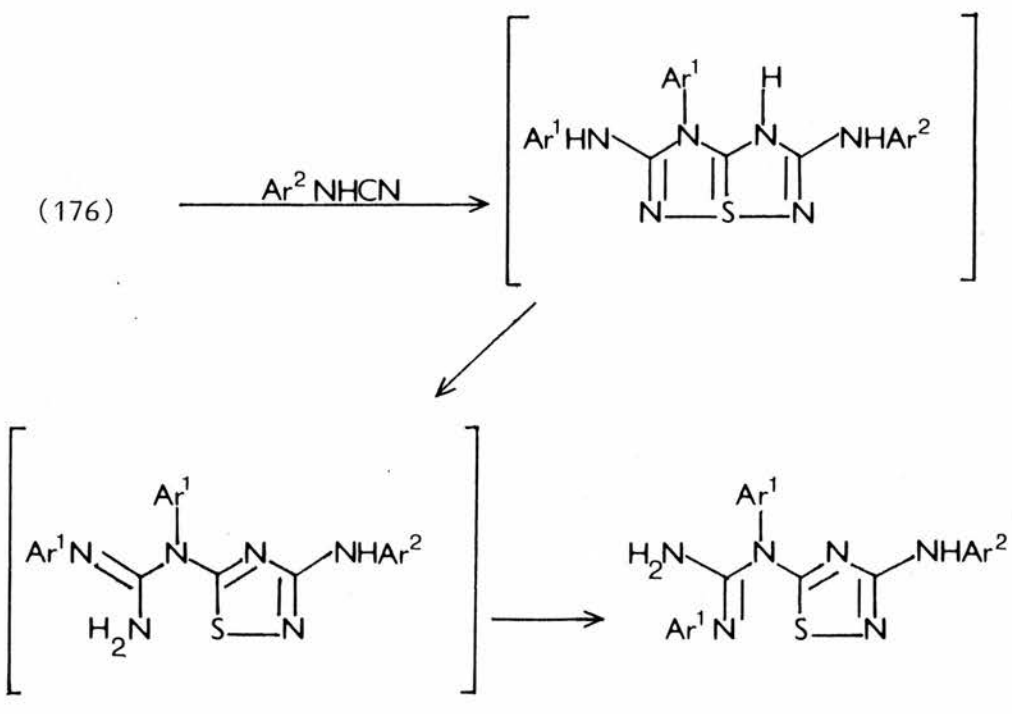
More recently[165,166], a crystal structure determination of Hector's base has been carried out. This shows the correct structure to be (176) and not (173) as previously suggested. In addition this structure, (176), is also known to be adopted in solution[167].



(176)

Under these circumstances, a revised scheme of reaction could be that which is set out in Scheme 16.

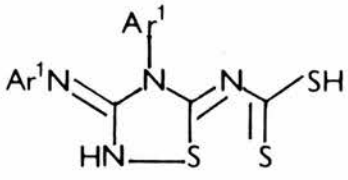
Scheme 16



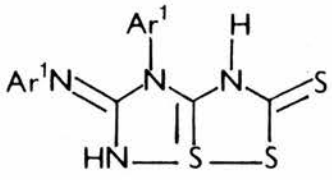
(175)

This hypothesis also proposes the mechanism of formation to involve prototropy and a bond switch as originally suggested by Akiba.

Hector's base forms a 1:1 adduct with carbon disulphide[168] for which alternative structures (177) and (178) have been suggested[169].

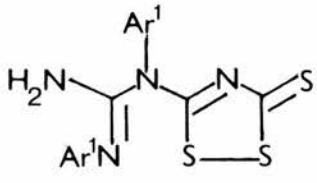


(177)

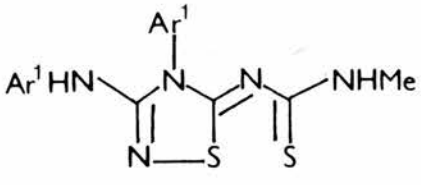


(178)

Glidewell[170] has shown the correct structure to be (179). Thus the reaction of Hector's base with carbon disulphide must involve a bond switch similar to that previously described for the reaction with arylcyanamides.



(179)



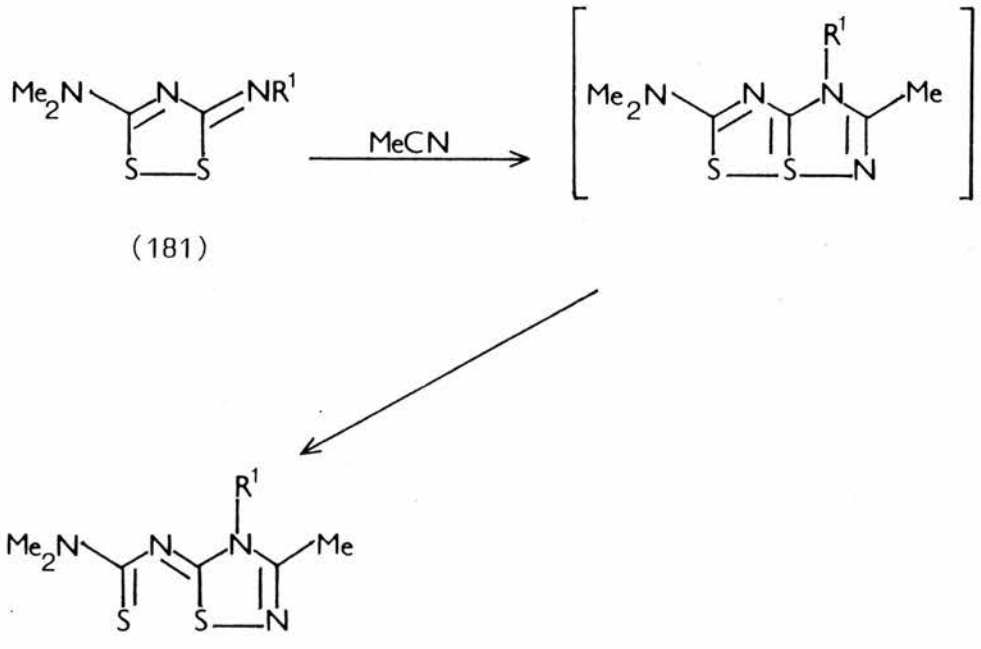
(180)

In marked contrast to this is the formation of the 1:1 adduct of Hector's base with methyl isothiocyanate[171]. This forms the adduct (180) without a heterocyclic rearrangement.

Glidewell and Cuthbertson[172] have carried out a MNDO study of model compounds to elucidate the nature of isomerism and adduct formation of Hector's base. They conclude that the occurrence or otherwise of a bond switch in these compounds is determined by thermodynamic rather than by mechanistic factors, the thermodynamically most favoured isomers being formed in each case.

On investigating the alkylation reactions of the imino-1,2,4-dithiazoles (181) in acetonitrile solvent, Oliver[106] observed a side reaction with the solvent leading to the bond switch products (182) (Scheme 17).

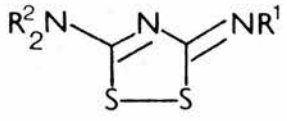
Scheme 17



(181)

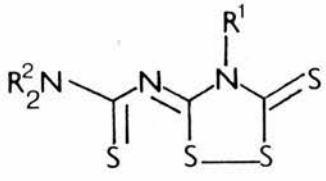
(182)

Goerdeler[173] and Oliver[126] have reported many examples of cycloadditions of heterocumulenes to compounds of type (183), [c.f. (181), R^2=Me].

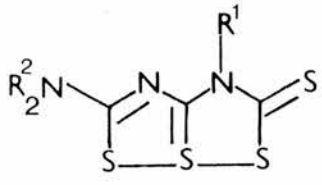


(183)

The carbon disulphide adducts of compounds (183) have been formulated as the bond switch products (184). However in this case, the structure of the product has not been determined and may in fact be the triheterapentalene (185).



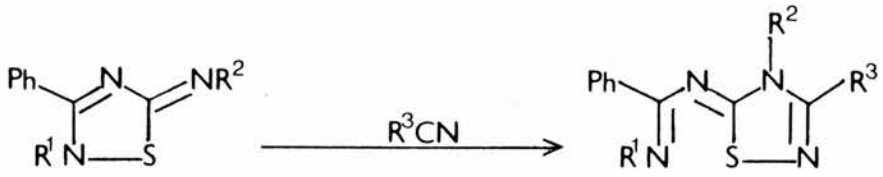
(184)



(185)

Goerdeler and Lobach[134] have reported the reactions of imino-1,2,4-thiadiazoles (186) with nitriles. These apparently proceed via a bond switch mechanism similar to that described by Oliver[106] (Scheme 18).

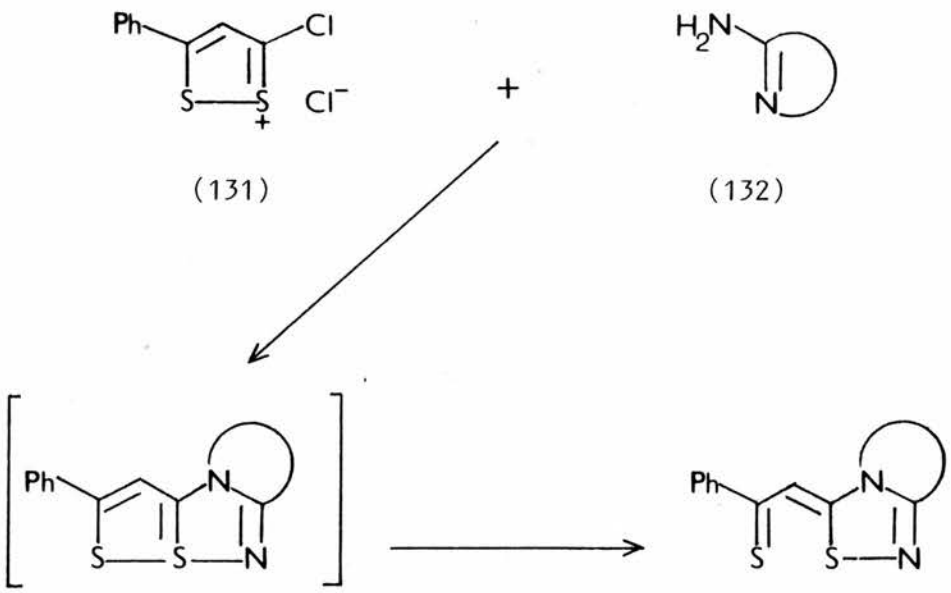
Scheme 18



(186)

Reid and Mitchell[141] have described a bond switch reaction resulting from the condensation of the dithiolylium salt (131) with various 2-amino-N-heterocycles (132). One of the products thus obtained could be formed via the triheterapentalene intermediate (187) as indicated in Scheme 19.

Scheme 19



(131) (132)

(187) (134)

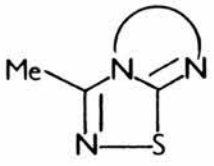
Much of the work described in the latter part of this thesis involves 1,3-dipolar cycloaddition reactions. As has been demonstrated in the preceeding pages, 1,3-dipolar cycloadditions form an ever expanding area of chemistry of great synthetic potential.

PART B

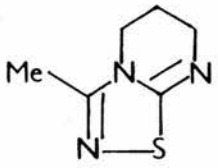
DISCUSSION

I (i) Condensation of 5-Amino-1,2,4-thiadiazoles with α,ω-Dihaloalkanes, and Related Reactions

One important aim of this work was to synthesise a variety of compounds corresponding to the general structure (188).



(188)



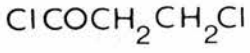
(189)

The compound (189) is already known[174] and it was decided to attempt to synthesise other such structures to see what effect varying the nature of the bridging substituent would have on reactions, if any.

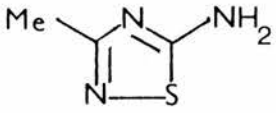
(a) Attempted Synthesis of 5,6-Dihydro-3-methyl-6-oxopyrimido [1,2-d][1,2,4]thiadiazole

5-Amino-3-methyl-1,2,4-thiadiazole was prepared by the method of Goerdeler[175].

The reaction of 3-chloropropionyl chloride (190) with 5-amino-3-methyl-1,2,4-thiadiazole (191) was attempted under a variety of conditions.



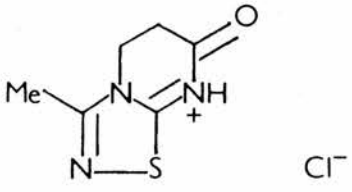
(190)



(191)

The product obtained at room temperature in acetonitrile was 5-amino-3-methyl-1,2,4-thiadiazolium chloride, the hydrochloride of the thiadiazole (191).

In refluxing acetonitrile, a different product was obtained whose physical properties (^{1}Hnmr, mass spectrum, microanalysis) were consistent with 5,6-dihydro-3-methyl-6-oxopyrimido[1,2-d][1,2,4] thiadiazolium chloride (192), the salt of the desired product.

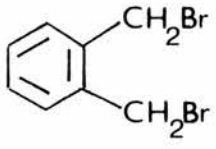


(192)

However, all attempts to deprotonate this compound were fruitless, suggesting that the product may not be the simple structure (192) originally envisaged.

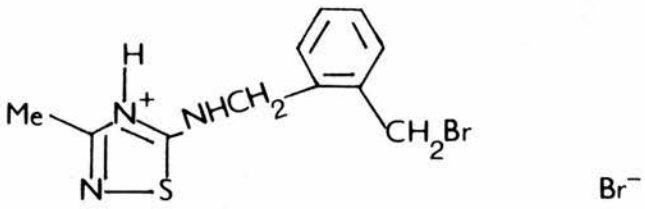
(b) Synthesis of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4] thiadiazolo[1,3]diazepine and Related Compounds

The reaction of 5-amino-3-methyl-1,2,4-thiadiazole (191) with α,α'-dibromo-o-xylene (193) was carried out initially in refluxing acetonitrile.

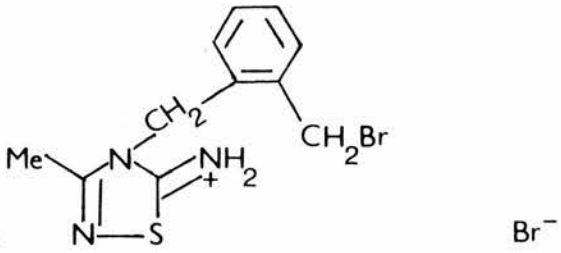


(193)

This yielded a salt which was formulated as (194) rather than the expected structure (195)[136,174] since two quite distinct N-H signals at δ9.5 and δ10.1 appear in the ^{1}Hnmr spectrum of this product.



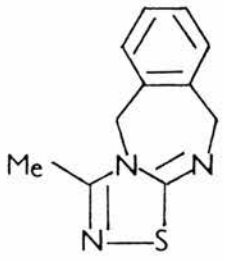
(194)



(195)

This salt was, however, extremely insoluble even in very polar solvents such as N,N-dimethylformamide, methanol, and water, and all attempts to deprotonate it were unsuccessful.

It had been hoped that the salt (194), once deprotonated, would cyclise to give, on subsequent deprotonation, a structure of type (196).



(196)

As this method was proving unsuccessful, an alternative route to the desired product (196) was investigated.

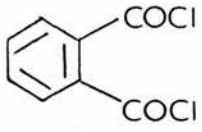
A solution of α,α'-dibromo-o-xylene (193) and 5-amino-3-methyl-1,2,4-thiadiazole (191) in N,N-dimethylformamide was brought to reflux and boiled for 15 minutes. Subsequent basification with aqueous sodium hydroxide followed by extraction into dichloromethane gave the product (196).

It is of interest that neither the salt (194) nor the salt (195) was detected throughout the course of this reaction. This would tend to suggest that the thiadiazole (191) is sufficiently basic to effect the initial deprotonation.

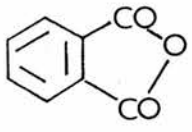
(c) Attempted Synthesis of 5,6-Benzo-4,7-dioxo-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine

Phthaloyl chloride (197) reacted violently and exothermically with 5-amino-3-methyl-1,2,4-thiadiazole (191) in N,N-dimethylformamide

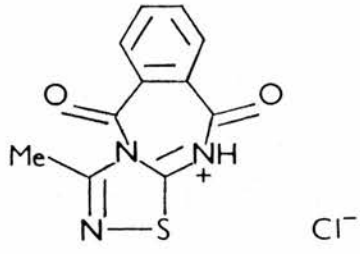
at room temperature yielding phthalic anhydride (198) and not the desired product (199).



(197)



(198)



(199)

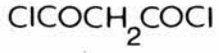
The possibility of carrying out the reaction in other solvents was investigated using acetonitrile, nitromethane and benzonitrile. In every case, the sole product was 5-amino-1,2,4-thiadiazolium chloride.

An attempt to carry out the reaction in the absence of solvent resulted in the formation of apparently polymeric material which was highly insoluble and involatile and would not melt up to 350°C.

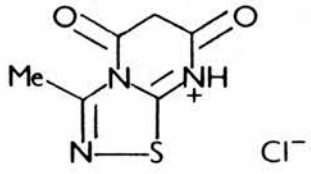
(d) Attempted Synthesis of 3-methyl-5H-4,6-dioxopyrimido[1,2-d][1,2,4]thiadiazole

Malonyl chloride (200) was added to a solution of 5-amino-3-methyl-

1,2,4-thiadiazole (191) in N,N-dimethylformamide. As with the product from phthalyl chloride mentioned previously, the product obtained appeared to be polymeric and not the desired compound (201). It was highly insoluble and involatile, which prevented any useful spectral data from being obtained, and would not melt up to 350°C.



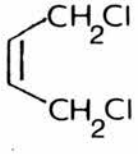
(200)



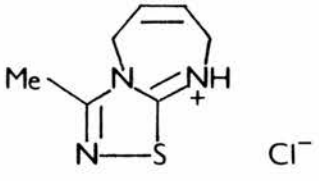
(201)

(e) Attempted Synthesis of 4,7-Dihydro-3-methyl[4,5-a][1,2,4] thiadiazolo[1,3]diazepine

All attempts to react the thiadiazole (191) with cis-1,4-dichlorobut-2-ene (202) to give the product (203) were unsuccessful.



(202)



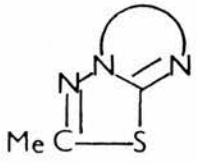
(203)

Both N,N-dimethylformamide and acetonitrile were tested as suitable solvents, and even in boiling acetonitrile (bp 81.6°C), compound (202) appears to decompose without any reaction taking place

with the thiadiazole (191). At room temperature no reaction was observed.

(ii) **Condensation of 5-Amino-1,3,4-thiadiazoles with α,ω-Dihaloalkanes and Related Reactions**

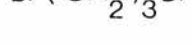
As a further variation, it was decided to attempt the syntheses of structures of type (204), which are isomeric to structure (188), to see what effect this might have on subsequent reactions.



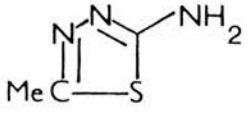
(204)

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

1,3-Dibromopropane (205) was added to a solution of 5-amino-2-methyl-1,3,4-thiadiazole (206) in acetonitrile.

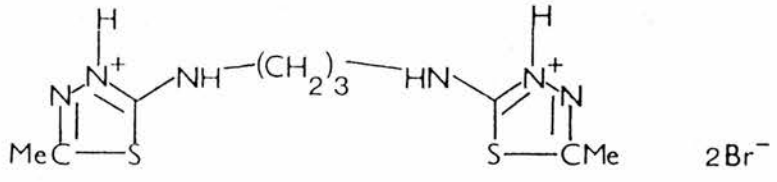


(205)



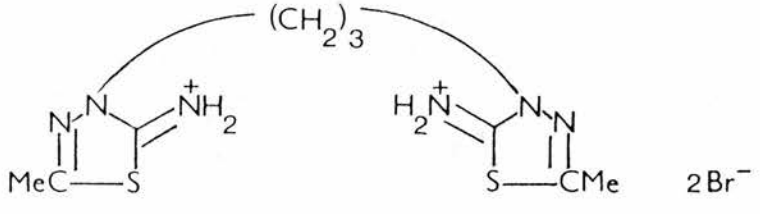
(206)

Three such solutions were boiled for 6 hours, 24 hours, and 72 hours respectively. In all cases, a small amount of material crystallised from the solution. Microanalysis and a ^{1}Hnmr spectrum indicated that the product was a bis adduct, $[(C_3H_5N_3S)_2(CH_2)_3]^{2+}$ $2Br^-$ (207).

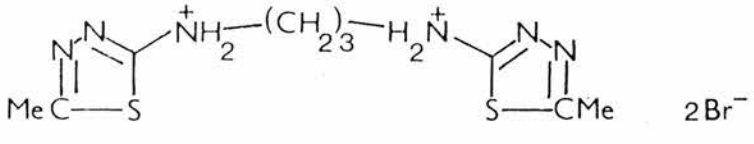


(208)

Possible structures for this adduct may be considered to be (208), (209(a)) or (209(b)), however, the two distinct Me signals present in the ^{1}Hnmr spectrum of this product are inconsistent with all of these structures.

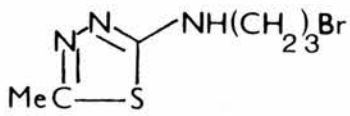


(209(a))



(209(b)

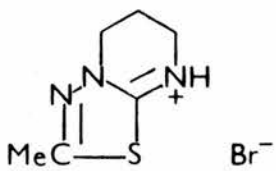
The mother liquors from the three experiments were treated in turn, after removal of the excess 1,3-dibromopropane, with aqueous sodium hydroxide. Extraction of this aqueous mixture with dichloromethane yielded a residue which was found on examination by ^{1}Hnmr spectroscopy to contain a mixture of the thiadiazole (206) and the uncyclised base (210).



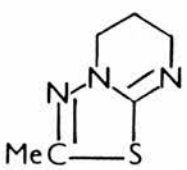
(210)

The ratios of thiadiazole (206) to base (210) were respectively 1:2.5, 1:7, and 1:4 for 6 hours, 24 hours and 72 hours reflux. Thus it appears that the optimum reaction time for the formation of the product (210) is 24 hours. This would tend to suggest that (210) is unstable and is subject to thermal decomposition on prolonged heating.

The product (210) was subsequently cyclised to form the salt (211). Treatment of (211) with sodium hydroxide gave the free base (212) in 4% yield.



(211)

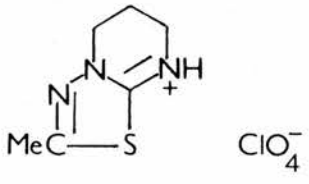


(212)

Due to the disappointingly low yield of (212), it was decided to investigate the effect of solvent on the reaction.

An identical reaction to that just described was carried out employing methanol as solvent. In this case none of the bis adduct (207) was detected. Presumably, (207) is sufficiently soluble in methanol to stay in solution throughout the course of the reaction and is at some stage broken down to form either the thiadiazole (206) or the base (210). After final work-up, the desired product (212) was obtained in 12% overall yield.

A sample of the base (212) was purified for analysis via the perchlorate (213) which was made by treating (212) with an excess of perchloric acid.



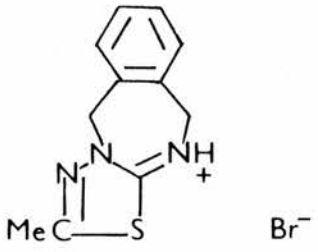
(213)

The perchlorate, which gave good analytical data, was reconverted to the free base, and the base (212) stored in a sealed tube prior to analysis. The base (212) was handled in an inert atmosphere when analysis was carried out.

A sample of the intermediate hydrobromide (211) was prepared from the base (212) for analysis.

(b) Attempted Synthesis of 5,6-Benzo-4,7-dihydro-2-methyl[4,5-a][1,3,4]thiadiazolo[1,3]diazepine

It was hoped that, as in the formation of the diazepine (196), the reaction of dibromo-o-xylene (193) and 5-amino-2-methyl-1,3,4-thiadiazole (206) could be carried out in one step to form the cyclised salt (214).



(214)

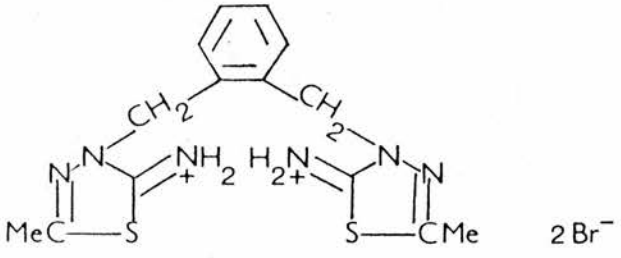
α,α'-Dibromo-o-xylene (193) dissolved in N,N-dimethylformamide was added to a solution of 5-amino-2-methyl-1,3,4-thiadiazole (206) and the resulting solution brought to reflux and boiled for 15 minutes.

However, after treatment with aqueous sodium hydroxide and work-up, examination of the residue by t.l.c. showed traces of three different products which were present in insufficient quantity for isolation.

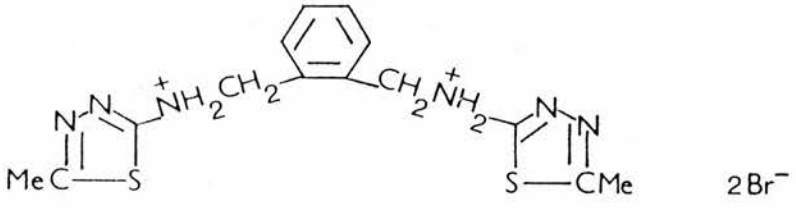
Subsequently it was envisaged that the desired reaction between (193) and (206) might be achieved in a similar manner to that employed in the formation of compound (212).

α,α'-Dibromo-o-xylene (193) and 5-amino-2-methyl-1,2,4-thiadiazole (206) were dissolved in acetonitrile and the solution was boiled for 24 hours. A product crystallised from the cold solution. The ^{1}Hnmr spectrum of this product was consistent with the formation of a bis

a bis adduct, $[(C_3H_5N_3S)_2.C_8H_8]^{2+}$ $2Br^-$ (215).

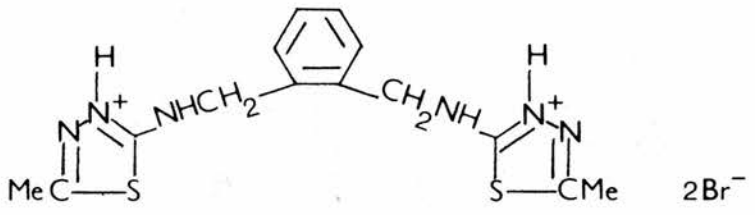


(216(a))



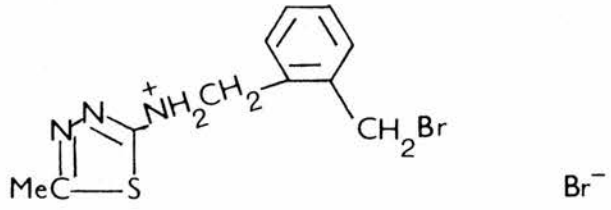
(216(b))

Again, in a manner analogous to the bis adduct (207) two distinct Me signals were observed in the ^{1}Hnmr spectrum, making it inconsistent with any of the structures (216(a)), (216(b)) and (216(c)).

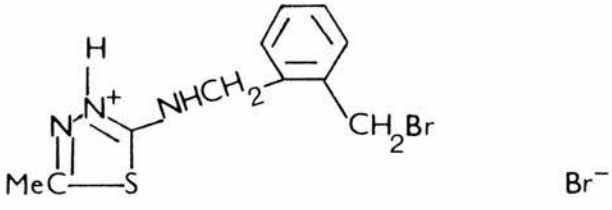


(216(c))

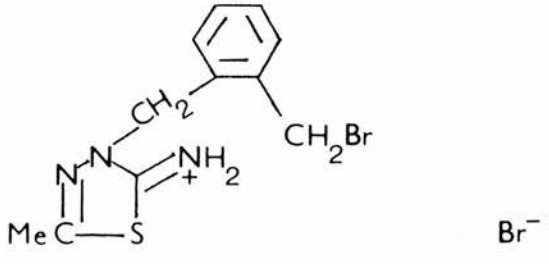
Investigation of the mother liquor showed only the presence of starting materials, and none of the uncyclised salt (217(a)), (217(b)) or (217(c)).



(217(a))

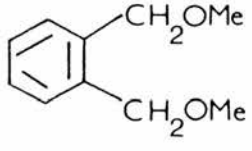


(217(b))



(217(c))

This reaction was also attempted using methanol as solvent. 5-Amino-2-methyl-1,3,4-thiadiazole (206) and α,α'-dibromo-o-xylene (193) were dissolved in methanol and boiled for 24 hours. On cooling, distilled water was added, and this mixture extracted with toluene in order to remove the excess α,α'-dibromo-o-xylene (c.f. the formation of (196)). However, on evaporation of the toluene, the residue was found to be a liquid and not the crystalline compound (193) anticipated. Investigation of this liquid by ^{1}Hnmr spectroscopy and mass spectrometry showed it to be the compound (218) i.e. the methanol solvent had reacted with the dibromo-o-xylene.



(218)

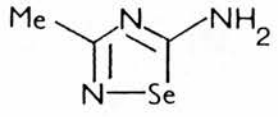
Addition of aqueous sodium hydroxide to the residual aqueous layer and subsequent extraction with dichloromethane did not yield any of the desired products i.e. the free bases of (217(a)), (217(b)) or (217(c)).

A final attempt was made to react the thiadiazole (206) and dibromo-o-xylene (193) in the absence of solvent. In this case, no significant amount of any product was detected after work-up.

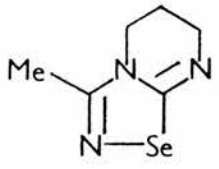
(iii) Attempted Formation of 5,6-Dihydro-3-methyl-4H-pyrimido [1,2-d][1,2,4]selenadiazole

5-Amino-3-methyl-1,2,4-selenadiazole (219) was prepared by the

method of Goerdeler et al[176].



(219)



(220)

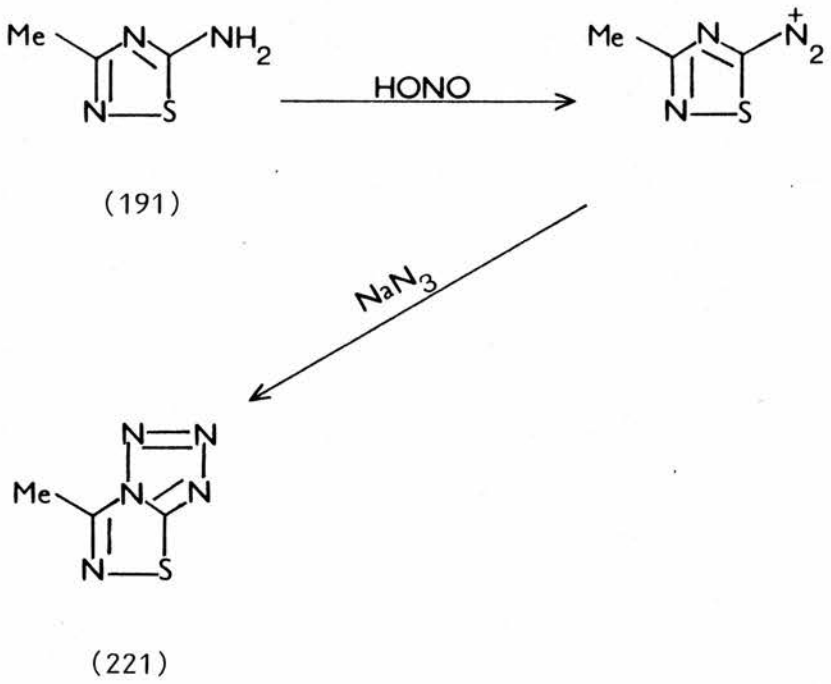
It had been hoped that the selenadiazole (219) would react with 1,3-dibromopropane (205) to yield the product (220). However, all attempts to effect this condensation/cyclisation reaction resulted in the decomposition of the selenadiazole due to loss of selenium.

(iv) Attempted Synthesis of 3-Methyl[4,5-a][1,2,4]thiadiazolo [2,3,4,5]tetrazole

This synthesis was attempted using a modification of the procedure described by Iddon et al[177].

If the thiadiazole (191) were to react according to Scheme 20, the tetrazole (221) would be produced.

Scheme 20



(191)

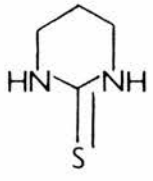
(221)

This route was investigated but apparently no reaction took place. However, it is not possible to say whether the product (221), if formed, would be sufficiently stable not to decompose with evolution of nitrogen. It may be that the reaction proceeds as anticipated, and that the desired product spontaneously decomposes on formation.

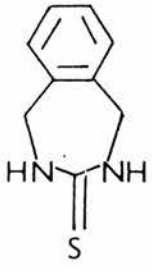
II Reactions of 5,6-Benzo-4,7-dihydro-3-methyl-[4,5-a][1,2,4]thiadiazolo[1,3]diazepine

(i) Thermolysis

The compound (189)[174] has previously been shown to thermolyse in a variety of solvents to give the cyclic thiourea (222).



(222)



(223)

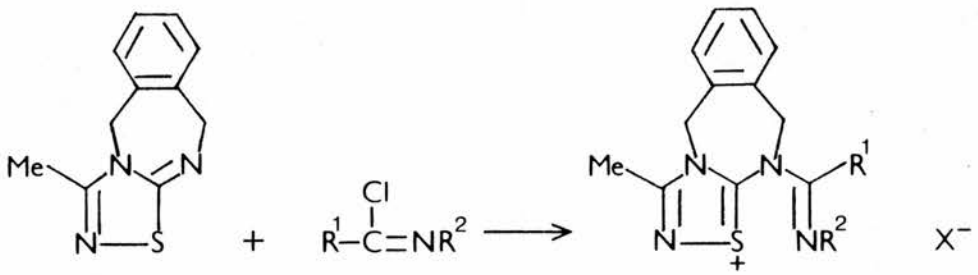
It was thought therefore, that the compound (196) would break down in an analogous manner to give the cyclic thiourea (223).

However, the diazepine (196) proved to be significantly less stable to heat than the pyrimidothiadiazole (189) and decomposed in boiling 1,2,3,4-tetrahydronaphthalene to give seven distinct trace products as shown by t.l.c.

(ii) With Imidoyl Chlorides

The diazepine (196) reacted with imidoyl chlorides (224) to give the chlorides [(225), X=Cl]. Subsequent treatment of these chlorides with perchloric acid yielded the more stable perchlorates [(225), $X=ClO_4$], (Scheme 21).

Scheme 21



(196) (224) (225)

	R^1	R^2
(a)	Ph	Me
(b)	Ph	Ph

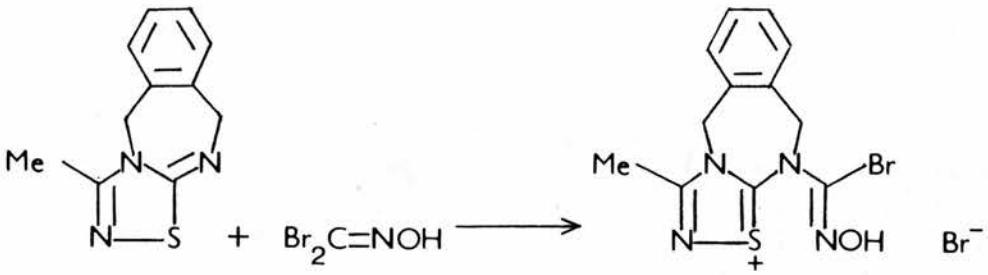
It would also have been desirable to have prepared other analogues of (225) in which R^1 was an alkyl substituent. However, all attempts to prepare the imidoyl chlorides [(224), R^1=Me, R^2=Me,Ph] were unsuccessful. Similarly, attempts to prepare the imidoyl chlorides [(224), R^1=Et, R^2=Me,Ph] were abortive.

A final attempt to prepare a perchlorate [(225), R^1=alkyl, X=ClO_4] was made utilising N-phenyl trimethylacetimidoyl chloride [(224), R^1=CMe_3, R^2=Ph]. However, treatment of the reaction residue with perchloric acid yielded only the perchlorate salt of the diazepine (196).

(iii) With Dibromoformaldoxime

A similar reaction to those with imidoyl chlorides was anticipated for the reaction of the diazepine (196) with dibromoformaldoxine (226), (Scheme 22).

Scheme 22

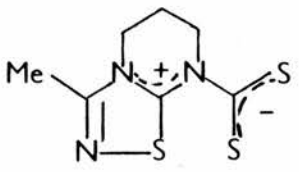


(196) (226)

This reaction did not appear to take place. Instead, it seems that the diazepine (196) effected dehydrobromination of the oxime (226) resulting in the hydrobromide salt of the diazepine.

(iv) With Carbon Disulphide

The compound (189) has been shown to react with carbon disulphide[174] to form a product which was assigned the zwitterionic structure (227) on the basis of its high insolubility and the absence of an $M^{+\cdot}$ peak in the mass spectrum.



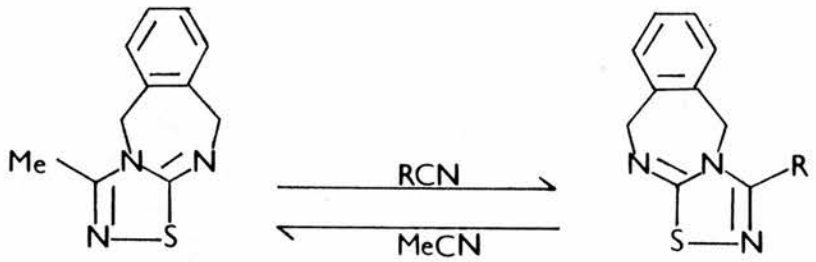
(227)

It was decided to attempt a similar reaction between the diazepine (196) and carbon disulphide. However, even after stirring a solution of the base (196) with excess carbon disulphide, no reaction was observed.

(v) With Nitriles

It was hoped that the diazepine (196) would react with nitriles in a similar manner to the pyrimidothiadiazole (189)[174], (Scheme 23).

Scheme 23



(196) (228)

Firstly, a simple exchange reaction was attempted using acetonitrile-d_3. The diazepine (196) was dissolved in acetonitrile-d_3 and the resulting solution boiled. After 26 hours, the ratio of deuterated product [(228), R=CD_3] to non-deuterated product (196), as monitored by the reduction in the methyl integral of the methyl signal in the ^{1}Hnmr spectrum, was 1:3.

This contrasts markedly with the behaviour of the pyrimidothiadiazole (189) which had undergone complete exchange with deuterated acetonitrile under analogous conditions after a period of 14 hours.

A second reaction was carried out identical to the first except that a small volume of dimethylsulphoxide-d_6 was added, resulting in an increase in internal temperature of the refluxing solution to ca. 90°C.

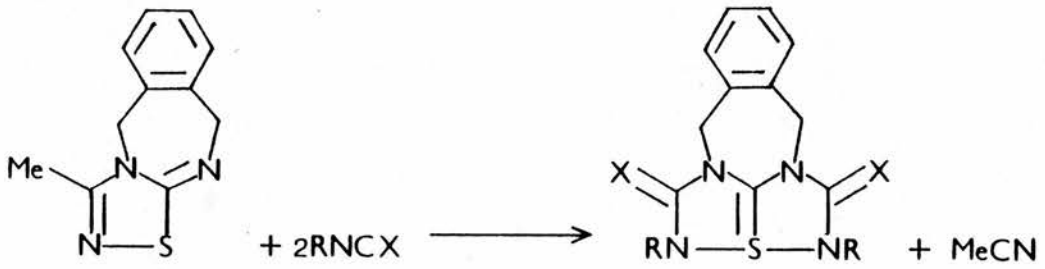
This increase in temperature resulted, after 24 hours, in a ratio of 7:2 in favour of the deuterated product. Complete exchange was never observed.

An analogous reaction employing benzonitrile in place of deuterated acetonitrile was attempted. However, none of the desired product, [(228), R=Ph], was detected. Instead, the diazepine (196) appeared to decompose at the temperatures employed, and at lower temperatures no reaction was observed.

(vi) With Isocyanates and Isothiocyanates

The diazepine (196) reacted with isocyanates and isothiocyanates (229) to give compounds of type (230), (Scheme 24).

Scheme 24

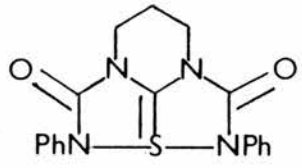


(196) (229) (230)

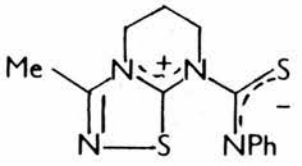
	R	X
(a)	Me	O
(b)	cyclohexyl	O
(c)	Ph	O
(d)	$PhCH_2$	O
(e)	p-tolyl	O
(f)	Me	S
(g)	Bu	S
(h)	Ph	S
(i)	$PhCH_2$	S

These compounds are similar to those obtained by Beer[112].

The structures of compounds (230) were assigned on the basis of the symmetry shown in their ^{1}Hnmr spectra, and their similarity to the compound (231), prepared by Beer[112] for which a crystal structure was obtained[130].



(231)

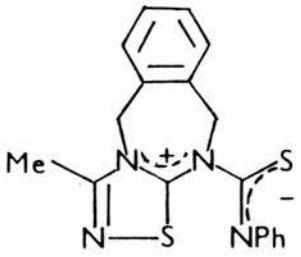


(232)

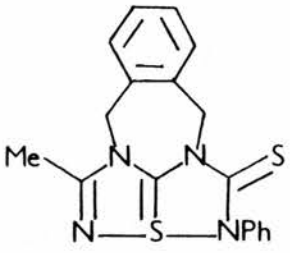
It is of interest that when the diazepine (196) was treated with phenyl isothiocyanate at room temperature, the product obtained was not (230(h)), but a compound which, from its ^{1}Hnmr spectrum and its microanalysis, was a 1:1 adduct of the diazepine and phenyl isothiocyanate.

A zwitterion of the type (232) was obtained from the reaction of the pyrimidothiadiazole (189) with phenyl isothiocyanate[174]. The structure of this zwitterion (232) was assigned by means of its ^{1}Hnmr spectrum which showed a positively charged pyrimidothiadiazole nucleus, and by an X-ray crystal structure determination.

In the case of the 1:1 adduct of the diazepine (196) with phenyl isothiocyanate, the ^{1}Hnmr shifts are not significantly different from those of the diazepine (196) itself, and hence in the absence of an X-ray crystal structure determination the product may be formulated as either (233(a)) or (233(b)).



(233(a))



(233(b))

The mass spectrum of this 1:1 adduct did not show an $M^{+\cdot}$ peak, but only the superimposed spectra of the diazepine (196) and phenyl isothiocyanate. This compares with the behaviour of the zwitterion (232). It should, however, be mentioned that the compounds (230) also do not show an $M^{+\cdot}$ peak in their mass spectra and so this behaviour is not conclusive evidence for an open, zwitterionic structure.

The reaction between the diazepine (196) and the isocyanate [(229), R=tosyl, X=O] gave a sticky solid which on examination by ^{1}Hnmr spectroscopy showed three methyl signals at δ2.318, δ2.477 and δ3.477. This observation is consistent neither with a 1:1 adduct nor with the anticipated product [(230), R=tosyl, X=O]. In the former case two methyl signals should be present, and in the latter case one signal for the two equivalent methyl groups.

Reactions of the diazepine (196) with the isothiocyanates [(229): R=t-butyl, allyl, cyclohexyl, p-tolyl; X=S] were unsuccessful.

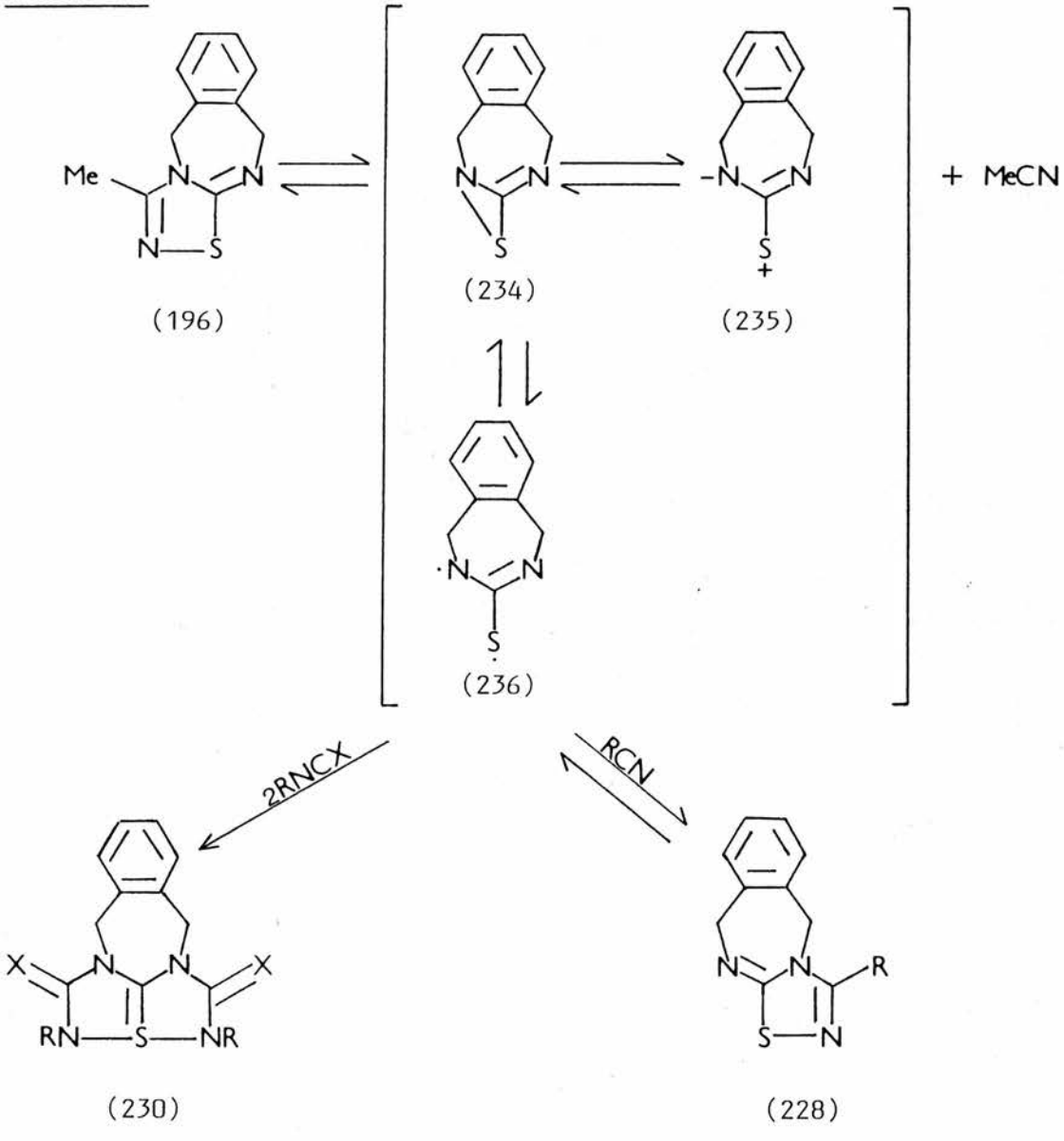
(vii) Mechanism of the Reaction of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine with nitriles or iso(thio)cyanates

Two general mechanisms of formation of the products (228) and (230) can be postulated. The first is an elimination/cycloaddition reaction. Alternatively the reaction could proceed by a cycloaddition/elimination mechanism.

(a) Elimination/Cycloaddition Mechanism

This is a two step process involving initially a unimolecular decomposition of compound (196) with loss of acetonitrile to form a thiaziridineimine (234) or its ring-opened dipolar form (235) or a singlet diradical species (236), [which could be formed either from compound (196) directly or via the thiaziridineimine (234)]. Subsequent addition of the appropriate nitrile or iso(thio)cyanate would then result in the observed products, (Scheme 25).

Scheme 25

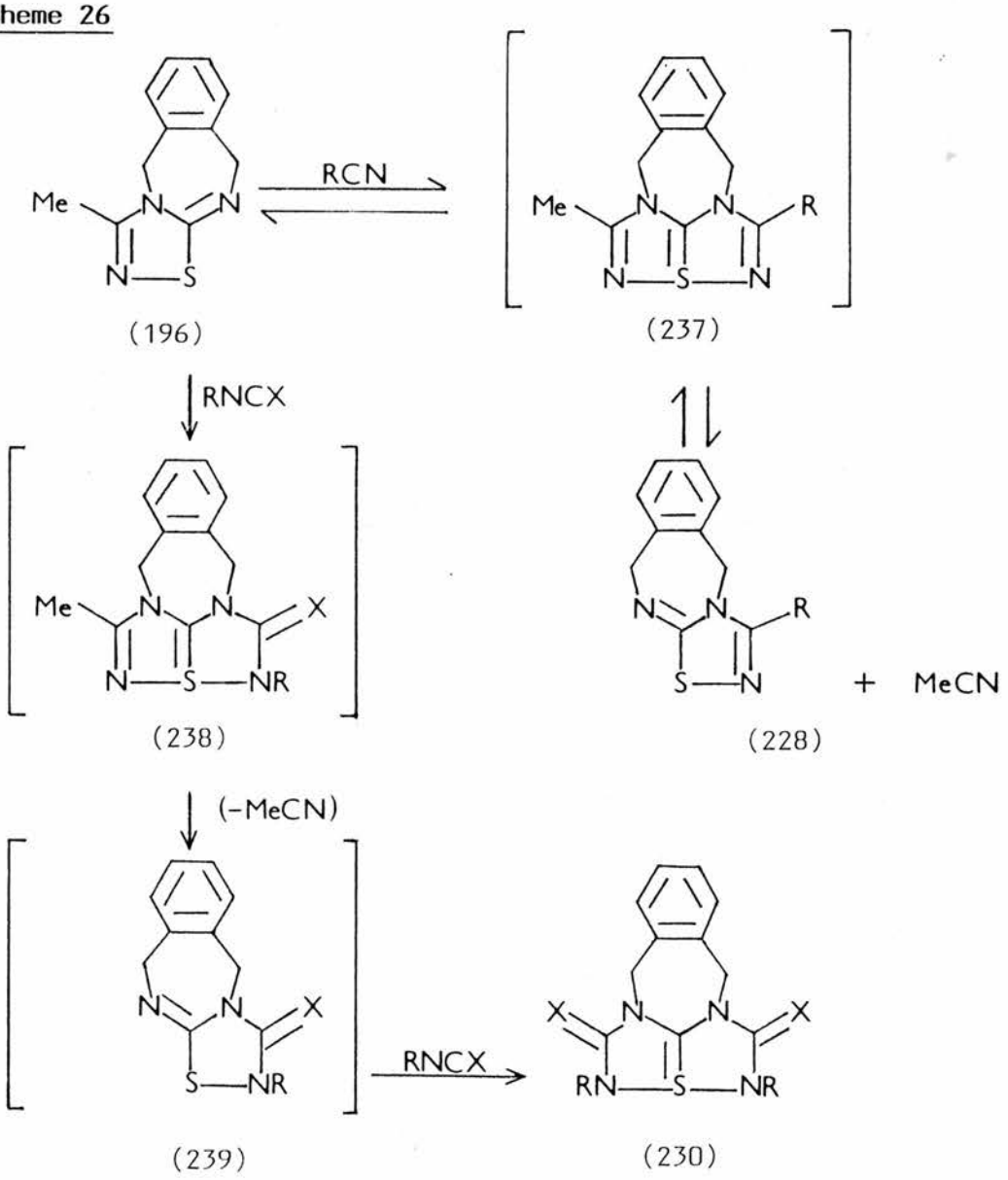


A two-step unimolecular decomposition mechanism of this type has been proposed by L'abbé[150] on the grounds of kinetic data to describe the reaction of 1,2,3,4-thiatriazolines (141) with isothiocyanates.

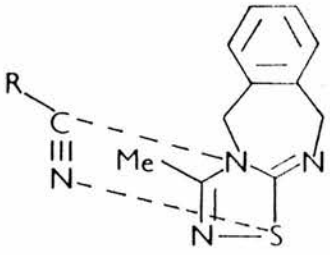
(b) Cycloaddition/Elimination Mechanism

This mechanism is bimolecular and involves firstly the addition of the nitrile or the isothiocyanate to give pentaheterapentalenes of type (237) or (238) with subsequent loss of acetonitrile to give the products (228), or loss of acetonitrile to give (239) followed by addition of a second mole of iso(thio)cyanate to give the products (230). In such a mechanism, (196) would be behaving as a masked 1,3-dipole, (Scheme 26).

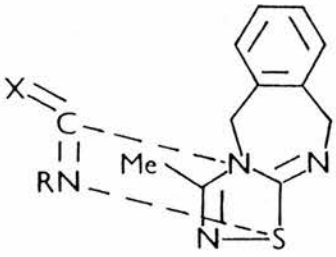
Scheme 26



An alternative to this bimolecular triheterapentalene intermediate could be proposed in which the incoming nitrile or iso(thio)cyanate attacks the same side of the diazepine (196) as the outgoing acetonitrile, viz. (240) or (241).



(240)



(241)

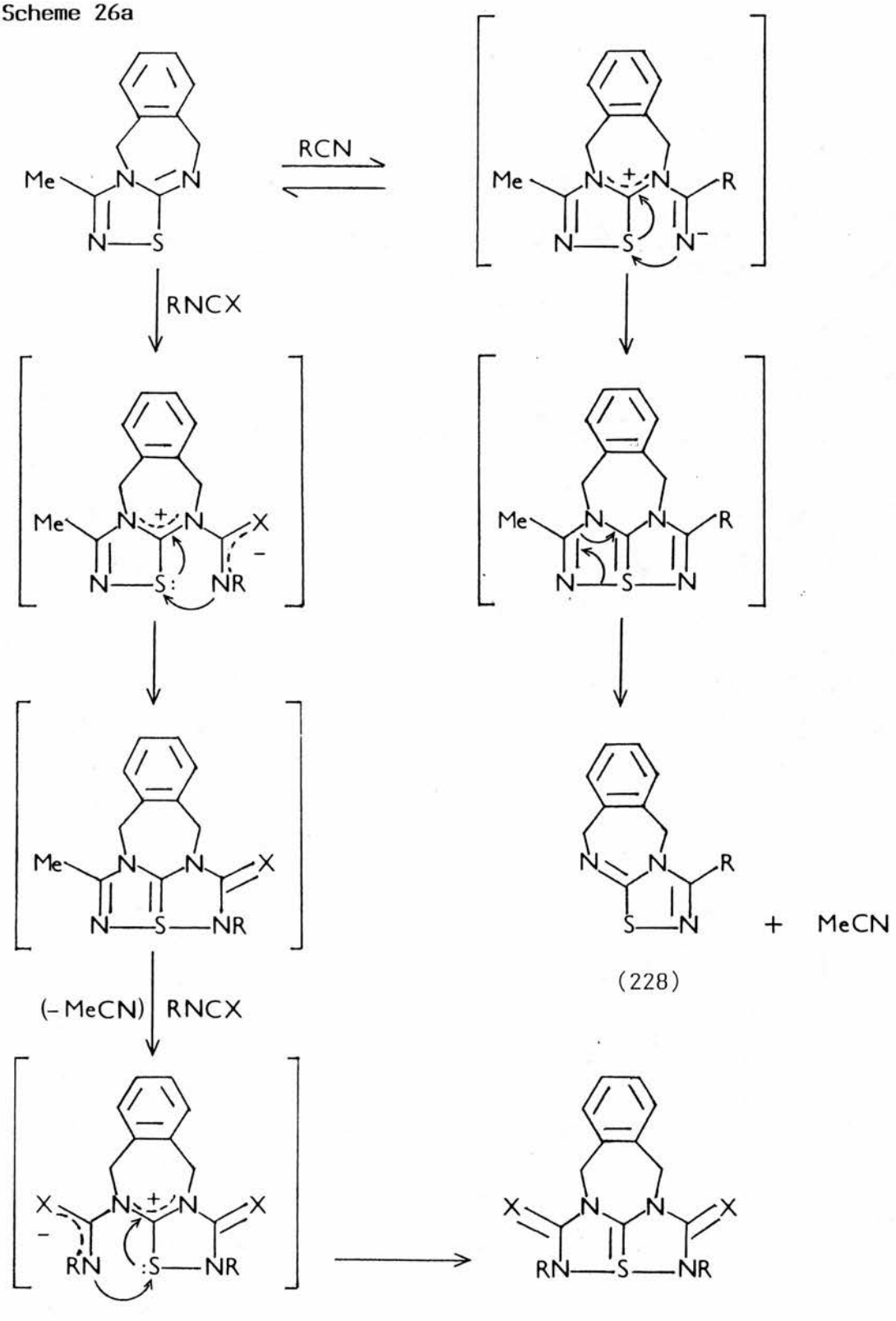
These two bimolecular mechanisms are practically indistinguishable due to the symmetrical nature of the bridging substituent in the diazepine (196).

A bimolecular mechanism was proposed by L'abbé[110] for the reaction of 5-arylimino-1,2,3,4-thiatriazolines (150) with isothiocyanates, again, on the basis of kinetic data.

A stepwise mechanism for the addition of nitrile or iso(thio)-cyanate cannot be excluded i.e. in which the formation of a zwitterionic intermediate[145,153] is involved, (Scheme 26(a)).

It is impossible with the information available to make any definite distinction between these two general mechanisms (a) or (b). However, the formation of the 1:1 adduct (233) lends weight to the idea that these reactions, at least in the case of the iso(thio)cyanates, proceed via a bimolecular mechanism.

Scheme 26a



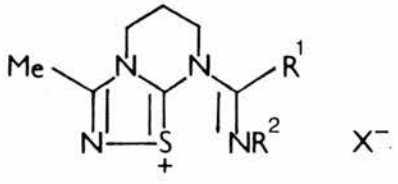
(228)

(230)

III Reactions of 5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole

(i) With Imidoyl Chlorides

The pyrimidothiadiazole (189) reacted with imidoyl chlorides to give compounds [(242), X=Cl]. Treatment of these chlorides with perchloric acid yielded the more stable perchlorates [(242), $X=ClO_4$].



(242)

	R^1	R^2
(a)	Ph	Me
(b)	Ph	Ph

Various attempts were again made to form compounds of type (242) in which R^1=alkyl.

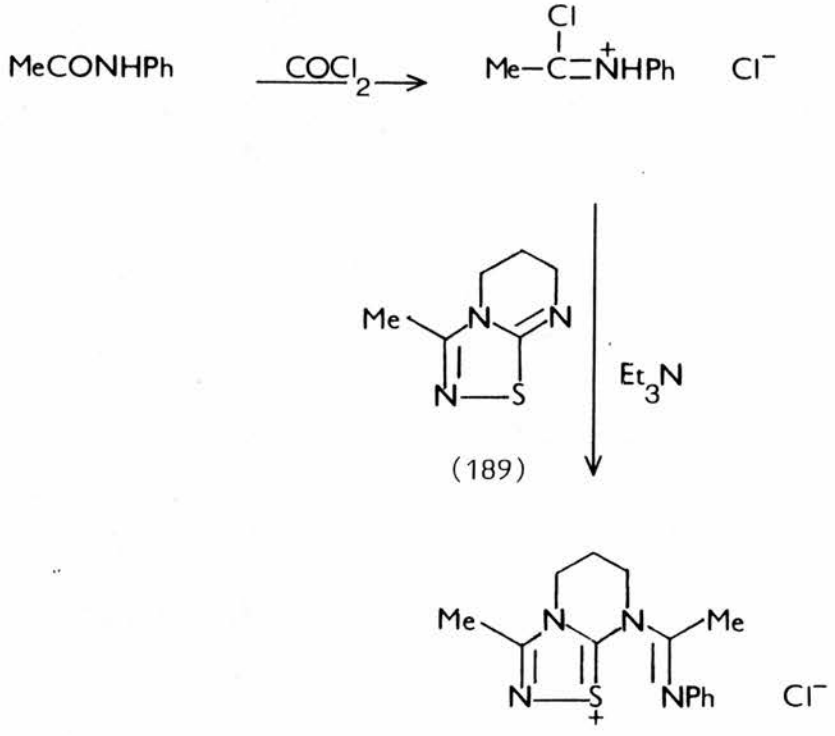
Formation of both N-methyl acetimidoyl chloride and N-phenyl acetimidoyl chloride [(242), R^1=Me, R^2=Me,Ph] was investigated. Syntheses were attempted by treating the corresponding amides, N-methyl acetamide and N-phenyl acetamide, with either thionyl chloride or oxalyl chloride. Again, the C-alkyl group appears to cause the imidoyl chlorides to be too unstable to isolate.

In the light of this observation, it was decided to try to form the imidoyl chloride in situ.

N-Phenyl acetamide was treated with phosgene for 1.5 hours after which time a solution of the pyrimidothiadiazole (189) was

added to the reaction mixture followed by triethylamine, (Scheme 27).

Scheme 27

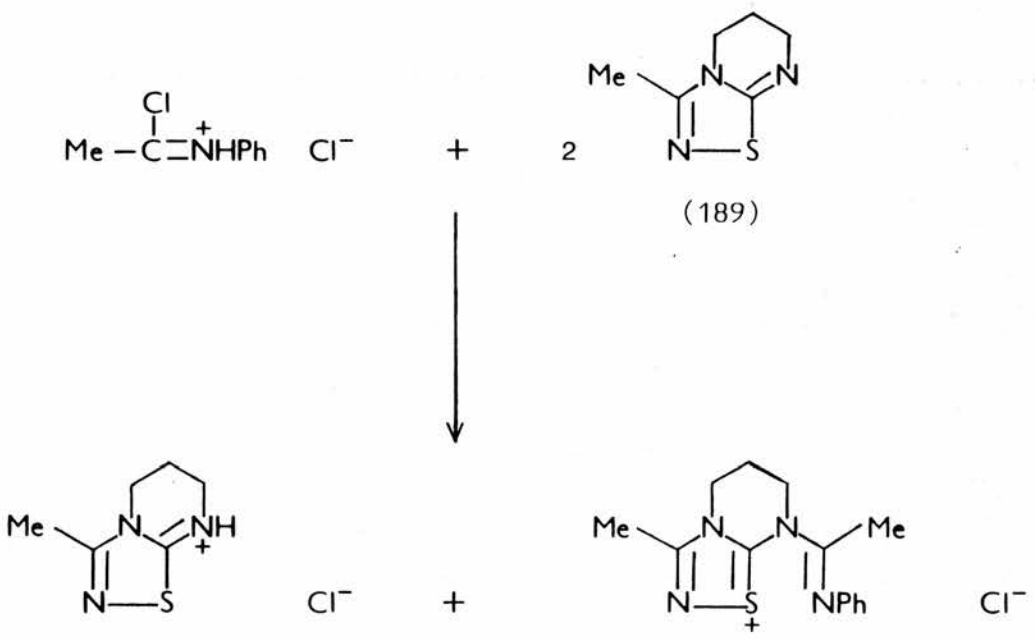


Triethylamine hydrochloride was indeed obtained from this reaction. The other product, obtained in trace amount, was not the anticipated imidoyl chloride but the hydrochloride salt of (189). It would appear that the pyrimidothiadiazole (189) is sufficiently basic to deprotonate the imidoyl chloride salt.

Deprotonation of the imidoyl chloride prior to addition of the pyrimidothiadiazole is thus ruled out due to the instability of the imidoyl chloride. Deprotonation by the addition of a base after the addition of (189) is unsuccessful. A remaining possibility appeared to be to treat the imidoyl chloride salt with a 2:1 excess of the pyrimidothiadiazole (189) in the hope that the first equivalent

of (189) would deprotonate the salt which would then react with the second equivalent of (189) to give the desired product, (Scheme 28).

Scheme 28



On examination by ^{1}Hnmr spectroscopy of the solid thus obtained, it was found to contain a mixture of the hydrochloride salt of (189) and the pyrimidothiadizole (189) itself.

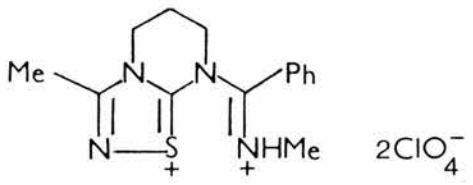
Thus it seems that N-phenyl acetimidoyl chloride is not stable for a sufficient length of time to react with the pyrimidothiadiazole.

The reactions of the pyrimidothiadiazole (189) with N-methyl trimethylacetimidoyl chloride and N-phenyl trimethylacetimidoyl chloride were also attempted. In these cases, ^{1}Hnmr data obtained indicated the presence of a mixture of the desired products

[(242), R^1=CMe_3, R^2=Me,Ph] and the hydrochloride of (189). Further investigation of the reaction with N-phenyl trimethylacetimidoyl chloride was carried out. Two identical reaction mixtures were prepared. The first was worked up after standing at room temperature for 30 minutes and the second after standing at room temperature for 24 hours.

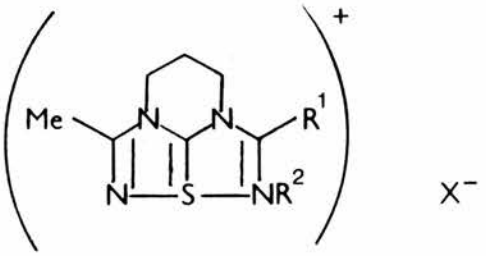
The ratio of the apparent product [(242), R^1= CMe_3, R^2=Ph] to hydrochloride salt was higher for the reaction time of 30 minutes. This observation appears to suggest that the desired product is not stable and decomposes immediately.

Treatment of the pyrimidothiadiazole (189) with N-methyl benzimidoyl chloride followed by perchloric acid gave not only the product (242(a)), but by varying the amount of perchloric acid used, also the product (243).



(243)

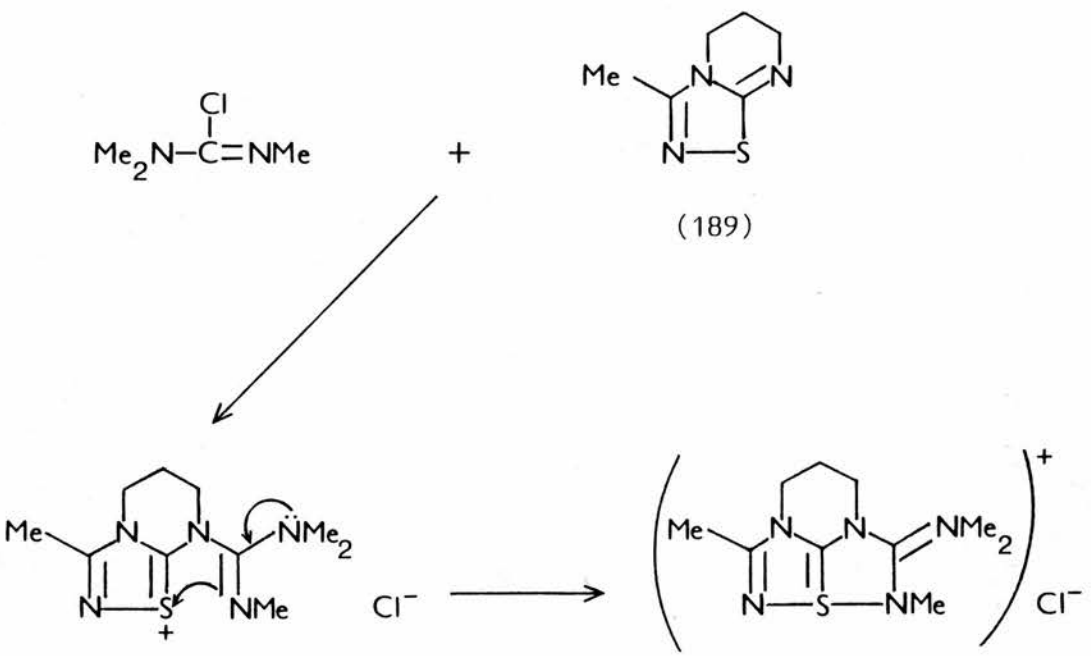
This is an interesting observation because it suggests that there may be sufficient electron density on the nitrogen atom (N-R^2) in the products (242) to effect ring closure and give the triheterapentalenium salt (244).



(244)

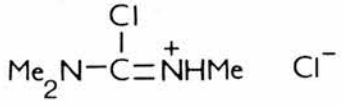
With this in mind, the formation of N-methyl dimethylcarbamidoyl chloride was attempted. It was hoped that this would react with the pyrimidothiadiazole (189), and that the higher electron density on the imino nitrogen atom would result in ring closure, (Scheme 29).

Scheme 29



(189)

However, although the salt of the imidoyl chloride (245) was formed, any attempts to deprotonate it were unsuccessful.



(245)

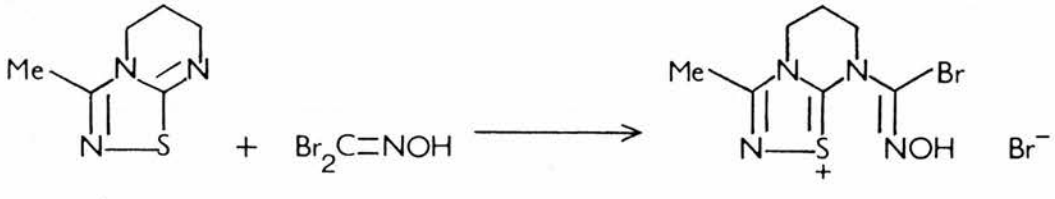
Moreover, an attempt to react the imidoyl chloride in situ by utilising a 2:1 excess of the pyrimidothiadiazole (189), thus allowing (189) to act as a base and deprotonate the salt (245) in the initial stage of the reaction, was unsuccessful.

It is possible that the greater electron density generated on the imidoyl nitrogen atom binds the proton more tightly to the imidoyl chloride moiety thus preventing deprotonation.

(ii) With Dibromoformaldoxime

An analogous reaction to that of the imidoyl chlorides with (189) was expected for the reaction of the pyrimidothiadiazole (189) with dibromoformaldoxime, (Scheme 30).

Scheme 30



(189) (226)

However, as with the diazepine (196), the sole product was the hydrobromide of (189) and not the expected addition product.

It was thought that the reactive fragment (246) which must be formed on loss of hydrogen bromide from the oxime (226) could still react with (189) to give the desired product.

(246)

A solution of the pyrimidothiadiazole (189), and dibromoformaldoxime (226) in acetonitrile was treated with triethylamine and subsequently boiled for 10 minutes. Triethylamine hydrobromide was obtained as a crystalline precipitate. Examination of the mother liquor by t.l.c. indicated the presence of at least ten distinct products and hence this approach was pursued no further.

(iii) With Isocyanates and Isothiocyanates

The pyrimidothiadiazole (189) reacted with isocyanates and isothiocyanates (229) to give compounds of the type (247), (Scheme 31), in a similar manner to those reactions of the diazepine (196) with isocyanates and isothiocyanates which have been discussed previously, (Scheme 24).

Scheme 31

(189) (229) (247)

	R	X
(a)	Me	O
(b)	cyclohexyl	O
(c)	Ph	O
(d)	p-tolyl	O
(e)	Me	S
(f)	Bu	S
(g)	allyl	S
(h)	cyclohexyl	S
(i)	Ph	S
(j)	$PhCH_2$	S
(k)	p-tolyl	S

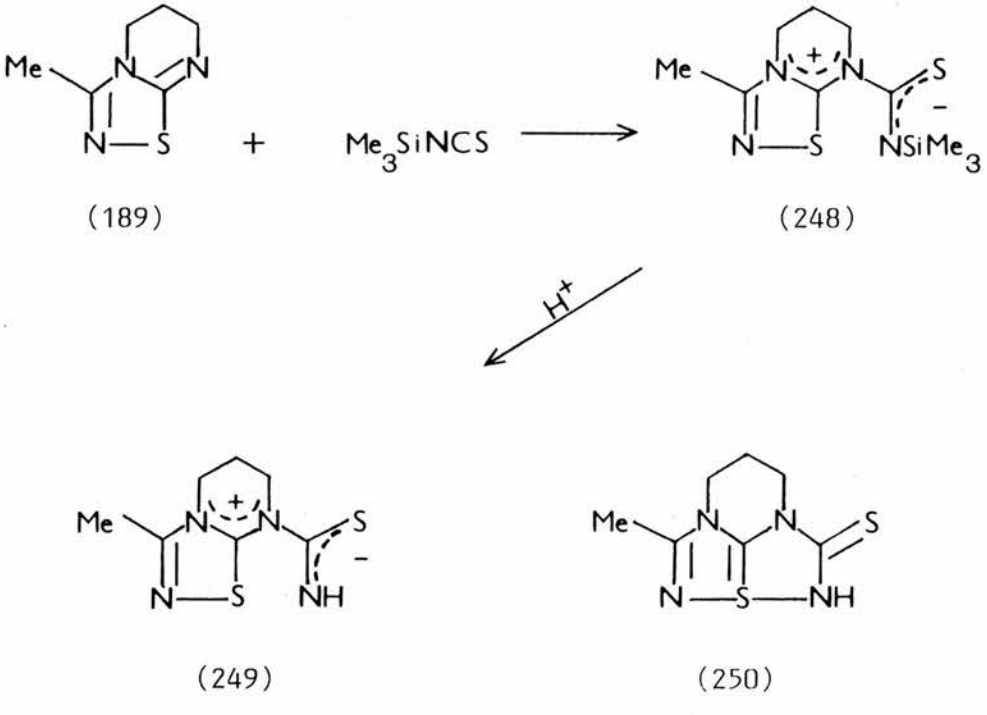
Analogous reactions of (189), with the isocyanates [(229), R=$PhCH_2$, $ClSO_2$, X=O] and the isothiocyanates [(229), R=t-butyl, t-octyl, X=S] were attempted with no success. In the case of the tertiary butyl and tertiary octyl isothiocyanates, the lack of reaction may simply be a consequence of steric hindrance both of these groups being large and bulky.

The reaction of the pyrimidothiadiazole (189) with p-toluenesulphonyl isocyanate [(229), R=tosyl, X=O] gave a tacky solid which on examination of its ^{1}Hnmr spectrum did not show the expected symmetrical structure. Again, as with the diazepine (196), the ^{1}Hnmr spectrum showed three methyl signals. These had chemical shift values of δ2.352, δ2.419, and δ2.529. If either a 1:1 adduct

or a product of type (247) had been formed, two methyl signals at most should have been observed.

It is known[174] that the pyrimidothiadiazole (189) reacts with isothiocyanates to give zwitterions of type (232). Since stable triheterapentalenes containing N-H in the heteroatom three-centre bond sequence have not previously been prepared, it was decided to attempt the reaction of the pyrimidothiadiazole (189) with trimethylsilyl isothiocyanate. If the zwitterion (248) were to be formed, the trimethylsilyl group could then be hydrolysed off leaving a product which may be formulated as either the zwitterion (249) or the triheterapentalene (250), (Scheme 32).

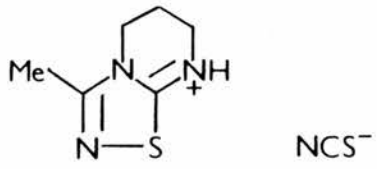
Scheme 32



(189) (248)

(249) (250)

The product obtained from the initial reaction was not the zwitterion (248), but the salt (251), whose structure was confirmed by an unequivocal synthesis from the hydrochloride salt of (189) and sodium thiocyanate.



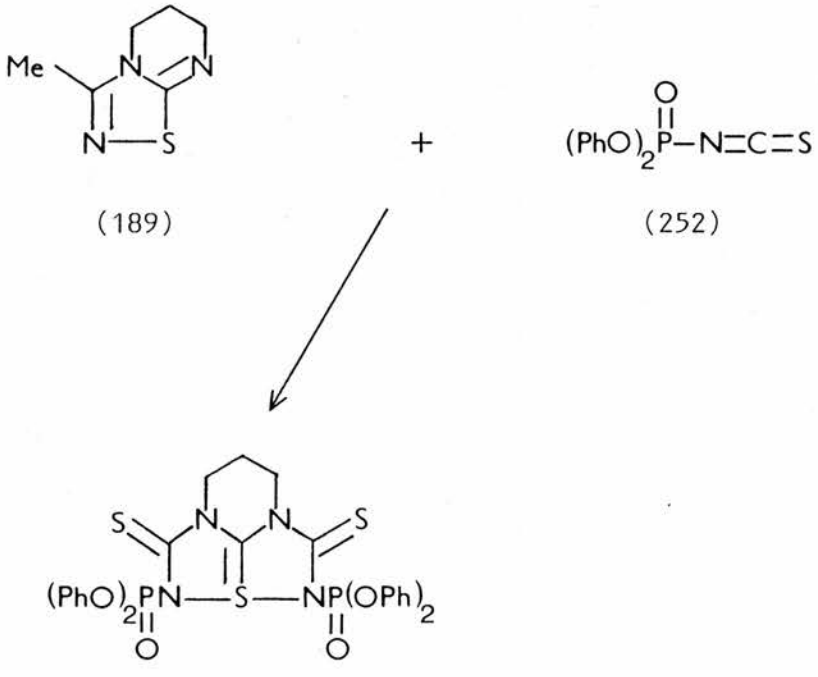
(251)

In a parallel experiment a solution of trimethylsilyl isothiocyanate in toluene was left standing at room temperature for 24 hours. The solution was then tested with ferric chloride, and only a faint red colouration arising from the presence of free thiocyanate was observed. This suggests that the hydrolysis reaction resulting in the product (251) must be base catalysed by the pyrimidothiadiazole (189).

(iv) With Diphenyl Phosphoroisothiocyanatidate

It was hoped that the pyrimidothiadiazole (189) would react with diphenyl phosphoroisothiocyanatidate (252) to produce a product (253), (Scheme 33).

Scheme 33



(189) (252)

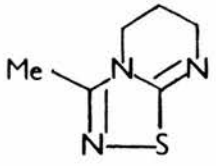
(253)

A mixture of (189) and (252) was heated at 145°C on an oil bath. Addition of ether to the cooled mixture yielded a dark brown precipitate which became oily on attempted filtration. This reaction was pursued no further.

(v) With Chloromethyl Thiocyanate

It was thought that chloromethyl thiocyanate (254) might react with (189) in the manner shown in Scheme 34 to give compound (255) or (256).

Scheme 34

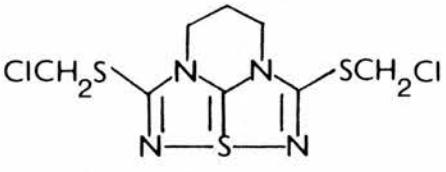


(189)

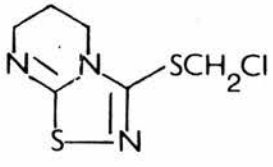
+

$ClCH_2SCN$

(254)



(255)

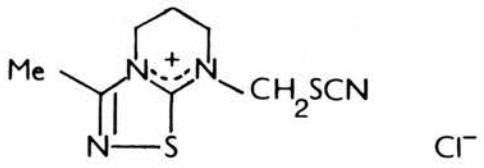


(256)

Two sets of conditions were employed. The first involved heating a mixture of the pyrimidothiadiazole (189) and chloromethyl thiocyanate (254) at 145°C for 15 minutes. Alternatively, a solution of the two reactants, (189) and (254), in dichloromethane was left standing at room temperature for 4 hours.

In both cases, a tacky oil resulted which showed no worthwhile products on examination by t.l.c.

It is possible that the reaction taking place involves the cleavage of the carbon-chlorine bond of the thiocyanate to form a product of the type (257) which is not stable and subsequently decomposes.

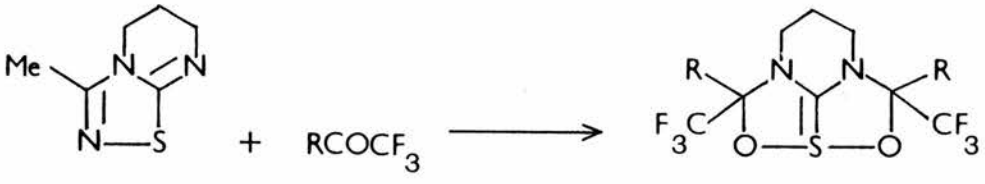


(257)

(vi) With 2,2,2-Trifluoroacetophenone or Hexafluoroacetone

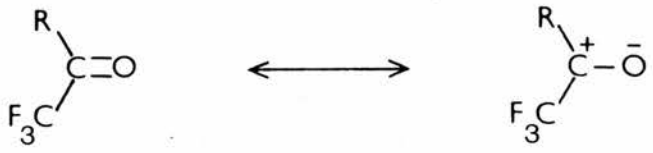
It was thought that the reaction between the pyrimidothiadiazole (189) and trifluoroacetophenone [(258), R=Ph] or hexafluoroacetone [(258), R=CF_3] might proceed according to scheme 35.

Scheme 35



(189) (258)

It was envisaged that the large number of fluorine groups present in (258) might sufficiently polarise the carbon-oxygen double bond (259) to allow reaction with the masked 1,3-dipole of (189) to take place.



(259)

The reactants (189) and (258) were heated at 145°C for 15 minutes but no reaction was observed.

On increasing the temperature by ca. 25°C a trace of a product was observed by t.l.c. Increasing the temperature still further to 179°C by employing o-dichlorobenzene, a high boiling, inert solvent, resulted again in the aforementioned product.

This trace product was tentatively identified as the cyclic thiourea (222) by t.l.c. comparison with an authentic sample.

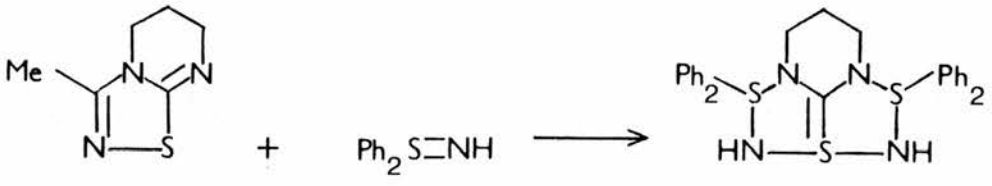
The cyclic thiourea (222) is known to be the product attained on thermolysis of the pyrimidothiadiazole (189) in high boiling solvents[174]. It would appear, therefore, that the reaction taking place is not the desired addition reaction but, as a consequence of the high temperatures employed, the thermolysis of the pyrimidothiadiazole (189). Analogous addition reactions between (189) and iso(thio)cyanates (229), which have been discussed previously, went to completion under similar conditions

with no thermolysis products being detected. These observations suggest that neither 2,2,2-trifluoroacetophenone nor hexafluoroacetone are sufficiently reactive to effect the postulated addition reaction.

(vii) With S,S-Diphenyl Sulphilimine

If the pyrimidothiadiazole (189) were to behave as a masked 1,3-dipole towards S,S-diphenyl sulphilimine (260), the reaction shown in Scheme 36 could take place.

Scheme 36



(189) (260) (261)

S,S-Diphenyl sulphilimine (260) and pyrimidothiadiazole (189) were mixed and heated at 145°C for 15 minutes.

No reaction was observed, however, and attempts to employ more vigorous reaction conditions were not pursued because it was thought that such reaction media would result in the thermolysis product (222) of the pyrimidothiadiazole rather than the desired product (261).

IV Reactions of 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole

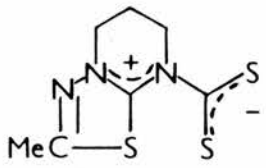
(i) Thermolysis

As compound (189) had been shown to produce the cyclic thiourea (222) on thermolysis[174], it was thought that the pyrimidothiadiazole (212) might behave in an analogous manner on thermolysis to produce the same cyclic thiourea (222).

A solution of compound (212) in 1,2,3,4-tetrahydronaphthalene was boiled in an inert atmosphere for 90 hours. After this time, t.l.c. examination of the reaction mixture showed only the presence of the pyrimidothiadiazole (212). Thus, compound (212) was found to be thermally very stable under conditions in which the base (189) undergoes reduction thermolysis.

(ii) With Carbon Disulphide

The pyrimidothiadiazole (212) was treated with an excess of carbon disulphide. After stirring at room temperature for five minutes, the excess carbon disulphide was removed leaving a pale pink powder which by analogy with the pyrimidothiadiazole adduct (227)[174] should have the structure (262).



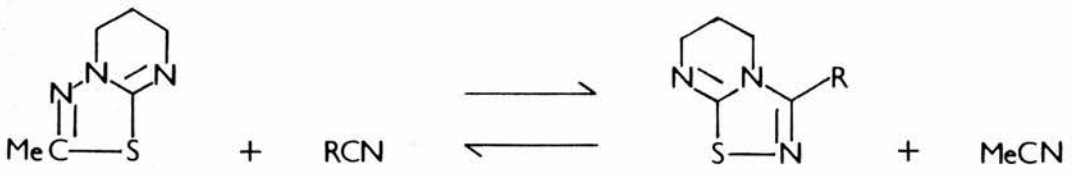
(262)

However, this product decomposed spontaneously on removal of the excess carbon disulphide to leave the pyrimidothiadiazole (212), and neither spectra nor analysis could be obtained.

(iii) With Nitriles

If the pyrimidothiadiazole (212) were to undergo exchange reactions with nitriles in a manner analogous to those undergone by the pyrimidothiadiazole (189)[174], it should yield identical products to those from the pyrimidothiadiazole (189) because the masked 1,3-dipole present in both of the pyrimidothiadiazoles (189) and (212) directs the mode of addition of the nitrile, (Scheme 37).

Scheme 37



(212) (263)

If in fact such a reaction between compound (212) and acetonitrile were to take place, the resulting product would be the pyrimidothiadiazole (189).

The pyrimidothiadiazole (212) was dissolved in acetonitrile, and the resulting solution boiled for 8 days. An examination of the reaction mixture by t.l.c. after this time showed only the presence of the pyrimidothiadiazole (212). Thus no rearrangement had taken place.

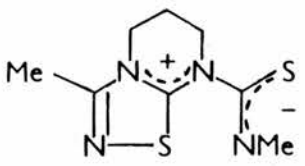
This reaction mixture was left at room temperature for a further 11 days after which time none of the desired product (189) was detected.

An analogous exchange reaction was attempted utilising benzonitrile in place of acetonitrile. Again, after work-up, the pyrimidothiadiazole (212) was recovered in 80% yield, and none of the anticipated product [(263), R=Ph] was observed. This was ascertained by running a t.l.c. of the reaction mixture against an authentic sample[174] of [(263), R=Ph].

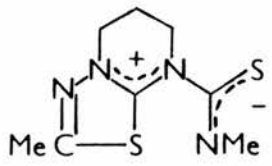
Thus, the compound (212) was found to be chemically very stable under conditions in which the pyrimidothiadiazole (189) undergoes complete exchange.

(iv) With Methyl Isothiocyanate

It is known[174] that the pyrimidothiadiazole (189) reacts with methyl isothiocyanate in toluene to give the zwitterion (264).



(264)



(265)

The pyrimidothiadiazole (212) was found to react in a similar manner to give the product (265).

As has already been discussed, (Scheme 31), the pyrimidothiadiazole (189) has been found to react with methyl isothiocyanate in dichloromethane to give compound (247(e)). Similarly, it was thought that the reaction of (212) with methyl isothiocyanate would also yield the product (247(e)).

The compound (212) was dissolved in dichloromethane, methyl isothiocyanate added, and the resulting solution left to stand at room temperature for 72 hours, and subsequently worked up as before.

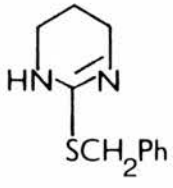
However, the product thus obtained was found to be the zwitterionic product (265), and not the anticipated product (247(e)).

An attempt to attain (247(e)) from the pyrimidothiadiazole (212) and methyl isothiocyanate by employing more vigorous reaction conditions (boiling the solution in the absence of solvent) was unsuccessful.

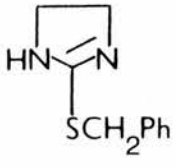
V Reactions of Possible Monocyclic Precursors of Triheterapentalenes

(i) Thermolysis

During the course of this work as a result of investigations already carried out in this area[174], the thermolysis reactions of compounds of type (266) and (267) were studied over a range of temperatures.



(266)



(267)

Compounds (266) and (267) were synthesised by treating the corresponding cyclic thioureas with benzyl bromide. Compound (266) has been prepared by an alternative route by D'Angeli et al[178].

This work was undertaken in order to investigate the possibility of a diradical species being formed during the reaction of the pyrimidothiadiazole[174] (189) or the diazepine (196) with heterocumulenes and nitriles.

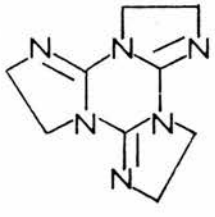
Solvents capable of functioning as hydrogen donors, namely isopropyl benzene and 1,2,3,4-tetrahydronaphthalene, were employed in the hope that they would reduce any radical intermediates formed on thermolysis.

2-Benzylthio-3,4,5,6-tetrahydropyrimidine (266) was found to decompose slowly in boiling isopropyl benzene [bp 152-154°C] to give 2-hexahydropyrimidinethione (222) in 23% yield.

2-Benzylthio-3,4,5,6-tetrahydropyrimidine (266) decomposed similarly in boiling 1,2,3,4-tetrahydronaphthalene (bp 207°C) to give the thiourea (222) in 21% yield after recrystallisation from ethanol. These results are in accordance with previous findings[174].

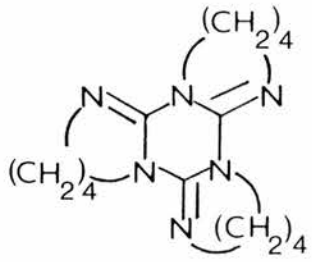
The thiourea (222) formed on thermolysis of (266) is a reduction product. This is indicative of radical formation under the conditions employed for thermolysis.

In contrast to these observations, 2-benzylthioimidazolidine (267) decomposed slowly in refluxing isopropyl benzene resulting in a product which is tentatively formulated as (268).

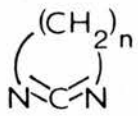


(268)

A similar trimeric species (269) was obtained by Richter et al[179] while attempting to synthesise the carbodiimide [(270), n=4].



(269)



(270)

They assumed that the trimer (269) was formed via the carbodiimide [(270), n=4] which they considered to be very labile.

This trimer (269) showed an intense I.R. absorption at 1630cm^{-1} for C=N. This absorption is near that (1650cm^{-1}) obtained for the thermolysis product of 2-benzylthioimidazolidine.

The microanalytical data obtained for the thermolysis product are consistent with the postulated structure (268).

[Found : 52.76%C 5.92%H 41.53%N

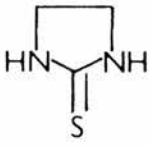
Required for (268): 52.93%C 5.92%H 41.15%N]

The sole singlet at δ3.725 in the ^{1}Hnmr spectrum of the thermolysis product could be the result of accidental magnetic equivalence of the hydrogen atoms, and as such could be consistent with structure (268).

Finally, the mass of the proposed structure (268) is 204. This corresponds to the highest m/z value present in the mass spectrum of the thermolysis product of 2-benzylthioimidazolidine.

Thermolysis of 2-benzylthioimidazolidine in 1,2,3,4-tetra-

hydronaphthalene yielded a mixture of products. Examination of the ^{1}Hnmr spectrum obtained for this mixture showed it to be the superimposed spectra of 2-imidazolidinethione (271) and the thermolysis product obtained in isopropyl benzene.



(271)

The mass spectrum obtained for this mixture was also consistent with the superimposed spectra of (271) and the thermolysis product obtained in isopropyl benzene.

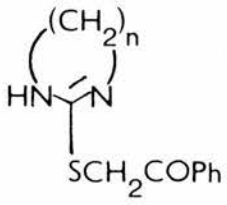
Richter et al[179] found that lower temperatures were more favourable to the formation of the trimer (269). The foregoing results are consistent with this observation, the postulated trimer (268) alone being formed at a temperature of ca. 152°C, while a mixture of this product and the thiourea (271) was formed at the higher temperature of 207°C.

The results obtained for the thermolysis of 2-benzylthio-3,4,5,6-tetrahydropyrimidine (266) and for the thermolysis of 2-benzylthioimidazolidine (267) offer an interesting contrast. In the former case sulphur is retained in the new heterocycle, while in the latter case sulphur is lost possibly resulting in the formation of the labile carbodiimide [(270), n=2]. Prior to this discovery, it had been suggested[174] that retention of sulphur and hence non-formation of

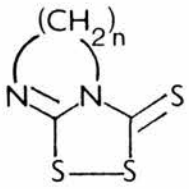
carbodiimide was a result of ring strain. However, these latter results suggest that the process may indeed be more complex.

(ii) With Heterocumulenes and Nitriles

It has been reported[112,174] that compounds of type (272) react with carbon disulphide and nitriles to give products of type (273) and (274).

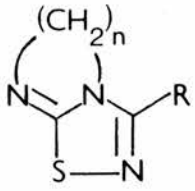


(272)



(273)

n = 2, 3

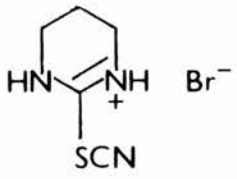


(274)

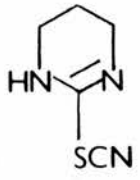
n = 3

In view of this, the reactions of (266), (267) and (276) with both carbon disulphide and benzonitrile were investigated.

2-Thiocyano-3,4,5,6-tetrahydropyrimidinium bromide (275) was prepared from 2-hexahydropyrimidinethione (222) and cyanogen bromide.



(275)



(276)

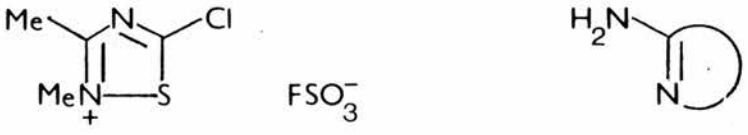
Attempts to deprotonate (275) to obtain the free base (276) were unsuccessful. It would appear that the product obtained reacted further on formation. Attempts to react(276) in situ by treating (275) with triethylamine were therefore made.

Reactions of 2-benzylthio-3,4,5,6-tetrahydropyrimidine (266), 2-benzylthioimidazolidine (267), and 2-thiocyano-3,4,5,6-tetrahydropyrimidinium bromide (275) (and triethylamine) both with carbon disulphide and benzonitrile were attempted.

In all cases, t.l.c. showed trace amounts of two or three products present in insufficient quantities to isolate.

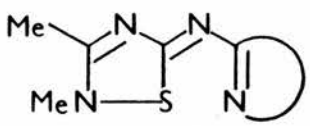
VI Condensation Reactions of 5-Chloro-2,3-dimethyl-1,2,4-thiadiazolium Fluorosulphonate with 2-Amino-N-heterocycles

The salt (277) reacts with 2-amino-N-heterocycles (132) in refluxing 1,2-dichloroethane to give condensation products.

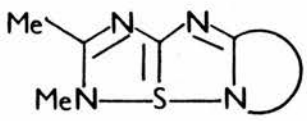


(277) (132)

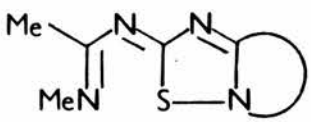
Theoretically, two isomeric products may be formed in this reaction arising either from condensation at the amino nitrogen or from reaction at the ring nitrogen atom. Each of the two possible products may be formulated in three different ways. The product arising from condensation at the amino nitrogen could be formulated as (278), (279) or (280); the product arising from reaction at the ring nitrogen could possess structure (281), (282) or (283). It is, however, extremely unlikely that a product would exist in the dipolar form (281), as the energy required to prevent a positive and negative charge held in such close proximity from combining, would be very great.



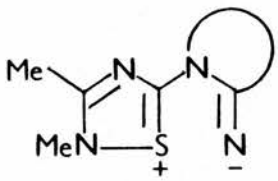
(278)



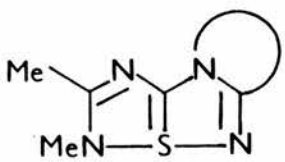
(279)



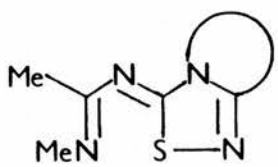
(280)



(281)

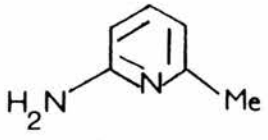


(282)

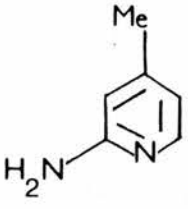


(283)

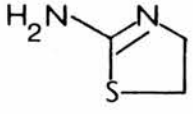
This reaction was investigated using three 2-amino-N-heterocycles, namely (284), (285) and (286).



(284)



(285)



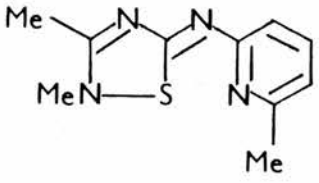
(286)

In all three cases only one condensation product was isolated. These products are tentatively formulated as having the structure (278), (279) or (280), arising from condensation at the amino nitrogen.

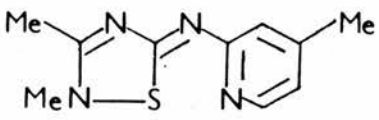
This assignment is based on a comparison with a similar series of condensation reactions carried out by Mitchell and Reid[141] in which the heterocycle (284) condensed with 5-phenyl-1,2-dithiolylium salts (131) to give only compounds of type (133) i.e. no product was formed from condensation at the ring nitrogen. A possible explanation of this behaviour could be steric blocking of the ring nitrogen atom in (284) by the neighbouring methyl and amino substituents.

It seems likely that for the condensation of (284) with the thiadiazolium salt (277), a product arising from condensation at the amino nitrogen would be the only one formed. On the basis that each

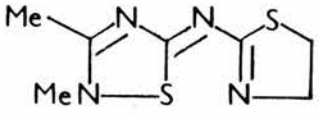
of the three condensation reactions resulted in only one product, it could further be suggested that the condensation reactions of (277) with heterocycles (285) and (286) would take place at the amino nitrogen. If this analogy is continued, the structure of the products obtained would be represented by (278) rather than (279) or (280). The three products would then be (287), (288) and (289) respectively.



(287)

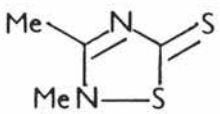


(288)

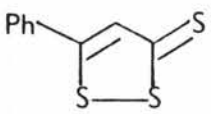


(289)

The condensation reaction between (277) and (286) also resulted in the solvolysis product (290) of the thiadiazolium salt (277).



(290)



(291)

Reid and Mitchell[141] found similar solvolysis products (291) throughout the course of their work.

PART C

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.

Infra-red spectra were recorded with a Perkin Elmer 1330 spectrometer, and refer to solids dispersed in KBr discs or liquid films. Mass spectra and accurate mass determinations were carried out by Mr C. Miller, Department of Chemistry, University of St Andrews. These spectra were recorded on an AEI MS902 instrument.

Nmr spectra were executed by Mrs M. Smith, Department of Chemistry, University of St Andrews. ^{1}Hnmr spectra were recorded at ambient temperature using a Bruker WP80 operating at 80 MHz. Solutions in chloroform-d ($CDCl_3$) and dimethylsulphoxide-d_6 (DMSO-d_6) were 0.4M, except where this concentration could not be attained, when saturated solutions were employed. Chemical shift values (δ) are given in p.p.m. downfield from tetramethylsilane as internal reference.

Carbon, hydrogen and nitrogen elementary microanalyses were executed by Miss C. Jack and 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 magnesium sulphate, and solvents were evaporated at reduced pressure using a Buchi rotary film evaporator. Solids were dried *in vacuo* over phosphoric anhydride.

Materials:

"40-60 Petrol" refers to petroleum ether of boiling range 40-60°C and "ether" refers to diethyl ether. Benzene, cyclohexane, ethanol, hexane, methanol, nitromethane, 40-60 petrol, propan-2-ol and toluene were all redistilled commercial solvents.

Ether was pre-dried over calcium chloride for ca. 24 hours before refluxing and distilling.

Acetonitrile was refluxed over sodium hydride (50% dispersion in oil, 2g/l) for 30 minutes, distilled, then refluxed over phosphoric anhydride for one hour and distilled twice.

Dichloromethane, 1,2-dichloroethane and chloroform were refluxed for one hour over phosphoric anhydride and distilled twice.

Ethyl acetate was refluxed for one hour over calcium hydride and distilled.

N,*N*-Dimethylformamide was dried for one week over calcium hydride and then distilled at 15mm of Hg.

o-Dichlorobenzene was spectroscopic grade solvent.

Isopropyl benzene and 1,2,3,4-tetrahydronaphthalene were refluxed over lithium aluminium hydride (ca. 2g/l) for 30 minutes and distilled.

Benzonitrile was a commercial reagent and was purified by distillation.

All reagents, unless otherwise stated, were commercially available. The solids were purified by recrystallisation while the liquids were purified by distillation.

Tables of ^{1}Hnmr and mass spectral data are to be found in the appendices I and II at the end of this section.

I (i) Condensation of 5-Amino-1,2,4-thiadiazoles with α,ω-Dihaloalkanes and Related Reactions

5-Amino-3-methyl-1,2,4-thiadiazole was prepared by the method of Goerdeler[175].

(a) Attempted Synthesis of 4,5-Dihydro-3-methyl-6-oxopyrimido [1,2-d][1,2,4]thiadiazole

(1) In Refluxing Acetonitrile.

3-Chloropropionyl chloride (190) (25mmol, 2.39ml) was added to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5785g) in acetonitrile (35ml), and the resultant boiled for 24 hours. On cooling, 4,5-dihydro-3-methyl-6-oxopyrimido[1,2-d][1,2,4] thiadiazolium chloride (192) crystallised out of the acetonitrile as cream needles, (0.9856g, 96%), mp 222-225°C.

Microanalysis: An analytical sample was obtained by taking a crop at less than 24 hours reflux.

		%C	%H	%N
	Found:	34.50	3.89	20.14
$C_6H_8N_3ClOS$	Requires:	35.04	3.92	20.43

^{1}Hnmr (see Table A)

Mass Spectrum (see Table 1).

If reaction is not allowed to go to completion i.e. is not boiled for 24 hours, then the intermediate uncyclised base 3-chloro-N([3]methyl[1,2,4]thiadiazolo)propanamide (292) can be isolated from the mother liquor. This may be achieved by removing the acetonitrile, adding distilled water (50ml) [to hydrolyse any excess 3-chloropropionyl chloride] followed by sodium hydroxide, (1M, 10ml) [to deprotonate any salt present] and extracting the aqueous solution with dichloromethane (3 x 50ml). The product thus obtained was recrystallised from ethanol (1ml), mp 175-178°C.

Microanalysis:

		%C	%H	%N
	Found:	35.02	3.88	19.87
$C_6H_8N_3ClOS$	Requires:	35.04	3.92	20.43

Accurate Mass Found: 205.008751

$C_6H_8N_3ClOS$ Requires: 205.00764

^{1}Hnmr (see Table 8)

Mass Spectrum (see Table 2)

Deprotonation of the chloride (192) thus obtained was attempted under a variety of conditions:

(1) In aqueous solution using 1M sodium hydroxide and repeated extraction with dichloromethane (8 x 30ml).

(2) In aqueous solution using sodium carbonate and repeated extraction with dichloromethane (8 x 30ml).

(3) In aqueous solution using sodium carbonate and repeated extraction with ethyl acetate (8 x 30ml).

(4) In aqueous solution using sodium carbonate, followed by removal of water and extraction for 24 hours with dichloromethane using a

soxlet apparatus.

(5) As a stirred suspension in acetonitrile and triethylamine.

(6) As a stirred suspension in dichloromethane and triethylamine.

(7) As a stirred suspension in methanol with amberlite 45(OH) ion exchange resin for 2 hours.

In all cases, very little material was isolated. The material which was isolated displayed peculiar solubility characteristics in that it was insoluble in dichloromethane, diethyl ether, ethyl acetate, benzene, and toluene, but was soluble in alcohols and N,N-dimethylformamide. However, once dissolved, the material could not be re-isolated from solution.

(2) At Room Temperature.

3-Chloropropionyl chloride (190) (25mmol, 2.3872g) was added to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in boiling acetonitrile (35ml) and the reaction mixture allowed to cool spontaneously to room temperature over a period of 0.5 hours. 5-Amino-3-methyl-1,2,4-thiadiazolium chloride (293) was obtained as white needles (0.6634g, 88%), mp 178-180°C.

^{1}Hnmr (see Table C)

Mass Spectrum: the product lost HCl to give a spectrum identical to that of the thiadiazole (191).

(b) Synthesis of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine and Related Compounds

Formation of 5(α-Bromo-xylyl)-3-methyl-1,2,4-thiadiazolium Bromide.

A solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in acetonitrile (35ml) was added to a solution of α,α'-dibromo-o-xylene (193) (25mmol, 6.5990g) in acetonitrile (10ml) and the resultant solution brought to reflux, boiled for 24 hours, and allowed to cool slowly overnight. 5(α-Bromo-xylyl)-3-methyl-1,2,4-thiadiazolium bromide (194) was obtained as white prisms (1.0205g,54%), mp 210-212°C.

Microanalysis:

		%C	%H	%N
	Found:	34.85	3.60	11.03
$C_{11}H_{13}N_3SBr_2$	Requires:	34.85	3.46	11.08

^{1}Hnmr (see Table D)

Mass Spectrum (see Table 3)

The mother liquor was evaporated to dryness and a ^{1}Hnmr spectrum obtained of the residue which showed a mixture of both reactants. This residue was extracted with boiling toluene (3 x 50ml), the extracts taken to dryness, and α,α'-dibromo-o-xylene (193) (4.9164g, 75%) obtained in ^{1}Hnmr pure form.

Deprotonation of the bromide (194) was attempted under a variety of conditions:

(1) In aqueous solution using 1M sodium hydroxide, followed by extraction with dichloromethane.

(2) In aqueous solution using sodium carbonate, followed by extraction with dichloromethane.

(3) In aqueous solution using 1M sodium hydroxide, followed by direct filtration. This yielded starting material (0.2585g, 68%), mp 208-210°C [^{1}Hnmr identical to the authentic sample].

(4) As a solution in N,N-dimethylformamide added to a 4:1 excess of aqueous alkali.

(5) As a solutiuon in methanol/ethanol [1:1] added to a 4:1 excess of aqueous alkali.

(6) As a solution in methanol using sodium methoxide.

In all cases no deprotonated material was detected, and it was concluded that the insolubility of the starting material hinders deprotonation.

A further attempt to deprotonate the salt was made as follows:

5(α-Bromo-xylyl)-3-methyl-1,2,4-thiadiazolium bromide (194) (1mmol, 0.3791g) was dissolved in N,N-dimethylformamide (10ml) and to this added a solution of potassium-tert-butoxide (1mmol, 0.1122g) in N,N-dimethylformamide (10ml). The resulting solution was heated to reflux, boiled for 0.25 hours and allowed to cool. Distilled water (50ml) was added to the cooled solution and the mixture extracted with dichloromethane (6 x 50ml) to remove the N,N-dimethylformamide. Sodium hydroxide (1M, 2ml) was added to the aqueous layer and this extracted with dichloromethane (6 x 50ml), the extracts dried over anhydrous magnesium sulphate, and taken to dryness. This black/brown

oil was extracted into dichloromethane/cyclohexane (9:1, 50ml), however none of the desired product was detected.

Finally deprotonation was attempted using di-tert-butylpyridine as follows:

5(α-Bromo-xylyl)-3-methyl-1,2,4-thiadiazolium bromide (194) (3mmol, 1.1373g) was dissolved in N,N-dimethylformamide (75ml) and to this added di-tert-butylpyridine (3mmol, 0.5739g, 0.67ml) and the resultant heated to reflux and boiled for 0.25 hours.

On cooling, distilled water (50ml) was added and the resultant extracted with dichloromethane (6 x 50ml). The aqueous layer was subsequently treated with sodium hydroxide (1M, 10ml) followed by extraction with dichloromethane (6 x 50ml). These dichloromethane extracts were dried over anhydrous magnesium sulphate, the solvent removed, and a ^{1}Hnmr spectrum obtained of the residue. No useful material was detected and hence this line of approach was abandoned.

Formation of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4] thiadiazolo[1,3]diazepine.

α,α'-Dibromo-o-xylene (193) (25mmol, 6.5990g) in N,N-dimethylformamide (15ml) was added to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (10mmol, 1.1516g) in N,N-dimethylformamide (7ml), and the resultant brought to reflux and boiled for 0.25 hours.

On cooling, distilled water (150ml) was added and the solution extracted with dichloromethane (6 x 75ml) to remove the N,N-dimethylformamide and the excess α,α'-dibromo-o-xylene. Sodium hydroxide (1M, 20ml) was added to the aqueous layer which was subsequently extracted with dichloromethane (6 x 75ml).

The above process was repeated five times. The final dichloromethane extracts were combined, dried over anhydrous magnesium sulphate, and the solvent evaporated. 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196) was obtained as white prisms (2.7545g, 25%), mp 206-209°C.

Microanalysis:

		%C	%H	%N
	Found:	60.93	5.09	19.43
$C_{11}H_{11}N_3S$	Requires:	60.80	5.10	19.34

Accurate Mass Found: 217.067470

$C_{11}H_{11}N_3S$ Requires: 217.06735

^{1}Hnmr (see Table E)

Mass Spectrum (see Table 4)

A 10mmol scale reaction as previously described was carried out with the modification that on work up, instead of adding distilled water, 2M hydrochloric acid (150ml) was used to prevent any disproportionation of the salt to free base during the first extraction with dichloromethane. Sufficient sodium hydroxide to neutralise both the hydrochloric acid and the salt was then added. However, no improvement in the yield was observed (0.5444g, 25%).

A larger scale reaction, namely 50mmol, was also carried out in the following manner:

α,α'-Dibromo-o-xylene (193) (125mmol, 32.9949g) dissolved in N,N-dimethylformamide (50ml) was added to a solution of 5-amino-3-

methyl-1,2,4-thiadiazole (191) (50mmol, 5.7578g) in N,N-dimethyl-formamide (50ml) and the resultant boiled for 0.25 hours.

On cooling, distilled water (500ml) was added and the solution extracted with dichloromethane (6 x 250ml). Sodium hydroxide (1M, 100ml) was added to the aqueous layer and the resultant extracted with dichloromethane (6 x 250ml), dried over anhydrous magnesium sulphate, and the solvent removed at the water pump. 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196) was obtained as white prisms after recrystallisation from dichloromethane/cyclohexane (10:1, 550ml; the solution being concentrated to approximately half its original volume), (2.7557g, 25%), mp 205-209°C.

The hydrobromide of the base was obtained by treating the base with hydrobromic acid thus:

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo [1,3]diazepine (1mmol, 02173g) was dissolved in dichloromethane (30ml) and hydrobromic acid (48% w/w, 3mmol, 0.34ml) added, followed by ether (50ml). 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo [1,3]diazepinium bromide (294) was obtained as white needles (0.2982g, 100%), mp 272-273°C.

Microanalysis:

		%C	%H	%N
	Found:	44.11	4.04	14.06
$C_{11}H_{12}N_3SBr$	Requires:	44.31	4.06	14.09

^{1}Hnmr (see Table F)

Mass Spectrum: the product lost HBr to give a spectrum identical to that of compound (196), (see Table 4).

(c) Attempted Synthesis of 5,6-Benzo-4,7-dioxo-3-methyl [4,5-a][1,2,4]thiadiazolo[1,3]diazepine (199)

(1) In N,N-dimethylformamide.

Phthaloyl chloride (197) (25mmol, 3.6ml) was added at room temperature to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in N,N-dimethylformamide (3ml). A violent reaction took place. On recrystallisation from chloroform (10ml), phthalic anhydride (198) was obtained as white needles (2.2373g, 60%), mp 127-128°C.

^{1}Hnmr: identical to authentic sample of phthalic anhydride.
Mass Spectrum showed $M^{+\cdot}$=148 and spectrum identical to authentic sample of phthalic anhydride.
IR: Identical to authentic sample.
Mixed melting point: 127-128°C.

(2) In acetonitrile.

Phthaloyl chloride (197) (25mmol, 3.6ml) was added to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in warm acetonitrile (30ml). 5-Amino-3-methyl-1,2,4-thiadiazolium chloride (293) crystallised immediately as white needles (0.2425g, 32%), mp 175-180°C.

^{1}Hnmr (see Table C)
Mass spectrum: the product lost HCl to give a spectrum identical to that of 5-amino-3-methyl-1,2,4-thiadiazole (191).

(3) In nitromethane.

Phthaloyl chloride (197) (7mmol, 1ml) was added to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in warm nitromethane (35ml). 5-amino-3-methyl-1,2,4-thiadiazolium chloride (293) was obtained as white needles (0.3697g, 49%), mp 175-180°C.

^{1}Hnmr (see Table C)

Mass spectrum: the product lost HCl to give a spectrum identical to that of 5-amino-3-methyl-1,2,4-thiadiazole (191).

(4) In benzonitrile.

Phthaloyl chloride (197) (7mmol, 1ml) was added to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in benzonitrile (15ml). 5-Amino-3-methyl-1,2,4-thiadiazolium chloride (293) was obtained as white needles (0.4175g, 55%), mp 175-180°C.

^{1}Hnmr (see Table C)

Mass spectrum: the product lost HCl to give a spectrum identical to that of 5-amino-3-methyl-1,2,4-thiadiazole.

(5) With no solvent.

5-Amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) was dissolved in phthaloyl chloride (197) (4ml) and the resulting solution heated in an oil bath for 20 minutes (oil bath temperature: 180°C).

The product thus obtained appears to be polymeric as it is insoluble in all solvents and will not melt at temperatures of up

to 350°C.

(d) Attempted Synthesis of 3-methyl-5H-4,6-dioxopyrimido [1,2-d][1,2,4]thiadiazole

Malonyl chloride (200) (25mmol, 2.4287ml) was added dropwise with stirring to a cooled solution (ice bath) of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in N,N-dimethylformamide (3ml). A vigorous reaction took place, yielding a solid which appears to be polymeric. A ^{1}Hnmr spectrum of this product was unable to be obtained due to low solubility, and the product showed no signs of melting at temperatures of up to 350°C. The mass spectrum did not show any significant peaks above a mass of m/z=80 and it was concluded that the material was very involatile.

(e) Attempted Synthesis of 4,7-Dihydro-3-methyl[4,5-a][1,2,4] thiadiazolo[1,3]diazepine

(1) In N,N-dimethylformamide

Cis-1,4-dichlorobut-2-ene (202) (25mmol, 2.59ml) was added to a solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in N,N-dimethylformamide (10ml) and the resulting solution heated in an oil bath (oil bath temperature: 130°C) for 0.5 hours and allowed to cool.

On cooling, distilled water (100ml) was added and the solution extracted with dichloromethane (4 x 75ml) to remove the N,N-dimethylformamide. The aqueous layer was treated with sodium hydroxide (1M, 10ml) and subsequently extracted with dichloromethane (4 x 75ml). The dichloromethane extracts were dried over anhydrous magnesium sulphate

and taken to dryness. A small amount of solid residue was obtained, which, on t.l.c., (10% methanol in ether) was shown to be the starting thiadiazole (191).

(2) In acetonitrile.

Cis-1,4-dichlorobut-2-ene (202) (25mmol, 2.59ml) was added to a filtered solution of 5-amino-3-methyl-1,2,4-thiadiazole (191) (5mmol, 0.5758g) in acetonitrile (35ml), and the resulting solution brought to reflux and boiled for 24 hours (oil bath temperature: 120°C).

On cooling, the mother liquor was filtered as extensive charring had occured, and the filtrate taken to dryness. The residue was extracted into boiling benzene (150ml) and concentrated to approximately half its original volume whereupon the product crystallised. The product was found to be 5-amino-3-methyl-1,2,4-thiadiazole by comparison with an authentic sample (mp, mixed mp, ^{1}Hnmr, mass spectrum were identical to authentic sample).

An identical reaction to the above was carried out at room temperature. After standing for 24 hours 5-amino-3-methyl-1,2,4-thiadiazole was recovered in quantitative yield.

(ii) Condensation of 5-Amino-1,3,4-thiadiazoles with α,ω-dihaloalkanes and Related Reactions

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

Preparation of 5-Amino-2-methyl-1,3,4-thiadiazole.

Thiosemicarbazide (1mol, 91.1346g) was stirred with acetyl chloride (1000ml) at room temperature for 15.5 hours. The product was filtered off, washed with a little ether, and dissolved in water (1500ml). The aqueous solution was then filtered (to remove traces of the acetyl compound which are also formed), and sodium carbonate

decahydrate (750mmol, 214.6056g) added with stirring for 5 minutes until all signs of gas evolution had ceased.

The water was removed at the water pump, the residue extracted with boiling ethanol, and the ethanolic extracts taken to dryness. 5-Amino-2-methyl-1,3,4-thiadiazole (206) was obtained as white needles (53.0345g, 46%), mp 234-236°C(literature: 234-236°C)[180].

(1) In acetonitrile.

5-Amino-2-methyl-1,3,4-thiadiazole (206) (5mmol, 0.5758g) was dissolved in acetonitrile (25ml) and to this added 1,3-dibromopropane (205) (25mmol, 2.55ml). This solution was brought to reflux and boiled for:

(a) 6 hours

(b) 24 hours

(c) 72 hours

On cooling, a small amount of crystalline solid was formed which was filtered off and recrystallised from ethanol (15ml, concentrated to approximately half its original volume). The bis adduct

(207), was obtained as white prisms (a: 0.0670g, 6.2%; b: 0.0663g, 6.1%; c: 0.0693g, 6.4%), mp 245-247°C.

Microanalysis:

		%C	%H	%N
	Found:	25.14	3.79	19.39
$C_9H_{16}N_6Br_2S_2$	Requires:	25.01	3.73	19.44

^{1}Hnmr (see Table G)

Mass Spectrum was unable to be obtained due to the low volatility of the salt.

The mother liquor was taken to dryness and distilled water (100ml) added. This aqueous solution was extracted with dichloromethane (6 x 75ml) to remove the excess 1,3-dibromopropane. The aqueous layer was then treated with sodium hydroxide (1M, 10ml) and extracted with dichloromethane (6 x 75ml). The extracts were dried over anhydrous magnesium sulphate, taken to dryness, and a ^{1}Hnmr spectrum obtained of the residue, (Table X).

On examination of the ^{1}Hnmr data obtained after (a) 6 hours, (b) 24 hours, and (c) 72 hours, all of which showed a mixture of starting thiadiazole and uncyclised base (210), the optimum conditions appeared to employ a reaction time of 24 hours. Hence a larger scale reaction was carried out with a reaction time of 24 hours.

5-Amino-2-methyl-1,3,4-thiadiazole (206) (25mmol, 2.8789g) was dissolved in acetonitrile (150ml) and to this added 1,3-dibromopropane (205) (125mmol, 12.73ml) and the resulting solution boiled for 24 hours.

The reaction was allowed to cool and the bis adduct filtered off. The filtrate was taken to dryness, distilled water (100ml) added to the residue and this extracted with dichloromethane (6 x 75ml) to remove the excess 1,3-dibromopropane. Sodium hydroxide (1M, 50ml) was added to the aqueous layer and this was subsequently extracted with dichloromethane (6 x 75ml).

The dichloromethane extracts were dried over anhydrous magnesium sulphate and taken to dryness. The residue was dissolved in

N,N-dimethylformamide (15ml), taken to the boil and allowed to cool. On cooling, ether (250ml) was added and the solution allowed to crystallise slowly overnight.

The ether layer was decanted off, and the residue recrystallised from propan-2-ol (6ml). 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazolium bromide (211) was obtained as pale yellow prisms (0.6248g, 11%), mp 167-169°C.

^{1}Hnmr (see Table H)

The cyclised salt was then dissolved in distilled water (100ml) and sodium hydroxide (1M, 50ml) added. This solution was extracted with dichloromethane (6 x 75ml), dried over anhydrous magnesium sulphate, and the solvent evaporated. 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) was purified by distillation at the oil pump (0.1622g, 4%), bp 100°C at 1mbar.

^{1}Hnmr (see Table I)

(2) In methanol, 100mmol scale.

5-Amino-2-methyl-1,3,4-thiadiazole (206) (100mmol, 11.5157g) was dissolved in methanol (600ml, redistilled AR methanol), 1,3-dibromopropane (205) (500mmol, 50.93ml) added to this, and the resultant brought to reflux and boiled for 24 hours.

The methanol was removed, and distilled water (400ml) added to the residue. This aqueous solution was extracted with dichloromethane (6 x 250ml) to remove the excess 1,3-dibromopropane, and the aqueous

layer treated with sodium hydroxide (1M, 200ml). This was subsequently extracted with dichloromethane (6 x 250ml), dried over anhydrous magnesium sulphate and the extracts taken to dryness.

The residue was dissolved in N,N-dimethylformamide (40ml), taken to its boiling point and allowed to cool. On cooling, ether (1000ml) was added and the solution left to recrystallise overnight. The ether layer was decanted and distilled water (400ml) added to the remaining crystalline solid which was then treated with sodium hydroxide (1M, 200ml). The aqueous solution was extracted with dichloromethane (6 x 250ml), dried over anhydrous magnesium sulphate, and the solvent evaporated. 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (212) was obtained, after purification by distillation at the oil pump, as white needles (1.8452g, 12%), bp 100°C/1mbar, mp 23-24°C.

A sample of the base was purified for analysis via the perchlorate thus:

5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) (2mmol, 0.3104g) in dichloromethane (25ml) was treated with perchloric acid (70% w/w, 4mmol, 0.34ml). Distilled water (20ml) was then added to this reaction mixture and the dichloromethane layer removed. The perchlorate was subsequently deprotonated by means of sodium carbonate decahydrate (8mmol, 2.2891g) and the purified base extracted from the aqueous layer with dichloromethane (6 x 25ml) and dried over anhydrous potassium carbonate. The solvent was evaporated, the base redistilled at the oil pump, and the purified sample stored in a sealed glass tube prior to analysis being carried out. The sample for analysis was handled in an inert atmosphere.

Microanalysis: (Carried out by Dr H. Mallissa and G. Reuter, Analytische Laboratorien, Germany).

		%C	%H	%N
	Found:	46.40	5.86	27.21
$C_6H_9N_3S$	Requires:	46.43	5.89	27.07

Accurate Mass Found: 155.051386

$C_6H_9N_3S$ Requires: 155.05171

^{1}Hnmr (see Table I)

Mass Spectrum (see Table 5)

t.l.c.: single spot r_F 0.2

G.L.C.: One peak both on 2% NPGS and OV225.

(3) In methanol, 500mmol scale.

5-Amino-2-methyl-1,3,4-thiadiazole (206) (500mmol, 57.5783g) was dissolved in redistilled AR methanol (1350ml) and to this added 1,3-dibromopropane (205) (2500mmol, 254.6ml). This solution was boiled for 24 hours, after which time the methanol was removed at the water pump.

Distilled water (1000ml) was added to this residue and the resulting aqueous solution extracted with dichloromethane (6 x 1400ml) to remove the excess 1,3-dibromopropane. The aqueous layer was subsequently treated with sodium hydroxide (1M, 1000ml), and extracted with dichloromethane (12 x 400ml).

These extracts were dried over anhydrous magnesium sulphate, the

solvent removed, and the residue dissolved in N,N-dimethylformamide (100ml). The resulting solution was taken to the boil and allowed to cool.

On cooling, ether (1000ml) was added and the resulting precipitate allowed to crystallise slowly overnight. The ether layer was decanted, distilled water (1000ml) added, and this solution treated with sodium hydroxide (1M, 1000ml). Subsequently the reaction mixture was extracted with dichloromethane (6 x 400ml), dried over anhydrous magnesium sulphate, and the solvent removed. The product (212) was purified by distillation at the oil pump (8.7281g, 11%), mp 23-25°C, bp 112°C/3mbar.

(b) Preparation of 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazolium bromide (211).

As the hydrobromide was proving difficult to isolate at the intermediate stage of the cyclisation reaction, it was decided to prepare it directly from the free base.

5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) (1mmol, 0.1552g) was dissolved in dichloromethane (5ml) and to this added hydrobromic acid (48% w/w, 3mmol, 0.3394ml). Ether (25ml) was added to this solution, the resulting oil allowed to settle, and the ether layer decanted off.

The oil was dissolved in propan-2-ol (2ml) and precipitated as a white crystalline solid by means of ether (15ml). 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazolium bromide (211) was obtained as white prisms (0.0475g, 20%), mp 175-175.5°C.

Microanalysis:

		%C	%H	%N
	Found:	30.67	4.26	17.86
$C_6H_{10}N_3SBr$	Requires:	30.52	4.27	17.80

^{1}Hnmr (see Table H)

Mass Spectrum: the product lost HBr to give a spectrum identical to that of compound (212) (see Table 5).

(c) Preparation of 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazolium perchlorate.

5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) (1mmol, 0.1552g) was dissolved in dichloromethane (5ml) and to this added perchloric acid (70% w/w, 2mmol, 0.168ml). Ether (25ml) was added to this solution and 5,6-dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazolium perchlorate (213) obtained as a white crystalline powder (0.2556g, 99%), mp 166-167°C.

Microanalysis:

		%C	%H	%N
	Found:	28.19	3.90	16.48
$C_6H_{10}N_3SClO_4$	Requires:	28.19	3.94	16.43

^{1}Hnmr (see Table H)

Mass Spectrum: the product lost $HClO_4$ to give a spectrum identical to that of compound (212) (see Table 5).

(d) Attempted Preparation of 5,6-Benzo-4,7-dihydro-2-methyl [4,5-a][1,3,4]thiadiazolo[1,3]diazepine.

(1) In N,N-Dimethylformamide.

α,α'-Dibromo-o-xylene (193) (25mmol, 6.5990g) was dissolved in N,N-dimethylformamide (15ml) and added to a solution of 5-amino-2-methyl-1,3,4-thiadiazole (206) (10mmol, 1.1516g) in N,N-dimethylformamide (7ml) and the resulting solution boiled for 15 minutes and allowed to cool spontaneously to room temperature. Distilled water (150ml) was added to the cooled solution and the resultant extracted with dichloromethane (6 x 75ml). Sodium hydroxide (1M, 20ml) was added to the aqueous layer and this extracted with dichloromethane (6 x 75ml), dried over anhydrous magnesium sulphate, and taken to dryness. The residue was extracted with dichloromethane/cyclohexane (10:1, 220ml) and a t.l.c. (10% methanol in ether) obtained of these extracts. However on examination, the t.l.c. showed the presence of three different products and further work up was not carried out.

(2) In acetonitrile.

5-Amino-2-methyl-1,3,4-thiadiazole (206) (5mmol, 0.5758g) was dissolved in acetonitrile (35ml) and added to a solution of α,α'-dibromo-o-xylene (193) (25mmol, 6.5990g) in acetonitrile (10ml) and the resulting solution boiled in an oil bath for 24 hours.

On cooling, the crystalline product was filtered off. The excess α,α'-dibromo-o-xylene was recovered by evaporating the mother liquor and extracting the residue with toluene (3 x 50ml). These extracts were taken to dryness and the α,α'-dibromo-o-xylene recrystallised from chloroform (20ml). α,α'-Dibromo-o-xylene

(3.0144g, 46%) was obtained in pure form.

The filtered product was recrystallised from methanol (10ml), and a ^{1}Hnmr spectrum obtained. This was found to be consistent with the bis adduct (215), however the microanalysis was incorrect, (Table Y).

On monitoring this reaction over a period of 48 hours, it was found that all of this product (215) was formed after 4 hours and no subsequent precipitation was observed.

(3) In Methanol.

5-Amino-2-methyl-1,3,4-thiadiazole (206) (5mmol, 0.5758g) was dissolved in methanol (30ml) and added to a solution of α,α'-dibromo-o-xylene (193) (25mmol, 6.5990g) in methanol (80ml). The resulting solution was brought to reflux and boiled for 24 hours.

The methanol was removed and distilled water (50ml) added to the residue. This mixture was extracted with toluene (6 x 30ml), the toluene extracts dried over anhydrous magnesium sulphate, and taken to dryness. These extracts yielded a liquid which was purified by distillation at the oil pump.

Sodium hydroxide (1M, 10ml) was added to the residual aqueous layer which was then extracted with dichloromethane (6 x 30ml), dried over anhydrous magnesium sulphate, and taken to dryness. The residue was dissolved in N,N-dimethylformamide (5ml), taken to the boil and allowed to cool. The N,N-dimethylformamide was removed at the oil pump and a ^{1}Hnmr spectrum obtained of the residue. On examination of this ^{1}Hnmr spectrum none of the desired product (214) was detected.

A ^{1}Hnmr spectrum obtained of the purified liquid arising from

the toluene extracts showed it to be α,α'-dimethoxy-o-xylene (218) (3.5694g), 86%), bp 79°C/1.9mbar.

^{1}Hnmr (see Table J)

Mass Spectrum (see Table 6)

(4) With no solvent.

5-Amino-2-methyl-1,3,4-thiadiazole (206) (1mmol, 0.1152g) and α,α'-dibromo-o-xylene (193) (5mmol, 1.3198g) were mixed and heated in an oil bath at 200°C for five minutes.

On cooling, distilled water (50ml) was added and this mixture extracted with dichloromethane (4 x 50ml) to remove the excess α,α'-dibromo-o-xylene.

The aqueous layer was subsequently treated with sodium hydroxide (1M, 2ml) and extracted with dichloromethane (4 x 50ml). The dichloromethane extracts were dried over anhydrous magnesium sulphate and the solvent evaporated.

The residue thus obtained was negligable and hence the reaction was pursued no further.

(iii) Attempted Formation of 3-Methyl[4,5-a][1,2,4]thiadiazolo [2,3,4,5]tetraazole (221)

This synthesis was attempted by using a modification of the procedure described by Iddon et al[177].

A stirred mixture of 5-amino-3-methyl-1,2,4-thiadiazole (191) (29.5mmol, 3.3971g), concentrated hydrochloric acid (36% w/w, 87.4mmol, 7.5ml) and water (7.5ml) was treated dropwise with sodium nitrite

(32.5mmol, 2.25g) in water (30ml). [The sodium nitrite was added over a period of 0.25 hours with cooling in an acetone/cardice bath to keep the internal temperature below -5°C]. A solution of sodium azide (34.5mmol, 2.25g) and sodium acetate (275mmol, 22.5g) in water (75ml) was added to this, keeping the temperature at 0°C. The resulting solution was stirred at 0°C for 0.5 hours, extracted with dichloromethane (7 x 80ml), dried over anhydrous magnesium sulphate, and the solvent evaporated. After recrystallisation from benzene (150ml concentrated to approximately 100ml), 5-amino-3-methyl-1,2,4-thiadiazole was obtained as colourless prisms (0.6520g, 19%), mp 195-198°C. The product was identical with an authentic sample (^{1}Hnmr, Mass spectrum, mp, mixed mp).

(iv) Attempted Formation of 5,6-Dihydro-3-methyl-4H-pyrimido-[1,2-d][1,2,4]selenadiazole.

1,3-Dibromopropane (25 mmol, 2.55 ml) was added to a solution of 5-amino-3-methyl-1,2,4-selenadiazole (5 mmol, 0.8103 g) in N,N-dimethylformamide (3 ml), and the resulting solution heated for 0.5 hours on an oil bath (temperature: 130°C).

On cooling ether (10 ml) was added and after standing for 1 hour, the ether layer was decanted. Water (10 ml) was added to the residue followed by sodium hydroxide (1 M, 10 ml). The resulting mixture was subsequently extracted with dichloromethane (4 x 30 ml), the extracts dried over anhydrous magnesium sulphate, and the solvent evaporated.

Examination of the residue by t.l.c. (10% methanol in ether) showed no worthwhile products.

II Reactions of 5,6-Benzo-4,7-dihydro-3-methyl [4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196)

(i) Thermolysis

(a) 4 hour reflux

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (5mmol, 1.0865g) was added to 1,2,3,4-tetrahydronaphthalene (10ml) and the resulting solution boiled under nitrogen for 4 hours.

(b) 0.5 hour reflux

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (5mmol, 1.0865g) was added to 1,2,3,4-tetrahydronaphthalene (35ml) and the resulting solution boiled for 0.5 hours under nitrogen.

In both cases, t.l.c. in ether showed 7 products at r_F 0.9, 0.8, 0.7, 0.6, 0.5, 0.3 and 0.1. The product at r_F 0.5 was darker staining than the others, however, attempts to isolate this or any of the other products by chromatographing on silica were unsuccessful.

(ii) With Imidoyl Chlorides

(a) With N-Methyl Benzimidoyl Chloride

N-Methyl benzimidoyl chloride was prepared by the method of Braun J. and Pinkernelle W.[181].

To a solution of 5,6-benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]-thiadiazolo[1,3]diazepine (196) (1mmol, 0.2173g) in dichloromethane (5ml) was added N-methyl benzimidoyl chloride (1.5mmol, 0.2304g) and the resultant brought to reflux and boiled for 1 hour, allowed to cool, and ether (20ml) added.

After standing, the ether was decanted and the residue dissolved in ethanol (2ml). Perchloric acid (3mmol, 0.252ml) was added, followed by ether (20ml). The resulting crystalline product was filtered off, washed with ether and dried. The product was recrystallised from acetonitrile/ether (2ml:30ml). 5,6-Benzo-4,7-dihydro-3-methyl-7-(N-benzylidine-methylamino)[4,5-a][1,2,4]thiadiazolo-[1,3]diazepinium perchlorate (225(a)) was obtained as white prisms (0.3104g, 71%), mp 185-189°C.

Microanalysis:

		%C	%H	%N
	Found:	52.17	4.52	12.94
$C_{18}H_{19}N_4SClO_4$	Requires:	52.47	4.40	12.88

^{1}Hnmr (see Table K)

Mass Spectrum: product dissociates to give spectra of diazepine (196) and N-methyl benzimidoyl chloride.

(b) With N-Phenyl Benzimidoyl Chloride

N-Phenyl benzimidoyl chloride was prepared by the method of Braun J. and Pinkernelle W.[181].

N-Phenyl benzimidoyl chloride (1.5mmol, 0.3235g) and 5,6-benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196) (1mmol, 0.2173g) were dissolved in dichloromethane/acetonitrile (1:1, 12ml), boiled for 2 hours, and the solvent removed at the water pump. The residual oil was redissolved in acetonitrile (1ml) and ether (25ml) added. After standing for approximately 2 hours, the ether was decanted off and the residue dissolved in ethanol (3ml). Perchloric acid (3mmol, 0.252ml) was added to this solution, followed by ether (30ml), and the resulting mixture allowed to stand for a further 2 hours. After this time, the ether layer was decanted off and the residue recrystallised from propan-2-ol (45ml concentrated to approximately half its original volume). 5,6-Benzo-4,7-dihydro-3-methyl-7-(N-benzylidine-phenylamino)[4,5-a][1,2,4]thiadiazolo[1,3]diazepinium perchlorate (225(b)) was obtained as white prisms (0.3425g, 69%), mp 175-177°C.

Microanalysis:

		%C	%H	%N
	Found:	57.73	4.29	11.10
$C_{24}H_{21}N_4SClO_4$	Requires:	58.00	4.26	11.27

^{1}Hnmr (see Table K)

Mass Spectrum: No mass spectrum was able to be obtained due to the high involatility of the salt.

(c) With N-Phenyl Trimethylacetimidoyl Chloride

Preparation of Trimethylacetanilide.

Aniline (400mmol, 36.46ml) was added dropwise over 0.5 hours

to a solution of trimethyl acetylchloride (100mmol, 12.0579g, 12.32ml) in benzene (500ml). The aniline hydrochloride was filtered off, the filtrate taken to dryness, and the residue recrystallised from ether (400ml) to give trimethylacetanilide (295) as white needles (14.8600g, 84%), mp 134-135°C.

Microanalysis:

		%C	%H	%N
	Found:	74.32	8.50	7.92
$C_{11}H_{15}NO$	Requires:	74.54	8.53	7.90

Accurate Mass Found: 177.114647

$C_{11}H_{15}NO$ Requires: 177.11534

^{1}Hnmr (see Table L)

Mass Spectrum (see Table 7)

N-Phenyl trimethylacetimidoyl chloride was prepared by the method of Cramer F. and Baer K.[182].

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) and N-phenyl trimethylacetimidoyl chloride (1.5mmol, 0.2935g) were dissolved in dichloromethane/ acetonitrile (1:1 10ml). The resulting solution was brought to reflux and boiled for 2 hours. On cooling, ether (60ml) was added and the resultant left to stand overnight. The ether was decanted and the residue dissolved in methanol (5ml). Perchloric acid (3mmol, 0.252ml) was added, followed by ether (80ml) and the

resulting precipitate filtered and recrystallised from ethanol (10ml) to give 5,6-benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4] thiadiazolo[1,3]diazepinium perchlorate (296) as white prisms (0.1436g, 45%), mp 258-259°C.

^{1}Hnmr (see Table F)

Mass Spectrum: product lost $HClO_4$ to give a spectrum identical to that of the free base (196), (see Table 4).

(iii) With Dibromoformaldoxime (226)

Dibromoformaldoxime was prepared by the method of Vyas, Chiang and Doyl[183]. Recrystallisation from 40-60 petrol yielded the product (226) as white prisms, mp 69-70°C.

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) was dissolved in dichloromethane/ acetonitrile (1:1, 10ml) and dibromoformaldoxime (226) (1.5mmol, 0.3042g) added. The resulting solution was boiled for 0.5 hours and allowed to cool. 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4] thiadiazolo[1,3]diazepinium bromide (294) was obtained as white prisms, (0.1193g, 40%), mp 274-275°C. This was identical (^{1}Hnmr, mp, mixed mp) with an authentic sample of the hydrobromide.

(iv) With Carbon Disulphide

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo [1,3]diazepine (196) (1mmol, 0.2173g) was dissolved in dichloromethane (10ml) and to this added carbon disulphide (83mmol, 5ml). The resulting solution was left stirring at room temperature for 96 hours

and subsequently taken to dryness.

On inspection, the crystalline residue was found to be 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (0.1437g, 66%). This was identical (^{1}Hnmr, mp, mixed mp, mass spectrum) with an authentic sample of the base.

(v) With Nitriles

(a) With Acetonitrile

(1) With acetonitrile-d_3: 2 hour reflux.

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (0.5mmol, 0.1086g) and acetonitrile-d_3 (1ml) were refluxed for 2 hours on an oil bath. On cooling, the solvent was evaporated and ^{1}Hnmr spectra of the residue obtained both in DMSO-d_6 and in $CDCl_3$. No significant reduction in the methyl integral was observed.

(2) With acetonitrile-d_3: 26 hour reflux.

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) was added to deuterated acetonitrile (2ml) and the resultant brought to reflux and boiled for 6 hours, after which time a further volume of deuterated acetonitrile (3ml) was added and boiling continued for an additional 20 hours.

The excess deuterated acetonitrile was removed and the residue examined by ^{1}Hnmr spectroscopy. Calculations based on the reduction in the methyl integral indicate that the ratio of deuterated product [(228), R=CD_3] to non-deuterated product (196) is ca. 1:3. The residue was in the form of white prisms (0.2000g), mp 214-216°C.

(3) With acetonitrile-d_3 and dimethylsulphoxide-d_6.

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) was added to dimethylsulphoxide-d_6 (2.5ml) and acetonitrile-d_3 (5ml) and the resulting solution brought to reflux and boiled for 24 hours.

The solvent was removed, firstly at the water pump, and subsequently at the oil pump yielding a white crystalline solid (0.2021g), mp 209-210°C. The internal temperature of the liquid was 92°C, and of the vapour was 80°C.

On examination by ^{1}Hnmr spectroscopy, the reduction in the methyl integral indicated that the ratio of deuterated product [(228), R=CD_3] to non-deuterated product (196) was approximately 7:2.

Mass Spectrum: The ratio of $M^{+\cdot}$ for deuterated to non-deuterated compound was 6.7:2 which is similar to that calculated from the ^{1}Hnmr spectrum.

(b) With Benzonitrile

(1) With no solvent.

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) and benzonitrile (10mmol, 1.02ml) were boiled for 0.5 hours. On cooling, the solution was chromatographed on silica (40cm x 2.2cm). The first 650ml of ether eluates contained the benzonitrile, the next 250ml of 10% methanol in ether showed only decomposed starting material, as did the next 1250ml of 10% methanol in ether and 250ml of methanol. The methanol/ether and methanol extracts were evaporated and examined by ^{1}Hnmr spectroscopy, however,

this showed many small peaks none of which could be assigned to the desired product [(228), R=Ph]. A mass spectrum obtained of the residue showed the highest m/z value to be 78.

(2) In toluene.

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo]1,3] diazepine (196) (1mmol, 0.2173g), benzonitrile (9.8mmol, 1ml) and toluene (2ml) were mixed and boiled for 18 hours. The resulting solution was examined by t.l.c., however, no useful material was detected.

(3) In benzene.

5,6-benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g), benzonitrile (9.8mmol, 1ml) and benzene (2ml) were mixed and boiled for 24 hours. Chromatographing on silica yielded no worthwhile product.

(vi) With Isocyanates

(a) Formation of 2,3,4,5-Tetrahydro-1,6-dimethyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) was dissolved in dichloromethane (10ml) and methyl isocyanate (20mmol, 1.1410g, 1.24ml) added to this solution. The resultant was brought to reflux, and boiled for 4 hours.

The solvent and the excess methyl isocyanate were subsequently removed and the residual crystalline solid recrystallised from benzene (20ml) concentrated to ca. half volume). A second crop was

obtained from acetonitrile (7ml concentrated to ca. half volume). 2,3,4,5-Tetrahydro-1,6-dimethyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (230(a)) was obtained as white needles (0.1462g, 50%), mp 160-165°C.

Microanalysis: a satisfactory analysis could not be obtained.

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(b) Formation of 2,3,4,5-Tetrahydro-1,6-dicyclohexyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]-thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) and cyclohexyl isocyanate (20mmol, 2.5034g, 2.55ml) were mixed in a round-bottomed flask and heated for 15 minutes at 145°C on an oil bath.

After the solution had cooled, ether (10ml) was added and the product allowed to crystallise slowly overnight. After recrystallisation from acetonitrile (4ml) 2,3,4,5-tetrahydro-1,6-dicyclohexyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (230(b)) was obtained as white prisms (0.0878g, 21%), mp 225-226°C.

Microanalysis: A satisfactory analysis could not be obtained.

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(c) Formation of 2,3,4,5-Tetrahydro-1,6-diphenyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]

diazepine (196) (1mmol, 0.2173g) and phenyl isocyanate (20mmol, 2.2ml) were heated at 140°C on an oil bath for 15 minutes.

On cooling, ether (15ml) was added and the product filtered and washed with more ether. Recrystallisation from acetonitrile (35ml concentrated to ca. 25ml), yielded 2,3,4,5-Tetrahydro-1,6-diphenyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (230(c)) as white needles (0.1043g, 25%), mp 204-205°C.

Microanalysis:

		%C	%H	%N
	Found:	66.57	4.32	13.62
$C_{23}H_{18}N_4SO_2$	Requires:	66.65	4.38	13.52

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(d) Formation of 2,3,4,5-Tetrahydro-1,6-dibenzyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) and benzyl isocyanate (20mmol, 2.6630g, 2.47ml) were mixed in a round-bottomed flask and subsequently heated at 145°C on an oil bath for 15 minutes.

After the reaction mixture had cooled, ether (25ml) was added and the product allowed to crystallise slowly overnight. The product was filtered off and washed with ether. Recrystallisation from acetonitrile (4ml) yielded 2,3,4,5-tetrahydro-1,6-dibenzyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (230(d)) as white

prisms (0.0895g, 20%), mp 162-163°C.

Microanalysis:

		%C	%H	%N
	Found:	67.61	4.69	12.59
$C_{25}H_{22}N_4SO_2$	Requires:	67.85	5.01	12.66

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(e) Formation of 2,3,4,5-Tetrahydro-1,6-di(p-tolyl)-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) and p-tolyl isocyanate (20mmol, 2.6630g) were placed in a round-bottomed flask and the resulting reaction mixture heated at 145°C on an oil bath for 15 minutes.

The crystalline precipitate was filtered off and washed with ether. After recrystallisation from acetonitrile (43ml), 2,3,4,5-tetrahydro-1,6-di(p-tolyl)-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (230(e)) was obtained as white microprisms (0.1747g, 39%), mp 185-187°C.

Microanalysis:

		%C	%H	%N
	Found:	67.51	4.86	12.64
$C_{25}H_{22}N_4SO_2$	Requires:	67.85	5.01	12.66

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(f) Attempted Reaction of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine and p-toluenesulphonyl isocyanate

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]-diazepine (196) (1mmol, 0.2173g) was placed in a round-bottomed flask along with p-toluenesulphonyl isocyanate (20mmol, 3.9442g) and the resulting mixture heated for 15 minutes at 145°C on an oil bath.

On cooling, the crystalline precipitate was filtered and thoroughly washed with ether. The precipitate was recrystallised from acetonitrile (86ml concentrated to ca. 20ml).

Examination of this tacky solid by ^{1}Hnmr spectroscopy showed three methyl signals, and two methylene signals which are inconsistant with the anticipated product, or a 1:1 adduct.

(vii) With Isothiocyanates

(a) Formation of 2,3,4,5-Tetrahydro-1,6-dimethyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) was dissolved in dichloromethane (20ml), and to this added methyl isothiocyanate (10mmol, 0.7ml), and the resulting solution left to stand at room temperature for 4 hours.

After this time, the solvent was removed, ether (50ml) added, and the white, crystalline product filtered and washed with more ether. After recrystallisation from acetonitrile (37ml concentrated

to ca. 20ml) 2,3,4,5-tetrahydro-1,6-dimethyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (230(f)) was obtained as white spars (0.2009g, 62%), mp 150-167°C.

Microanalysis:

		%C	%H	%N
	Found:	48.32	4.40	17.43
$C_{13}H_{14}N_4S_3$	Requires:	48.42	4.38	17.37

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(b) Formation of 2,3,4,5-Tetrahydro-1,6-dibutyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]-diazepine (196) (1mmol, 0.2173g) was placed in a round-bottomed flask and butyl isothiocyanate (20mmol, 2.3039g, 2.41ml) added. The resulting reaction mixture was heated at 145°C on an oil bath for 45 minutes.

On cooling, ether (25ml) was added and the product allowed to crystallise slowly overnight. The product, thus obtained, was filtered off and washed with ether. A first crop of the product was obtained from benzene (5ml concentrated to ca. half volume), and a further crop was obtained from acetonitrile (3ml). 2,3,4,5-Tetrahydro-1,6-dibutyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraaza-pentalene-2,5-dithione (230(g)) crystallised as white needles (0.1597g, 39%), mp 126-127°C.

Microanalysis:

		%C	%H	%N
	Found:	56.43	6.33	13.78
$C_{19}H_{26}N_4S_3$	Requires:	56.12	6.44	13.78

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(c) Attempted Reaction of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine and t-Butyl Isothiocyanate

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196) (1mmol, 0.2173g) and t-butyl isothiocyanate (20mmol, 2.3039g, 2.54ml) were mixed in a round-bottom flask and heated for 15 minutes at 145°C on an oil bath.

On cooling, the crystalline precipitate was filtered off and washed with ether. Recrystallisation from acetonitrile (4ml) yielded 5,6-benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine as white prisms (0.1337g, 63%), mp 204-206°C. This was identical (^{1}Hnmr, mass spectrum, mp, mixed mp) with an authentic sample.

(d) Attempted Reaction of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine with allyl isothiocyanate

Method A

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196) (1mmol, 0.2173g) was placed with allyl isothiocyanate (20mmol, 1.9831g, 1.96ml) in a round-bottomed flask, and the resulting

mixture heated at 145°C on an oil bath for 15 minutes.

On cooling, ether (50ml) was added, however, no crystalline precipitate was observed. Examination of the reaction mixture by t.l.c. (10% methanol in ether and 1:1 ether/benzene) showed mainly tar at the origin and a trace of unreacted diazepine (196).

Method B

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) was dissolved in dichloromethane (20ml) and to this added allyl isothiocyanate (10mmol, 0.9915g, 0.98ml). The resulting solution was left to stand at room temperature for 24 hours.

After 24h, the solvent was removed and ether (50ml) added. No crystalline precipitate was subsequently observed, suggesting that not even the zwitterion is formed. Examination of the reaction mixture by t.l.c. as previously, showed only reactants.

(e) Attempted Reaction of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a] [1,2,4]thiadiazolo[1,3]diazepine with cyclohexyl isothiocyanate

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) was placed in a round-bottomed flask and to this added cyclohexyl isothiocyanate (20mmol, 2.8247g, 2.84ml). This reaction mixture was heated at 145°C on an oil bath for 15 minutes.

On cooling, no crystalline precipitate was observed even on addition of ether (75ml). An examination of the reaction mixture by t.l.c. (10% methanol in ether and 1:1 ether/benzene) showed only starting materials.

(f) With Phenyl Isothiocyanate

(1) Formation of 2,3,4,5-Tetrahydro-1,6-diphenyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione.

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196) (1mmol, 0.2173g) was heated, at 140°C on an oil bath, with phenyl isothiocyanate (20mmol, 2.4ml) for 15 minutes.

On cooling, the product was filtered off, and washed with ether (10ml). After recrystallisation from N,N-dimethylformamide (4ml), 2,3,4,5-tetrahydro-1,6-diphenyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (230(h)) was obtained as pale yellow spars (0.3659g, 82%), mp 161-163°C.

Microanalysis:

		%C	%H	%N
	Found:	61.56	4.12	12.91
$C_{23}H_{18}N_4S_3$	Requires:	61.85	4.06	12.54

^{1}Hnmr: could not be obtained due to low solubility.

Mass Spectrum (see Table 8)

(2) Formation of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepinium-7-(phenylthiocarbamate).

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196) (1mmol, 0.2173g) was dissolved in dichloromethane (25ml) and the solution filtered. Phenyl isothiocyanate (10mmol, 1.2ml) was added to this filtered solution, and the resulting reaction mixture left to stand for 4 hours.

After this time, the solvent was removed, ether (50ml) added to the residue and the resulting white precipitate filtered and washed with more ether. 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4] thiadiazolo[1,3]diazepinium-7-(phenylthiocarbamate) (233) was obtained as white prisms (0.2180g, 62%), mp 192-195°C (with decomposition from 130°C).

Microanalysis:

		%C	%H	%N
	Found:	61.29	4.53	15.89
$C_{18}H_{16}N_4S_2$	Requires:	61.34	4.58	15.90

^{1}Hnmr (see Table N)

Mass Spectrum: the product broke down to give the spectra of the diazepine (196) and PhNCS superimposed.

(g) Formation of 2,3,4,5-Tetrahydro-1,6-dibenzyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3] diazepine (196) (1mmol, 0.2173g) and benzyl isothiocyanate (20mmol, 2.9843g, 2.65ml) were placed in a round-bottomed flask and heated at 145°C on an oil bath for 15 minutes.

On cooling, the crystalline precipitate was filtered off and washed with ether. Recrystallisation from acetonitrile (70ml concentrated to ca. half volume) yielded 2,3,4,5-tetrahydro-1,6-dibenzyl-3,4-xylyl-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione

(230(i)) as white prisms (0.2923g, 62%), mp 193-194°C.

Microanalysis: A sample for analysis was recrystallised from benzene.

		%C	%H	%N
	Found:	63.48	4.65	11.62
$C_{25}H_{22}N_4S_3$	Requires:	63.26	4.67	11.80

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(h) Attempted Reaction of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine with p-tolyl isothiocyanate

5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine (196) (1mmol, 0.2173g) was placed in a round-bottom flask and to this added p-tolyl isothiocyanate (20mmol, 2.9843g). The resultant was heated at 145°C on an oil bath for 15 minutes.

On cooling, ether (50ml) was added and the solution left to stand overnight. However, no crystalline precipitate was observed. Examination of the reaction mixture by t.l.c. (10% methanol in ether and 1:1 ether/benzene) showed only decomposition products at the origin, and traces of reactants.

III Reactions of 5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189)

(i) With Imidoyl Chlorides

(a) With N-Methyl Benzimidoyl Chloride

(1) 1.5 : 1 excess of perchloric acid.

N-Methyl benzimidoyl chloride was prepared by the method of Braun J. and Pinkernelle W.[181].

N-Methyl benzimidoyl chloride (1.5mmol, 0.2304g) and 5,6-dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) were dissolved in acetonitrile (1ml) and the resulting solution brought to reflux and boiled for 10 minutes.

On cooling, ether (20ml) was added and the precipitate allowed to settle. The ether layer was decanted and the residue was dissolved in ethanol (1.5ml). Perchloric acid (1.5mmol, 0.126ml) was added to the ethanol solution and the resulting crystalline precipitate filtered off and washed with a little ether. After recrystallisation from ethanol (5ml), 5,6-dihydro-3-methyl-4H-7-(N-benzylidine-methylamino)-pyrimido[1,2-d][1,2,4]thiadiazolium perchlorate (242(a)) was obtained as pale yellow needles (0.2306g, 55%), mp 185-190°C.

Microanalysis:

		%C	%H	%N
	Found:	45.10	4.57	14.89
$C_{14}H_{17}N_4ClO_4S$	Requires:	45.10	4.60	15.03

^{1}Hnmr (see Table 0)

Mass Spectrum: product breaks down to give spectra of (189) and imidoyl chloride superimposed.

(2) 3:1 excess of perchloric acid.

N-Methyl benzimidoyl chloride (1.5mmol, 0.2304g) and 5,6-dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) were dissolved in acetonitrile (1ml) and the resulting solution was boiled for 10 minutes.

On cooling, ether (20ml) was added and the precipitate allowed to settle. The ether layer was decanted and perchloric acid (3mmol, 0.252ml) added to the residue. The crystalline precipitate thus formed was filtered off, washed with a little ether, and recrystallised from acetonitrile (5ml, a second crop being obtained on addition of 25ml of ethyl acetate). 5,6-dihydro-3-methyl-4H-7-(N-benzylidine-methylammonio)-pyrimido[1,2-d][1,2,4]thiadiazolium diperchlorate (243) was obtained as white needles (0.1996g, 42%), mp 225-227°C.

Microanalysis:

		%C	%H	%N
	Found:	35.48	3.84	11.73
$C_{14}H_{18}N_4Cl_2O_8S$	Requires:	35.53	3.83	11.84

^{1}Hnmr (see Table 0)

Mass Spectrum: No spectrum was able to be obtained due to the low volatility of the product.

(b) With N-Phenyl Benzimidoyl Chloride

N-Phenyl benzimidoyl chloride was prepared by the method of Braun J. and Pinkernelle W.[181].

N-Phenyl benzimidoyl chloride (1.5mmol, 0.3235g) and 5,6-dihydro-3-methyl-4H-pyrimido[1,2—d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) were dissolved in acetonitrile (4ml) and the resulting solution boiled for 10 minutes. On cooling, ether (20ml) was added and the precipitate allowed to settle. The ether layer was decanted and the residue dissolved in ethanol (2ml). Perchloric acid (3mmol, 0.252ml) was added to the ethanolic solution and the resulting crystalline precipitate filtered off and washed with a little ether. After recrystallisation from acetonitrile/ether (1:5, 30ml), 5,6-dihydro-3-methyl-4H-7-(N-benzylidine-phenylamino)-pyrimido-[1,2-d][1,2,4]thiadiazolium perchlorate (242(b)) was obtained as white prisms (0.2923g, 67%), mp 238-239°C.

Microanalysis:

		%C	%H	%N
	Found:	52.27	4.40	12.74
$C_{19}H_{19}N_4ClO_4S$	Requires:	52.47	4.40	12.88

^{1}Hnmr (see Table 0)

Mass Spectrum: product breaks down to give spectra of (189) and imidoyl chloride superimposed.

(c) With N-Phenyl Trimethylacetimidoyl Chloride.

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189)

(1mmol, 0.1552g) and N-phenyl trimethylacetimidoyl chloride (1.5mmol, 0.2935g) were dissolved in acetonitrile (1ml) and the resulting solution boiled for 10 minutes.

On cooling, ether (20ml) was added and the precipitate left to settle. The ether layer was decanted and the residue dissolved in ethanol/methanol (2:1, 6ml). Perchloric acid (3mmol, 0.252ml) was added to this solution, followed by ether (20ml), and the resulting crystalline precipitate filtered off.

On examination of a ^{1}Hnmr spectrum obtained of the crystaline precipitate there would appear to be a mixture of protonated base and the desired 1:1 adduct [(242), R^{1}=CMe_3, R^{2}=Ph]. With this in mind several modifications of this reaction were carried out.

Reaction time ; Temperature

(1) 1 hour ; boiling acetonitrile

(2) 30 minutes ; room temperature

(3) 24 hours ; room temperature

^{1}Hnmr data were obtained for the above reaction conditions and in all cases there appeared to be a mixture of the desired product and the protonated base. The reaction carried out at room temperature for 30 minutes appears to be the most favourable to the desired product and it was thought that this may indicate that the desired product was unstable and decomposed on formation, (see Table Z).

(d) With N-Methyl Trimethylacetimidoyl Chloride

Formation of N-Methyl Trimethylacetamide.

Methylamine gas was bubbled through a solution of trimethylacetyl chloride (100mmol, 12.3165g) in ether (500ml) for approximately 1.5 hours. The methylamine hydrochloride was filtered off and discarded, the filtrate taken to dryness, and recrystallised from hexane (15ml). N-Methyl trimethylacetamide (297) was obtained as white needles (10.13g, 88%), mp 89-91°C.

Microanalysis:

		%C	%H	%N
	Found:	62.37	11.54	12.18
$C_6H_{13}NO$	Requires:	62.57	11.38	12.16

Accurate Mass Found: 115.099256

$C_6H_{13}NO$ Requires : 115.09970

^{1}Hnmr (see Table P)

Mass Spectrum (see Table 9)

Formation of N-Methyl Trimethylacetimidoyl Chloride.

N-Methyl trimethylacetamide (50mmol, 5.7587g) was added portionwise over a period of 15 minutes to a stirred suspension of phosphorus pentachloride (50mmol, 0.4119g) in benzene (60ml) and the resulting mixture brought slowly to reflux and boiled for 1 hour.

On cooling, the solution was transferred to a vigreux flask and fractionally distilled at room temperature to remove the benzene and the phosphorus oxychloride. N-Methyl trimethylacetimidoyl chloride (298) was purified by distillation at the water pump

(1.7298g, 26%), bp 34°C/15mmHg.

A microanalysis of this product was unable to be obtained as the product appeared to react with the capsules used to contain the material for analysis.

Accurate Mass Found: 133.066401

$C_6H_{12}NCl$ Requires : 133.06582

^{1}Hnmr: The ^{1}Hnmr spectrum obtained suggests that the product is a mixture of cis and trans isomers (see Table P), E:Z ratio ca. 1:1.

Mass Spectrum (see Table 9).

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) and N-methyl trimethylacetimidoyl chloride (1.5mmol, 0.2004g) were dissolved in acetonitrile (4ml) and the resulting solution boiled for 5 minutes.

On cooling, ether (20ml) was added and the precipitate filtered, dried and dissolved in ethanol/methanol (2.5ml:3ml). Perchloric acid (3mmol, 0.252ml) was added to this solution, followed by ether (20ml) and this precipitate filtered and dried *in vacuo*.

On examination of the ^{1}Hnmr spectrum obtained of the precipitate it would appear that a mixture of products was formed and hence this reaction was abandoned.

(e) With N-Phenyl Acetamide, Phosgene and Triethylamine.

N-Phenyl acetamide (5mmol, 0.6758g) was dissolved in benzene (60ml) and treated at 60°C with phosgene gas for 1.5 hours.

On cooling, a solution of 5,6-dihydro-3-methyl-4H-pyrimido-[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) in benzene (5ml) was added to the reaction mixture followed by triethylamine (10mmol, 1.39ml). The resulting solid was filtered, washed with benzene and then with ether. The solid thus obtained was disslved in propan-2-ol (10ml) and reprecipitated with ether (50ml). This precipitate was filtered off and a ^{1}Hnmr spectrum obtained.

On examination by ^{1}Hnmr spectroscopy, a mixture of signals was observed. The main signals appeared to be due to triethylamine hydrochloride, but there were, however, trace signals which corresponded to the hydrochloride of the base (189). No phenyl residue was detected and hence this line of approach was abandoned.

(f) With N-Methyl Dimethylcarbamidoyl Chloride.

Formation of 1,1,3-trimethylurea.

Methylamine gas was bubbled through a solution of dimethyl-carbamyl chloride in ether. The methylamine hydrochloride was filtered off, and the filtrate taken to dryness. The product was recrystallised from ether to give 1,1,3-trimethylurea as white prisms, mp 72-74°C (literature: 75.5°C).

Attempted Formation of N-Methyl Dimethylcarbamidoyl Chloride.

1,1,3-Trimethylurea (20mmol, 2.0427g) was dissolved in dichloromethane (10ml) and treated with oxalyl chloride (40mmol, 3.43ml). Subsequently the reaction mixture was heated on a water bath at 50°C for a period of 20 minutes.

On cooling, ether (20ml) was added to ensure complete precipitation and the product (245) was then filtered rapidly due to its extremely hygroscopic nature.

^{1}Hnmr (see Table Q)

On examination by ^{1}Hnmr spectroscopy, the product was found to be the chloride salt (245) as anticipated, however attempts to deprotonate this salt using anhydrous potassium carbonate and triethylamine proved unsuccessful.

In order to see whether the imidoyl chloride would react with 5,6-dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole, a small scale reaction employing the salt (245) and a 2:1 excess of the base (189) was carried out. Both reactants were dissolved in acetonitrile and this solution boiled for 10 minutes and allowed to cool. On cooling, ether was added and the cloudy precipitate allowed to settle for 2 hours. The ether layer was decanted, the residue treated with perchloric acid, and a ^{1}Hnmr spectrum of the resulting solid obtained. On examination of the ^{1}Hnmr spectrum thus obtained it was found that there were insufficient signals for the desired product.

(ii) With Dibromofomaldoxime (226)

Dibromoformaldoxime was prepared by the method of Vyas, Chiang and Doyle[183].

Method A

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189)

(1mmol, 0.1552g) was dissolved in acetonitrile (5ml), dibromoformaldoxime (226) (1.5mmol, 0.3042g) added, and the resultant boiled for 20 minutes.

On cooling, ether (25ml) was added and the precipitate filtered off and dried in vacuo. The product was recrystallised from ethanol (10ml, precipitation with 25ml ether). 5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazolium bromide[174] was obtained as white needles (0.0949g, 40%), mp 293-294°C.

Microanalysis:

		%C	%H	%N
	Found:	30.53	4.20	17.57
$C_6H_{10}N_3SBr$	Requires:	30.52	4.27	17.80

Method B

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was dissolved in acetonitrile (15ml) and dibromoformaldoxime (226) (1mmol, 0.2028g) added to this solution, followed by triethylamine (10mmol, 1.39ml). This solution was boiled for 10 minutes and allowed to cool. The small amount of crystalline material formed was filtered off and recrystallised from acetonitrile (5ml, precipitating with 25ml of ether). Triethylamine hydrobromide was obtained as white needles (0.1254g, 69%), mp 248-250°C. Examination of the mother liquor by t.l.c. (10% methanol in ether) showed the presence of at least 10 different products.

(iii) With Isocyanates

(a) Formation of 2,3,4,5-Tetrahydro-1,6-dimethyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was dissolved in dichloromethane (20ml) and to this added methyl isocyanate (10mmol, 0.62ml) and the resulting solution left to stand for 4 hours at room temperature.

The solvent was subsequently removed, ether (50ml) added, and this mixture left to crystallise slowly overnight. The ether was carefully decanted and the residue recrystallised from acetonitrile (2ml), yielding 2,3,4,5-tetrahydro-1,6-dimethyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (247(a)) as white spars (0.1136g, 50%), mp 105-125°C (with slow decomposition).

Microanalysis: A satisfactory analysis could not be obtained. (A sample was recrystallised from acetonitrile three times in succession, and another was recrystallised from benzene).

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(b) Formation of 2,3,4,5-Tetrahydro-1,6-dicyclohexyl-3,4-propano-6aλ-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) and cyclohexyl isocyanate (20mmol, 2.5034g, 2.55ml) were heated at 145°C on an oil bath for 15 minutes.

On cooling, the crystalline precipitate was filtered off and washed with ether. Recrystallisation from acetonitrile (5ml)

afforded 2,3,4,5-tetrahydro-1,6-dicyclohexyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (247(b)) as white spars (0.2274g, 62%), mp 140-141°C.

Microanalysis: A correct analysis could not be obtained.

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(c) Formation of 2,3,4,5-Tetrahydro-1,6-diphenyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) and phenyl isocyanate (20mmol, 2.2ml) were heated at 145°C on an oil bath for 15 minutes.

On cooling, the product was filtered and washed with a little ether. Recrystallisation from acetonitrile (11ml) yielded 2,3,4,5-tetrahydro-1,6-diphenyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (247(c)) as white needles (0.2821g, 80%), mp 209-212°C.

Microanalysis:

		%C	%H	%N
	Found:	61.45	4.50	15.97
$C_{18}H_{16}N_4SO_2$	Requires:	61.35	4.58	15.90

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(d) With Benzyl Isocyanate

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask and benzyl isocyanate (20mmol, 2.6630g, 2.47ml) added. This reaction mixture was heated at 145°C on an oil bath for 15 minutes.

On cooling, ether (25ml) was added, but the precipitate thus obtained, oiled on filtering. Examination of the reaction mixture by t.l.c. (10% methanol in ether and 1:1 ether/benzene) showed no products.

(e) Formation of 2,3,4,5-Tetrahydro-1,6-di(p-tolyl)-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask, p-tolyl isocyanate (20mmol, 2.6630g, 2.52ml) added, and the resulting reaction mixture heated at 145°C on an oil bath for 15 minutes.

On cooling, the crystalline product was filtered and washed with ether. Recrystallisation from acetonitrile (25ml) yielded 2,3,4,5-tetrahydro-1,6-di(p-tolyl)-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dione (247(d)) as white spars (0.2721g, 72%), mp 217-218°C.

Microanalysis:

		%C	%H	%N
	Found:	63.15	5.17	14.77
$C_{20}H_{20}N_4SO_2$	Requires:	63.14	5.30	14.73

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(f) With p-Toluenesulphonyl Isocyanate

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) and p-toluenesulphonyl isocyanate (20mmol, 3.9442g) were added to a round-bottomed flask and the resulting reaction mixture was heated at 145°C on an oil bath for 15 minutes.

On cooling, ether (25ml) was added and the resulting crystalline precipitate recrystallised from acetonitrile (5ml).

However, examination by ^{1}Hnmr spectroscopy of the tacky solid thus obtained did not show the triplet expected for the desired product. In addition, as with the diazepine, there were too many methyl signals for either a 1:1 or a 2:1 adduct. (Three methyl signals at 2.352 δ, 2.419 δ, 2.529 δ).

(g) With Chlorosulphonyl Isocyanate

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask and to this added chlorosulphonyl isocyanate (20mmol, 2.8307g, 1.74ml) and the resulting mixture taken to reflux and boiled for 15 minutes.

On cooling, ether (25ml) was added however, no crystalline precipitate was observed nor indeed was any product observed on t.l.c. (10% methanol in ether and 1:1 ether/benzene).

(iv) With Isothiocyanates

(a) Formation of 2,3,4,5-Tetrahydro-1,6-dimethyl-3,4-propano-6aλ^{4}-thia-1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was dissolved in dichloromethane (20ml) and to this

added methyl isothiocyanate (10mmol, 0.7ml). The resulting solution was allowed to stand at room temperature for 4h.

The solvent was subsequently removed, ether (50ml) added, and the product filtered and washed with further ether. After recrystallisation from acetonitrile (13ml concentrated to ca. 8ml), 2,3,4,5-tetrahydro-1,6-dimethyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (247(e)) was obtained as white needles (0.1606g, 62%), mp 203-204°C.

Microanalysis:

		%C	%H	%N
	Found:	37.09	4.50	21.64
$C_8H_{12}N_4S_3$	Requires:	36.90	4.64	21.52

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(b) Formation of 2,3,4,5-Tetrahydro-1,6-dibutyl-3,4- propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask and to this added butyl isothiocyanate (20mmol, 2.3039g, 2.41ml). The resultant was heated at 145°C on an oil bath for 15 minutes.

On cooling, the product was filtered and washed with ether. After recrystallisation from acetonitrile (12ml concentrated to ca. half volume), 2,3,4,5-tetrahydro-1,6-dibutyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (247(f)) was obtained as white needles (0.2508g, 73%), mp 140-145°C.

Microanalysis:

		%C	%H	%N
	Found:	48.63	6.94	16.21
$C_{14}H_{24}N_4S_3$	Requires:	48.80	7.02	16.26

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(c) With t-Butyl Isothiocyanate

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask, t-butyl isothiocyanate (20mmol, 2.3039g, 2.54ml) added, and the resultant heated for 15 minutes at 145°C on an oil bath.

On cooling, ether (25ml) was added, and the solution left to stand overnight. After this time, no crystalline precipitate was observed, and subsequent examination of the reaction mixture by t.l.c. (10% methanol in ether) showed only starting materials and the thermolysis product of the base (189) i.e. 2-hexahydro-pyrimidinethione (222).

(d) Formation of 2,3,4,5-Tetrahydro-1,6-diallyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapetalene-2,5-dithione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask, and to this added allyl isothiocyanate (20mmol, 1.9831g, 1.96ml). The resulting mixture was heated at 145°C on an oil bath for 15 minutes.

The crystalline precipitate was subsequently filtered and

washed with ether. Recrystallisation from acetonitrile (6ml concentrated to ca. 4ml), yielded 2,3,4,5-tetrahydro-1,6-diallyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (247(g)) as white needles (0.2131g), 68%), mp 154-157°C.

Microanalysis:

		%C	%H	%N
	Found:	45.86	5.10	17.86
$C_{12}H_{16}N_4S_3$	Requires:	46.13	5.16	17.93

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(e) With t-Octyl Isothiocyanate

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask and to this added t-octyl isothiocyanate (20mmol, 3.4261g, 2.86ml). The resultant was heated at 150°C on an oil bath for 15 minutes.

On cooling, the crystalline precipitate was filtered and washed with ether. On recrystallisation from acetonitrile (10ml concentrated to ca. half volume), 5,6-dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]-thiadiazole was obtained as white needles (0.0375g, 24%). The product was identical (^{1}Hnmr, mass spectrum, mp, mixed mp) with an authentic sample.

(f) Formation of 2,3,4,5-Tetrahydro-1,6-dicyclohexyl-3,4-propano-6aλ^4-thia -1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189)

(1mmol, 0.1552g) was placed in a round-bottomed flask and to this added cyclohexyl isothiocyanate (20mmol, 2.8247g, 2.84ml). The resulting mixture was heated at 145°C on an oil bath for 15 minutes.

On cooling, the product was filtered and washed with ether. After recrystallisation from acetonitrile (40ml concentrated to ca. 8ml), 2,3,4,5-tetrahydro-1,6-dicyclohexyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (247(h)) was obtained as white needles (0.0482g, 12%), mp 183-185°C.

Microanalysis:

		%C	%H	%N
	Found:	54.14	7.22	14.28
$C_{18}H_{28}N_4S_3$	Requires:	54.51	7.12	14.13

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(g) Formation of 2,3,4,5-Tetrahydro-1,6-diphenyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was heated with phenyl isothiocyanate (20mmol, 2.4ml) at 140°C on an oil bath for 15 minutes.

On cooling, the product was filtered and washed with a little ether, 2,3,4,5-Tetrahydro-1,6-diphenyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (247(i)) was obtained, after recrystallisation from acetonitrile (47ml concentrated to ca. 30ml),

as white spars (0.2341g, 61%), mp 175-182°C.

Microanalysis:

		%C	%H	%N
	Found:	56.05	4.17	14.78
$C_{18}H_{16}N_4S_3$	Requires:	56.22	4.19	14.57

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(h) Formation of 2,3,4,5-Tetrahydro-1,6-dibenzyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask with benzyl isothiocyanate (20mmol, 2.9843g, 2.65ml) and the resultant heated at 145°C on an oil bath for 15 minutes.

On cooling, the product was filtered off and washed with ether. Recrystallisation from acetonitrile (185ml concentrated to 150ml) yielded 2,3,4,5-tetrahydro-1,6-dibenzyl-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (247(j)) as white needles (0.3591g, 87%), mp 207-208°C.

Microanalysis:

		%C	%H	%N
	Found:	57.91	4.83	13.54
$C_{20}H_{20}N_4S_3$	Requires:	58.22	4.89	13.58

^{1}Hnmr (see Table M)

Mass Spectrum (see Table 8)

(i) Formation of 2,3,4,5-Tetrahydro-1,6-di(p-tolyl)-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was placed in a round-bottomed flask and to this added p-tolyl isothiocyanate (20mmol, 2.9843g). The resulting reaction mixture was heated at 145°C on an oil bath for 15 minutes.

On cooling, the product was filtered and washed thoroughly with ether to remove any traces of solid p-tolyl isothiocyanate. Recrystallisation from acetonitrile (40ml) concentrated to ca. 8ml) yielded 2,3,4,5-tetrahydro-1,6-di(p-tolyl)-3,4-propano-6aλ^4-thia-1,3,4,6-tetraazapentalene-2,5-dithione (247(k)) as pale yellow prisms (0.1526g, 37%), mp 175-179°C.

Microanalysis: A sample for analysis was recrystallised from benzene.

		%C	%H	%N
	Found:	58.17	4.83	13.47
$C_{20}H_{20}N_4S_3$	Requires:	58.22	4.89	13.58

^{1}Hnmr (see Table M)

Mass Spectrum: unable to be obtained due to low volatility.

(j) With Trimethylsilyl Isothiocyanate

Trimethylsilyl isothiocyanate (8mmol, 1.13ml) was added to a filtered solution of 5,6-dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) in toluene (5ml). A cream

coloured precipitate was formed immediately on mixing and this was filtered off and washed, firstly with toluene, and then with ether. On testing the product with ferric chloride a deep red colouration arising from the presence of free thiocyanate was observed. 5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazolium thiocyanate (251) was obtained as white prisms (0.1799g, 84%), mp 215-216°C. A small sample was recrystallised from acetonitrile for microanalysis.

Microanalysis:

		%C	%H	%N
	Found:	39.34	4.74	26.26
$C_7H_{10}N_4S_2$	Requires:	39.23	4.70	26.14

^{1}Hnmr (see Table R).

As a parallel experiment, a solution of trimethylsilyl isothiocyanate in toluene and ferric chloride was left to stand at room temperature for 24 hours. After this time only a faint red colouration was observed on testing with ferric chloride suggesting that the formation of the thiocyanate salt is base catalysed by 5,6-dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189).

In order to confirm that it was indeed the thiocyanate salt (251) that was being formed, an authentic sample was prepared via the chloride.

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was dissolved in dichloromethane (20ml) and

treated with hydrochloric acid (36% w/w, 3mmol, 0.26ml). Ether (50ml) was added and the resulting oil allowed to settle before the ether layer was decanted. The residue was dissolved in ethanol (10ml) and the hydrochloride (299) precipitated as white prisms (0.1587g, 83%), mp 249-250°C.

Microanalysis:

		%C	%H	%N
	Found:	37.60	5.26	21.92
$C_6H_{10}N_3SCl$	Requires:	37.47	5.23	22.12

^{1}Hnmr (see Table S)

Mass Spectrum: the product lost HCl to give a spectrum identical to (189).

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazolium chloride (299) (0.5mmol, 0.0958g) was dissolved in boiling acetonitrile (25ml) and to this added a solution of sodium thiocyanate dihydrate (0.5mmol, 0.0586g) in boiling acetonitrile (10ml). The resulting reaction mixture was hot filtered to remove the sodium chloride formed, the filtrate taken to dryness, and the residue recrystallised from boiling acetonitrile (10ml). 5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazolium thiocyanate (251) was obtained as white prisms (0.0710g, 66%), mp 214-215°C. On testing with ferric chloride a deep red colouration was again observed.

Microanalysis:

		%C	%H	%N
	Found:	39.16	4.69	26.24
$C_7H_{10}N_4S_2$	Requires:	39.23	4.70	26.14

^{1}Hnmr (see Table R)

Mass Spectrum: The product lost HSCN to give a spectrum identical to (189).

Mixed mp with product previously obtained: 213-214°C.

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

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) and diphenyl phosphoroisothiocyanatidate (252) (20mmol, 5.8253g, 4.52ml) were heated at 145°C on an oil bath for 15 minutes.

On cooling, no crystalline product was observed and hence ether (25ml) was added. The precipitate, thus obtained, oiled on filtering and hence the reaction was pursued no further.

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

Method A

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) and chloromethylthiocyanate (254) (20mmol, 2.1512g,

1.57ml) were heated at 145°C on an oil bath for 15 minutes.

On cooling, no crystalline product was obtained even after addition of ether (50ml). Examination of the reaction mixture by t.l.c. (10% methanol in ether or 1:1 benzene/ether) showed no worthwhile products, only a black tar on the origin.

Method B

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was dissolved in dichloromethane (20ml) and to this added chloromethylthiocyanate (254) (10mmol, 0.79ml) and the resulting solution allowed to stand at room temperature for 4 hours.

The dichloromethane was subsequently removed and ether (50ml) added. Again, no crystalline product was obtained, and examination by t.l.c. showed, as before, no worthwhile products.

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

Method A

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) was mixed with 2,2,2-trifluoroacetophenone [(258), R=Ph] (20mmol, 3.4824g, 2.81ml) and the resultant heated at 145°C on an oil bath for 15 minutes.

On cooling, examination of the reaction mixture by t.l.c. (10% methanol in ether and 1:1 ether/benzene) showed only the presence of starting materials.

Method B

The reaction mixture was prepared as before and subsequently boiled (bp of 2,2,2-trifluoroacetophenone 165-166°C) for 30 minutes.

Examination of the reaction mixture by t.l.c. (10% methanol in ether and 1:1 ether/benzene) showed a trace product at r_F 0.5.

Method C

The reaction mixture was prepared as Method A and to this added a high boiling inert solvent, o-dichlorobenzene [(10ml), bp 179-180°C]. This solution was boiled for 2 hours and a product, r_F 0.5, was again observed.

However, running the reaction mixture against a standard, 2-hexahydropyrimidinethione (222), showed the product to be (222) i.e. the thermolysis product of the base (189).

(b) Attempted Reaction of 5,6-Dihydro-3-methyl-4H-pyrimido [1,2-d][1,2,4]thiadiazole with Hexafluoroacetone [(258), R=CF_3]

This reaction was attempted under analogous conditions to methods B and C previously described. Again, only the thermolysis product, 2-hexahydropyrimidinethione (222), was detected.

(viii) Attempted Reaction of 5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d]-[1,2,4]thiadiazole and S,S-Diphenyl Sulphilimine

5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazole (189) (1mmol, 0.1552g) and S,S-diphenyl sulphilimine (260) (4mmol, 0.8052g) were mixed and heated for 15 minutes at 145°C on an oil bath.

On cooling, a small amount of crystalline material was observed.

Examination by ^{1}Hnmr spectroscopy showed this material to be unreacted sulphilimine.

IV Reactions of 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole

(i) Thermolysis

5,6-Dihydro-2-methyl-4H-pyrimido-[1,2-d][1,3,4]thiadiazole (212) (5mmol, 0.7761g) was dissolved in 1,2,3,4-tetrahydronaphthalene (50ml), and boiled under argon for ninety hours.

On examination by t.l.c. (10% methanol in ether) only thiadiazole (212) was detected, and further attempts to thermolyse this compound were not made.

(ii) With Carbon Disulphide

5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) (1mmol, 0.1552g) was added to carbon disulphide (83mmol, 5ml). After 5 minutes, the excess carbon disulphide was removed at the water pump leaving a pale pink powder. However, the product spontaneously decomposed at room temperature with loss of carbon disulphide to give the thiadiazole (212) (^{1}Hnmr, mass spectrum and t.l.c. identical to authentic sample), and hence neither spectra nor analysis of the product were able to be obtained.

(iii) With Nitriles

(a) With Acetonitrile

5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) (1mmol, 0.1552g) was dissolved in acetonitrile (10ml) and the resulting solution boiled for 8 days. A further 5ml of acetonitrile was added after every 24 hour interval.

On examination of the reaction mixture by t.l.c. (10% methanol in ether) only reactant (212) was detected.

On standing at room temperature for a further 11 days, no exchange product was obtained.

(b) With Benzonitrile

5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) (5mmol, 0.7761g) was added to benzonitrile (24.5mmol, 2.5ml) and the resulting solution boiled for 0.5 hours on an oil bath.

On cooling, the reaction mixture was chromatographed on silica (40cm x 2.7cm) eluting with ether. The first 700ml of eluates brought off the benzonitrile. Thereafter the polarity of the solvent was stepped up in 250ml amounts to 50% methanol in ether and no product was detected in these eluates. Subsequently, methanol (750ml) was put through the column and this brought off the original base. 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) was obtained as a colourless liquid (0.6029g, 80%), which was identical (t.l.c., mass spectrum) to an authentic sample.

(iv) With Methyl Isothiocyanate

(a) In toluene

5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) (1mmol, 0.1552g) was dissolved in toluene (5ml) and to this added methyl isothiocyanate (10mmol, 0.7ml).

After standing for 15 minutes, 5,6-dihydro-2-methyl-4H-pyrimido [1,2-d][1,3,4]thiadiazolium-7-(methylthiocarbamate) (265) was obtained as white prisms (0.2193g, 96%), mp 70-80°C.

Microanalysis:

		%C	%H	%N
	Found:	42.15	5.24	24.64
$C_8H_{12}N_4S_2$	Requires:	42.08	5.30	24.54

^{1}Hnmr (see Table T).

Mass Spectrum: The mass spectrum shows the superimposed spectra of thiadiazole (212) and methyl isothiocyanate.

(b) In dichloromethane

5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole (212) (1mmol, 0.1552g) was dissolved in dichloromethane (20ml) and to this solution added methyl isothiocyanate (10mmol, 0.7ml).

The resulting solution was left at room temperature for a period of 72 hours, and the solvent subsequently removed. Ether (50ml) was added to the residue and the crystalline product filtered and washed with more ether. 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4] thiadiazolium-7-(methylthiocarbamate) (265) was obtained as white spars (0.1895g, 83%), mp 78-79°C.

^{1}Hnmr: Identical to the ^{1}Hnmr spectrum of the product obtained in toluene.

Mixed mp with product obtained in toluene: 70-80°C.

(c) A further reaction on a similar scale heating the reactants to reflux (bp MeNCS: 117-118°C) on an oil bath in the absence of solvent was attempted. However, this did not yield any worthwile product.

V Synthesis of Possible Monocyclic Precursors of Triheterapentalenes

(i) 2-Benzylthioimidazolidine

2-Imidazolidinethione (271) (50mmol, 5.1079g) and benzyl bromide (62.5mmol, 7.44ml) were placed in a 50ml round-bottomed flask fitted with a reflux condenser, and the flask heated in an oil bath until all the solid had dissolved (oil bath temperature 200°C). Once a solution had been obtained, the resultant was heated for 0.5 hours. On cooling, the glass which was formed was extracted with boiling ethanol (100ml) and the desired product precipitated using ether (180ml). This yielded 2-benzylthioimidazolidinium bromide (300) as a white powder (8.2488g, 60%), mp 169-171°C.

Microanalysis:

		%C	%H	%N
	Found:	43.92	4.82	10.18
$C_{10}H_{13}N_2BrS$	Requires:	43.97	4.80	10.25

^{1}Hnmr (see Table U).

Mass Spectrum: product lost HBr to give a spectrum identical to that of (267).

2-Benzylthioimidazolidinium bromide (300), (25mmol, 6.8288g) was dissolved in distilled water (200ml) and concentrated ammonia (33% w/w, 85.3mmol, 5ml) added. The resulting white precipitate was

immediately extracted with dichloromethane (3 x 125ml). The dichloromethane extracts were dried over anhydrous magnesium sulphate and the solvent evaporated. On recrystallisation from ether/cyclohexane (250ml:25ml), 2-benzylthioimidazolidine (267) was obtained as white plates (4.0300g, 84%), mp 68-69°C.

Microanalysis:

		%C	%H	%N
	Found:	62.58	6.28	14.58
$C_{10}H_{12}N_2S$	Requires:	62.46	6.29	14.57

Accurate Mass Found: 192.073299

$C_{10}H_{12}N_2S$ Requires: 192.07210

^{1}Hnmr (see Table U).

Mass Spectrum (see Table 10).

(ii) 2-Benzylthio-3,4,5,6-tetrahydropyrimidine

2-Hexahydropyrimidinethione (222) (50mmol, 5.8092g) and benzyl bromide (62.5mmol, 7.48ml) were placed in a 50ml round-bottomed flask fitted with a reflux condenser and the flask heated in an oil bath (oil bath temperature 160°C) until a solution was formed. Once a solution was obtained, the reaction mixture was heated for 0.5 hours. On cooling, the glass which was formed was extracted with boiling ethanol (100ml) and concentrated to approximately 50ml. 2-Benzylthio-3,4,5,6-tetrahydropyrimidinium bromide (301) crystallised from the cooled solution as a white, microcrystalline solid (12.1130g, 84%), mp 139-142°C.

Microanalysis:

		%C	%H	%N
	Found:	46.13	5.24	9.72
$C_{11}H_{15}N_2BrS$	Requires:	46.00	5.26	9.75

^{1}Hnmr (see Table U).

Mass Spectrum: product lost HBr to give a spectrum identical to that of (266).

2-Benzylthio-3,4,5,6-tetrahydropyrimidinium bromide (301) (25mmol, 7.1805g) was dissolved in distilled water (200ml) and to this added concentrated ammonia (33% w/w, 85.3mmol, 5ml). The resulting white precipitate was immediately extracted with dichloromethane (3 x 125ml), the extracts dried over anhydrous magnesium sulphate, and the solvent evaporated. 2-Benzylthio-3,4,5,6-tetrahydropyrimidine (266) was obtained as white needles after recrystallisation from ether/cyclohexane (200ml:50ml), (3.5584g, 69%), mp 79-81°C.

Microanalysis:

		%C	%H	%N
	Found:	64.29	6.86	13.61
$C_{11}H_{14}N_2S$	Requires:	64.04	6.84	13.58

Accurate Mass Found: 206.08893

$C_{11}H_{14}N_2S$ Requires: 206.08774

^{1}Hnmr (see Table U).

Mass Spectrum (see Table 10).

(iii) 2-Thiocyano-3,4,5,6-tetrahydropyrimidinium Bromide

2-Hexahydropyrimidinethione (222) (50mmol, 5.8092g) dissolved in N,N-dimethylformamide (40ml) was added to a solution of cyanogen bromide (50mmol, 5.2961g) in N,N-dimethylformamide (25ml). The resulting white crystalline product was filtered off and dried in vacuo. 2-Thiocyano-3,4,5,6-tetrahydropyrimidinium bromide (275) was obtained as white needles after recrystallisation from methanol/ether (400ml:500ml; 2nd crop on addition of a further 250ml of ether), (8.7265g, 79%), mp 175-176°C.

Microanalysis:

		%C	%H	%N
	Found:	27.02	3.62	18.75
$C_5H_8N_3SBr$	Requires:	27.04	3.63	18.92

^{1}Hnmr (see Table U).

Mass Spectrum (see Table 10).

VI Thermolysis of Possible Monocyclic Precursors of Triheterapentalenes

(i) 2-Benzylthioimidazolidine (267)

(a) In isopropylbenzene

2-Benzylthioimidazolidine (267), (5mmol, 0.9614g) was dissolved in isopropylbenzene (25ml). The solution was brought to reflux and boiled under argon for 24 hours (all apparatus being lagged with aluminium foil to exclude light), and allowed to cool overnight.

The mother liquor was decanted, the residue being the product which had crystallised on the flask wall. The product was washed with 40-60 petrol (5ml) and transferred to a sublimation tube by dissolving in dichloromethane. The product was sublimed at the oil pump (0.5mbar) and then recrystallised from N,N-dimethylformamide (8ml). The product, formulated as (268), was obtained as white prisms, (0.0358g), subliming at approximately 260°C.

Microanalysis:

		%C	%H	%N
	Found:	52.76	5.92	41.53
$C_xH_yN_zS_w$	Requires:		?	

^{1}Hnmr (see Table V).

^{13}Cnmr: unable to be obtained due to low solubility of product.

IR Spectrum: KBr disc and CsI disc show a strong absorption at $1650cm^{-1}$.

Mass Spectrum (see Table 11).

(b) In 1,2,3,4-tetrahydronaphthalene

2-Benzylthioimidazolidine (267), (5mmol, 0.9614g) was dissolved in 1,2,3,4-tetrahydronaphthalene (10ml). The resulting solution was brought to reflux and boiled under argon for 4 hours (all apparatus being lagged with aluminium foil to exclude light) and allowed to cool overnight. The product crystallised on the flask wall.

The mother liquor was decanted and the residue washed with 40-60 petrol (5ml) and transferred to a sublimation tube by dissolving in dichloromethane. The residue was sublimed at the oil pump (0.2mbar, heating block temperature: 200°C), yielding a white crystalline material, (0.1384g).

^{1}Hnmr: by comparison with the spectra of 2-imidazolidinethione (271) and the product obtained from the thermolysis of (267) in isopropylbenzene, the solid obtained was shown to be a mixture of the thiourea (271) and the product previously obtained from the thermolysis of 2-benzylthioimidazolidine in isopropylbenzene.

Mass Spectrum: shows superimposed spectra of 2-imidazolidinethione (271) and the product obtained from the thermolysis of 2-benzylthioimidazolidine in isopropylbenzene.

(ii) 2-Benzylthio-3,4,5,6-tetrahydropyrimidine (266)

(a) In isopropylbenzene

2-Benzylthio-3,4,5,6-tetrahydropyrimidine (266) was dissolved in isopropylbenzene (30ml). The solution was brought to reflux and

boiled under argon for 24 hours (all apparatus being lagged with aluminium foil to exclude light) and allowed to cool overnight. The product crystallised out on the flask walls. The mother liquor was decanted and brought to reflux for a further 24 hours whereupon a second crop of product was obtained on cooling. The solid product was combined, washed with 40-60 petrol, and sublimed at the oil pump (0.2mbar). After recrystallisation from ethanol (5ml), 2-hexahydropyrimidinethione (222) was obtained as white needles (0.1336g, 23%), mp 210-211°C.

Accurate Mass Found:	116.041666
$C_4H_8N_2S$ Requires:	116.04081
Mixed mp:	210-211°C.
^{1}Hnmr:	Identical to authentic sample.
Mass Spectrum:	Identical to authentic sample.

(b) In 1,2,3,4-tetrahydronaphthalene

2-Benzylthio-3,4,5,6-tetrahydropyrimidine (266) was dissolved in 1,2,3,4-tetrahydronaphthalene (25ml), the solution brought to reflux, boiled under argon for 4 hours (all apparatus being lagged with aluminium foil to exclude light), and allowed to cool overnight. The product crystallised out on the flask walls.

The mother liquor was decanted and the residue washed with 40-60 petrol (5ml) and transferred to a sublimation tube by dissolving in dichloromethane. The residue was sublimed at the oil pump (0.3mbar). 2-Hexahydropyrimidinethione (222) was obtained as white leaves after recrystallisation from ethanol (6ml), (0.1206g, 21%), mp 208-209°C.

Accurate Mass Found:	116.040298
$C_4H_8N_2S$ Requires:	116.04081
Mixed mp:	209-211°C
^{1}Hnmr:	Identical to authentic sample.
Mass Spectrum:	Identical to authentic sample.

VII Reactions of 5-Chloro-2,3-dimethyl-1,2,4-thiadiazolium Fluorosulphonate with 2-Amino-N-heterocycles

(i) With 2-Amino-6-methyl-pyridine

5-Chloro-3-methyl-1,2,4-thiadiazole was prepared by the method of Goerdeler[184].

5-chloro-3-methyl-1,2,4-thiadiazole (10mmol, 1ml) was dissolved in dichloromethane (5ml), methyl fluorosulphonate (10mmol, 0.8ml) added, and the resultant allowed to stand overnight.

The salt (277), thus obtained, was filtered off, washed with ether, and transferred by means of 1,2-dichloroethane (10ml) into a solution of 2-amino-6-methyl-pyridine (284) (20mmol, 2.1629g) in 1,2-dichloroethane (50ml). The resulting solution was subsequently boiled for 10 minutes.

On cooling, the reaction mixture was filtered to remove any traces of fluorosulphonate salt of (284) which may have formed. Aqueous sodium carbonate (300ml of distilled water, 17.1684g of $Na_2CO_3.10H_2O$, 60mmol) was added to the filtered solution. This mixture was extracted with benzene (2 x 500ml), and washed with distilled water (3 x 500ml). The benzene extracts were dried over anhydrous magnesium sulphate, and the benzene evaporated.

The residue was chromatographed on silica (2.8cm x 60cm), eluting with benzene. The first 1l of benzene and 3l of 10% ether in benzene contained traces of several compounds which appeared to be dissociating on the column and hence, were discarded. The next 1.75l of 20% ether in benzene and 300ml of ether brought off the

product. The product formulated as (287) was obtained after recrystallisation from cyclohexane (25ml concentrated to ca. 15ml, charcoal screen) as white prisms (0.2999g, 14%), mp 127-128°C.

Microanalysis:

		%C	%H	%N
	Found:	54.80	5.49	25.21
$C_{10}H_{12}N_4S$	Requires:	54.52	5.49	25.43

Accurate Mass Found: 220.078358

$C_{10}H_{12}N_4S$ Requires: 220.07825

^{1}Hnmr (see Table W)

Mass Spectrum (see Table 12)

(ii) With 2-Amino-4-methyl-pyridine

5-Chloro-3-methyl-1,2,4-thiadiazole was prepared by the method of Goerdeler[184].

5-Chloro-3-methyl-1,2,4-thiadiazole (10mmol, 1ml) was dissolved in dichloromethane (5ml) and to this added methyl fluorosulphonate (10mmol, 0.8ml). This reaction mixture was left to stand overnight. The resulting salt (277) was filtered, washed with ether, and by means of 1,2-dichloroethane (10ml), washed into a solution of 2-amino-4-methyl-pyridine (285) (20mmol, 2.1629g) in 1,2-dichloroethane (50ml). This reaction mixture was subsequently boiled for 10 minutes.

On cooling, any crystalline product was filtered off (this being

the fluorosulphonate salt of the aminopyridine), and the mother liquor added to aqueous sodium carbonate (300ml distilled water, 17.1684g of $Na_2CO_3,10H_2O$, 60mmol). This aqueous solution was extracted with benzene (2x500ml), and the benzene extracts washed with distilled water (3x500ml). These extracts were dried over anhydrous magnesium sulphate, and the benzene removed.

The residue was chromatographed on silica (2.8cm x 50cm), eluting with benzene. The first 1l of benzene and 1.25l of 10% ether in benzene contained traces of several compounds which appeared to be dissociating on the column. The next 750ml of 10% ether in benzene brought off the product. After recrystallisation from cyclohexane (60ml concentrated to ca. half volume), the product formulated as (288) was obtained as pale yellow prisms (0.5427g, 25%), mp 137-138°C.

Microanalysis:

		%C	%H	%N
	Found:	54.52	5.49	25.51
$C_{10}H_{12}N_4S$	Requires:	54.52	5.49	25.43

Accurate Mass Found: 220.079015

$C_{10}H_{12}N_4S$ Requires: 220.07825

^{1}Hnmr (see Table W)

Mass Spectrum (see Table 12)

(iii) With 2-Amino-2-thiazoline

5-Chloro-3-methyl-1,2,4-thiadiazole was prepared by the method of Goerdeler[184].

5-Chloro-3-methyl-1,2,4-thiadiazole (10mmol, 1ml) was dissolved in dichloromethane (5ml), methyl fluorosulphonate (10ml, 0.8ml) added, and the resultant allowed to crystallise overnight.

The salt (277) was subsequently filtered off, washed with ether, and transferred by means of 1,2-dichloroethane (10ml) into a solution of 2-amino-2-thiazoline (286) (20mmol, 2.0432g) in 1,2-dichloroethane (50ml). The resulting solution was boiled for 10 minutes.

On cooling, the reaction mixture was filtered, to remove any traces of fluorosulphonate salt of (286) that may have been formed, and added to an aqueous solution of sodium carbonate (300ml of distilled water, 17.1684g of $Na_2CO_3.10H_2O$, 60mmol). The resulting mixture was extracted with benzene (2x500ml), and the benzene extracts washed with distilled water (3x500ml). The extracts were dried over anhydrous magnesium sulphate, and the solvent evaporated.

The residue was chromatographed on silica (2.8cm x 50cm), eluting with benzene. The first 750ml of benzene and 500ml of 10% ether in benzene contained no material and were discarded. The next 750ml of 10% ether in benzene contained a product running at r_F 0.6 (t.l.c. on silica, 1:1 ether/benzene) with traces of products at r_F 0.9 and r_F 0.8 also present. The next 250ml of 10% ether in benzene was a mixed fraction, containing products running at r_F 0.6 and r_F 0.5, and was discarded. The following 2l of 10% ether in benzene contained the desired product running at r_F 0.5 on t.l.c. (1:1 ether/benzene).

The product running at r_F 0.6 was found to be a hydrolysis product. After recrystallisation from hexane (15ml concentrated to ca. 5ml), 2,3-dimethyl-1,2,4-thiadiazolo-5-thione (290) was obtained as white spars (0.0346g, 2.4%), mp 101-102°C.

Microanalysis:

		%C	%H	%N
	Found:	32.89	4.11	19.20
$C_4H_6N_2S_2$	Requires:	32.85	4.14	19.16

Accurate Mass Found: 145.997669

$C_4H_6N_2S_2$ Requires: 145.99723

^{1}Hnmr (see Table W)

Mass Spectrum (see Table 12)

The product running at r_F 0.5 was the anticipated product. Recrystallisation from cyclohexane (25ml concentrated to ca. half volume) yielded the product formulated as (289) as white spars (0.2104g, 10%), mp 143-145°C.

Microanalysis:

		%C	%H	%N
	Found:	39.56	4.65	26.24
$C_7H_{10}N_4S_2$	Requires:	39.23	4.70	26.14

Accurate Mass Found: 214.033940

$C_7H_{10}N_4S_2$ Requires: 214.03467

^{1}Hnmr (see Table W)

Mass Spectrum (see Table 12)

APPENDIX I

Nmr solvents:

(a) = Dimethylsulphoxide-d_6 (DMSO-d_6)

(b) = Chloroform-d ($CDCl_3$)

Key to Tables.

(s) = singlet

(d) = doublet

(t) = triplet

(q) = quartet

(qi) = quintet

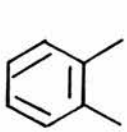
(bs) = broad singlet

(b) = broad signal

(m) = multiplet

Chemical shift values (δ) are given in p.p.m. downfield from tetramethylsilane as internal reference.

* = proton exchanges in D_2O.

R^1 = 

R^2 = 

Table A

^{1}Hnmr Spectrum of 4,5-Dihydro-3-methyl-6-oxopyrimido[1,2-d][1,2,4]thiadiazolium Chloride

Compound No.	Solvent	Chemical Shift
(192)	(a)	2.556 (s) [Me]
		2.953 (t) [CH_2]
		4.487 (t) [CH_2]
		5.512 (bs) [NH]

Table B

^{1}Hnmr Spectrum of 3-Chloro-N([3]methyl[1,2,4]-thiadiazolo)-propanamide

Compound No.	Solvent	Chemical Shift
(292)	(a)	2.452 (s) [Me]
		3.050 (t) [CH_2Cl]
		3.926 (t) [CH_2]
		10.475 (bs) [NH]

Table C

^{1}Hnmr Spectrum of 5-Amino-3-methyl-1,2,4-thiadiazolium Chloride

Compound No.	Solvent	Chemical Shift
(293)	(a)	2.339 (s) [Me]
		10.378 (bs) [NH_3]

Table D

^{1}Hnmr Spectrum of 5(α-Bromo-xylyl)-
-3-methyl-1,2,4-thiadiazolium Bromide

Compound No.	Solvent	Chemical Shift
(194)	(a)	2.571 (s) [Me]
		4.859 (s) [CH_2]
		5.473 (s) [CH_2]
		7.300- 7.596 (m) [R^1]
		9.5 (bs) [NH]
		10.1 (bs) [NH]

Table E

^{1}Hnmr Spectrum of 5,6-Benzo-4,7-dihydro-3-
methyl[4,5-a][1,2,4]thiadiazolo[1,3]diazepine

Compound No.	Solvent	Chemical Shift
(196)	(a)	2.315 (s) [Me]
		4.719 (s) [CH_2]
		5.174 (s) [CH_2]
		7.303- 7.358 (m) [R^1].
	(b)	2.285 (s) [Me]
		4.780 (s) [CH_2]
		5.018 (s) [CH_2]
		7.294- 7.306 (m) [R^1].

Table F

^{1}Hnmr Spectra of the Bromide and Perchlorate Salts of (196)

Compound No.	Solvent	Chemical Shift
(294)	(a)	2.629 (s) [Me]
		5.021 (s) [CH_2]
		5.625 (s) [CH_2]
		7.381- 7.761 (m) [R^1].
		11.5 (bs) [NH]
(296)	(a)	2.629 (s) [Me]
		4.997 (s) [CH_2]
		5.589 (s) [CH_2]
		7.474- 7.694 (m) [R^1].
		11.0 (bs) [NH]

Table G

^{1}Hnmr Spectrum of (207).

Compound No.	Solvent	Chemical Shift
(207)	(a)	2.3 (b) [CH_2]
		2.538 (s) [Me]
		2.886 (s) [Me]
		4.405 (b) [2xCH_2]
		8.6 (bs) [2xNH]
		10.1 (bs) [2xNH]

Table H

^{1}Hnmr Spectra of the Bromide and Perchlorate Salts of 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazole

Compound No.	Solvent	Chemical Shift
(211)	(a)	2.135 (qi) [CH_2]
		2.556 (s) [Me]
		3.538 (t) [CH_2]
		4.222 (t) [CH_2]
		10.5 (bs) [NH]
(213)	(a)	2.135 (qi) [CH_2]
		2.547 (s) [Me]
		3.523 (t) [CH_2]
		4.207 (t) [CH_2]
		10.25 (bs) [NH]

Table I

^{1}Hnmr Spectrum of 5,6-Dihydro-2-methyl-4H-pyrimido-[1,2-d][1,3,4]thiadiazole

Compound No.	Solvent	Chemical Shift
(212)	(a)	1.806 (qi) [CH_2]
		2.251 (s) [Me]
		3.264 (t) [CH_2]
		3.850 (t) [CH_2]

Table I continued

(b)	1.918 (qi) [CH_2]
	2.272 (s) [Me]
	3.423 (t) [CH_2]
	3.908 (t) [CH_2]

Table J

^{1}Hnmr Spectrum of α,α'-Dimethoxy-o-xylene

Compound No.	Solvent	Chemical Shift
(218)	(a)	3.301 (s) [2xMeO]
		4.460 (s) [2xCH_2]
		7.199- 7.450 (m) [R^1].

Table K

^{1}Hnmr Spectra for the Imidoyl Chloride Adducts of (196)

Compound No.	Solvent	Chemical Shift
(225(a))	(a)	2.840 (s) [Me]
		3.142 (s) [Me]
		5.308 (s) [CH_2]
		5.988 (s) [CH_2]
		7.050- 7.852 (m) [Ph + R^1].
(225(b))	(a)	2.879 (s) [Me]
		5.338 (s) [CH_2]
		5.949 (s) [CH_2]
		6.794- 7.575 (m) [2xPh + R^1].

Table L

^{1}Hnmr Spectrum of Trimethylacetanilide

Compound No.	Solvent	Chemical Shift
(295)	(a)	1.235 (s) [CMe_3]
		7.016- 7.727 (m) [Ph]
		9.30 (bs) [NH]

Table M

^{1}Hnmr Spectra of the Tetrahydrotetraazapentalenes

Compound No.	Solvent	Chemical Shift
(230(a))	(b)	2.864 (s) [2xNMe]
		5.467 (s) [2xCH_2]
		7.431 (s) [R^1].
(230(b))	(b)	1- 2.1 (m) [2x$(CH_2)_5$: cyclohexyl]
		3.5 (bs) [2xNCH: cyclohexyl]
		5.451 (s) [2xCH_2]
		7.434 (s) [R^1].
(230(c))	(b)	5.549 (s) [2xCH_2]
		7.151- 7.480 (m) [2xPh + R^1]
(230(d))	(b)	4.426 (s) [2xNCH_2]
		5.424 (s) [2xCH_2]
		7.261 (s) [2xPh]
		7.413 (s) [R^1].
(230(e))	(b)	2.318 (s) [2xMe]
		5.537 (s) [2xCH_2]
		7.187- 7.346 (m) [2xR^2]
		7.471 (s) [R^1].

Table M continued

(230(f))	(b)	3.169 (s) [2xMe] 6.248 (s) [2xCH_2] 7.477- 7.514 (m) [R^1].
(230(g))	(b)	0.579- 1.022 (m) [2xMe] 1.232- 1.809 (m) [2x$(CH_2)_2$] 3.667 (t) [2xNCH_2] 6.260 (s) [2xCH_2] 7.480- 7.523 (m) [R^1]
(230(i))	(b)	4.805 (s) [2xCH_2(xylyl)] 6.223 (s) [2xCH_2(benzyl)] 7.273 (s) [2xPh] 7.468- 7.505 (m) [R^1]
(247(a))	(b)	2.224 (qi) [CH_2] 2.907 (s) [2xMe] 3.947 (t) [2xCH_2]
(247(b))	(b)	1- 2.230 (m) [2x$(CH_2)_5$ (cyclohexyl)] 2.272 (qi) [CH_2] 3.7 (bs) [2xNCH] 3.923 (t) [2xCH_2]

Table M continued

(247(c))	(b)	2.175 (qi) [CH_2] 3.917 (t) [2xCH_2] 7.087- 7.538 (m) [2xPh].
(247(d))	(b)	2.233 (qi) [CH_2] 2.333 (s) [2xMe] 3.972 (t) [2xCH_2] 7.090- 7.376 (m) [2xR^2]
(247(e))	(b)	2.352 (qi) [CH_2] 3.224 (s) [2xMe] 4.411 (t) [2xCH_2]
(247(f))	(b)	0.735- 1.842 (m) [2x$(CH_2)_2$Me] 2.437 (qi) [CH_2] 3.722 (t) [2xNCH_2] 4.414 (t) [2xCH_2]
(247(g))	(b)	2.358 (qi) [CH_2] 4.420 (m) [2xCH_2 (propano bridge) + 2xNCH_2] 5.253 (m) [2xCH_2 (allyl)] 6.022 (m) [2xCH (allyl)]
(247(h))	(b)	2.309 (m) [CH_2 + 2 x cyclohexyl] 4.429 (t) [2xCH_2]

Table M continued

(247(i))	(b)	2.5 (qi) [CH_2] 4.545 (t) [2xCH_2] 7.392 (m) [2xPh]
(247(j))	(b)	2.375 (qi) [CH_2] 4.399 (t) [2xCH_2] 4.847 (s) [2xNCH_2] 7.303 (s) [2xPh]
(247(k))	(b)	2.349 (s) [2xMe] 2.5 (qi) [CH_2] 4.512 (t) [2xCH_2] 7.230 (s) [2xR^2].

Table N

^{1}Hnmr Spectrum of 5,6-Benzo-4,7-dihydro-3-methyl-[4,5-a][1,2,4]thiadiazolo[1,3]diazepinium-7-(phenylthiocarbamate)

Compound No.	Solvent	Chemical Shift
(233)	(b)	2.300 (s) [Me] 4.789 (s) [CH_2] 5.043 (s) [CH_2] 7.261- 7.309 (m) [Ph+R^1].

Table O

^{1}Hnmr Spectra of the Imidoyl Chloride Adducts of (189)

Compound No.	Solvent	Chemical Shift
(242(a))	(a)	2.272 (qi) [CH_2]
		2.599 (s) [Me]
		3.166 (s) [NMe]
		3.685 (t) [CH_2]
		4.298 (t) [CH_2]
		7.505- 7.724 (m) [Ph]
(242(b))	(a)	2.474 (qi) [CH_2]
		2.660 (s) [Me]
		3.877 (t) [CH_2]
		4.374 (t) [CH_2]
		6.766- 7.495 (m) [2xPh].
(243)	(a)	2.510 (qi) [CH_2]
		2.596 (s) [Me]
		3.166 (s) [NMe]
		3.691 (t) [CH_2]
		4.298 (t) [CH_2]
		7.456- 7.724 (m) [Ph]
		9.0 (bs) [$NH^{*}+H_2O$]

Table P

^{1}Hnmr Spectra of N-Methyl Trimethylacetamide and N-Methyl Trimethylacetimidoyl Chloride

Compound No.	Solvent	Chemical Shift
(297)	(a)	1.083 (s) [t-Butyl]
		2.572 (d) [Me]
		8.5 (bs) [NH]
(298)	(a)	1.086 (s) [t-Butyl]
		1.238 (s) [Me]
		2.568 (s) [t-Butyl]
		3.035 (s) [Me]

Table Q

^{1}Hnmr Spectrum of N-Methyl Dimethylcarbamidoylium Dichloride

Compound No.	Solvent	Chemical Shift
(245)	(b)	2.866 (d) [Me]
		3.017 (s) [Me]
		3.423 (s) [Me]
		5.25 (bs) [NH]

Table R

^{1}Hnmr Spectrum of 5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazolium Thiocyanate

Compound No.	Solvent	Chemical Shift
(251)	(a)	2.06 (qi) [CH_2]
		2.446 (s) [Me]
		3.557 (t) [CH_2]
		4.112 (t) [CH_2]
		10.25 (bs) [NH]

Table S

^{1}Hnmr spectrum of 5,6-Dihydro-3-methyl-4H-pyrimido[1,2-d][1,2,4]thiadiazolium Chloride

Compound No.	Solvent	Chemical Shift
(299)	(a)	2.074 (qi) [CH_2]
		2.422 (s) [Me]
		3.538 (t) [CH_2]
		4.100 (t) [CH_2]
		11.544 (bs) [NH]

Table T

^{1}Hnmr Spectrum of 5,6-Dihydro-2-methyl-4H-pyrimido[1,2-d][1,3,4]thiadiazolium-7-(methylthiocarbamate)

Compound No.	Solvent	Chemical Shift
(265)	(b)	1.928 (qi) [CH_2]
		2.278 (s) [Me]
		3.279 (s) [NMe]
		3.423 (t) [CH_2]
		3.911 (t) [CH_2]

Table U

^{1}Hnmr Spectra of Possible Monocyclic Precursors of Triheterapentalenes

Compound No.	Solvent	Chemical Shift
(300)	(a)	3.880 (s) [2xCH_2]
		4.585 (s) [CH_2(benzyl)]
		7.42 (m) [Ph]
		10.3 (bs) [2xNH]
(267)	(a)	3.490 (s) [2xCH_2]
		4.255 (s) [CH_2(benzyl)]
		7.3 (m) [Ph]
	(b)	3.661 (s) [2xCH_2]
		4.112 (s) [NH]
		4.316 (s) [CH_2(benzyl)]
		7.3 (m) [Ph]

Table U continued

(301)	(a)	1.66 (qi) [CH_2]
		3.36 (t) [2xCH_2]
		4.55 (s) [CH_2(benzyl)]
		7.39 (s) [Ph]
		9.88 (bs) [2xNH]
(266)	(a)	1.65 (qi) [CH_2]
		3.24 (t) [2xCH_2]
		4.11 (s) [CH_2(benzyl)]
		7.28 (s) [Ph]
	(b)	1.79 (qi) [CH_2]
		3.38 (t) [2xCH_2]
		4.17 (s) [CH_2(benzyl)]
		7.30 (m) [Ph]
		NH signal appears as a shoulder on the singlet at 4.17.
(275)	(a)	1.91 (qi) [CH_2]
		3.50 (t) [2xCH_2]
		11.08 (bs) [2xNH]

Table V

^{1}Hnmr Spectrum of the Thermolysis Product of (267)

Compound No.	Solvent	Chemical Shift
(268)	(a)	3.725 (s)

Table W

^{1}Hnmr Spectra of the Condensation Products of 5-Chloro-2,3-dimethyl-1,2,4-thiadiazolium Fluorosulphonate and 2-Amino-N-heterocycles

Compound No.	Solvent	Chemical Shift
(287)	(a)	2.410 (s) [Me]
		2.510 (s) [Me]
		3.618 (s) [NMe]
		6.811 (d) [H]
		7.024 (d) [H]
		7.639 (t) [H]
	(b)	2.410 (s) [Me]
		2.581 (s) [Me]
		3.654 (s) [NMe]
		6.721 (d) [H]
		7.064 (d) [H]
		7.547 (t) [H]

Table W continued

(288)	(a)	2.312 (s) [Me]
		2.404 (s) [Me]
		3.606 (s) [NMe]
		6.827 (d) [H]
		7.047 (s) [H]
		8.292 (d) [H]
	(b)	2.333 (s) [Me]
		2.401 (s) [Me]
		3.636 (s) [NMe]
		6.718 (d) [H]
		7.068 (s) [H]
		8.313 (d) [H].
(289)	(a)	2.404 (s) [Me]
		3.423 (t) [CH_2]
		3.523 (s) [NMe]
		4.149 (t) [CH_2]
	(b)	2.422 (s) [Me]
		3.447 (t) [CH_2]
		3.587 (s) [NMe]
		4.258 (t) [CH_2]
(290)	(a)	2.510 (s) [Me]
		3.590 (s) [NMe]

Table X

^{1}Hnmr Spectra of Mixture of (210) and Thiadiazole (206).

Solvent (a).

No. of Hours of Reflux:	6	24	72	
Chemical Shifts:	1.897	1.949	1.928	(qi)[CH_2](210)
	2.327	2.385	2.361	(s)[Me](210)
	2.449	2.434	2.431	(s)[Me](206)
	3.343	3.389	3.365	(t)[CH_2](210)
	3.944	4.011	3.984	(t)[CH_2](210)
	4.673	5.763	5.363	(s)[NH](210)
	7.0	7.0	7.0	(bs)[NH_2](206)

The ratios of thiadiazole (206) to base (210) were respectively 1:2.5, 1:7, and 1:4 for 6 hours, 24 hours and 72 hours reflux.

Table Y

^{1}Hnmr Spectrum of (215).

Compound No.	Solvent	Chemical Shift
(215)	(a)	2.541 (a) [Me]
		5.616 (s) [Me]
		7.215 (m) [xylyl]
		10.3 (bs) [2xNH_2]

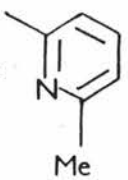
Table Z

Mixture of [242, R^1 = CMe_3, R^2 = Ph] and Hydrochloride of (189).

Solvent (a)	Chemical Shift
	1.250 (s) [Bu^t]
	2.022 (qi) [CH_2] (hydrochloride)
	2.390 (qi) [CH_2]
	2.431 (s) [Me] (hydrochloride)
	2.600 (s) [Me]
	3.501 (t) [CH_2] (hydrochloride)
	3.815 (t) [CH_2]
	4.022 (t) [CH_2] (hydrochloride)
	4.350 (t) [CH_2]
	7.016-7.767 (m) [Ph]
	10.5 (bs) [NH]

APPENDIX II

Key to Tables

R^3 = 

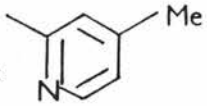
R^4 = 

Table 1

Mass Spectrum of 4,5-Dihydro-3-methyl-6-oxopyrimido[1,2-d][1,2,4]thiadiazolium Chloride

Compound No.		m/e	% height
(192)	$M^{+\cdot}$-HCl	169	14%
	$M^{+\cdot}$-(CO+HCl)	141	12%
	MeCNS	73	100%
	MeCN	41	9%

Table 2

Mass Spectrum of 3-Chloro-N([3]methyl[1,2,4]thiadiazolo)-propanamide

Compound No.		m/e	% height
(292)	$Me^{+\cdot}(Cl^{37})$	207	6%
	$M^{+\cdot}(Cl^{35})$	205	15%
	$M^{+\cdot}$-$CO(CH_2)_2Cl$	115	100%
	MeCNS	73	86%

Table 3

Mass Spectrum of 5(α-Bromo-xylyl)-3-methyl-1,2,4-thiadiazolium Bromide

Compound No.		m/e	% height
(194)	$M^{+\cdot}$-2HBr	217	8%
	xylyl	104	71%
	HBr^{81}	82	100%
	HBr^{79}	80	100%
	MeCNS	73	53%
	MeCN	41	71%

Table 4

Mass Spectrum of 5,6-Benzo-4,7-dihydro-3-methyl[4,5-a][1,2,4][thiadiazolo[1,3]diazepine

Compound No.		m/e	% height
(196)	$M^{+\cdot}$	217	82%
	xylyl-N	117	100%
	MeCNS	73	47%
	MeCN	41	22%

Table 5

Mass Spectrum of 5,6-Dihydro-2-methyl-4H-pyrimido [1,2-d][1,2,4]-thiadiazole

Compound No.		m/e	% height
(212)	$M^{+\cdot}$	155	100%
	MeCS	59	75%
	MeCN	41	28%

Table 6

Mass Spectrum of α,α'-dimethoxy-o-xylene

Compound No.		m/e	% height
(218)	$M^{+\cdot}$-MeOH	134	100%
	xylyl–O	119	83%
	xylyl	104	27%

Table 7

Mass Spectrum of Trimethylacetanilide

Compound No.		m/e	% height
(295)	$M^{+\cdot}$	177	99%
	$PhNH_2$	93	100%
	CMe_3	57	100%

Table 8

Mass Spectra of the Tetrahydrotetraazapentalenes

Compound No.		m/e	% height
(230(a))	$M^{+\cdot}$-MeNCO	233	12%
	xylyl-N	117	5%
	MeNCO	57	100%
(230(b))	$M^{+\cdot}$-cyclohexyl-NCO	301	4%
	cyclohexyl-NCO	125	22%
	CCHNCO	67	100%
(230(c))	$M^{+\cdot}$-PhNCO	295	27%
	PhNCO	119	100%
	PhN	91	55%
(230(d))	$M^{+\cdot}$-$PhCH_2NCO$	309	10%
	$PhCH_2NCO$	133	67%
	$PhCH_2$	91	100%
	CCHNCO	67	92%
(230(e))	M^{+}-p-tolyl-NCO	309	23%
	p-tolyl-NS	137	47%
	p-tolyl-NCO	133	100%

Table 8 continued

(230(f))	$M^{+\cdot}$-MeNCS	249	27%
	xylyl–N	117	31%
	MeNCS	73	100%
(230(g))	$M^{+\cdot}$-BuNCS	291	1%
	BuNCS	115	100%
	Bu	57	59%
(230(h))	$M^{+\cdot}$-PhNCS	311	7%
	PhNCS	135	100%
	Ph	77	83%
(230(i))	$M^{+\cdot}$-$PhCH_2NCS$	325	15%
	$PhCH_2NCS$	149	19%
	$PhCH_2$	91	100%
(247(a))	$M^{+\cdot}$-MeNCO	171	100%
	MeNS	61	77%
	MeNCO	57	100%
(247(b))	$M^{+\cdot}$-cyclohexyl–NCO	239	14%
	cyclohexyl–N(CO)S	157	67%
	cyclohexyl–NCO	125	21%
	CCHNCO	67	100%

Table 8 continued

(247(c))	$M^{+\cdot}$-PhNCO	233	42%
	PhNS	123	100%
	PhNCO	119	100%
	PhN	91	56%
(247(d))	$M^{+\cdot}$-p-tolyl-NCO	247	38%
	p-tolyl-NS	137	100%
	p-tolyl-NCO	133	94%
(247(e))	$M^{+\cdot}$-MeNCS	187	57%
	MeNCS	73	100%
(247(f))	$M^{+\cdot}$-BuNCS	229	6%
	Bu	57	29%
	$(CH_2)_2CH$	41	100%
(247(g))	$M^{+\cdot}$-allyl-NCS	213	33%
	allyl-NCS	99	40%
	CH_2NCS	72	50%
	allyl	41	100%
(247(h))	$M^{+\cdot}$-cyclohexyl-NCS	255	3%
	cyclohexyl-NCS	141	31%
	$(CH_2)_3CH$	55	100%

Table 8 continued

(247(i)	$M^{+\cdot}$-PhNCS	249	24%
	PhNCS	135	100%
	Ph	77	96%
(247(j))	$M^{+\cdot}$-$PhCH_2NCS$	263	11%
	$PhCH_2NCS$	149	25%
	$PhCH_2$	91	100%

Table 9

Mass Spectra of N-Methyl Trimethylacetamide and N-Methyl Trimethylacetimidoyl Chloride

Compound No.		m/e	% height
(297)	$M^{+\cdot}$	115	67%
	MeNHCO	58	89%
	t-Butyl	57	100%
(298)	$M^{+\cdot}(Cl^{37})$	135	0.7%
	$M^{+\cdot}(Cl^{35})$	133	2%
	$M^{+\cdot}$-Cl	98	75%
	t-Butyl	57	54%
	$(Me)_2C$	42	100%

Table 10

Mass Spectra of Possible Monocyclic Precursors of Triheterapentalenes

Compound No.		m/e	% height
(267)	$M^{+\cdot}$	192	24%
	$M^{+\cdot}-PhCH_2$	102	48%
	$PhCH_2$	91	100%
(266)	$M^{+\cdot}$	206	12%
	$M^{+\cdot}-PhCH_2$	115	33%
	$PhCH_2$	91	100%
(275)	$M^{+\cdot}-HBr$	141	22%
	$NHCNCH_2$	55	100%
	CS	44	67%

Table 11

Mass Spectrum of Thermolysis Product of (267)

Compound No.	m/e	% height
(268)	205	7%
	204	7%
	203	76%
	71	21%
	67	21%
	32	100%

Table 12

Mass Spectra of the Condensation Products of 5-Chloro-2,3-dimethyl-1,2,4-thiadiazolium Fluorosulphonate and 2-Amino-N-heterocycles

Compound No.		m/e	% height
(287)	$M^{+\cdot}$	220	100%
	$M^{+\cdot}$-MeCN	179	38%
	R^3	92	40%
	MeCN	41	41%
(288)	$M^{+\cdot}$	220	100%
	$M^{+\cdot}$-MeCN	179	32%
	R^4	92	43%
(289)	$M^{+\cdot}$	214	100%
	$M^{+\cdot}$-MeCN	173	17%
	MeCNS	73	67%
(290)	$M^{+\cdot}$	146	100%
	$M^{+\cdot}$-MeCN	105	56%
	MeCNS	73	44%

APPENDIX III

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