

THE SYNTHESIS AND REACTIONS OF 1,2-DIAZEPINES
AND THEIR IRON CARBONYL COMPLEXES

by

CARL B. ARGO, B.Sc.

Thesis presented for the degree of
DOCTOR OF PHILOSOPHY

University of Edinburgh

September 1983



T h a n k s M u m

Acknowledgements

I would like to sincerely thank Dr. J.T. Sharp for his excellent supervision of this work, and for his invaluable advice and encouragement throughout the period during which the work was carried out.

I am also indebted to the staff of the Department of Chemistry, University of Edinburgh, with particular thanks to Messrs. J. Grunbaum, J. Millar, J. Broom and D. Thomas for the technical services which they provided.

I would also like to thank the S.R.C. for financial support, Professor J.I.G. Cadogan for provision of laboratory facilities and Mrs. C.G. Ranken for her efficient typing of this manuscript.

Abstract

The rearrangement of 3*H*-1,2-diazepines by rapid [1,5] hydrogen migration has been studied in detail. The mechanism of the rearrangement was identified as an intramolecular sigmatropic type. The rapid rate of the migration compared to analogous cycloheptatriene systems was attributed to the electron withdrawing effect of the azo group rather than to stereochemical factors alone.

Conversion of 3*H*-1,2-diazepines into their dinuclear iron carbonyl complexes inhibited the [1,5] sigmatropic hydrogen rearrangement. Thus pure samples of the two isomeric diazepine complexes were isolated and characterised spectroscopically. Inhibition of the rearrangement was attributed partly to the change in the electronic effect of the diaza linkage and partly to a flattening of the diazepine ring due to complexation.

Complexation of the diazepine ring also reduced the activation energy for ring inversion by $\sim 40 \text{ kJ mol}^{-1}$.

A study was carried out on the factors affecting the reaction of $\alpha\beta,\gamma\delta$ -unsaturated aldehydes with *p*-toluenesulphonylhydrazide under acid conditions. Those with fixed cisoid geometry gave 3,4-dihydro-2-tosyl-1,2-diazepines, while similar acyclic dienals did not undergo cyclisation. Phenyl substituents at the terminus of $\alpha\beta,\gamma\delta$ -unsaturated *p*-toluenesulphonylhydrazones inhibited cyclisation to dihydro diazepine.

Three new synthetic routes to the $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds required for this study were devised.

Mild oxidation of 4-phenyl-1*H*-2,3-benzodiazepine gave the *N*-2 benzodiazepine *N*-oxide. A similar oxidation of the monocyclic diazepine 3,5,7-trimethyl-3*H*-1,2-diazepine, gave its *N*-2 oxide which was found to undergo a new rearrangement reaction to give 3,5-dimethyl-3-propenyl-3*H*-pyrazole *N*-2 oxide under very mild conditions. This isomerisation was found to be reversible and mechanisms for the interconversion were considered.

C O N T E N T S

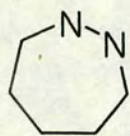
	Page No.
INTRODUCTION	1
DISCUSSION	84
EXPERIMENTAL	179
APPENDICES	242
REFERENCES	268

<u>INTRODUCTION</u>	
A.	<u>1,2-Diazepines</u> 3
1.	1 <i>H</i> -1,2-Diazepines 4
1.1	Synthesis 4
1.2	Reactions 8
2.	Dihydro-1 <i>H</i> -1,2-diazepines 13
3.	Tetrahydro-1 <i>H</i> -1,2-diazepines 14
4.	Hexahydro-1,2-diazepines 14
5.	3,4-Dihydro-2 <i>H</i> -1,2-diazepines 15
6.	3 <i>H</i> -1,2-Diazepines 16
6.1	Synthesis 17
6.2	Reactions 18
7.	4 <i>H</i> -1,2-Diazepines 19
7.1	Synthesis 19
7.2	Reactions 20
8.	Dihydro-4 <i>H</i> -1,2-diazepines 21
8.1	Synthesis 21
8.2	Reactions 22
9.	5 <i>H</i> -1,2-Diazepines 24
B.	<u>Benzodiazepines</u> 27
1.	1,2-Benzodiazepines 28
1.1	1 <i>H</i> -1,2-Benzodiazepines 28
1.2	3 <i>H</i> -1,2-Benzodiazepines 30
1.3	5 <i>H</i> -1,2-Benzodiazepines 31
2.	2,3-Benzodiazepines 32
2.1	1 <i>H</i> -2,3-Benzodiazepines 33

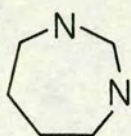
	Page No.
2.2 3 <i>H</i> -2,3-Benzodiazepines	35
2.3 5 <i>H</i> -2,3-Benzodiazepines	36
C. <u>Iron Carbonyl Complexes of 1,2-Diaza</u> <u>Compounds</u>	 39
1. 1,2-Diazepine Complexes	39
1.1 1 <i>H</i> -1,2-Diazepines	39
1.2 4 <i>H</i> -1,2-Diazepines	42
2. Cyclic Fe ₂ N ₂ Systems	43
2.1 Complexes derived from Azo Compounds	45
2.1.1 Aliphatic Azo Compounds	46
2.1.2 Azobenzene	51
2.2 Complexes derived from Azines	54
2.3 Complexes derived from Aromatic Vicinal Diaza Heterocycles	 56
2.4 Structural Information	61
2.4.1 X-Ray Diffraction Studies	61
2.4.2 Infrared Spectroscopy Analysis	62
D. <u>Thermal [1,5] Sigmatropic Migrations</u>	 64
1. Theoretical Considerations	64
2. Characteristics of the [1,5] migration reaction and its mechanism	 65
3. Literature examples	69
3.1 Hydrocarbon Systems	69
3.2 Diaza Heterocyclic Systems	72
E. <u>Azoxy Compounds</u>	 77

A. 1,2-Diazepines

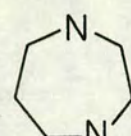
Diazepines are monocyclic seven-membered rings containing two nitrogen atoms. There are three basic ring structures, depending on the position of the two nitrogen atoms.



1,2 - diazepine



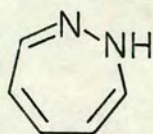
1,3 - diazepine



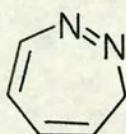
1,4 - diazepine

All three classes have been recently reviewed^{1,2}, and only the 1,2 class will be discussed here.

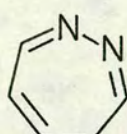
Fully unsaturated 1,2-diazepines are classified according to the position of the saturated atom in the ring system.



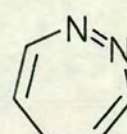
1H



3H



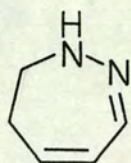
4H



5H

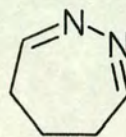
Saturated ring systems are described by the terms "dihydro" and "tetrahydro", and are named according to IUPAC nomenclature.

Structures (1) and (2) serve as examples of this nomenclature.



(1)

3,4-dihydro-2H-1,2-diazepine



(2)

5,6-dihydro-4H-1,2-diazepine

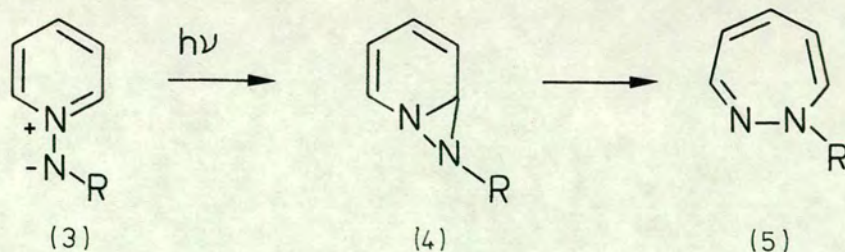
In this review the 1,2-diazepines will be considered under their 1H, 2H, 3H, 4H and 5H headings. The fully unsaturated diazepines will be treated first followed by those with increasing saturation.

1. 1H-1,2-Diazepines

This isomer is the most documented of the series : the large number of papers in this area is due to the work of Streith, Snieckus and Sasaki.

1.1 Synthesis

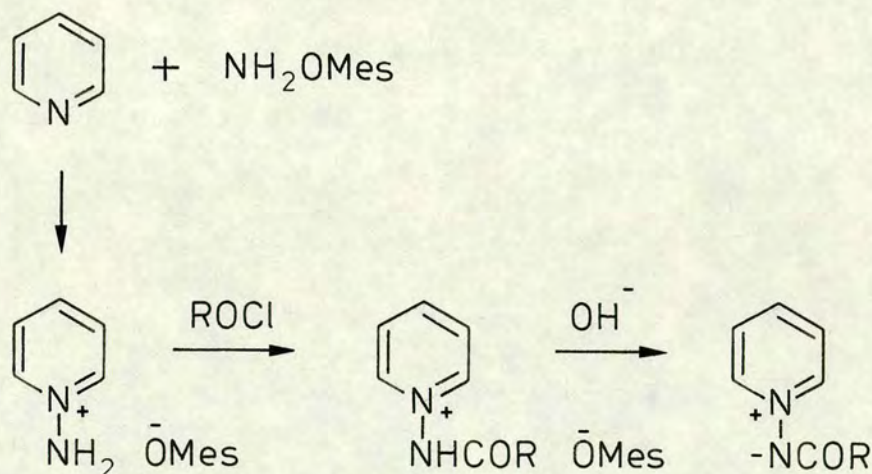
Streith and Cassal^{3,4,5} were the first to report the synthesis of 1H-1,2-diazepines (5), and the literature now contains many examples of their photolytic route (Scheme 1).



Scheme 1

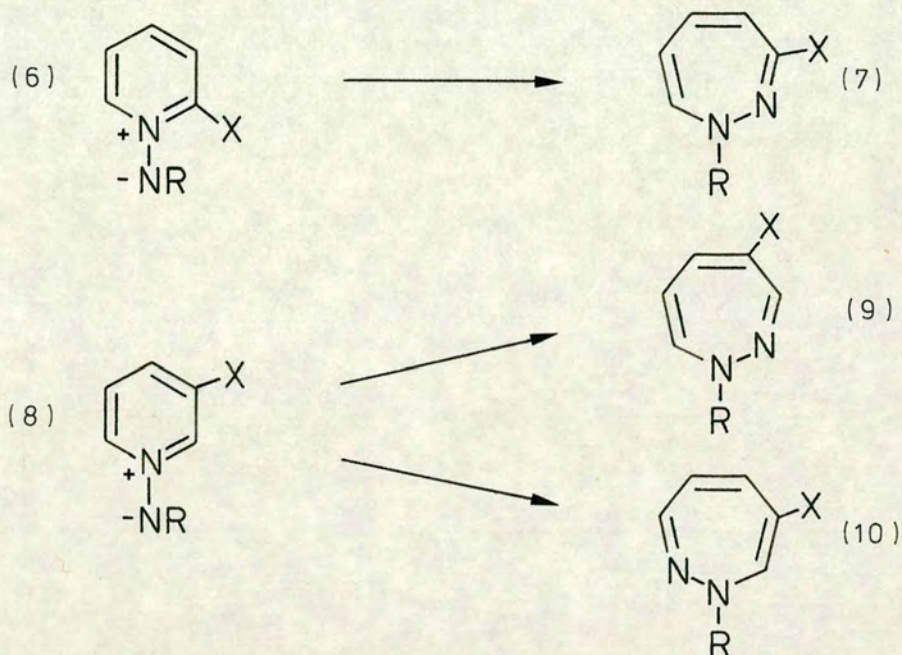
Photolysis of pyridine N-imines (3) is thought to give a diaziridine intermediate (4) which isomerises spontaneously to the seven membered ring.

A drawback of this synthesis was the difficult preparation of pyridine N-imines⁶; this problem has been solved by the use of *o*-mesitylsulphonylhydroxylamine (MSH) to effect the nitrogen-nitrogen coupling reaction to the pyridine^{7,8,9}, followed by treatment with an acyl chloride and deprotonation by base (Scheme 2). Thus a large number of ring substituted pyridine N-imines have been synthesised which in turn yield 1*H*-1,2-diazepines when photolysed.

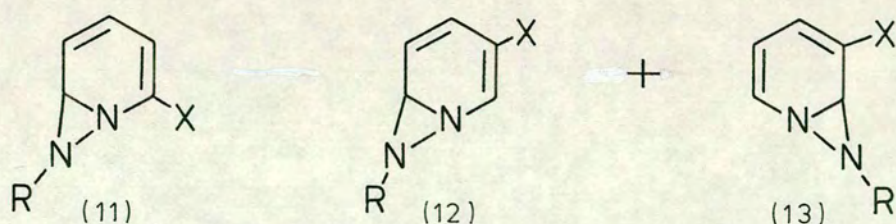


Scheme 2

A complication with ring substituted pyridine N-imines is that it is possible to obtain two diazepines upon photolysis. Pyridine N-imines bearing a substituent in the 2-position (6) cyclise exclusively to the C-6 position yielding the 3-substituted-1*H*-1,2-diazepines (7). However, most pyridine N-imines bearing a substituent in the 3-position (8) cyclise at both the C-2 and C-5 position to give the 6- and 4-substituted diazepines (9) and (10).

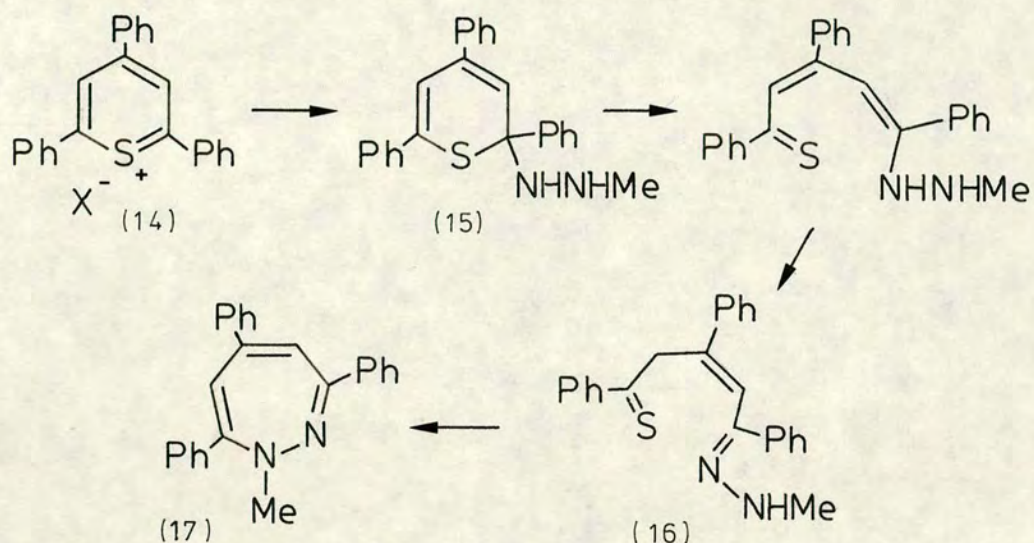


This has been explained in terms of the diaziridine intermediate; pyridine N-imines bearing a substituent in the 2-position only form one diaziridine (11), apparently for steric reasons, whereas pyridine N-imines bearing a substituent in the 3-position can form two (12) and (13).



1*H*-1,2-Diazepines have also been synthesised by a non-photochemical route devised by Klingsberg¹⁰. This method

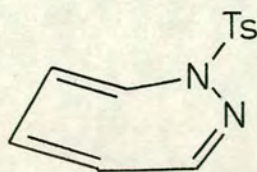
involves the reaction of methylhydrazine with pyrylium and thiopyrylium salts. The reaction is of limited scope and only three 1^H-1,2-diazepines have been synthesised in this manner. 1-Methyl-3,5,7-triphenyl-1^H-1,2-diazepine (17) is one example synthesised by this route^{11,12} (Scheme 3).



Scheme 3

Methylhydrazine reacts with the thiopyrylium salt (14) to give the non-aromatic adduct (15) which ring opens, isomerises to the hydrazone (16) and then ring closes to give the diazepine (17).

An X-ray crystal structure of 1-tosyl-1,2-diazepine (18) has shown that the 1^H ring system lies in a boat conformation, with a localised imine double bond and a conjugated butadiene unit¹³.

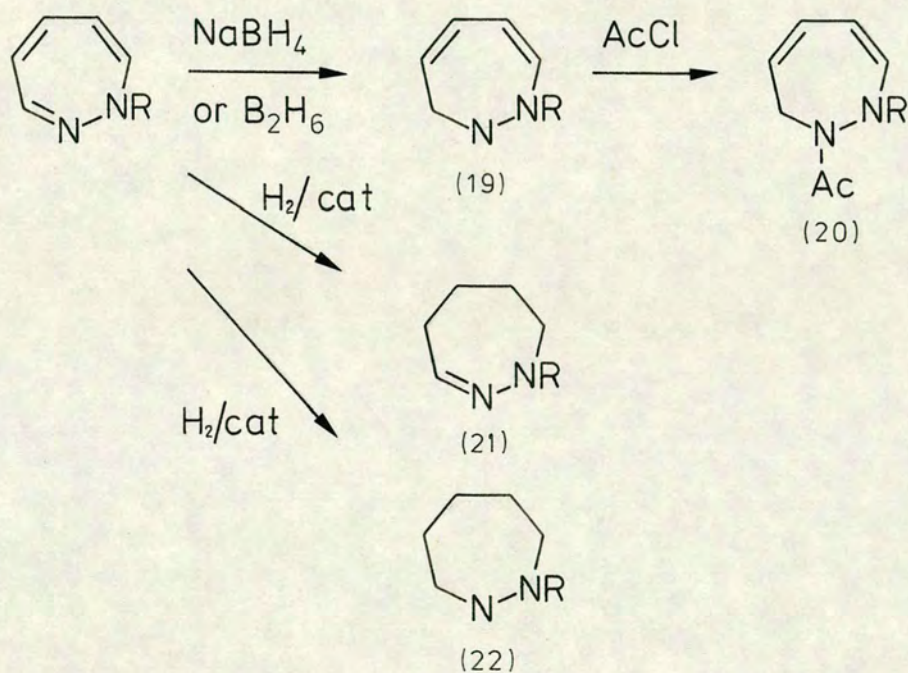


(18)

1.2 Reactions

Considerable work has been carried out on the reactions of 1*H*-1,2-diazepines, and has been reviewed by Nastasi². Some of the more interesting examples will be presented here.

Reduction.- Depending on the reducing agent used, either dihydro, tetrahydro or hexahydro derivatives can be prepared (Scheme 4).



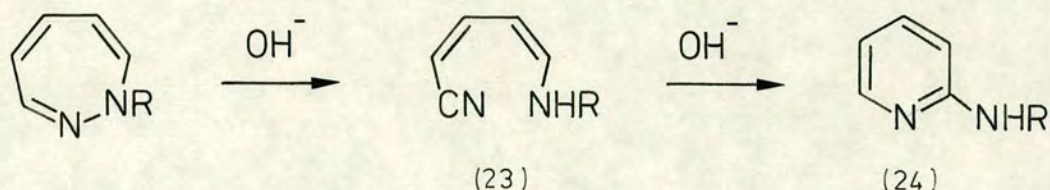
Scheme 4

Reduction with sodium borohydride¹⁴ or diborane¹⁵ gives the unstable 2,3-dihydro-1*H*-1,2-diazepines (19); these products can be stabilised by acylation to give (20).

Hydrogenation with a platinum catalyst gives the tetrahydro (21) and hexahydro (22) compounds^{4,15,16,17}.

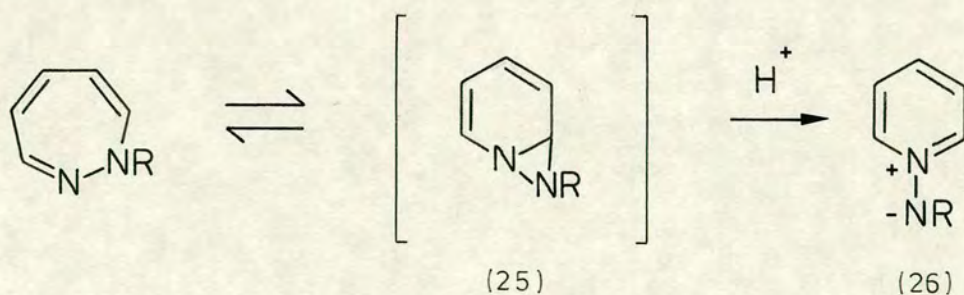
Reactions with acids and bases.- Base catalysed rearrangement

of 1*H*-1,2-diazepines bearing a hydrogen atom at the C-3 position leads to ring opening and formation of 2-aminopyridines (24). This reaction proceeds through a *Z,Z*-diene (23) which then ring closes¹⁸ (Scheme 5).



Scheme 5

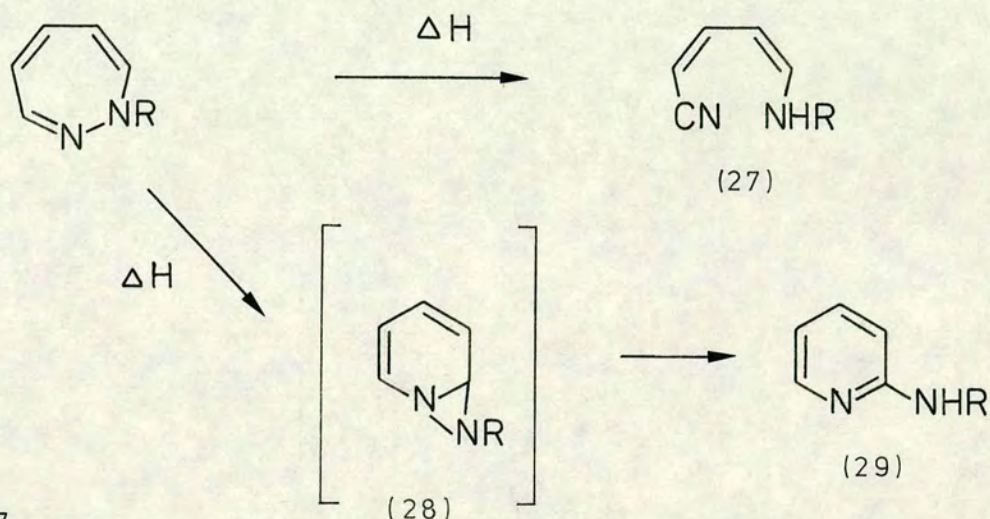
Treatment of 1*H*-1,2-diazepines with acid results in the formation of pyridine *N*-imines (26), probably proceeding through the diaziridine (25)^{19,20}. This reaction is the reverse of the photochemical synthesis of 1*H*-1,2-diazepines from pyridine *N*-imines. The role of the acid in the rearrangement is not understood (Scheme 6).



Scheme 6

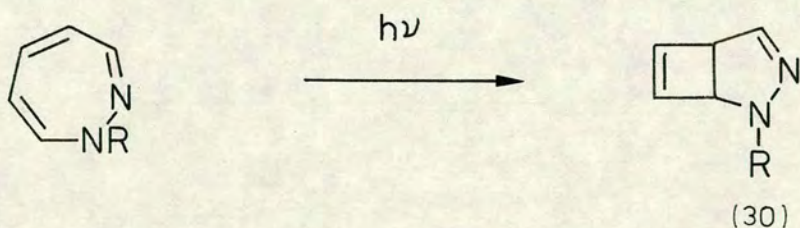
Thermal and photochemical reactions.- The thermal reactions of 1*H*-1,2-diazepines are interesting in that the products are the same as that for the base catalysed rearrangement, i.e. 2-aminopyridines (29) and *Z,Z*-dienes (27) (Scheme 7). However in this reaction it has been demonstrated that the

2-aminopyridines are formed via the diaziridine (28) and not via the *Z,Z*-diene (27)¹⁸⁻²¹.



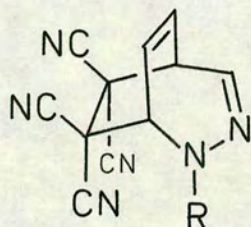
Scheme 7

Photolysis of 1*H*-1,2-diazepines results in electrocyclic ring-closure of the butadiene moiety (Scheme 8), to give 2,3-diaza[3.2.0]bicyclic heptadiene (30)²⁰⁻²². This type of reactivity is observed with many other seven-membered cyclic dienes.

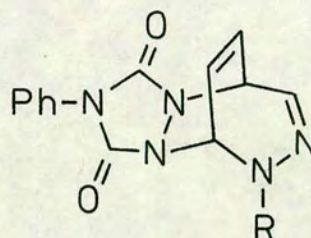


Scheme 8

Cycloaddition reactions.- 1*H*-1,2-Diazepines also undergo [4+2] cycloaddition reactions with dienophiles. Thus with highly reactive dienophiles such as tetracyanoethylene^{17,23,24} and 4-phenyl-1,2,4-triazoline-3,5-dione²⁴⁻²⁶ the expected cycloadducts (31) and (32) were formed.

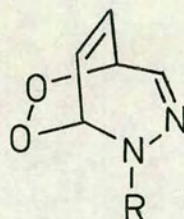


(31)



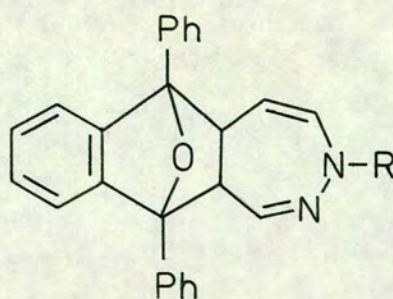
(32)

The cycloaddition of singlet oxygen leads to the novel photoxide²⁷ (33).



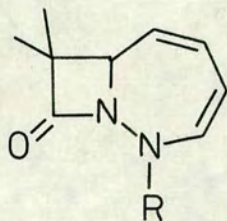
(33)

[2+4]Cycloadditions have also been performed, an example being the reaction with diphenylisobenzofuran to give the cycloadduct²⁶ (34).



(34)

Ketenes react in a [2+2] cycloaddition²⁸ with the imine double bond to give C₇-C₈-*E*-aza-9-nonanes (35).



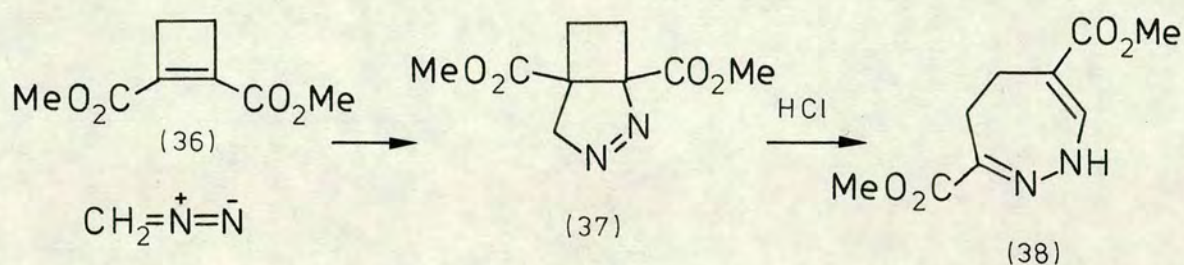
(35)

A number of 1*H*-1,2-diazepine iron tricarbonyl complexes have also been prepared and are reviewed separately in Section C.

2. Dihydro-1*H*-1,2-diazepines

The chemistry of the dihydro-, tetrahydro- and hexahydro-1*H*-1,2-diazepines is less extensive than for the fully unsaturated system.

2,3-Dihydro-1*H*-1,2-diazepines can be synthesised by hydrogenation of 1*H*-1,2-diazepines (discussed in section A.1.2). The 4,5-dihydro-1*H*-1,2-diazepines have been prepared by the cycloaddition of diazomethane to 1,2-disubstituted cyclobutenes²⁹ (Scheme 9).



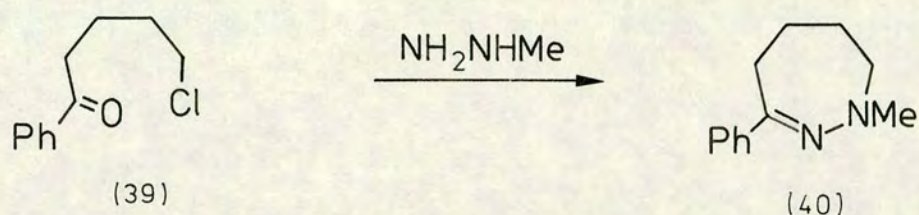
Scheme 9

Treatment of the 1-pyrazoline cycloadduct with hydrogen chloride gas results in ring expansion to give the diazepine, eg. dimethyl-1,2-cyclobutenedicarboxylate (36) adds to diazomethane to form the 1-pyrazoline (37) which subsequently gives the 4,5-dihydro-1*H*-1,2-diazepine-3,6-dimethylcarboxylate (38).

There are two important reactions of 2,3-dihydro-*H*-1,2-diazepines : these are the conversion to 3,4-dihydro-2*H*-1,2-diazepines (discussed in Section A.5) and their reactions with diiron nonacarbonyl (discussed in Section C).

3. Tetrahydro-1*H*-1,2-diazepines

4,5,6,7-Tetrahydro-1*H*-1,2-diazepines can be prepared from 1*H*-1,2-diazepines by hydrogenation (see Section A.1.2) They can also be prepared by the reaction of substituted hydrazines with δ -chloroarylketones³⁰, eg. the reaction of methylhydrazine with the ketone (39) to give the 3-phenyl substituted diazepine (40) as depicted in scheme 10.



Scheme 10

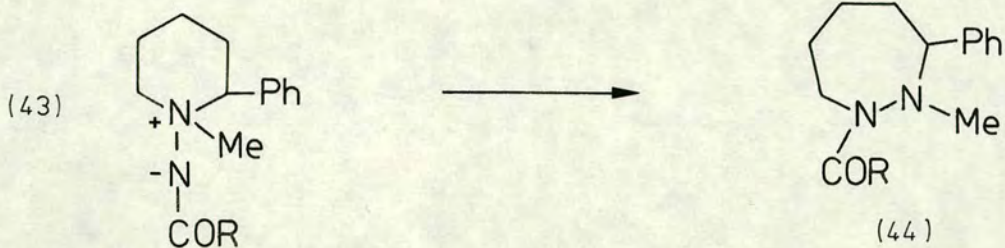
4. Hexahydro-1,2-diazepines

There are three different routes into this system. The first is the hydrogenation of the corresponding 1*H*-1,2-diazepine (see Section A.1.2). The second is the reaction of 1,5-dihalogenopentanes and a substituted hydrazine, this method has been in the literature for many years. An example is the reaction of hydrazobenzene with 1,5-diiodopentane (41) which gives 1,2-diphenylhexahydro-1,2-diazepine³¹ (42) (Scheme 11).



Scheme 11

The third method of synthesis is the vacuum pyrolysis of 1-methyl-2-phenylpiperidine-1-acylimides (43) which ring expands to hexahydro-1,2-diazepines (44) depicted scheme 12³². Confirmation of diazepine structure was obtained by independent synthesis.

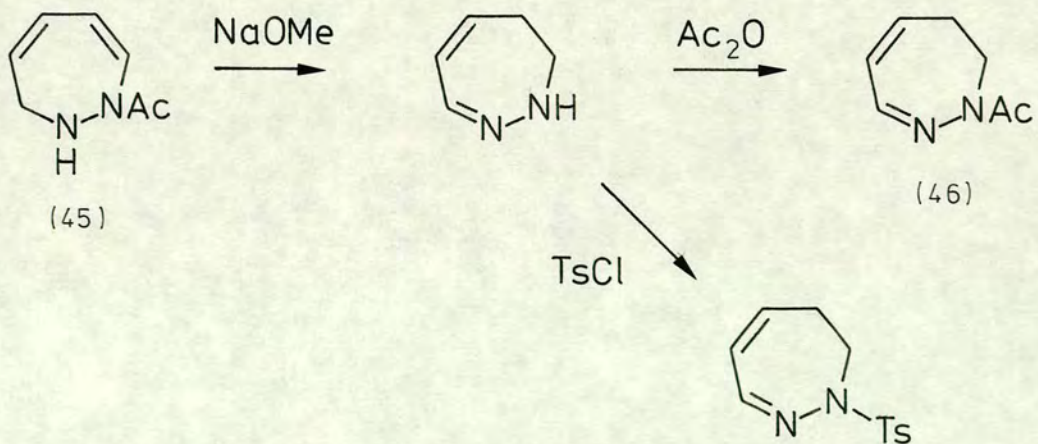


Scheme 12

5. 3,4-Dihydro-2H-1,2-diazepines

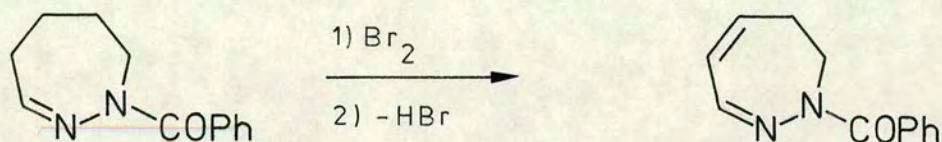
There are three methods of synthesis for this diazepine, all of which have been devised in recent years.

3,4-Dihydro-2H-1,2-diazepines (46) have been prepared by sodium methoxide deacylation of the corresponding 1H-2,3-dihydro-1,2-diazepine (45) followed by acylation or tosylation¹⁴ (Scheme 13).



Scheme 13

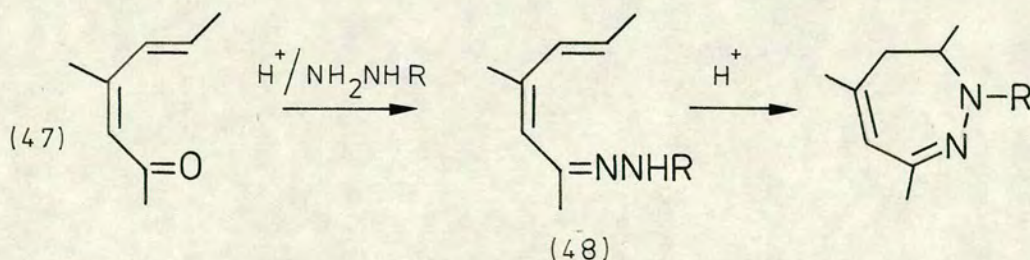
3,4-Dihydro-2*H*-1,2-diazepines have also been prepared by the bromination and dehydrobromination of 2,3,4,5-tetrahydro-1*H*-1,2-diazepines³⁰ (Scheme 14).



Scheme 14

The third method of synthesis is the acid-catalysed reaction of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds³³ (47) with *p*-toluenesulphonylhydrazide (Scheme 15). The ring closure step has been shown to be substituent dependent and in some cases the tosylhydrazone (48) could not be cyclised.

Further work on this topic is contained in this thesis.



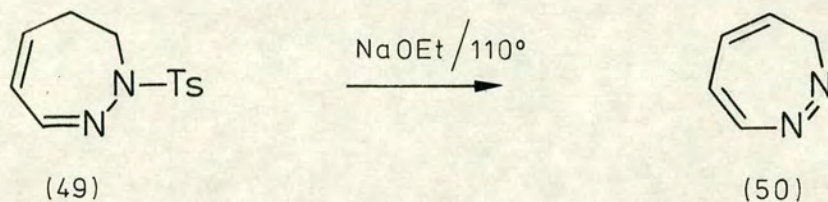
Scheme 15

6. 3*H*-1,2-Diazepines

This was the last of the 1,2-diazepine isomers to be prepared and further work on this interesting system is contained within this thesis.

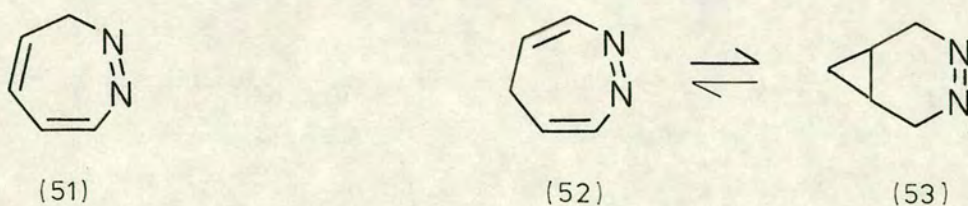
6.1 Synthesis

The 3*H*-1,2-diazepines (50) have been prepared by the base induced elimination of *p*-toluenesulphonic acid from 3,4-dihydro-2-tosyl-1,2-diazepines (49) (Scheme 16)³⁴. This reaction will be further reviewed in the Discussion, Section A.

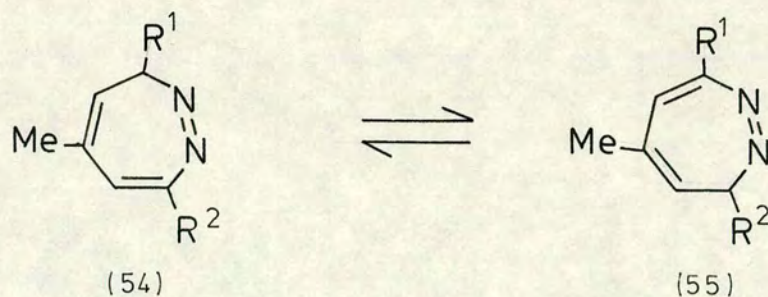


Scheme 16

It is interesting to note that these 3*H*-isomers (51) exist as diazepines where as the 5*H*-isomers (52), the only other 1,2-diazepine to be destabilised by an azo-group, favour the ring contracted diazanorcaradiene structure (53).

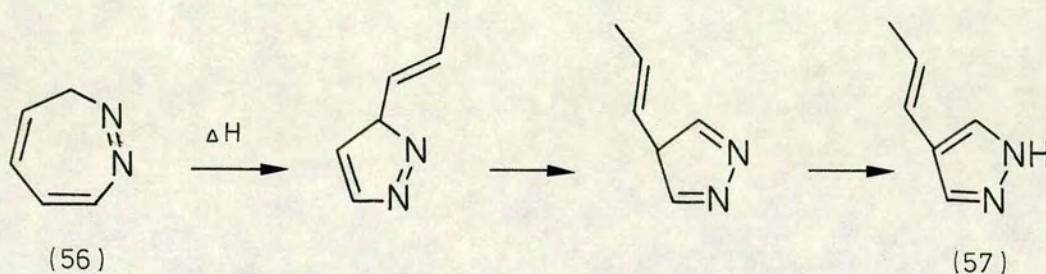


These 3*H*-1,2-diazepines exhibit 1,5-sigmatropic hydrogen shifts which interconvert (54) and (55); this interconversion is remarkably fast compared with analogous cycloheptatrienes so that the isomers are not isolable at room temperature.



6.2 Reactions

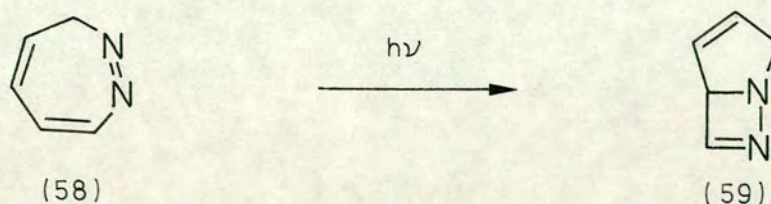
Two reactions of this system have been reported, the first reaction is the thermolytic ring contraction of 3*H*-1,2-diazepines (56) to 1*H*-pyrazoles (57) (Scheme 17) apparently by three consecutive rearrangements^{35,36}.



Scheme 17

The initial ring contraction is followed by a 1,5-migration of the vinyl group and then by a hydrogen shift.

In the second reaction 3*H*-1,2-diazepines (58) underwent ring contraction upon photolysis to give the [1,2] diazeto [4,1-*a*] pyroles (59) in high yield³⁷ (Scheme 18).



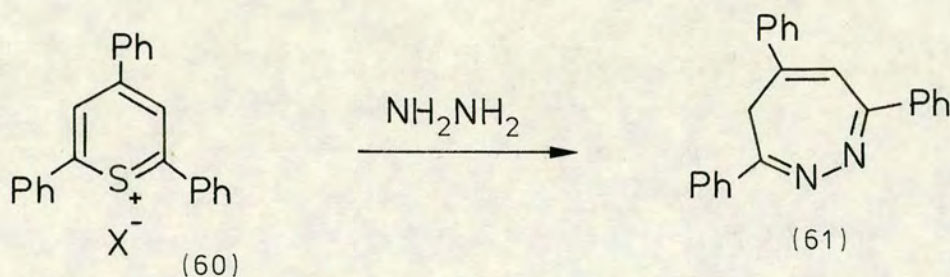
Scheme 18

7. 4H-1,2-Diazepines

This tautomer which contains an imine linkage and olefinic unsaturation is well documented in the literature.

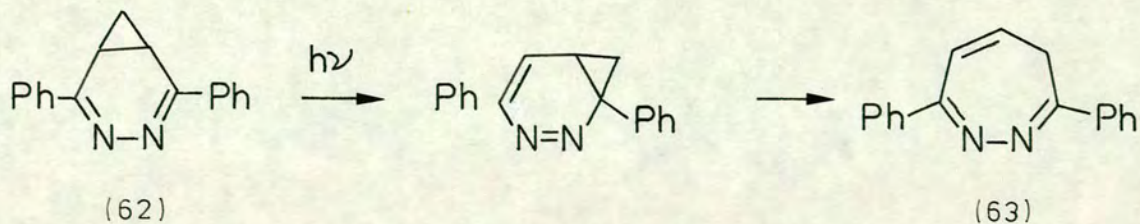
7.1 Synthesis

4H-1,2-Diazepines have been prepared by Klingsberg¹⁰, by the reaction of hydrazine with pyrylium or thiopyrylium salts. This reaction is similar to the synthesis of 1H-1,2-diazepines from thiopyrylium salts and methylhydrazine (see Section A.1.1). An example of this route is the preparation of 3,5,7-triphenyl-4H-1,2-diazepine (61) from a triphenylthiopyrylium salt (60) and hydrazine^{11,12} (Scheme 19).



Scheme 19

4H-1,2-Diazepines (63) have also been synthesised by photolysis of 3,4-diazanorcaradienes (62). This reaction proceeds via a photochemical walk process³⁸ (Scheme 20).



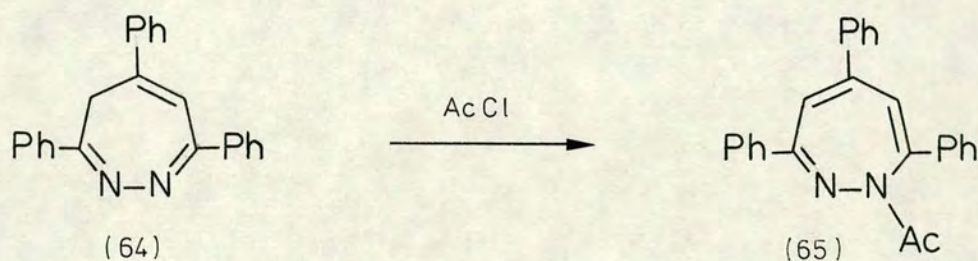
Scheme 20

Sauer et al.^{39,40} have further shown that 3,4-diazanorcaradienes will rearrange thermally to give 4*H*-1,2-diazepines also.

7.2 Reactions

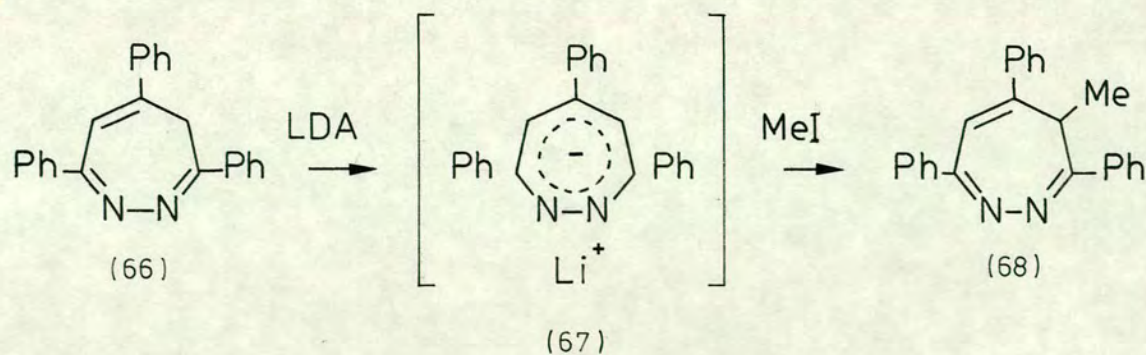
Few reactions on this class of 1,2-diazepine have been carried out. Those that are documented are, however, quite interesting.

Acylation of 3,5,7-triphenyl-4*H*-1,2-diazepine (64) with acetyl chloride occurs at N-2 to give the corresponding acylated 1*H*-1,2-diazepine (65)²¹ as depicted in Scheme 21.



Scheme 21

4*H*-1,2-Diazepines (66) have been deprotonated via treatment with lithium diisopropylamide and reaction of the anion (67) with alkyl halides gave 4-substituted-4*H*-1,2-diazepines⁴¹ (68) (Scheme 22).



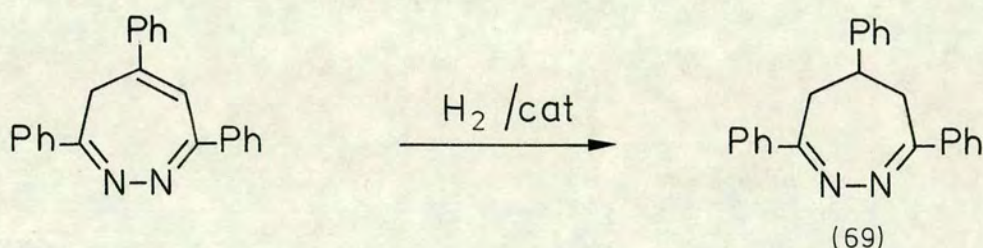
Scheme 22

This reaction provides a useful route to such systems which would be difficult to prepare by direct synthesis.

8. Dihydro-4H-1,2-diazepines

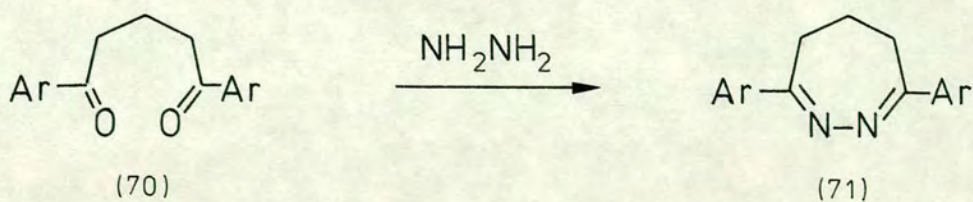
8.1 Synthesis

5,6-Dihydro-4H-1,2-diazepines have been prepared by catalytic hydrogenation of the fully unsaturated parent compound, an example being the preparation of 3,5,7-triphenyl-5,6-dihydro-4H-1,2-diazepine (69)¹² (Scheme 23).



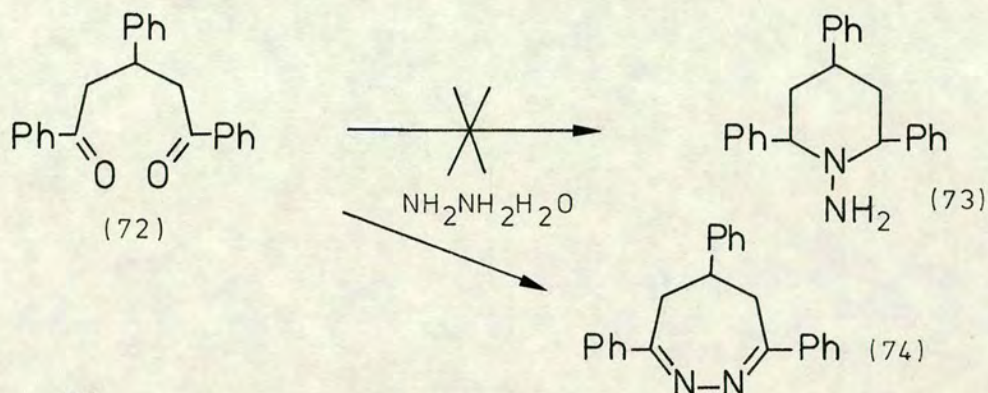
Scheme 23

Another method of synthesis reported in the literature involves the condensation of hydrazine with diaroylpropanes (70). In this way a variety of 3,7-diaryl-5,6-dihydro-4H-1,2-diazepines (71) have been prepared⁴² (Scheme 24).



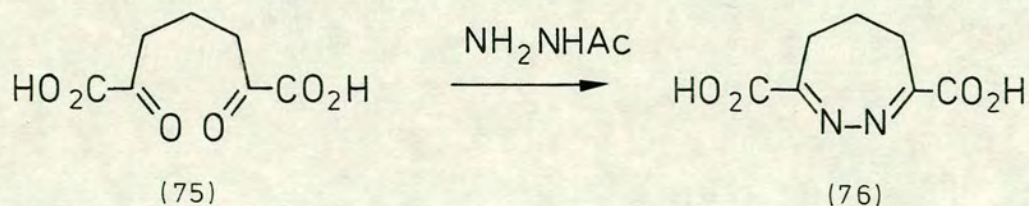
Scheme 24

The originators of this reaction, Merz and Richter⁴³, incorrectly assigned the product of the reaction between 1,3,5-triphenyl-1,5-pentanedione (72) with hydrazine hydrate as 2,4,6-triphenyl-1-amino-1,4-dihydropiperidine (73). Carpino⁴⁴ subsequently showed that the correct product was 3,5,7-triphenyl-5,6-dihydro-4*H*-1,2-diazepine (74) (Scheme 25).



Scheme 25

In a similar reaction Blaise and Gault⁴⁵ prepared 5,6-dihydro-4*H*-1,2-diazepine-3,7-dicarboxylic acid (76) from acetylhydrazide and α,α' -dioxopimelic acid (75) in Scheme 26, the diazepine is deposited almost immediately as a precipitate.



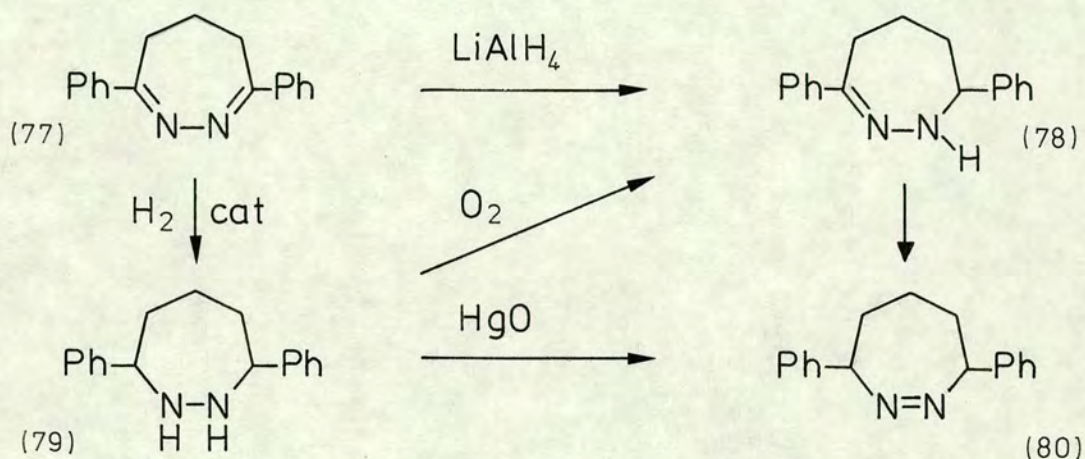
Scheme 26

8.2 Reactions

Two reactions of this system have been reported in the literature.

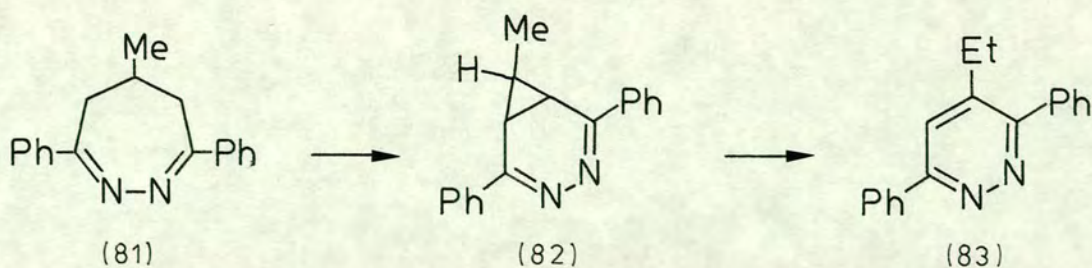
In one, 3,7-diphenyl-5,6-dihydro-4*H*-1,2-diazepine (77)

can be reduced to a tetrahydrodiazepine (78) by lithium aluminium hydride⁴⁶, and to the hexahydrodiazepine (79) by catalytic hydrogenation. Oxidation of the hexahydrodiazepine (78) with air gives the tetrahydrodiazepine (78) and with mercuric oxide gives the different tetrahydrodiazepine (80), which rearranges into the isomeric tetrahydrodiazepine (78)^{47,48} (Scheme 27).



Scheme 27

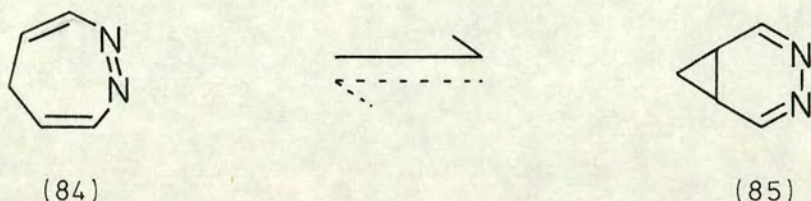
In the other reaction that has been reported, treatment of 5,6-dihydro-4*H*-1,2-diazepine (81) with *N*-bromo or *N*-chlorosuccinimide resulted in ring contraction to the pyridazine derivative (83), via the bicyclic intermediate (82)⁴⁹ (Scheme 28).



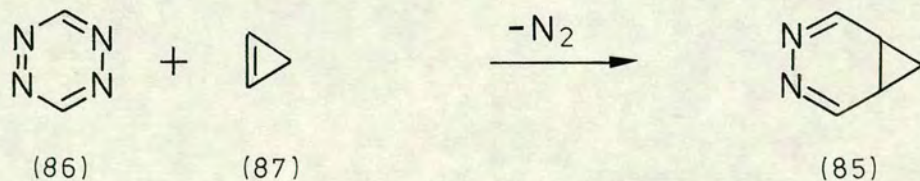
Scheme 28

9. 5H-1,2-Diazepines

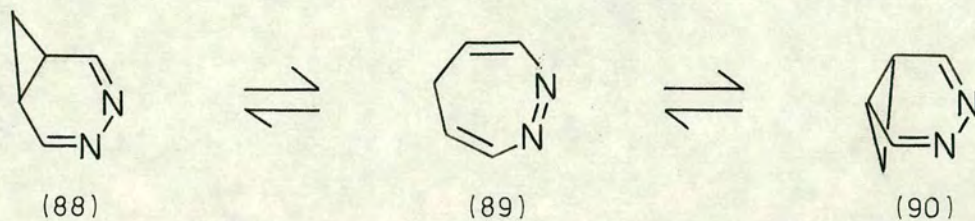
This is the last member of the monocyclic 1,2-diazepine series and this 5H-isomer (84) is so destabilised by the low bond energy of the azo-group that in all systems so far reported, it exists entirely as its diazanorcaradiene tautomer (85).



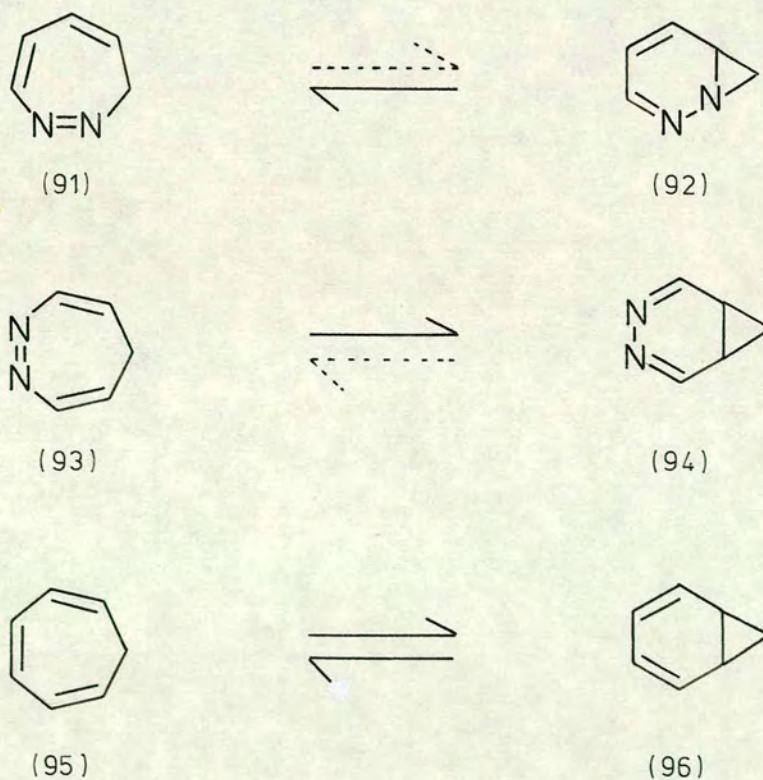
Sauer et al.⁵⁰ has synthesised these diazanorcaradienes (85) by a Diels-Alder type reaction between tetrazines (86) and cyclopropenes (87) (Scheme 29).



Evidence for the existence of the 5H-1,2-diazepine has been provided by variable temperature n.m.r. studies carried out by Maier^{51,52}. Thus, in the *exo-endo* equilibration between the two isomeric diazanorcaradienes (88) and (90), studied by variable temperature n.m.r., the monocyclic form (87) was inferred as a transient intermediate.



It is interesting to compare the stability of the 5*H*-isomer with the other 1,2-diazepine isomer destabilised by an azo group; the 3*H*-isomer. In the 3*H* series the compounds so far studied have the tautomeric equilibrium so strongly biased in favour of the diazepine structure (91) that the diazanorcaradiene form (92) is undetectable. This contrasts with the 5*H*-1,2-diazepine (93) case in which the equilibrium is as strongly biased in the opposite direction.



In the analogous hydrocarbon case, the equilibrium between cycloheptatriene (95) and norcaradiene (96) is affected by substituents on the ring⁵³.

The crossover in thermodynamic stability of the 3*H* and 5*H* systems has been explained in terms of bond energies³⁴. The average bond energies of C=N (607) and C=C (613) bonds are much higher than for N=N (385) bonds while for the single bonds (C-C) (348) is greater than C-N (302) which is greater than N-N (168 kJ mol⁻¹). Thus although both the 5*H* and the 3*H*-1,2-diazepines are similarly destabilised by having an azo-group, in the diazonorcaradienes (92) is destabilised relative to (91) by having two C-N bonds where (91) has the stronger C-C bond. In the 5*H*-isomer the gain in bonding energy on its conversion into the diazanorcaradiene more than off-sets the increased ring strain, but for the 3*H*-isomer it does not and so the diazepine structure is favoured.

B. Benzodiazepines

Benzodiazepines are bicyclic, heterocyclic compounds having a benzene ring fused to the diazepine ring. There are six basic ring structures depending on the position of the two nitrogen atoms and these are shown in figure 1.

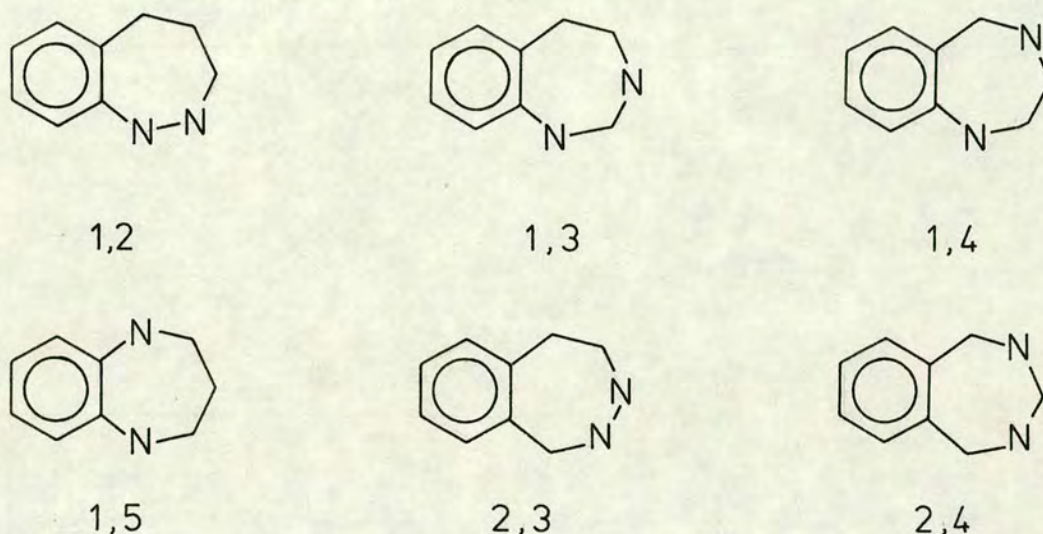


Figure 1

Benzodiazepines are numbered as shown; starting at the position adjacent to the carbocyclic ring and giving the first nitrogen the lowest number possible.

The chemistry of benzodiazepines has been reviewed^{1,2,54} and much of the literature is concerned with the biologically active 1,4-benzodiazepines. Two drugs which have 1,4-benzodiazepines as their active ingredients are the tranquilisers "Librium" and "Valium".

1,5-Benzodiazepines are synthetically easy to prepare and their chemistry has also been well studied. The literature on the remaining four classes of benzodiazepines is less

extensive. Only the two isomers which contain adjacent nitrogen atoms, namely the 1,2- and 2,3-benzodiazepines will be reviewed here.

1. 1,2-Benzodiazepines

There are three possible 1,2-benzodiazepine isomers (Figure 2), all of which have been reported.

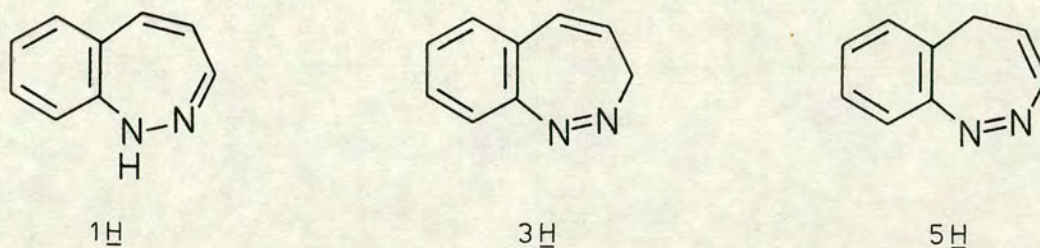
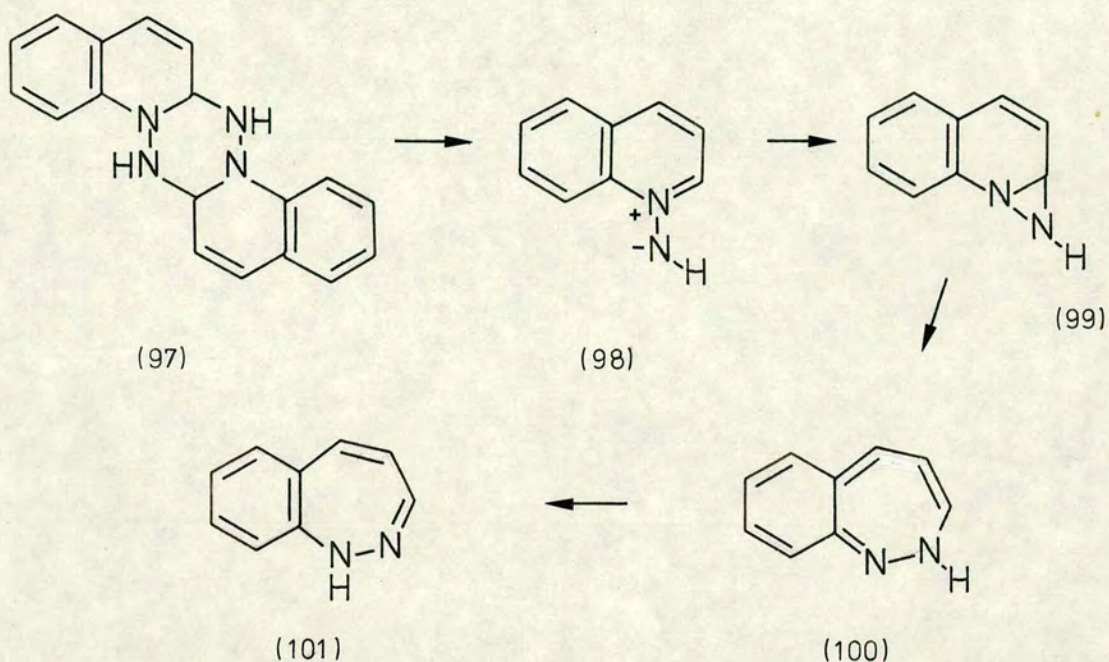


Figure 2

1.1 1H-1,2-Benzodiazepines

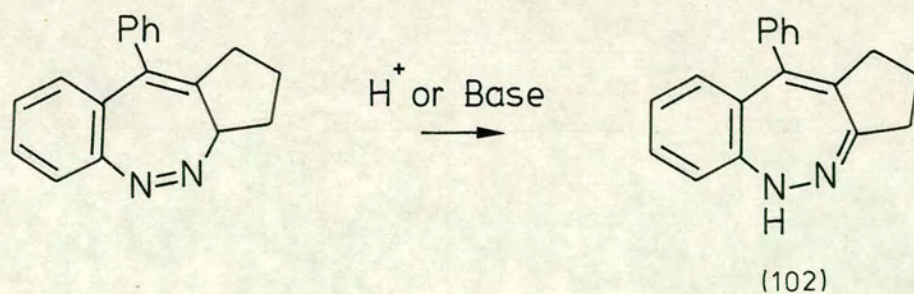
1H-1,2-Benzodiazepines have been prepared by photolysis of N-iminoquinolinium ylide dimers⁵⁵ (Scheme 30). The mechanism postulated for this interesting reaction is the equilibration of the N-iminoquinolinium dimer (97) to the monomer ylide (98), followed by photoinduced electrocyclisation to compound (99), ring expansion to the 2H-benzodiazepine (100) and finally a [1,7] hydrogen shift to restore aromaticity to the benzene nucleus to give the 1H-1,2-benzodiazepine (101).



Scheme 30

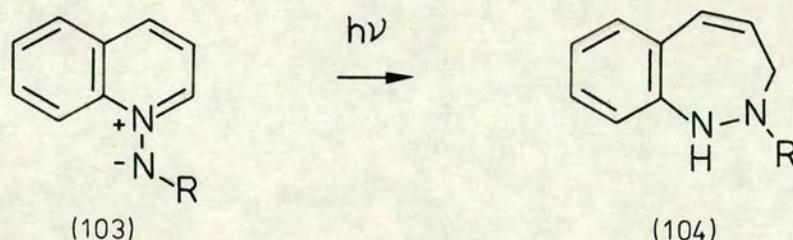
This synthetic route is analogous to the preparation of 1*H*-1,2-diazepines from pyridine *N*-imines (Section A.1.1).

1*H*-1,2-Benzodiazepines have also been prepared by the treatment of the 3*H*-isomer with acid or base⁵⁶, thus the 1*H*-1,2-benzodiazepine (102) was synthesised in this manner (Scheme 31).



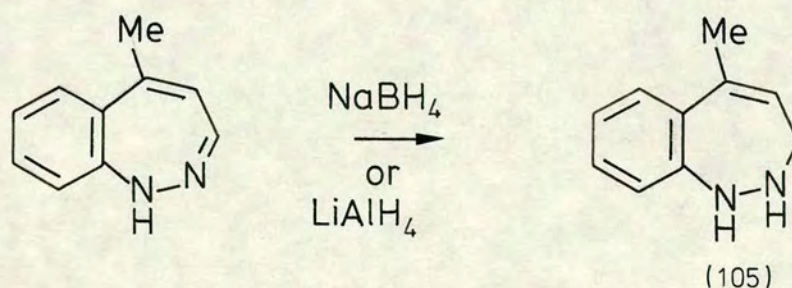
Scheme 31

2,3-Dihydro-1*H*-1,2-benzodiazepines (104) have been prepared by the photolysis of *N*-iminoquinolinium ylides (103) in ethanol or methanol (Scheme 32).⁵⁷⁻⁵⁹



Scheme 32

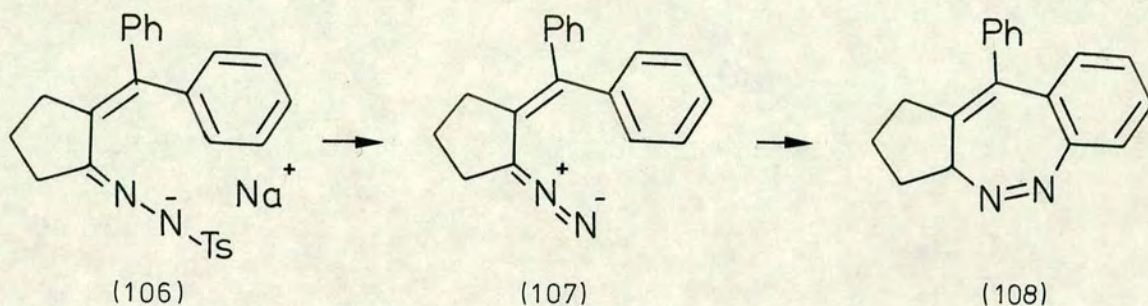
This 2,3-dihydro-1*H*-1,2-benzodiazepine (105) isomer has also been prepared by reduction of the corresponding fully unsaturated system⁵⁵ (Scheme 33).



Scheme 33

1.2 3*H*-1,2-Benzodiazepines

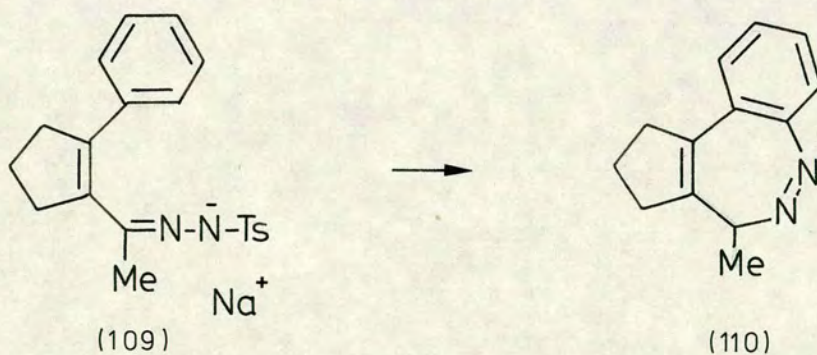
These compounds have been synthesised by Sharp and his co-workers by the thermal decomposition of tosylhydrazone salts of α -diarylmethylene cyclopentanones (106). The benzodiazepine (108) was obtained from the resulting diazoalkene (107) via 1,7-electrocyclic ring-closure^{56,60} (Scheme 34).



Scheme 34

This reaction was found to be extremely sensitive to steric factors.

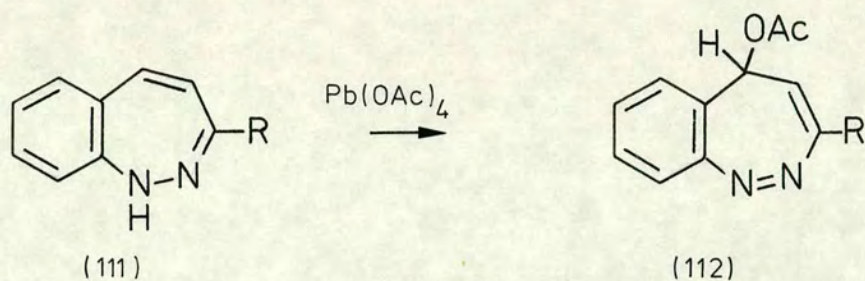
3*H*-1,2-Benzodiazepines of the type (110) have been obtained by using a similar method; the thermal decomposition of the tosylhydrazone salts of the type⁶¹ (109) (Scheme 35).



Scheme 35

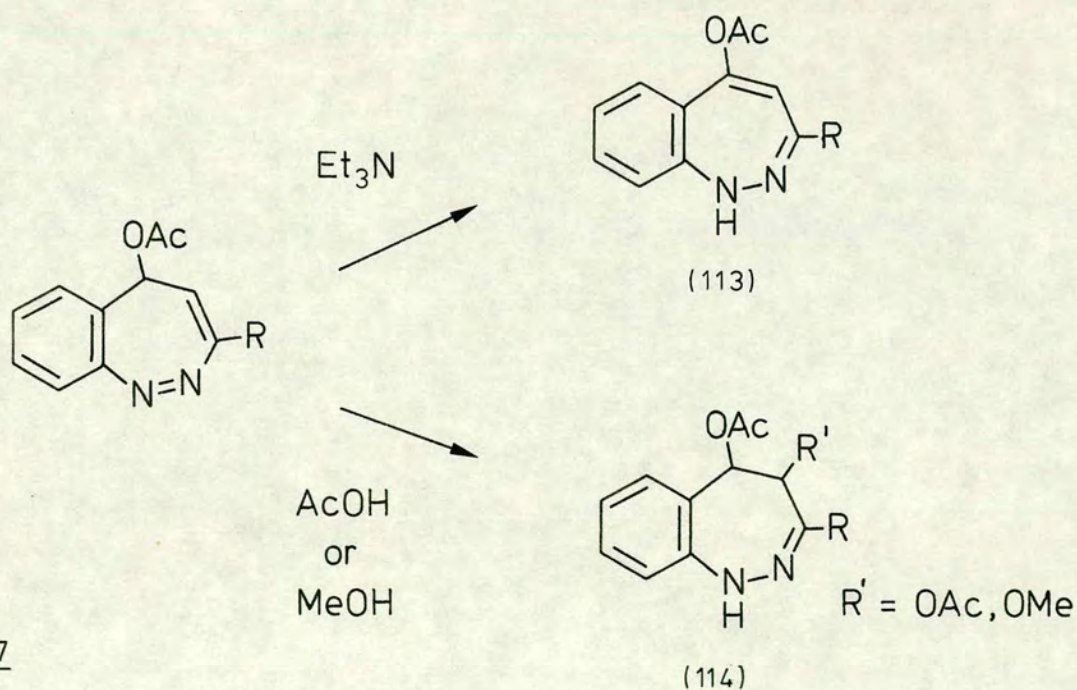
1.3 5*H*-1,2-Benzodiazepines

This isomer has recently been prepared for the first time by the treatment of 1*H*-1,2-benzodiazepines (111) with lead tetraacetate to give the previously unknown 5*H*-tautomer⁶² (112) (Scheme 36).



Scheme 36

The 5*H*-1,2-benzodiazepines are less stable than the 3*H*- and 1*H*-isomers, and can be isomerised to the latter (113) with base. They also react readily with acetic acid or methanol to give the corresponding 1,4-adducts⁶² (114), as shown in Scheme 37.



Scheme 37

2. 2,3-Benzodiazepines

Of the three possible 2,3-benzodiazepine isomers two, the 1*H* and 5*H*, are well known (Figure 3).

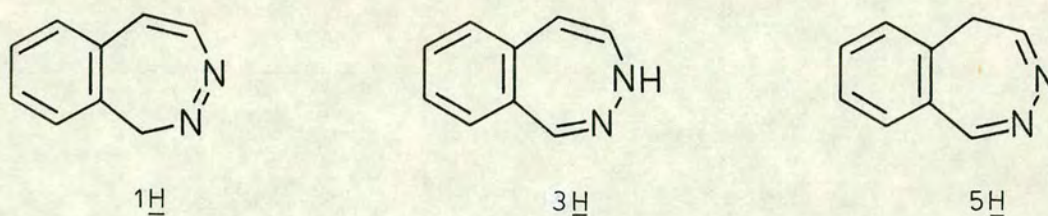
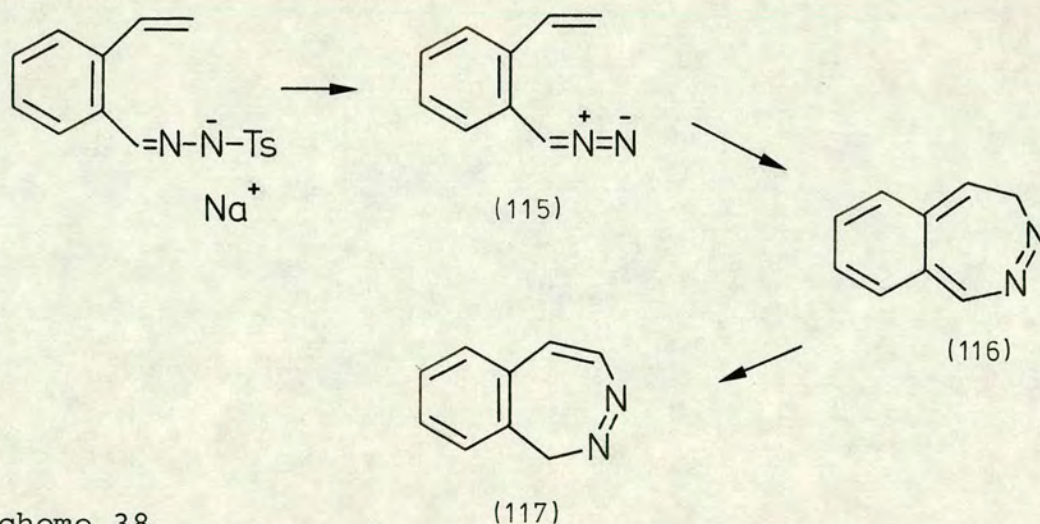


Figure 3

2.1 1H-2,3-Benzodiazepines

This isomer has been prepared by thermal decomposition of tosylhydrazone salts of α -aryldiazoalkenes^{63,64} (Scheme 38).



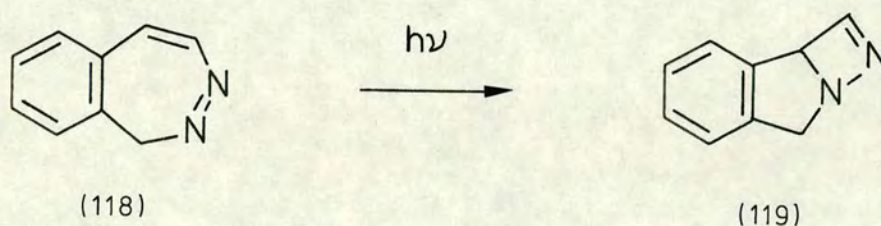
Scheme 38

The mechanism suggested for this reaction is the formation of the α -aryldiazoalkene (115) which undergoes 1,7-electrocyclic ring-closure to give the intermediate 4H-benzodiazepine (116) which converts to the stable 1H-2,3-benzodiazepine (117) via a 1,5-symmetry allowed sigmatropic hydrogen shift. The structure (117) has been confirmed by X-ray analysis.

1H-2,3-Benzodiazepines (118) are readily isomerised by

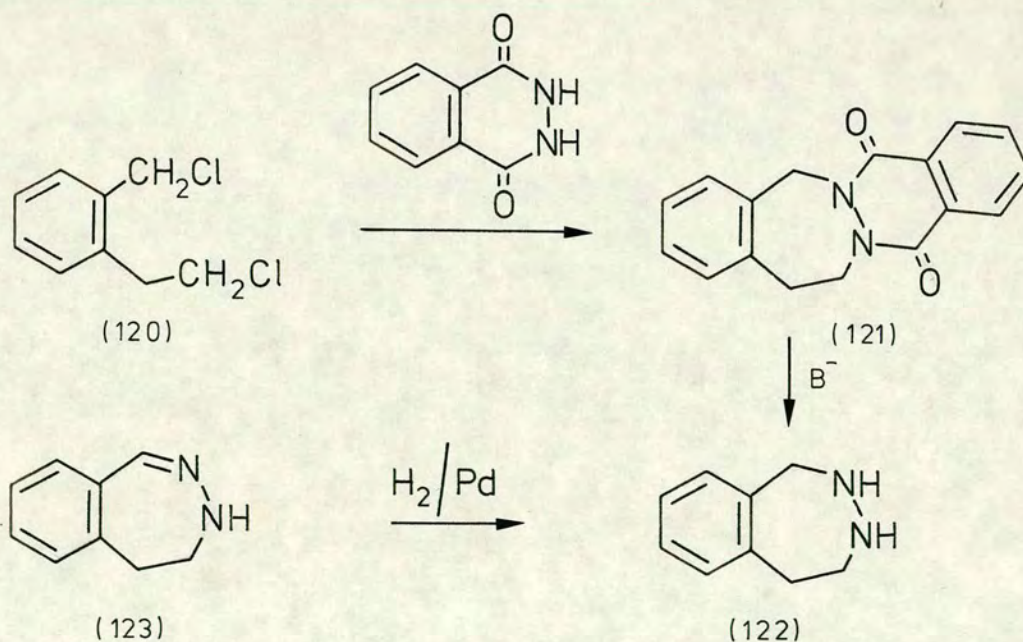
light to give azetido [1,2-*b*][1,2] diazepine (119)

(Scheme 39).



Scheme 39

A tetrahydro 1*H*-2,3-benzodiazepine (122) has been synthesised by the reaction of phthaloyl hydrazide and *o*-chloromethyl-2-phenylethyl chloride (120) followed by cleavage of the primary diazepine product (121) with base⁶⁵ (Scheme 40).

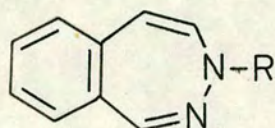


Scheme 40

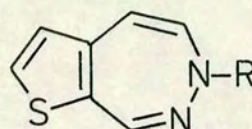
This 2,3,4,5-tetrahydro-1*H*-2,3-benzodiazepine (122) has also been prepared by catalytic hydrogenation of the corresponding 4,5-dihydro-3*H*-2,3-benzodiazepine⁶⁵ (123) (Scheme 40)

2.2 3H-2,3-Benzodiazepines

The parent unsaturated benzodiazepine (124) is unknown but the thieno analogue (125) has been prepared⁶⁶.

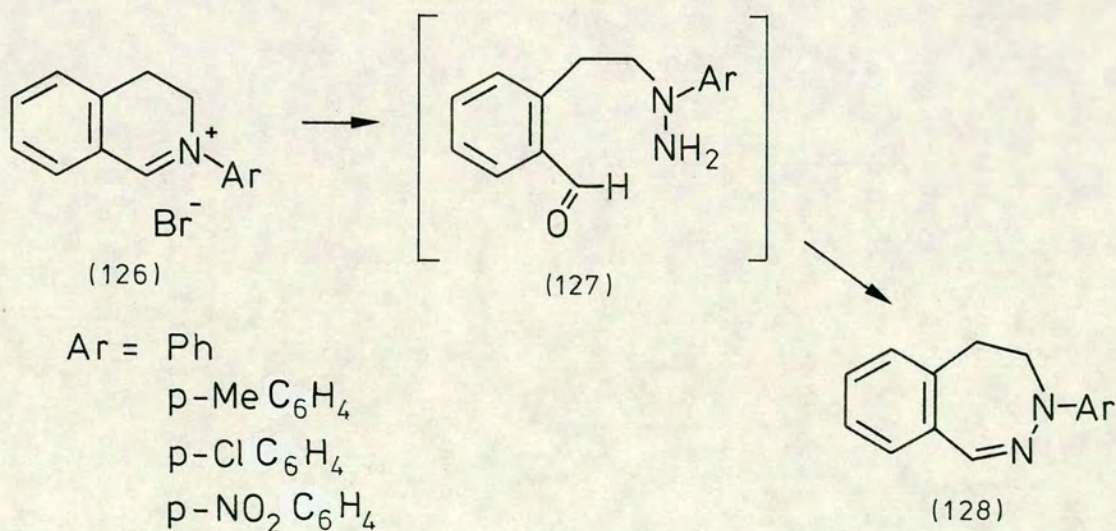


(124)



(125)

There are a few examples of saturated 3H-2,3-benzodiazepines, for example, 3-aryl-4,5-dihydro-3H-2,3-benzodiazepines (128) have been prepared by treatment of dihydroisoquinolinium salts (126) with alkali, followed by reaction with *o*-mesitylsulphonylhydroxylamine⁶⁷ (Scheme 41).

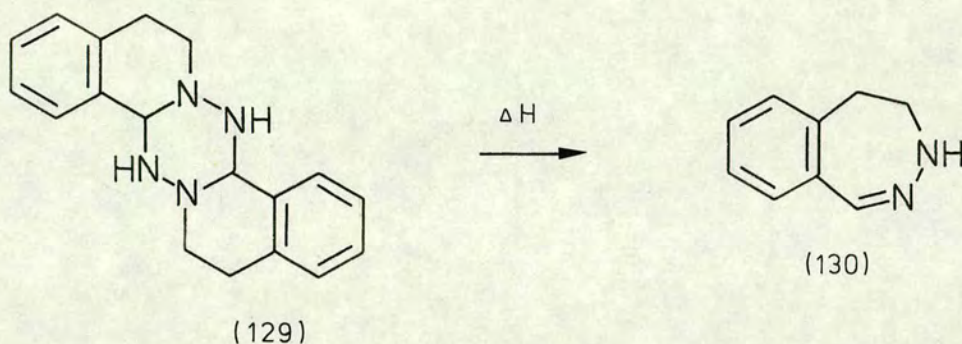


Scheme 41

The hydrazine derivative (127) has been postulated as an intermediate.

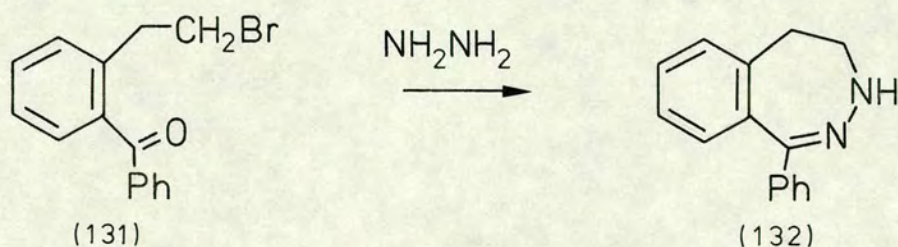
Schmitz and Ohme⁶⁵ found that 4,5-dihydro-3H-2,3-benzo-

diazepines (130) could be prepared by the pyrolysis of diisoquinolinotetrazines (129) as depicted in Scheme 42.



Scheme 42

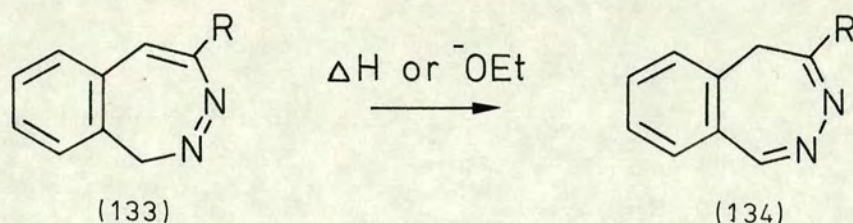
One other synthesis of a 3H-2,3-benzodiazepine has been reported⁶⁸, this is the reaction of 2-(2-bromoethyl)benzophenone (131) with hydrazine to give 4,5-dihydro-1-phenyl-3H-2,3-benzodiazepine (132) as depicted in Scheme 43.



Scheme 43

2.3 5H-2,3-Benzodiazepines

The 5H-isomer (134) has been prepared by thermal or basic treatment of the corresponding 1H-derivative (133)^{64,69} (Scheme 44).

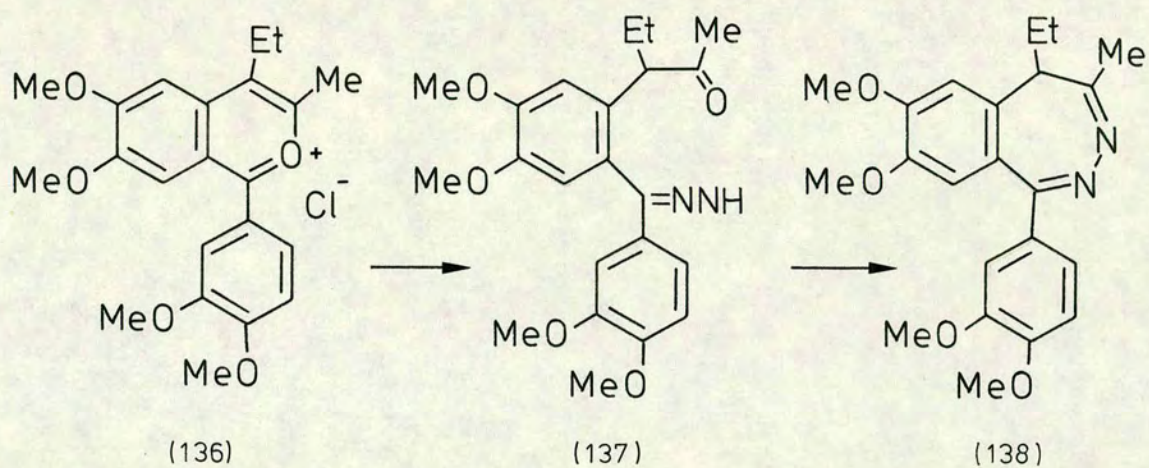


Scheme 44

The energy barrier to ring inversion has been calculated to be ~ 80 kJ mole from variable temperature n.m.r. experiments. These values are much higher than those reported for the parent monocyclic 4*H*-1,2-diazepine (135), which is consistent with the higher degree of ring-rigidity associated with the fused benzene ring.

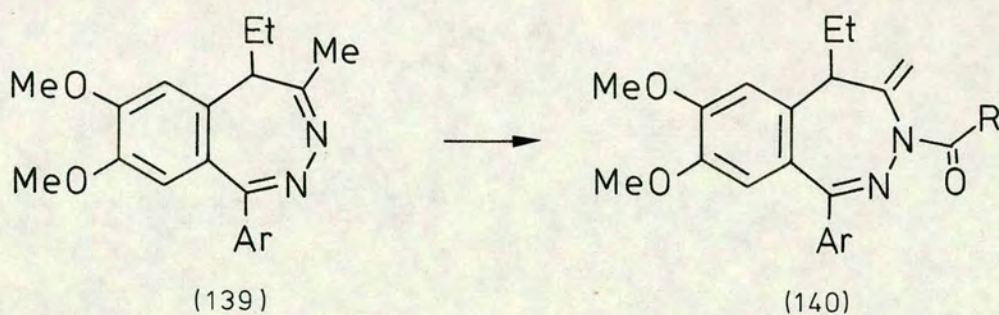


One other method of synthesis of this isomer (138) is reported in the literature.⁷⁰⁻⁷³ In this reaction a benzo-pyrylium salt (136) is treated with hydrazine hydrate, the reaction proceeds via the monohydrazone (137) (Scheme 45). This reaction is very similar to the preparation of monocyclic 4*H*-1,2-diazepines (see Section A.7.1).



Scheme 45

This benzodiazepine undergoes an interesting acylation reaction to give the novel 3-acyl-4-methylene derivative (140) (Scheme 46).



Scheme 46

Acylation occurs at N-3 with concomitant C=N bond migration to give (140).⁷⁴

C. Iron Carbonyl Complexes of 1,2-Diaza Compounds

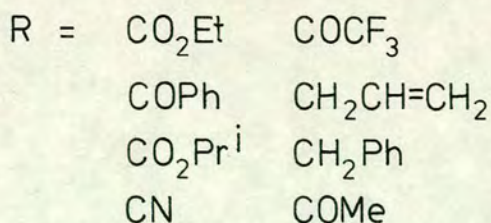
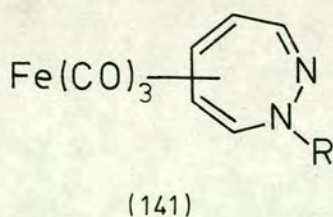
Nitrogen-containing organic compounds have provided a wide variety of transition metal complexes. This review will consider iron carbonyl complexes derived from organic compounds which contained two nitrogen atoms, and more specifically those in which the nitrogen atoms were initially adjacent. Analogous complexes of other transition metals will be mentioned briefly for comparison.

1. 1,2-Diazepine Complexes

To date the literature only contains examples of monocyclic 1,2-diazepine iron carbonyl complexes, and in particular only those of the 1*H*- and 4*H*-1,2-diazepine isomers.

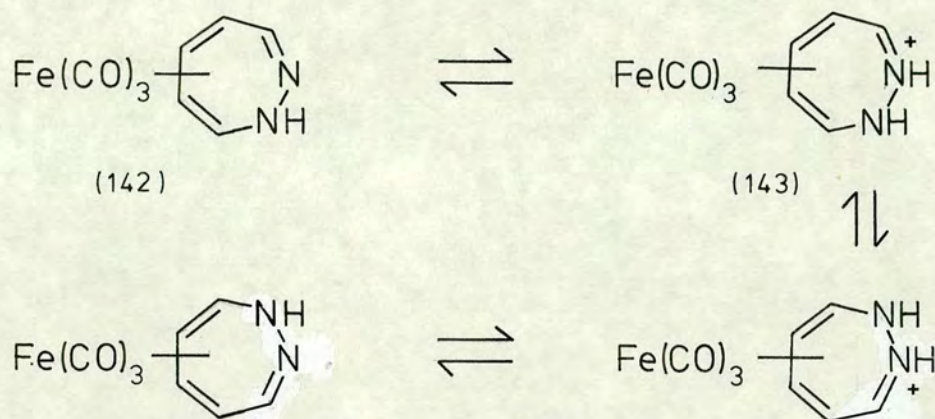
1.1 1*H*-1,2-Diazepine

Many examples of iron tricarbonyl 1*H*-1,2-diazepine complexes are reported in the literature^{3,75,76,77}. X-Ray diffraction studies⁷⁸ have shown that the iron tricarbonyl residue is coordinated to the diene fragment of the heterocycle (141).



This type of interaction between a butadiene unit and an iron tricarbonyl residue is well known in organometallic chemistry.⁷⁹

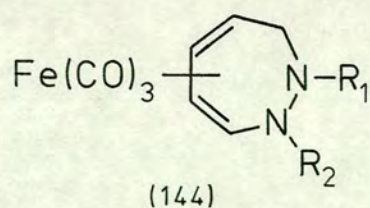
The iron tricarbonyl complex of the parent 1*H*-1,2-diazepine (142) exhibits novel fluxional behaviour via an intermediate protonated complex⁸⁰ (143) (Scheme 47).



Scheme 47

The intermediate iminium complex (143) is capable of iron tricarbonyl migration fluxional behaviour.

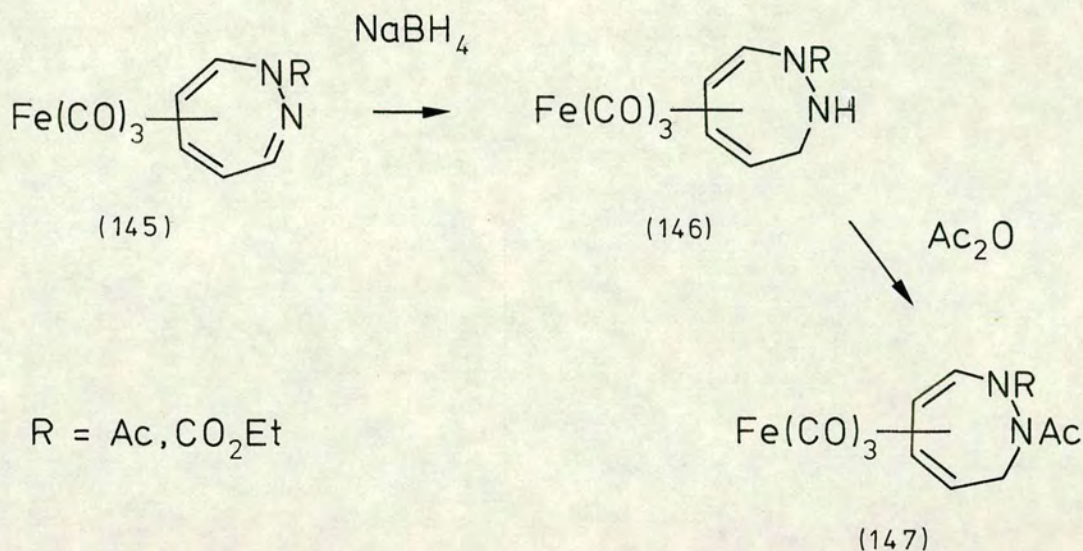
2,3-Dihydro-1*H*-1,2-diazepine iron tricarbonyl complexes (144) have been prepared by treating the corresponding free diazepines with a suspension of diiron nonacarbonyl in benzene.¹⁴



R ₁	R ₂
H	Ac
H	CO ₂ Et
Ac	CO ₂ Et
Ac	Ac

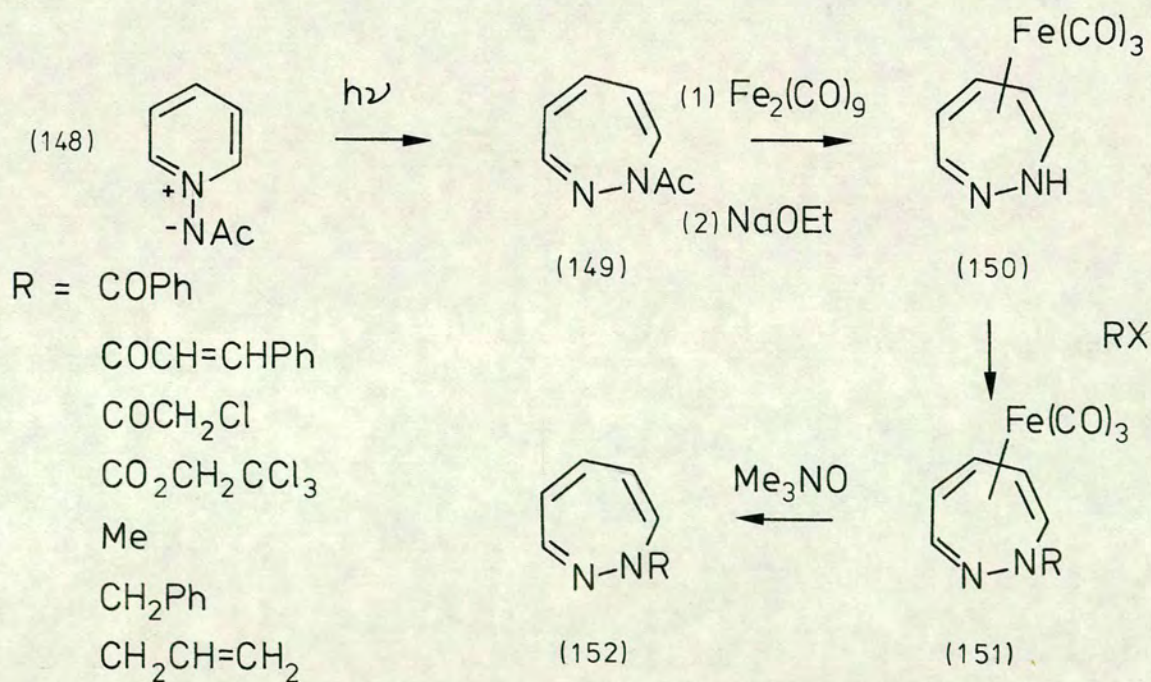
2,3-Dihydro-1*H*-1,2-diazepine iron tricarbonyl complexes (146) have also been prepared by reduction of the corresponding 1*H*-complex (145) with sodium borohydride. These dihydro

derivatives were found to be unstable and were converted into the more stable *N*-acetyl derivatives (147) by treatment with acetic anhydride (Scheme 48).



Scheme 48

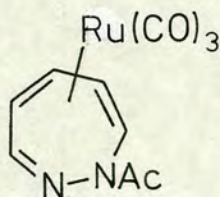
1*H*-1,2-Diazepine iron tricarbonyl complexes have provided a more versatile synthetic route to *N*-substituted 1*H*-1,2-diazepines (152)¹⁴ (Scheme 49).



Scheme 49

This organometallic approach uses the photolysis of an *N*-iminopyridinium ylide (148) as a source of the 1*H*-1,2-diazepine ring system (149), this is then treated with diiron nonacarbonyl to give the iron tricarbonyl complex (150). The acetyl group is removed by reaction with sodium ethoxide and various *N*-substituted derivatives (151) are then prepared by treatment with acyl and alkyl halides. Removal of the tricarbonyliron residue is achieved by Shvo's⁸¹ procedure in which the complex is treated with an excess of trimethylamine *N*-oxide. This method avoids the limitations associated with the synthesis via photolysis of *N*-iminopyridinium ylides, ie only substituted diazepines for which the corresponding ylide is stable can be prepared.

Ruthenium tricarbonyl complexes of 1*H*-1,2-diazepines (153) have also been prepared⁷⁶, and their structures are similar to that of the iron tricarbonyl complexes, the ruthenium residue coordinating via the butadiene unit of the heterocycle.

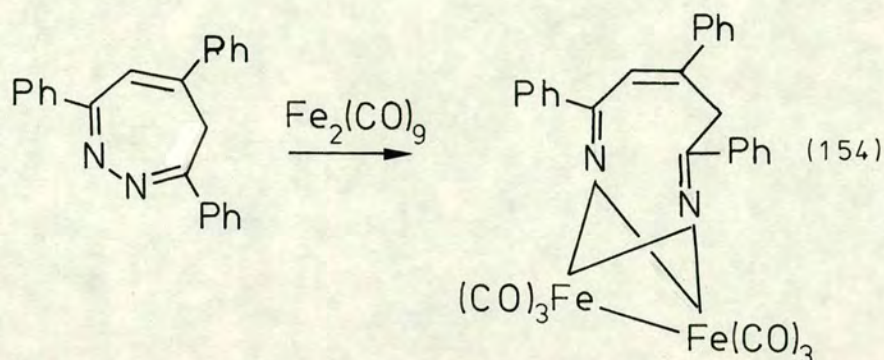


(153)

1.2 4*H*-1,2-Diazepines

The reactivity of this 1,2-diazepine isomer is quite different⁸²: reaction with iron carbonyls does not produce

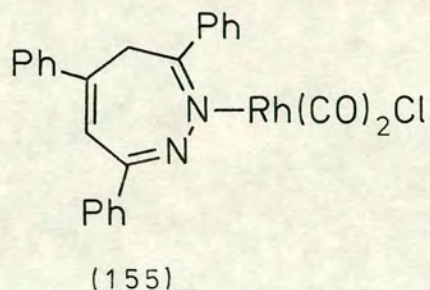
simple iron tricarbonyl diene complexes, but rather N-N bond cleavage occurs to yield a novel bicyclic eight membered metallocyclic ring system (154) (Scheme 50).



Scheme 50

This reactivity is consistent with the reactivity observed for other azine containing compounds (see Section C.2.2).

A rhodium carbonyl complex of a 4*H*-1,2-diazepine (155) has also been reported⁸³, in this case the ring system of the heterocycle is retained and coordination is via σ lone pair donation from one of the nitrogen atoms.



2. Cyclic Fe_2N_2 Systems

Many examples of dinuclear iron carbonyl complexes containing heteroatom bridges are reported in the literature⁸⁴. Included in these examples are compounds containing the diiron hexacarbonyl group, in which the iron atoms are linked by an

intermetallic bond as well as one six-electron or two three-electron heteroatom bridges.

These complexes can be divided into two types according to the electronic structure of the bridge (figure 3).

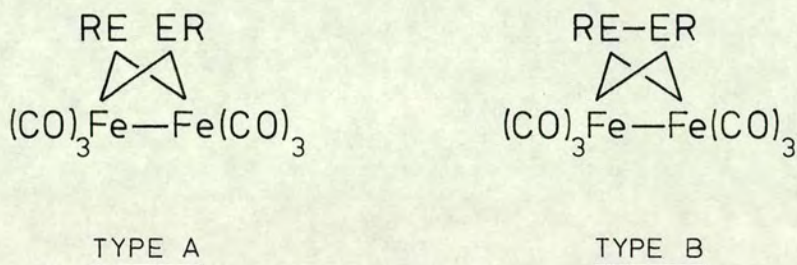


Figure 3

Among type A complexes; those with three-electron bridges, compounds with sulphur bridges have been known longest.⁸⁴⁻⁸⁷ Analogous nitrogen-containing complexes were discovered only comparatively recently.

Type B complexes; those containing one six-electron bridge, have been prepared from sulphur, nitrogen and phosphorus compounds (figure 4). Both type A and type B nitrogen complexes have recently been reviewed.⁸⁸

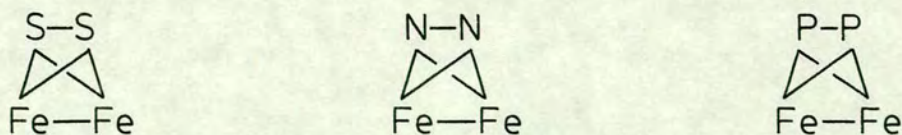


Figure 4

This section will survey the literature on dinuclear complexes containing the Fe_2N_2 system, and in particular those complexes derived from diaza containing compounds in which the nitrogen atoms were initially adjacent. Complexes will be reviewed according to the structural unit present in the original nitrogen containing compound.

Initial interest in these nitrogen complexes was due to the fact that compounds containing the diazene ligand ($\text{HN}=\text{NH}$) were regarded as possible intermediates in the enzymatic fixation of molecular nitrogen^{89,90}.

2.1 Complexes derived from Azo-compounds

Until 1963 there was almost no information in the literature about transition metal complexes of azo compounds; however, since the paper by Kleiman and Dubeck⁹¹ describing a nickel azobenzene complex, a steady stream of publications has appeared. These have dealt with complexes of other metals such as platinum⁹², palladium⁹³ and iron⁹⁴. The four different ways in which an azo bond can coordinate to transition metals has proved to be an irresistible attraction to chemists (figure 5).

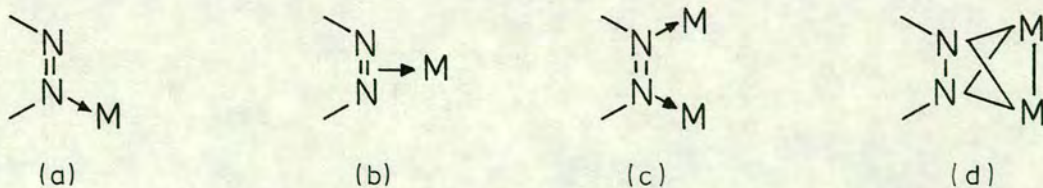


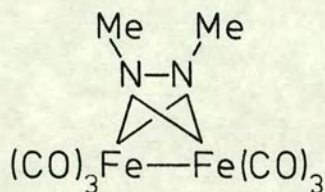
Figure 5

Considering iron carbonyl azo compound complexes, three

of the four possible types of coordination are known (a, c and d), in which the nitrogen-ligand behaves as a donor of two, four and six electrons respectively. Type (b) coordination is encountered in complexes of other transition metals such as nickel⁹⁵, titanium and vanadium⁹⁶.

2.1.1 Aliphatic Azo Compounds

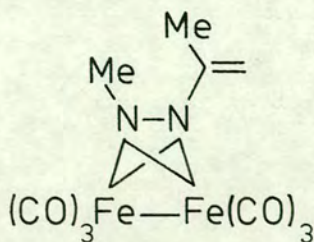
The reaction between azomethane and diiron nonacarbonyl gives a dinuclear complex (156) in which the initial skeleton of the azo-compound is retained.⁹⁷



(156)

This structure, in which the azo-compound behaves as a six electron donor, was confirmed by X-ray diffraction.

The interaction of 2-(methyl-azo)propene with diiron nonacarbonyl gives rise to a dinuclear complex to which the structure (157) has been attributed on the basis of spectroscopic data⁹⁸; interestingly the carbon carbon double bond is not involved in coordination.

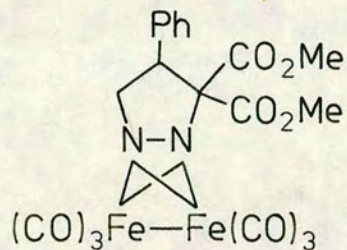


(157)

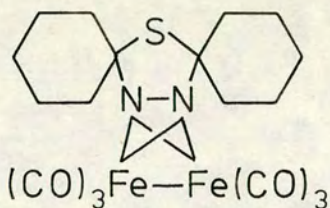
Cyclic azo-compounds also retain their skeleton in reactions with iron carbonyls. Dinuclear iron carbonyl complexes of type (B) have been obtained from 2,3-diazabicyclo[2.2.1]hept-2-ene⁹⁹⁻¹⁰¹ (158), derivatives of 1,2-diazacyclopent-1-ene¹⁰²⁻¹⁰⁴ (159), 1,3,4-thiazoline (160)¹⁰¹, and dibenzo[1,4,5]oxadiazepine^{105,106} (161).



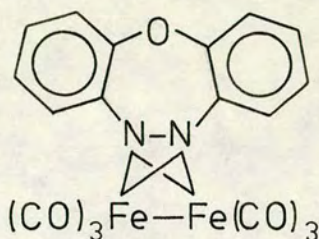
(158)



(159)

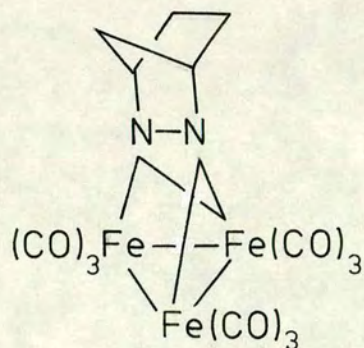


(160)



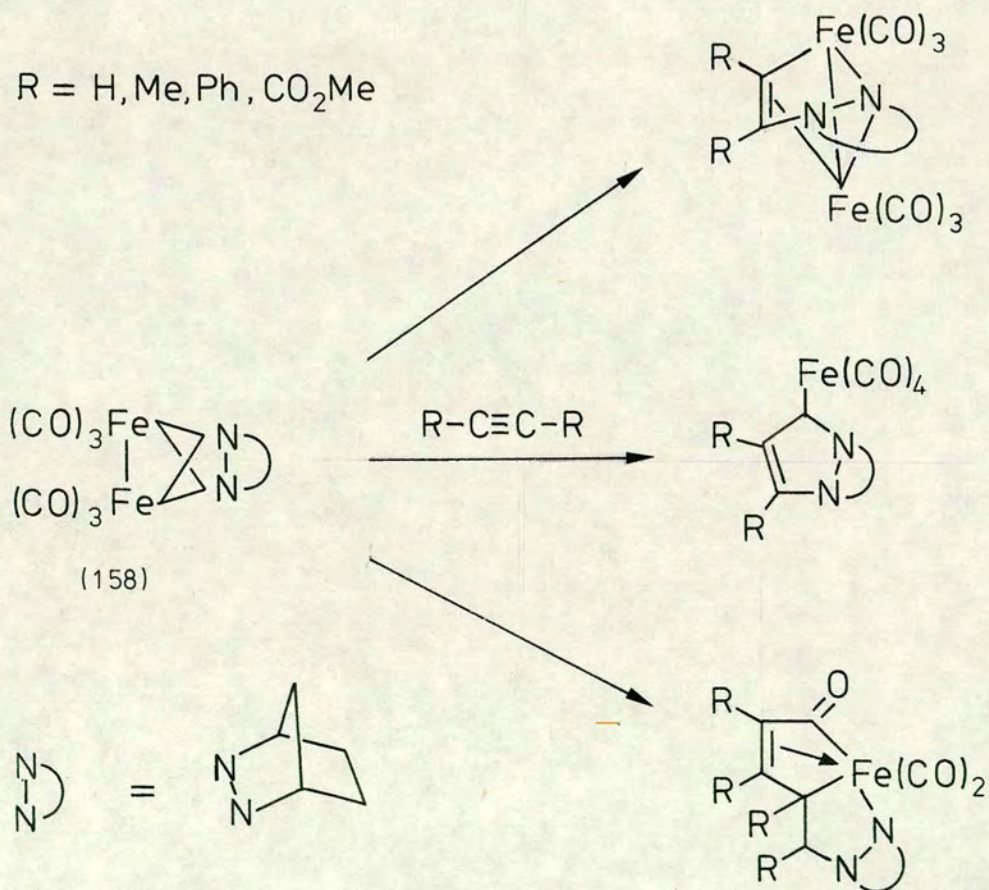
(161)

Reactions of 2,3-diazabicyclo[2.2.1]hept-2-ene diiron hexacarbonyl complex (158) have provided further interesting complexes. Thus irradiation of the complex in the presence of iron pentacarbonyl results in the formation trinuclear cluster (162)⁹⁹.



(162)

Reactions of the dinuclear complex (158) with alkynes, both thermally and photochemically, have produced complexes in which the alkyne molecules have been incorporated by insertion into the iron nitrogen bond (Scheme 51)¹⁰⁷⁻¹⁰⁹.

Scheme 51

Similar alkyne insertion reactions have also been reported

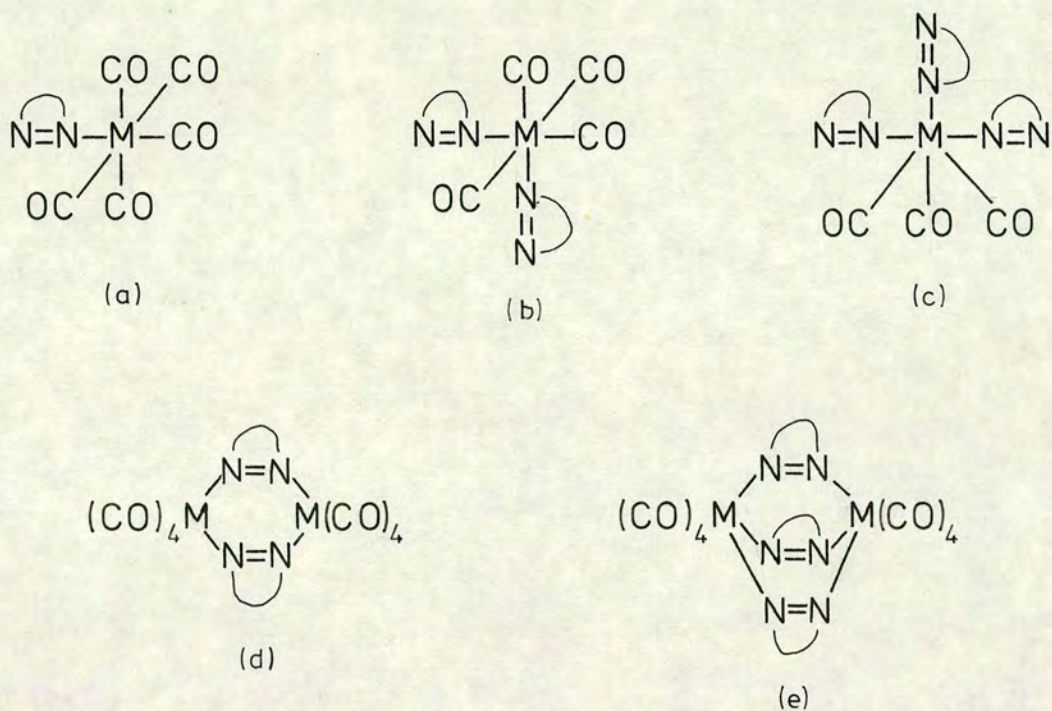


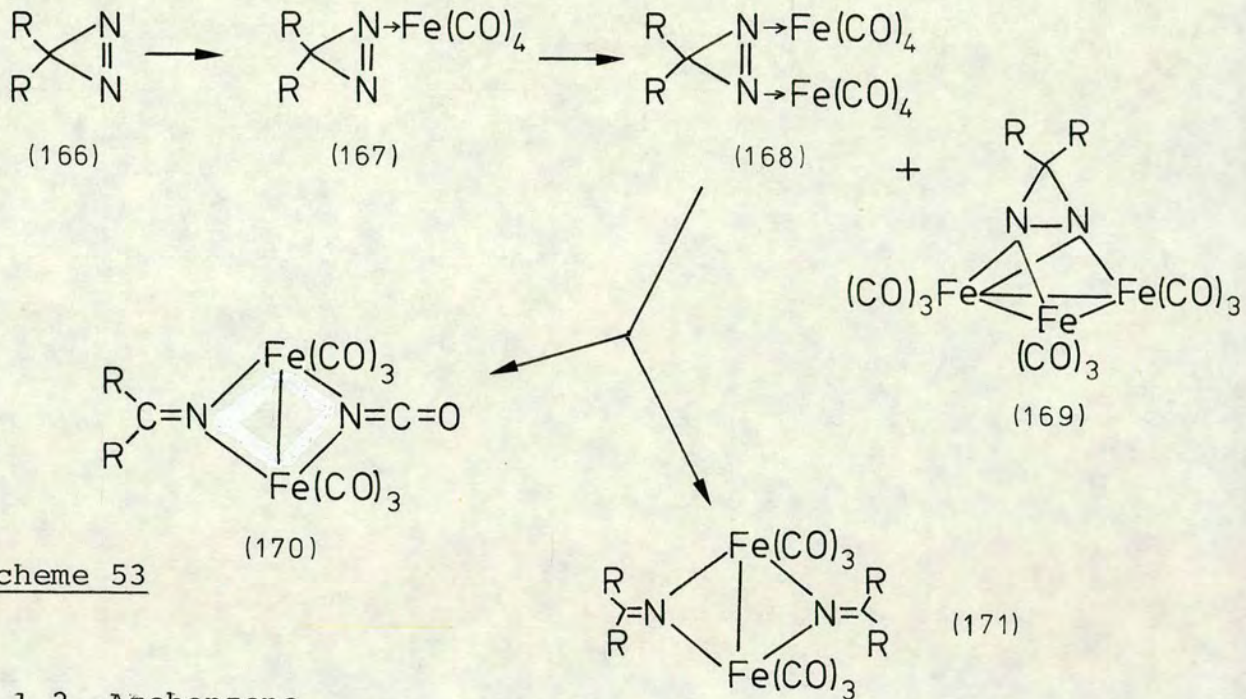
Figure 6

In these dinuclear complexes the azo compound behaves as a four-electron donor and there is no intermetallic bond. Group VIA metals form bonds with the nitrogen lone pair electrons, while the π electrons of the azo group are not involved, this is in marked contrast to the reactivity of iron carbonyl complexes.

The reaction of diiron nonacarbonyl with diazirines (166), which are strained cyclic azo-compounds, is a special case. MINDO/2 calculations¹¹⁵ have led to the conclusion that the distribution of electron density in these compounds differs significantly from that in other cyclic azo-compounds; the concept of a free electron pair on the nitrogen atoms is no longer valid.

Despite these differences, a series of unstable complexes (167→169) in which the diazirine skeleton is retained, have been prepared¹⁰⁷ (Scheme 53). These complexes decompose in

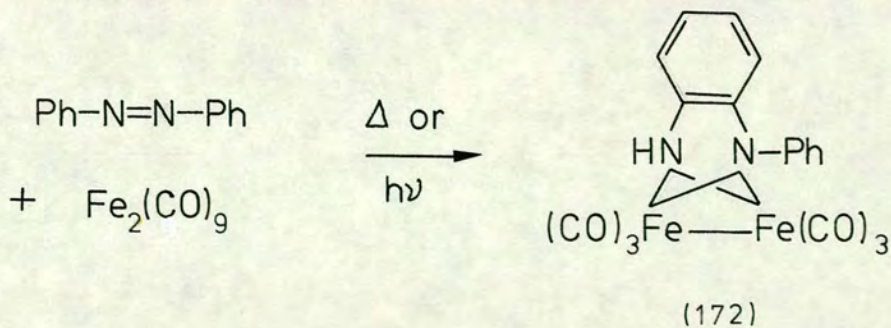
solution and form new, more stable, compounds (170) and (171).



Scheme 53

2.1.2 Azobenzene

The preparation of azobenzene iron carbonyl complexes was first investigated by Bagga *et al.*⁹⁴ The structure of the complex isolated was established by X-ray diffraction^{116,117} and it showed that dissociation of the azo bond had occurred and rearrangement to an orthosemidine complex (172) had taken place (Scheme 54).

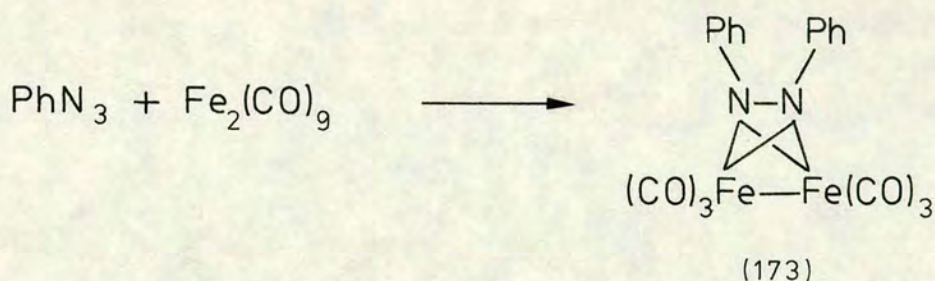


Scheme 54



This complex has been prepared both thermally and by photochemical routes; the yields however were very low 2-3%. It has been reported¹⁰⁵ that the reaction of azobenzene with diiron nonacarbonyl at room temperature results in the formation of an unstable complex in which the azobenzene ligand is probably incorporated without serious changes, since azobenzene is liberated in attempts to purify the complex chromatographically or by sublimation.

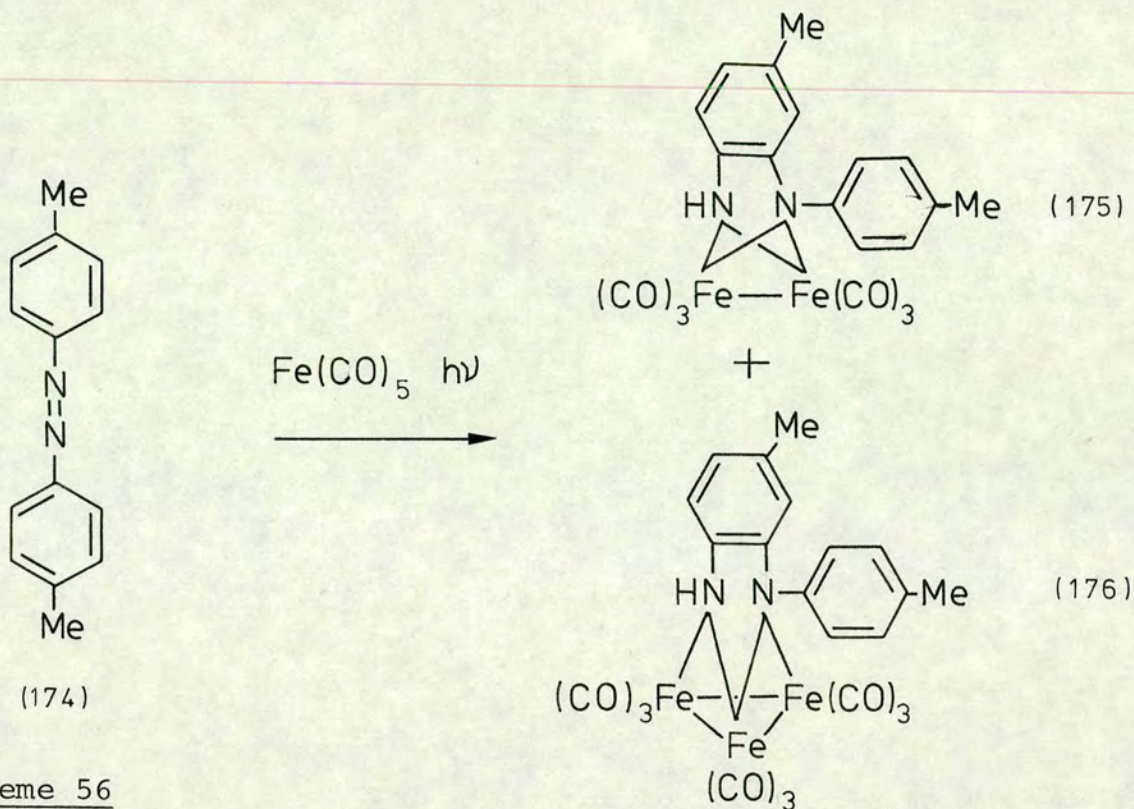
It is of interest that the complex which might be expected to be formed (173), is in fact the product from the reaction of phenyl azide and diiron nonacarbonyl and is found to be comparatively stable (Scheme 55).¹¹⁸



Scheme 55

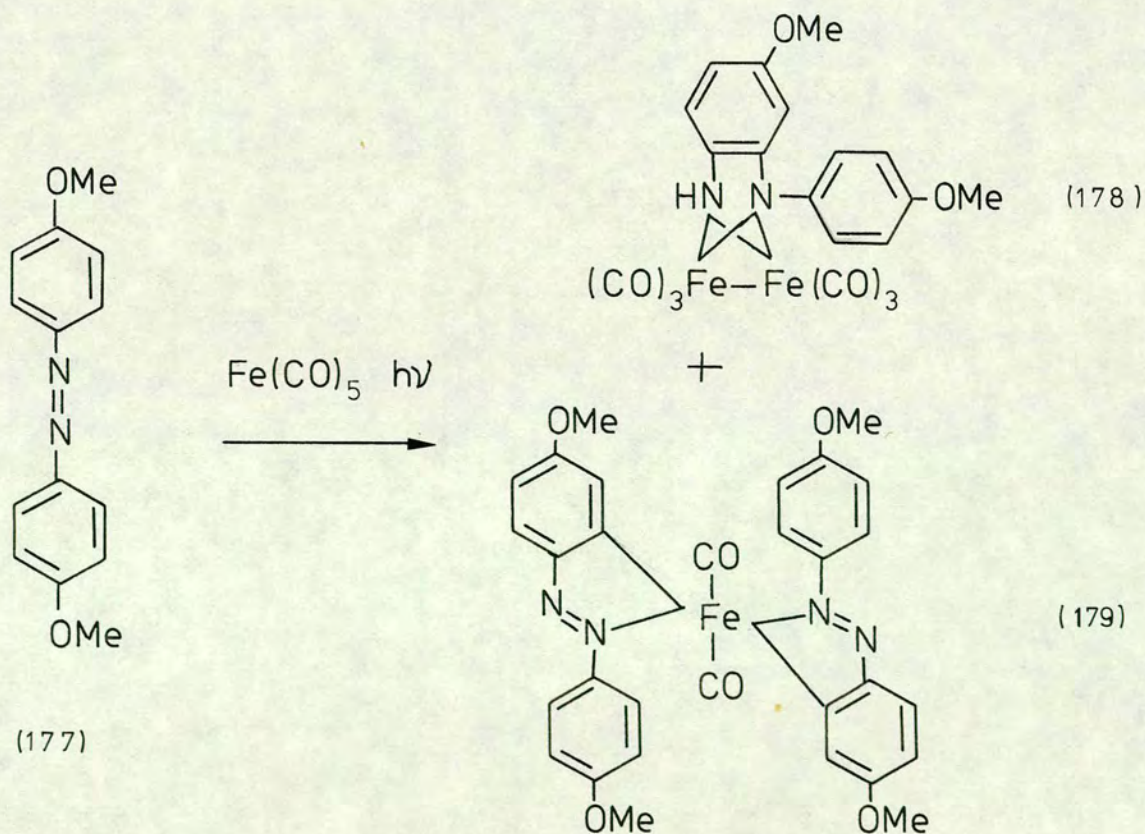
These observations suggest that there is some mechanistic feature which prevents the usual reaction pathway being followed when azobenzene interacts with iron carbonyls.

Ring-substituted azobenzenes behave slightly differently in reaction with iron carbonyls. Irradiation of 4,4'-dimethylazobenzene (174) with iron pentacarbonyl gives a trinuclear (176) as well as the expected dinuclear (175) complex¹¹⁸ (Scheme 56).



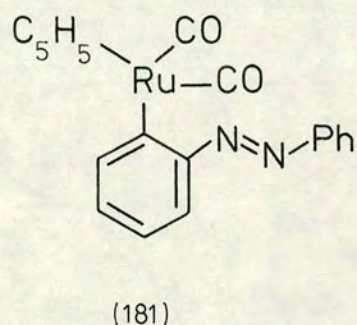
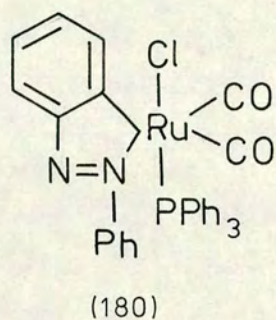
Scheme 56

Under the same conditions 4,4'-dimethoxyazobenzene (177) gives the dinuclear complex (178) plus a small amount of a completely new structure (179), which is a product of ring metallation (Scheme 57).¹¹⁸



Scheme 57

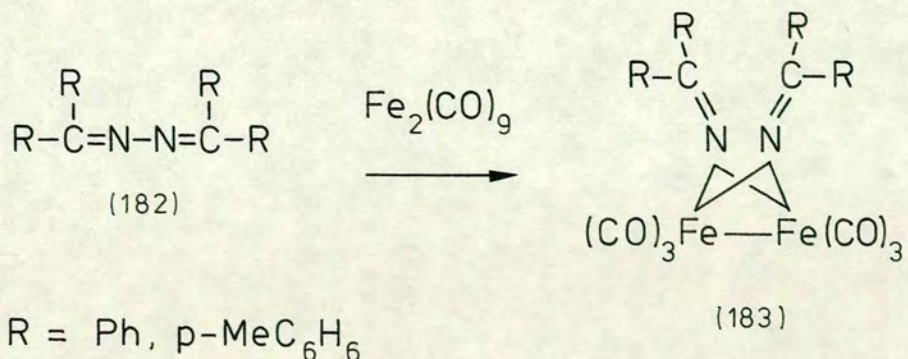
It should be noted that this last type of ring-metallated complex is encountered fairly frequently when other metal carbonyls are reacted with azobenzene¹¹⁹⁻¹²¹. Thus the following ruthenium complexes (180) and (181) have been prepared.¹²²



2.2 Complexes derived from Azines

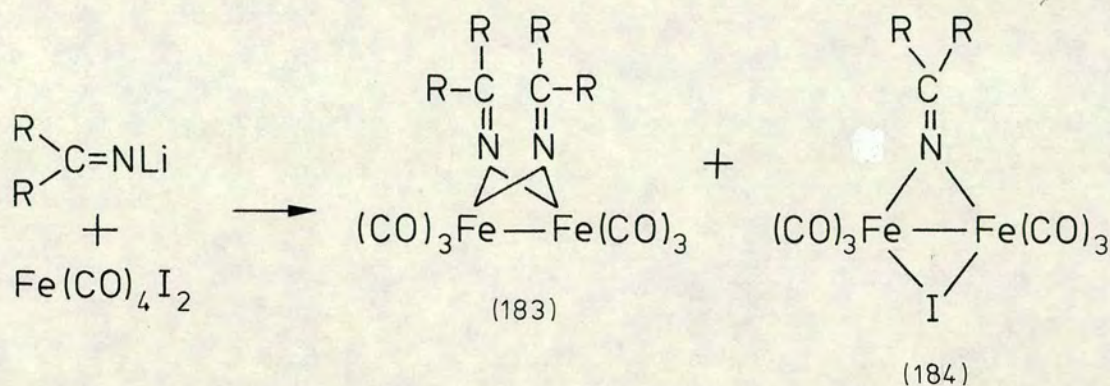
The reactivity of azines with iron carbonyls differs from that observed with azo-compounds; in this case complexes of type A; i.e. three-electron donor complexes, are predominately formed.

Thus benzophenone azine and its 4,4'-dimethyl derivative (182) have been reacted with iron carbonyls to give complexes (183) in which dissociation of the nitrogen nitrogen bond has occurred (Scheme 58)¹²³.



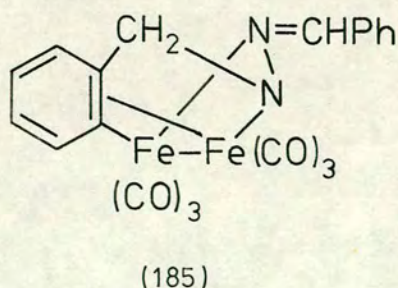
The structures of these complexes have been demonstrated by X-ray diffraction.

An alternative route to these complexes (183) has been devised, which also leads to the formation of a small amount of a further complex (184) (Scheme 59)¹²³.



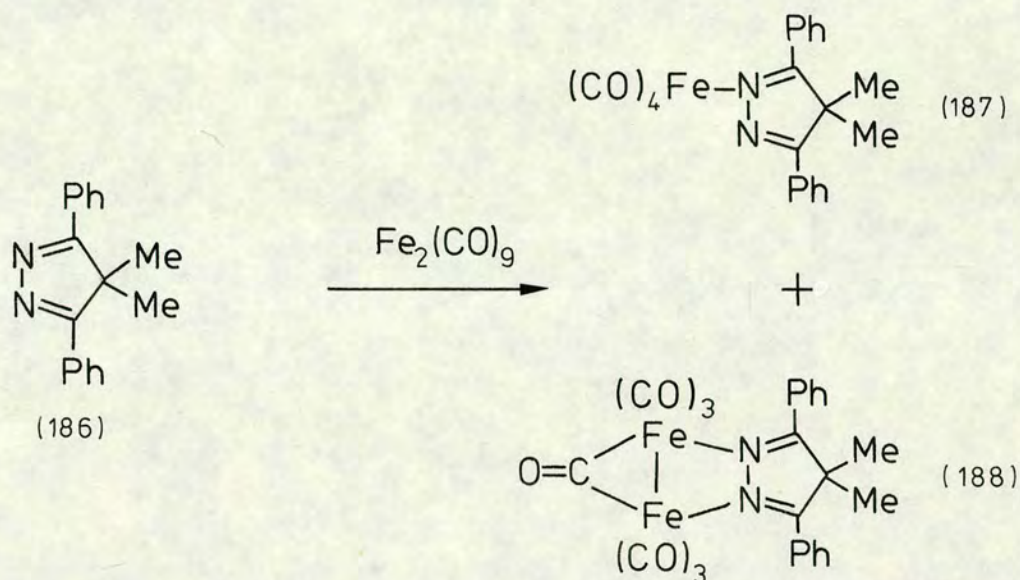
Scheme 59

The reactivity of benzylideneazine is markedly different; it reacts to give a complex in which the nitrogen bond is retained. The structure (185) was attributed on the basis of spectroscopic evidence⁹⁴.



The reaction of cyclic azines with iron carbonyls have also been investigated, thus the cyclic azine 5,5-dimethyl-1,4-diphenyldiazacyclopentadiene (186) reacts under mild

conditions with diiron nonacarbonyl to form two complexes: a mononuclear (187) and dinuclear¹²⁴ (188) (Scheme 60).



Scheme 60

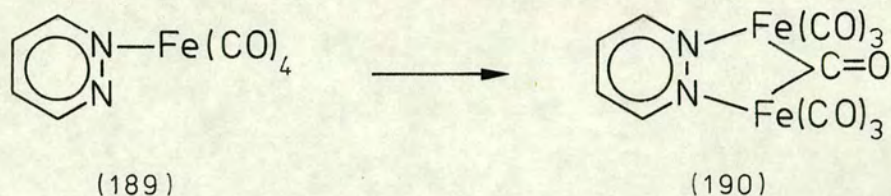
The dinuclear complex contains a bridging carbonyl absorption in its infra-red spectrum, and in this case the azine linkage behaves as a four-electron donor.

Cyclic seven membered azines are reviewed elsewhere (see section C.1.2).

2.3 Aromatic Vicinal Diaza Heterocyclic Systems

These heterocycles can be represented by resonance hybrids containing both azo and azine groups, thus it is not surprising that the reactivity of these heterocycles with iron carbonyls is the same as that encountered for azo-compounds and azines.

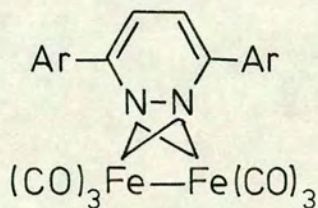
Pyridazine, the parent compound of this class of heterocycles, reacts with diiron nonacarbonyl to form initially a mononuclear complex (189) which reacts further to give a dinuclear complex (190) (Scheme 61).^{101,125}



Scheme 61

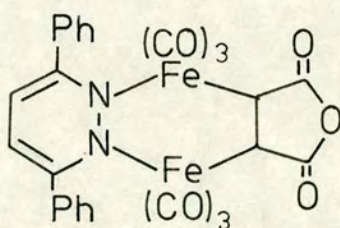
The bridging carbonyl is identified in the infra-red, and the presence of the seven carbonyl groups has been demonstrated convincingly by mass spectroscopy. Interestingly attempts to convert the bridging carbonyl complex into the more common diiron hexacarbonyl type of complex were unsuccessful.

3,6-Diarylpyridazine reacts with iron carbonyls to give a diiron hexacarbonyl complex (191), this structure was demonstrated by X-ray diffraction.^{126,127}



(191)

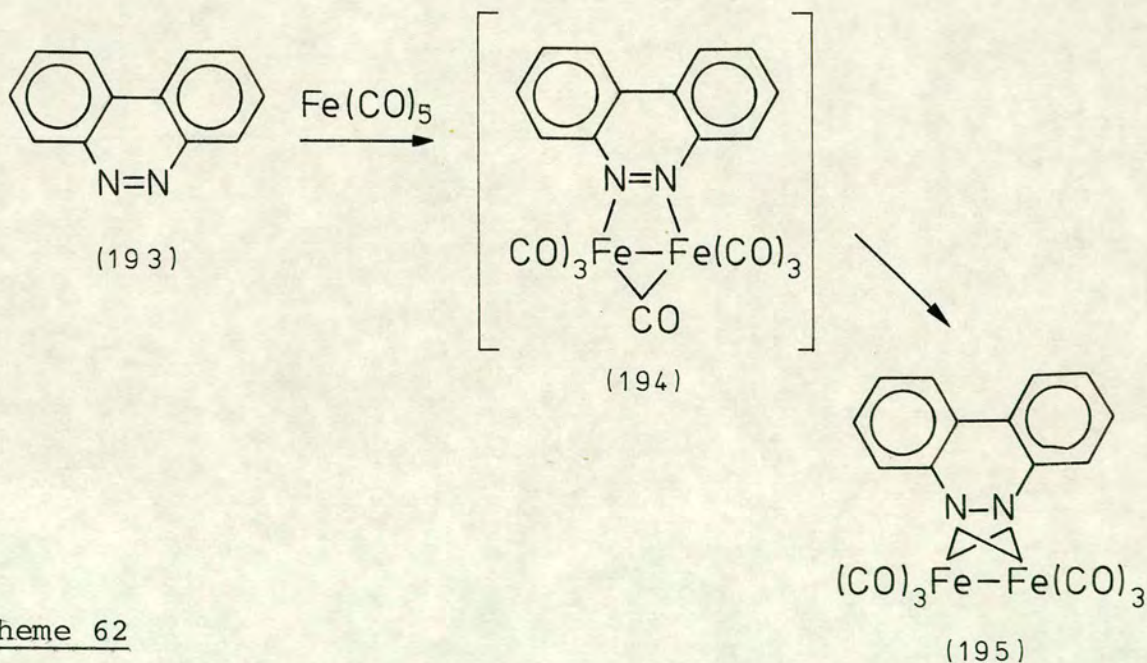
An interesting reaction of this complex has been reported¹⁰⁹. In this reaction maleic anhydride inserts into the iron nitrogen bond to give the novel adduct (192).



(192)

This reaction is similar to the alkyne insertion reactions reported for 2,3-diazabicyclo[2,2,1]hept-2-ene (see section C.2.1.1). Other workers¹⁰⁹ however, regard this reaction as a type of cycloaddition.

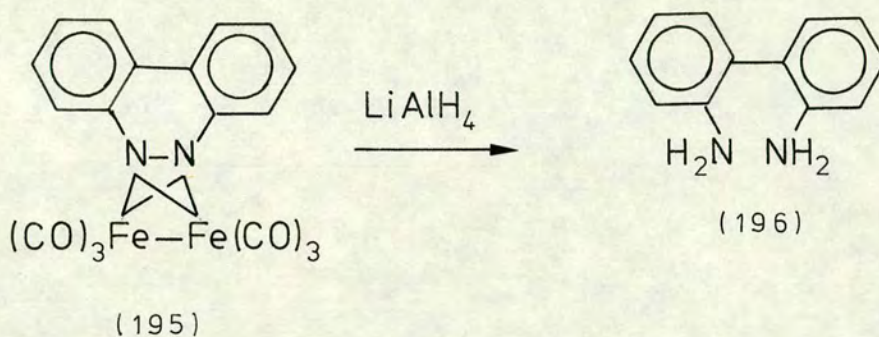
A diiron hexacarbonyl complex (195) was obtained in good yield from benzo[*c*]cinnoline (193)^{105,106}, the intermediate diiron heptacarbonyl complex (194) with the bridging carbonyl group was also identified (Scheme 62).

Scheme 62

This conversion of a heptacarbonyl complex to a hexacarbonyl complex suggests that the formation of the $N_2Fe_2(CO)_6$ group must be energetically favourable, since reaction occurs

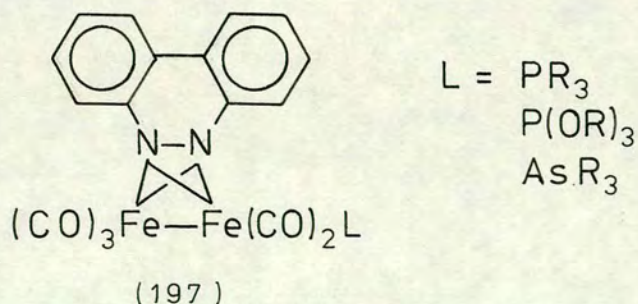
despite the loss of resonance energy due to the breakdown of the aromatic system of the heterocycle.

This hexacarbonyl complex (195) has been reduced with lithium aluminium hydride to give 2,2-diaminobiphenyl¹⁰⁵ (196) (Scheme 63).

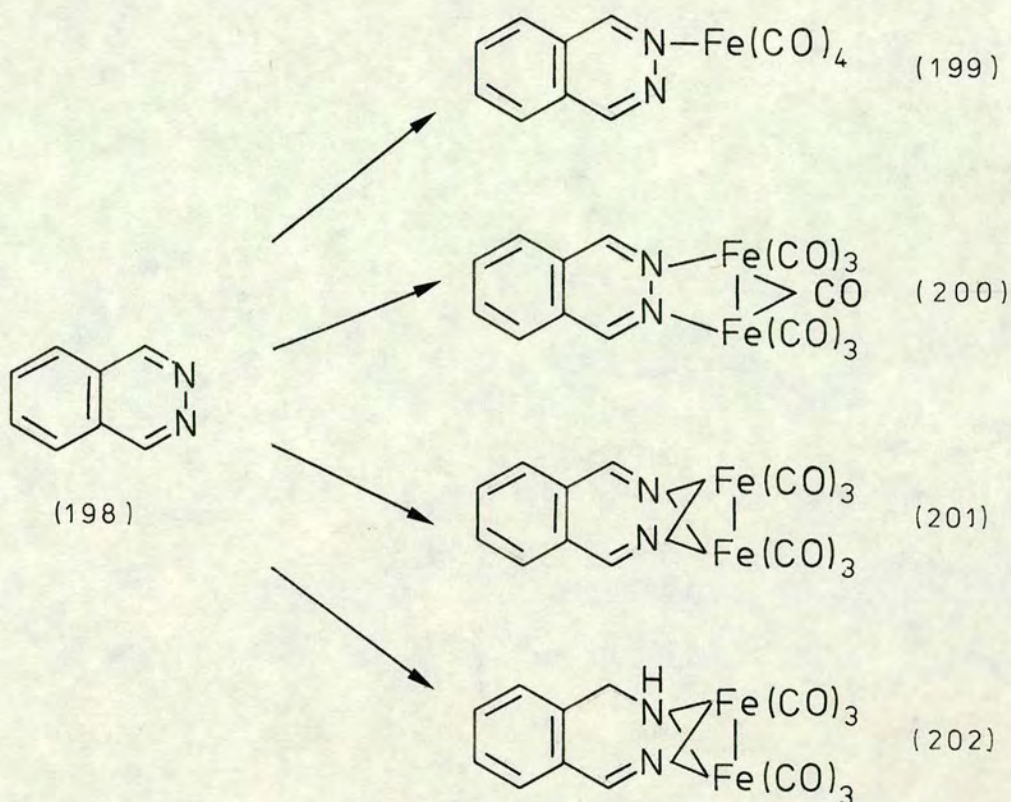


Scheme 63

Carbonyl ligand substitution reactions involving this complex have also been carried out. Many examples of phosphines, phosphites, arsines and isonitriles substituting one and sometimes two carbonyl groups have been reported^{109,128} (197).



Phthalazine (198) has been reacted with iron carbonyl to give a range of mononuclear and dinuclear complexes^{101,129} (199→202) (Scheme 64).

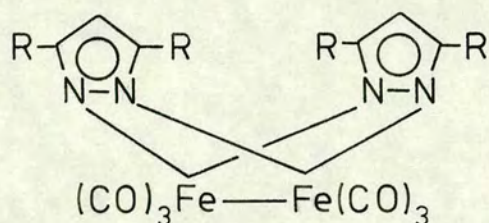


Scheme 64

In contrast to pyridazine complexes, phthalazine complexes retain the benzoid rather than the alternative *o*-quinoid structure, consequently the phthalazine complex (201) has no bond between the nitrogen atoms.

The unusual dihydrophthalazine complex (202) was obtained from reaction of phthalazine with triiron dodecacarbonyl in benzene in the presence of methanol.

The reactivity of pyrazoles with iron carbonyls has provided further unusual complexes, thus when pyrazole or 3,5-dimethylpyrazole was reacted with diiron nonacarbonyl in ether the dinuclear hexacarbonyl complex (203) was obtained.^{130,131}

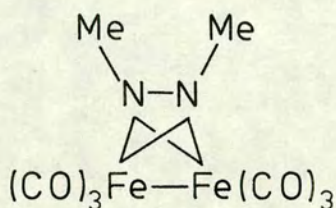


(203)

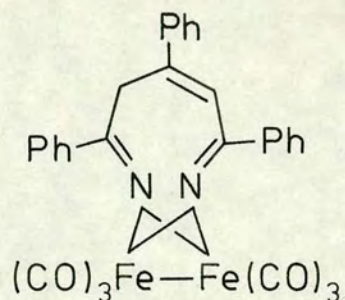
2.4 Structural Information

2.4.1 X-Ray Diffraction Studies

Considerable data have been assimilated from various X-ray studies concerning the N_2Fe_2 fragment, compounds (204) and (205) serve as two typical examples.



(204)



(205)

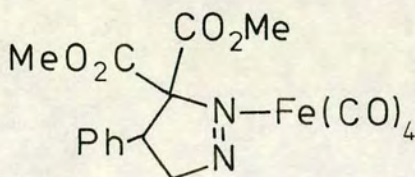
Complex	Fe-Fe	Fe-N	N-N	Fe-N-Fe	N-Fe-N	Ref
(204)	2.496	1.878	1.366	83.4	42.7	97
(205)	2.393	1.920 1.965	2.25	-	-	82

Structural parameters of dinuclear complexes, bond lengths in angstroms angles in degrees.

In complex (204) where a nitrogen-nitrogen bond is retained the distance measured is approximately 1.4\AA , which corresponds to a single bond. In the other complex (205) the distance between nitrogen atoms is 2.2\AA , which leads to the conclusion that there is no bonding interaction.

The iron-iron distances in the complexes of approximately 2.45\AA indicate the presence of bonding interaction.

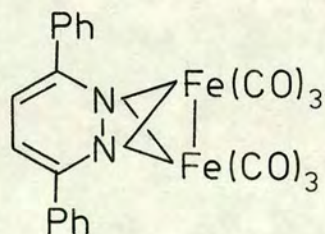
In complexes of the type $\text{LFe}(\text{CO})_4$, eg. complex (206), X-ray diffraction studies show that the Fe-N bond is 1.98\AA and the nitrogen-nitrogen bond is 1.24\AA . In this complex the azo linkage has been retained.



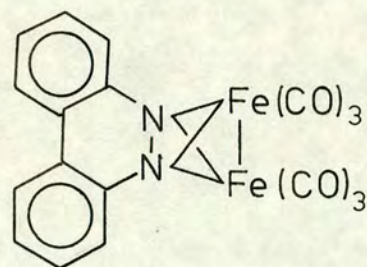
(206)

2.4.2 Infra-red Spectroscopy Analysis

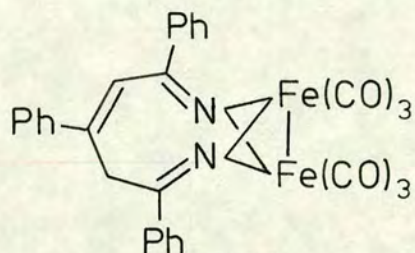
From X-ray diffraction studies it can be seen that the $\text{N}_2\text{Fe}_2(\text{CO})_6$ group present in these complexes has C_{2v} symmetry, group theoretical analysis predicts that the carbonyl groups should possess five infrared-active vibrations. The carbonyl bonds observed for complexes (207→210) are presented in Table 1



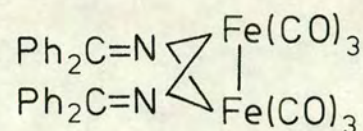
(207)



(208)



(209)



(210)

Table 1: Stretching vibration frequency of the carbonyl groups

Complex	$\nu(\text{C=O}) \text{ cm}^{-1}$	Refs
207	2065, 2025, 1985, 1970 (cyclohexane)	127
208	2073, 2033, 1982, 1972 (CS_2)	105
209	2068, 2031, 1998, 1986, 1972, 1967 (hexane)	132
210	2047, 2041, 1994, 1979 (cyclohexane)	123

It can be seen that the spectra for these complexes are very similar. Indeed the presence of such absorptions is now used as evidence for the existence of an $\text{N}_2\text{Fe}_2(\text{CO})_6$ residue.

Infrared spectra yield further important information when complexes of the type $\text{LFe}_2(\text{CO})_7$ are studied. Apart from the four stretching vibration bands of the terminal carbonyl groups, they also include an absorption at $1820\text{--}1730 \text{ cm}^{-1}$, which is characteristic of a bridging carbonyl group.

D. Thermal [1,5] Sigmatropic Migrations

Since the discovery of this class of reaction in 1961,¹³³ isomeric transformations of conjugated dienes and polyenes has become a rapidly expanding branch of organic chemistry.

1. Theoretical Considerations

Sigmatropic migrations are a type of pericyclic intramolecular rearrangement in which an atom or group migrates from an initial point of attachment in a molecule, across a conjugated system, to a new point of attachment.

The pattern of reactivity observed for sigmatropic migrations has been successfully explained by the Woodward-Hoffman rules.¹³⁴

Sigmatropic change of order $[i,j]$, is defined as the migration of a σ bond, flanked by one or more π -electron systems, to a new position whose termini are $(i-1)$ and $(j-1)$ atoms removed from the original bonded position in an uncatalysed intramolecular process.

Thermal sigmatropic rearrangements where $i=1$, collectively named $[1,j]$ rearrangements were reviewed in 1974,¹³⁵ a more recent review concerned solely with $[1,5]$ shifts appeared in 1981¹³⁶.

There are many kinds of sigmatropic rearrangement, those involving a total of $(4n+2)$ electrons are allowed in the all-suprafacial mode. These are the common reactions and the following are some examples¹³⁷⁻¹⁴⁰ (figure 7).

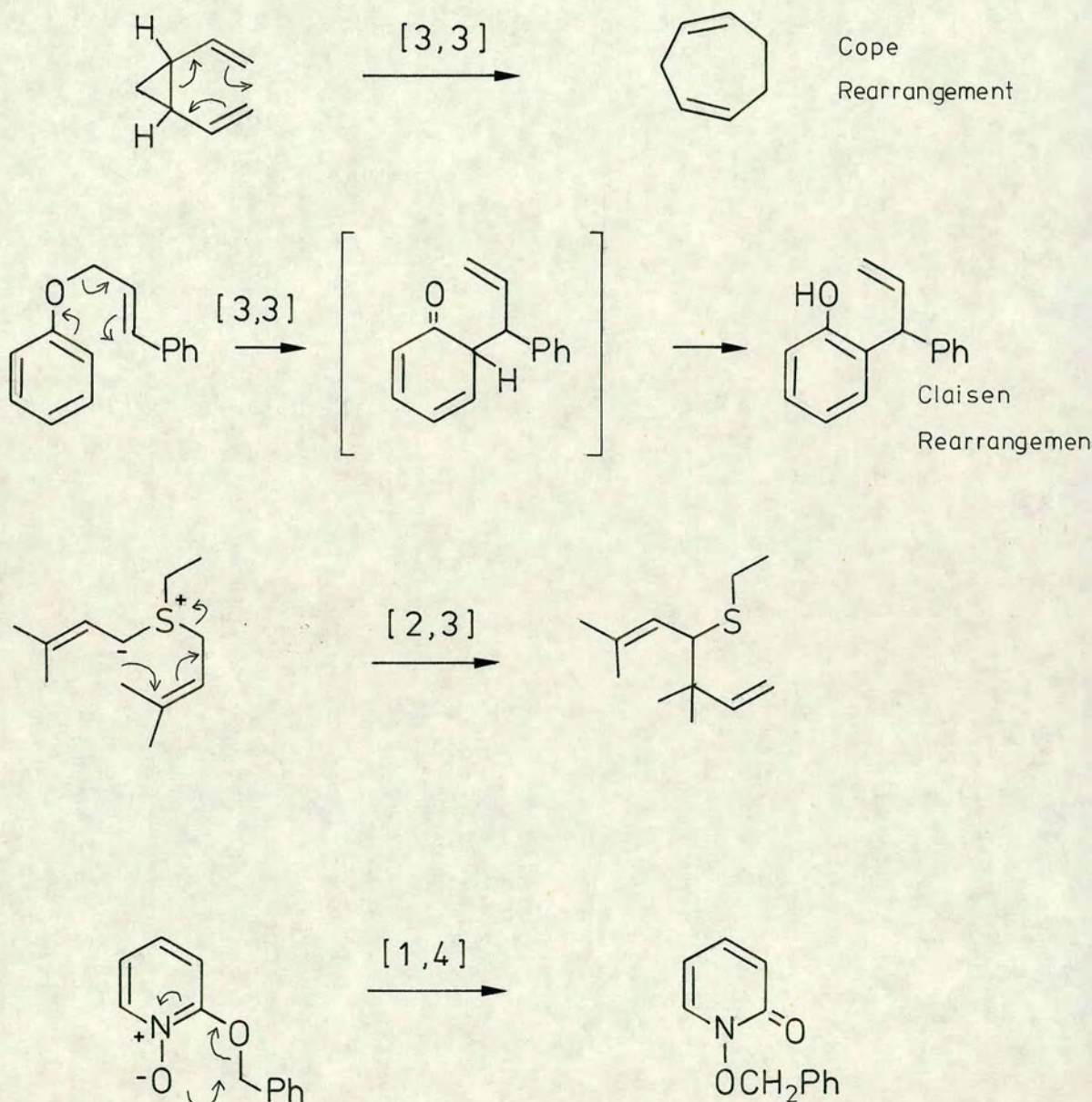
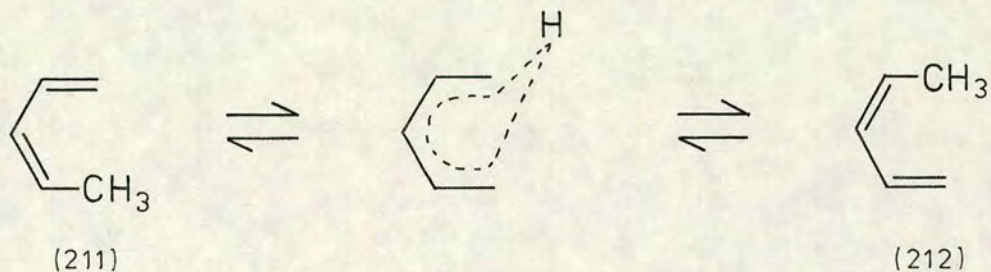


Figure 7

2. Characteristics of the [1,5] migration reaction and its mechanism

As the review of the experimental data in the following sections will show, the 1,5-shift of hydrogen or a substituent is an extremely common phenomenon in organic chemistry. This reaction can be performed by any *Z*-1,3-diene or polyene system

including cyclic, acyclic and heterocyclic systems. The simplest case; the 1,5-sigmatropic shift of hydrogen in *Z*-piperylene (211)→(212), is depicted in scheme 65.



Scheme 65

The migrating system of double bonds must have the *Z*-configuration, since acyclic *E*-dienes and cyclic dienes with a fixed transoid configuration do not undergo reaction.

It has been reliably established that these thermal rearrangements proceed *via* a 1,5-shift and not sequential 1,3-shifts, since the latter pathway would have led to a sequence of interconversions of isomers which has been reliably ruled out by experimental data. In polyene rings it has been further demonstrated that these thermal isomerisations involve 1,5- and not 1,7-shifts.

On the basis of the following five features it is possible to unambiguously identify an isomerisation of a diene or polyene as a [1,5] sigmatropic migration.

- i) The absence of hydrogen exchange in the isomerisation - an intramolecular mechanism.
- ii) Comparable reaction rates in both liquid and gas phase.
- iii) A high negative entropy of activation - a highly ordered transition state.

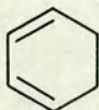
iv) A high primary kinetic isotope effect, $K_H/K_D > 6$ for hydrogen migration.

v) Stereospecificity of the reaction.

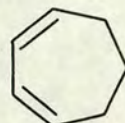
Interesting information about the 1,5-shift reaction mechanism can be obtained by examining the cyclopentadiene (213), cyclohexa-1,3-diene (214) and cyclohepta-1,3-diene (215) systems.



(213)



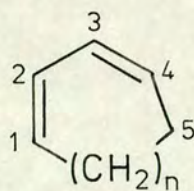
(214)



(215)

The rate of 1,5-hydrogen migration in these systems decreases in the sequence $C_5 > C_7 > C_6$, this should be compared with the acidity sequence of these hydrocarbons; $C_5 > C_6 \approx C_7$, thus it can be concluded that there is no charge separation in the transition state. This conclusion has been confirmed by the weak dependence of the rate of reaction with the nature of the solvent and also by the comparable rates of reaction observed both in the liquid and gas phases. These observations are entirely consistent with a concerted process.

The rate of reaction for 1,5-hydrogen migration is found to vary within fairly wide limits, the reaction is most facile in cyclopentadiene ($\Delta G^\ddagger \sim 84 \text{ kJ mol}^{-1}$) and most difficult in cyclohexadienes ($\Delta G^\ddagger \sim 163 \text{ kJ mol}^{-1}$). These differences in rate are related to the distance between the migrating centres, C(1) and C(5) of the diene fragment (216).



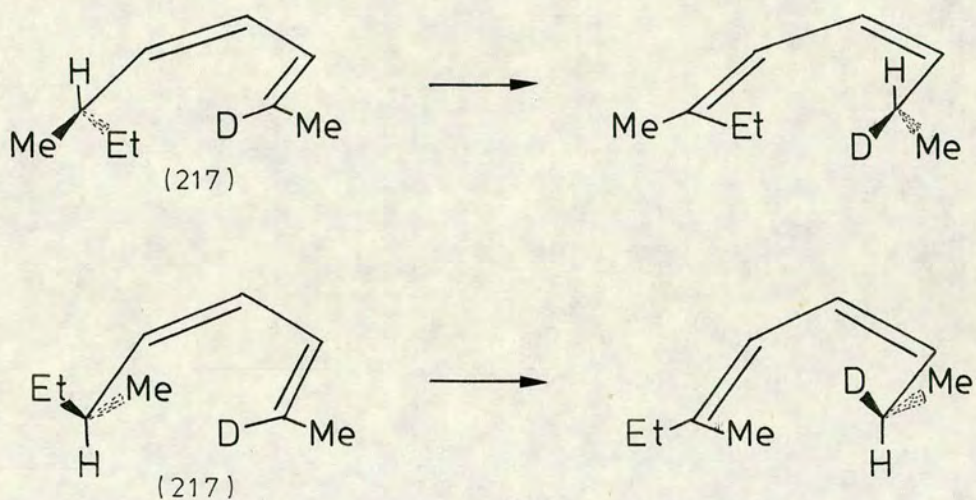
The ease of migration is determined by the distance of approach of the C(5)-H bond and the π orbital of C(1). The conformation of cyclopentadiene¹⁴¹ is planar and almost planar in the case of cyclohexa-1,3-diene¹⁴², cyclohepta-1,3-diene¹⁴³ and higher analogues possess non-planar conformation. An estimate of the distances migration centres can be arranged in the sequence $C_5 < C_7 - C_9 < C_6$, which is in good agreement with the experimentally observed rates of 1,5-hydrogen migration in these cyclic dienes.

The end product of 1,5-migration of hydrogen is the establishment of thermodynamic equilibrium between isomers. Two limiting situations can be envisaged, in one the difference between the free energies of the isomers is close to zero and their concentrations in the mixture are equal. An example of this situation is provided by deuterio-derivatives of dienes and polyenes. In the second limiting situation one of the isomers is much more favoured by energy factors ($\Delta\Delta G > 6 \text{ kJ mol}^{-1}$), and its concentration in the equilibrium mixture is close to 100%.

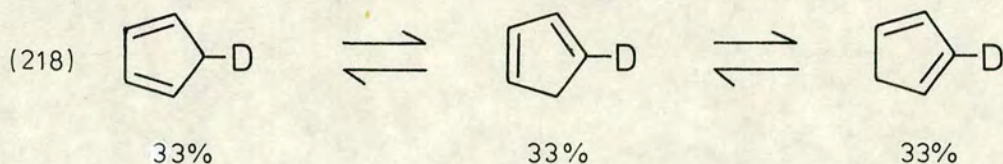
3. Selected Literature Examples

3.1 Hydrocarbon Systems

The suprafacial nature of [1,5] hydrogen migration in acyclic systems has been conclusively demonstrated by Roth et al.¹⁴⁴ The optically active diene (217) gave the two isomers expected from a suprafacial [1,5] shift, but gave neither of the isomers expected of an antarafacial migration.

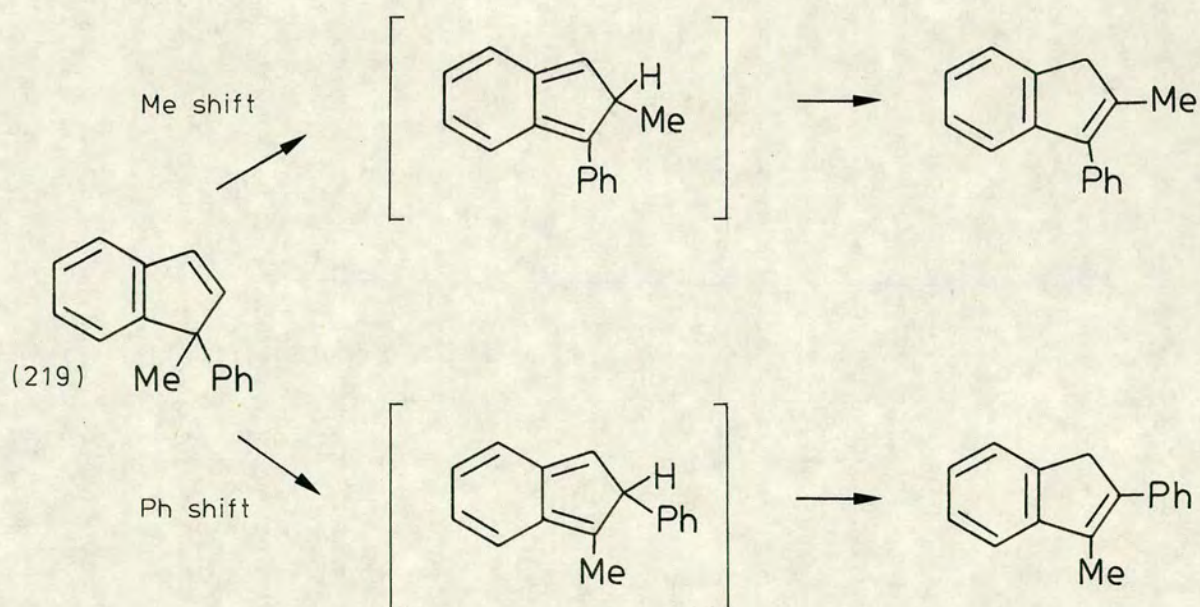


The 5-deuterocyclopentadiene (218) was synthesised by treating cyclopentadienylmagnesium bromide with deuterium oxide at -5°C ¹⁴⁵. Subsequent heating at 60°C for one hour resulted in the formation of equal amounts of the 1-, 2- and 5-deuterocyclopentadienes. It was noted that this interconversion was not accompanied by intermolecular hydrogen exchange (scheme 66).



Scheme 66

An example of 1,5-sigmatropic migration in an indene system is provided by the thermal isomerisation of 1-methyl-1-phenylindene ¹⁴⁵ (219 (scheme 67),

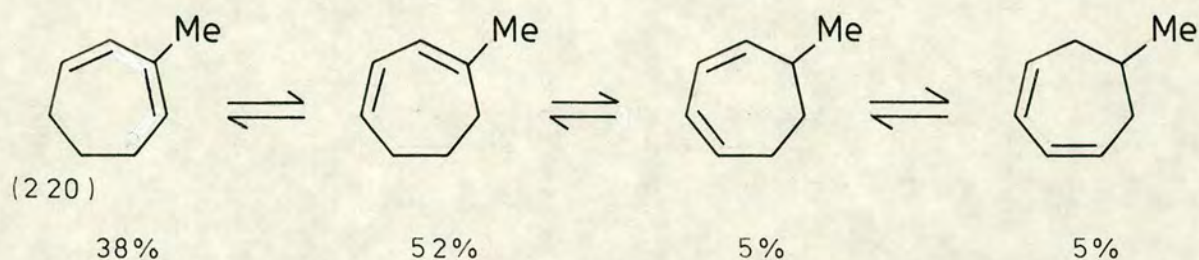


Scheme 67

The ratio of isomers in the product mixture made it possible to rank the substituents according to their ability to migrate; $H \gg Ph > Me$.

The cyclohepta-system has received comparatively little attention but Mirčnov has carried out some interesting studies. 2-Methylcyclohepta-1,3-diene (220) has been found to undergo

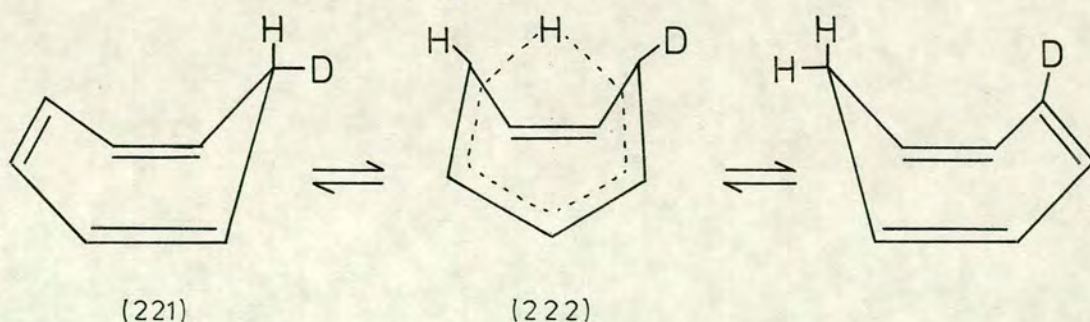
reversible thermal isomerisation at 120°C (scheme 68)¹⁴⁶.



Scheme 68

Isomerisation of the analogous 2-deutero derivative led to a uniform distribution of the label in all positions¹⁴⁶, this reaction proceeds in the absence of hydrogen exchange between molecules, indicating an intramolecular mechanism.

The 1,5-migration of hydrogen in cycloheptatrienes has been convincingly demonstrated; heating 7-deuterocyclohepta-1,3,5-triene (221) at 140°C resulted in scrambling of the label between all four possible positions¹⁴⁷, and this transformation took place *via* an intramolecular mechanism. A non-planar symmetrical transition state (222) has been suggested (scheme 69).

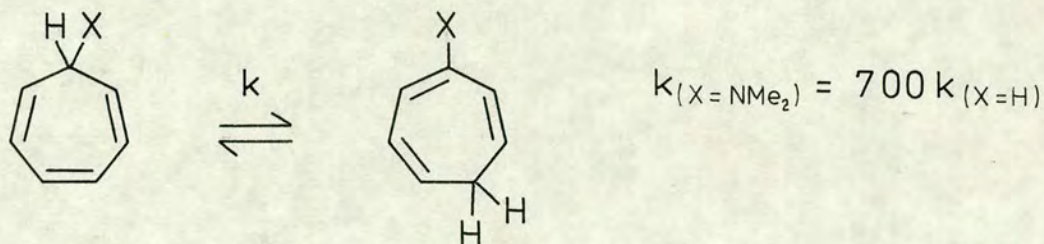


Scheme 69

A number of studies concerned with the thermal transformation of monosubstituted cycloheptatrienes have been reported.¹⁴⁸⁻

150 A general tendency identified was the thermodynamic

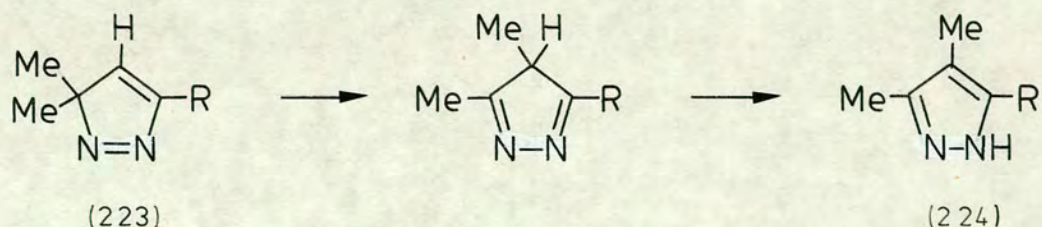
stability of the 7-isomer, and that the presence of methoxy and *N,N*-dimethyl substituents led to a sharp increase in the rate of 1,5-migration¹⁵⁰ (scheme 70).



Scheme 70

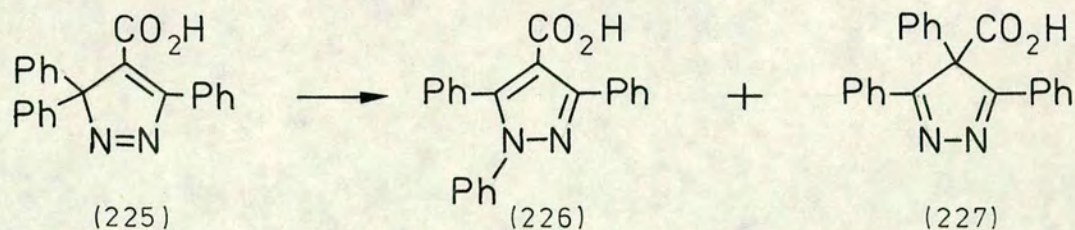
3.2 Diaza Heterocyclic Systems

The van Alphen-Huttel rearrangement of 3*H*-pyrazoles occurs *via* 1,5-sigmatropic shifts^{151,152}. Depending on the nature of the migrating group, rearrangement to nitrogen or carbon is favoured. Thus the 3,3-dimethyl-3*H*-pyrazole (223) rearranged *via* 1,5-methyl migration to C-4, followed by facile aromatization to give the 1*H*-pyrazole (224) (scheme 71).



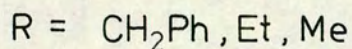
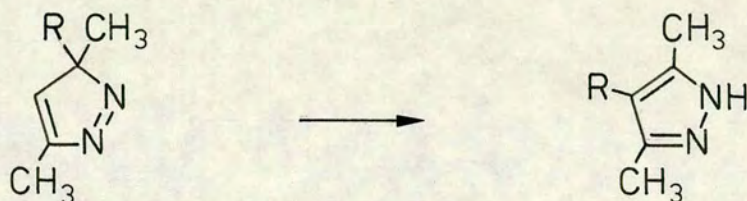
Scheme 71

The 3*H*-pyrazole (225) rearranged by 1,5-phenyl migration to both carbon and nitrogen giving compounds (226) and (227) respectively (scheme 72).



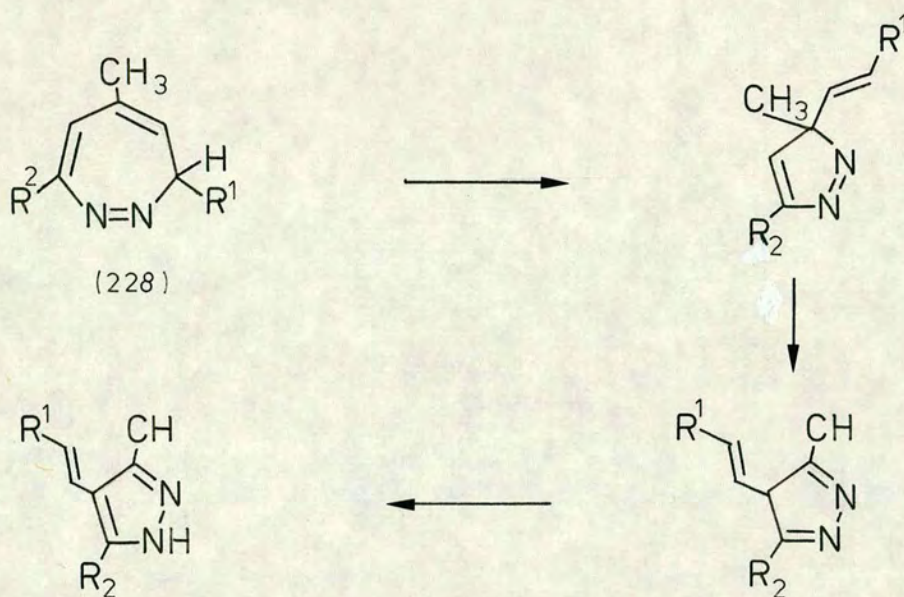
Scheme 72

A further study by Schiess and Stalder¹⁵³ showed that the migratory aptitude of various alkyl groups within the 3H-pyrazole system was benzyl >> ethyl > methyl (scheme 73).



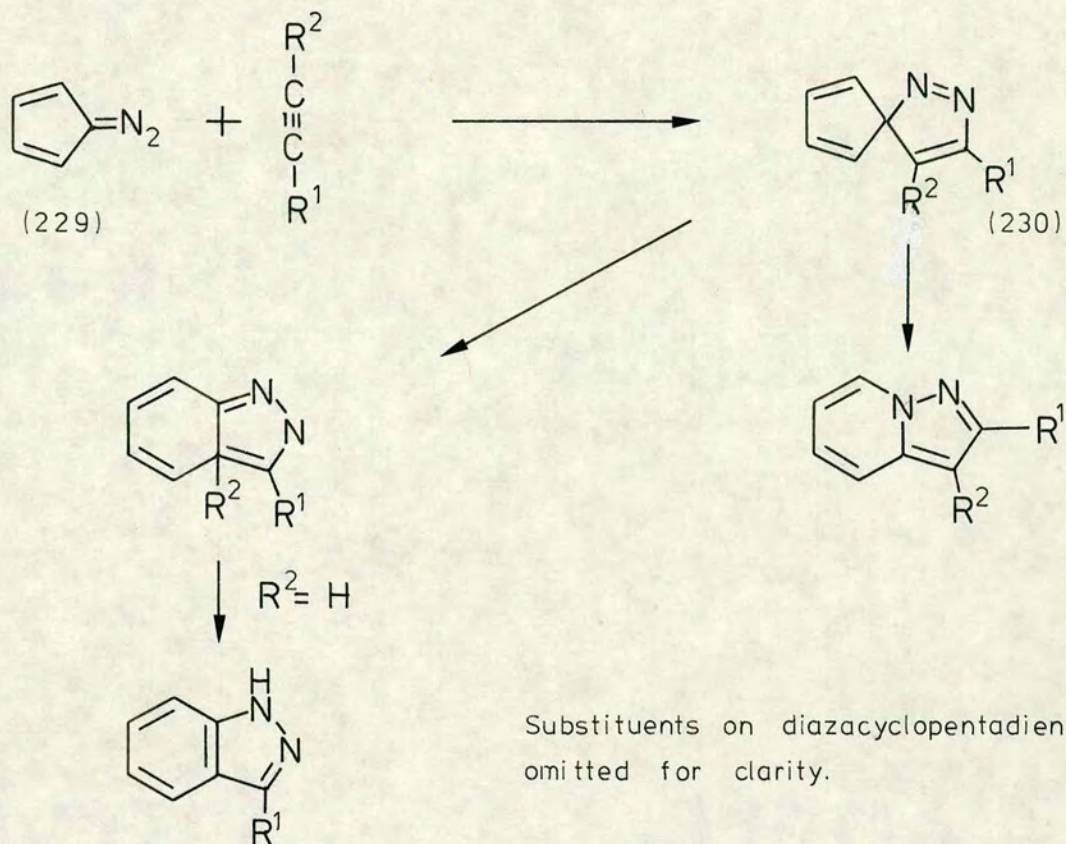
Scheme 73

Sharp *et al.*³⁶ have reported the 1,5-migration of a vinyl group in preference to a methyl group following the thermal rearrangement of a 3H-1,2-diazepine (228) (Scheme 74).



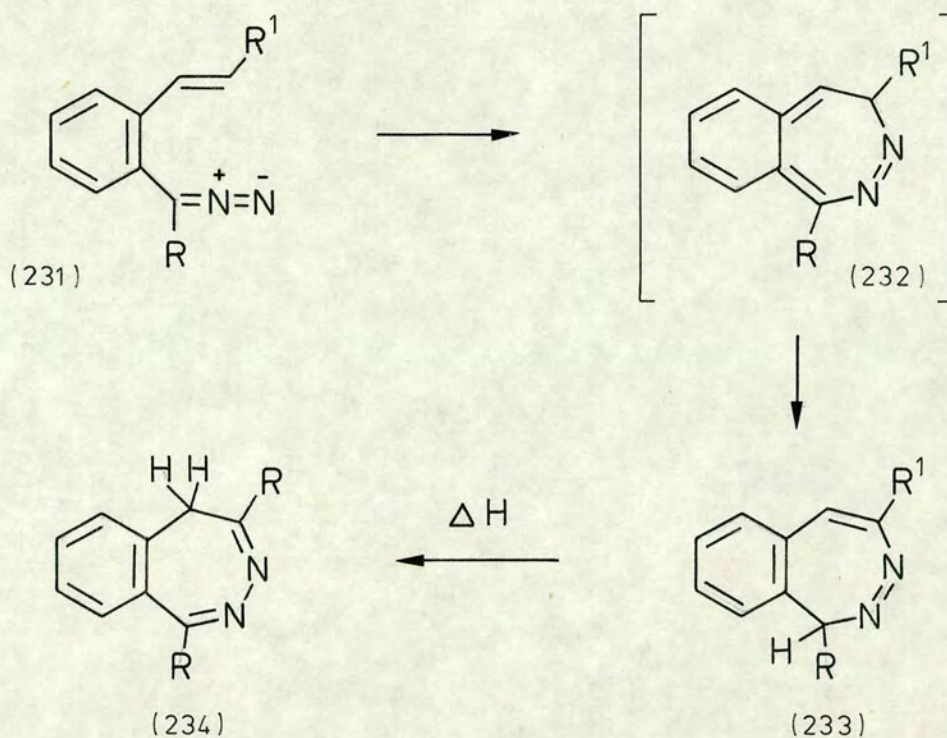
Scheme 74

A particular facile [1,5] alkyl shift has been reported by Sergio and co-workers^{154,155}. This occurs spontaneously in the intermediary pyrazoles (230) formed by the cycloaddition of disubstituted acetylenes to diazocyclopentadienes (229) (scheme 75). This should be contrasted with the hydrocarbon analogues¹⁵⁶ which rearrange at 280-380°.



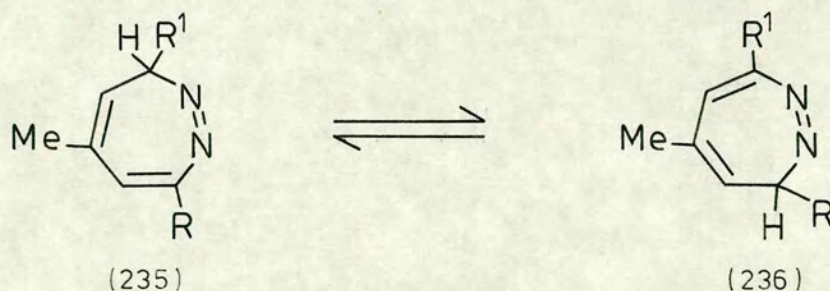
Scheme 75

A 1,5-sigmatropic hydrogen migration has been postulated by Sharp *et al.* in the mechanism of formation for 1*H*-2,3-benzodiazepines⁶⁴ (scheme 76). In these reactions $\alpha\beta,\gamma\delta$ -unsaturated diazoalkenes of the type (231) undergo 1,7-ring closure to give the 4*H*-2,3-benzodiazepine (232) which re-aromatises by a [1,5] sigmatropic hydrogen migration to give the product (233). This 1*H*-isomer (233) can undergo a further [1,5] sigmatropic hydrogen shift at elevated temperatures to give the 5*H*-isomer (234).



Scheme 76

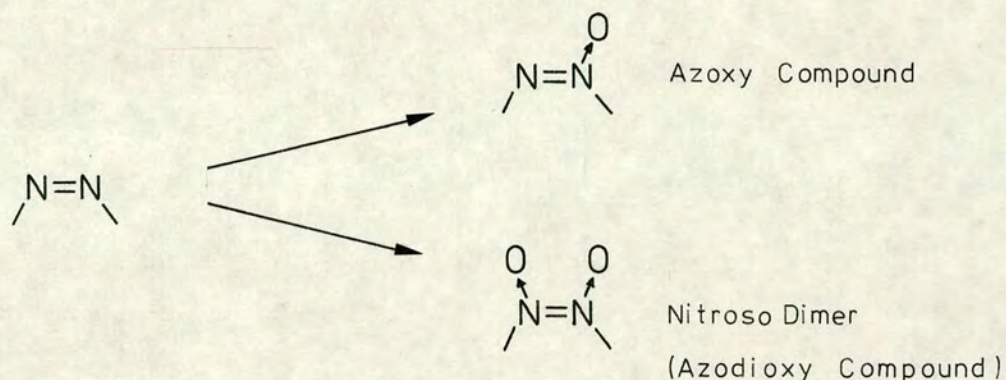
The 3*H*-1,2-diazepine system³⁴ possesses a particularly facile 1,5-hydrogen shift which interconverts the two diazepine isomers (235) and (236).



These shifts are remarkably fast compared with analogous cycloheptatrienes³⁴. This chemistry is the subject of further research contained in this thesis.

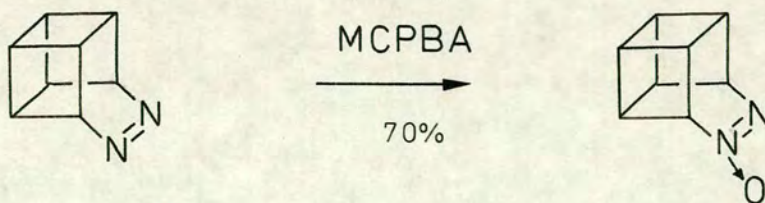
E. Azoxy Compounds

The lone-pair electrons of an azo group can form dative bonds with either one or two oxygen atoms to give azoxy compounds or nitroso dimers respectively (Scheme 77).

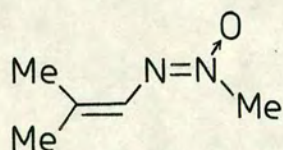
Scheme 77

Reviews of aromatic and aliphatic azoxy compounds are available^{157,158}, some relevant examples of aliphatic azoxy compounds and 1,2-diazepine N-oxides will be considered here.

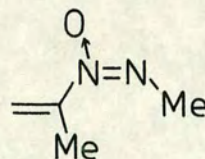
Oxidations of azo compounds have been carried out in good yields with peracids or hydrogen peroxide, an example is the oxidation of diazabasketene¹⁵⁹ (Scheme 78).

Scheme 78

Oxidation of α,β -unsaturated azo compounds with peracetic acid gave the corresponding azoxy compounds (237) and (238)¹⁶⁰.



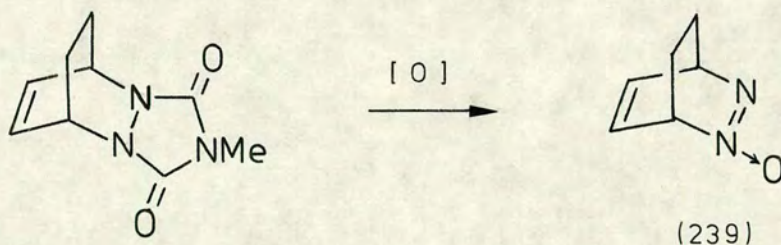
(237)



(238)

The location of the oxygen atom was found to be dependent on adjacent alkyl substitution. Interestingly the competing reaction to give epoxides was not observed.

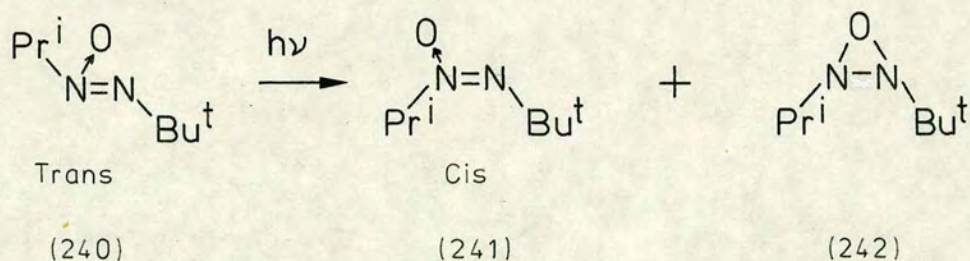
In one case an azo compound was very unstable even at -78°C , the stable azoxy compound (239) could however be prepared by an oxidative hydrolysis method¹⁶¹ (Scheme 79).



(239)

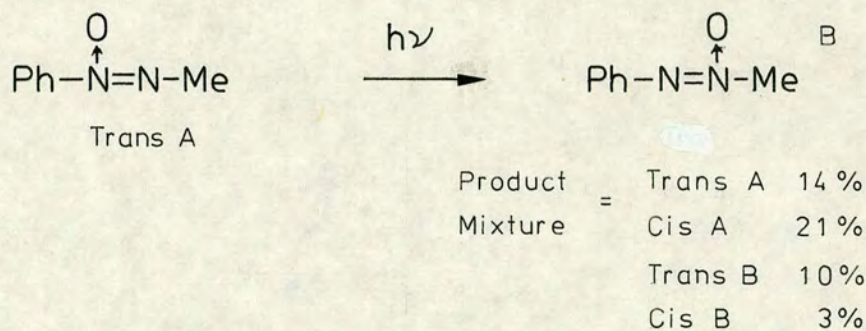
Scheme 79

The use of photolysis in azoxy compound synthesis enables isolation of the elusive *cis* isomer. In most cases irradiation of a *trans* azoxy compound (240) results in a mixture of the *cis* compound (241) together with the cyclic oxadiaziridene (242) (Scheme 80)¹⁶².



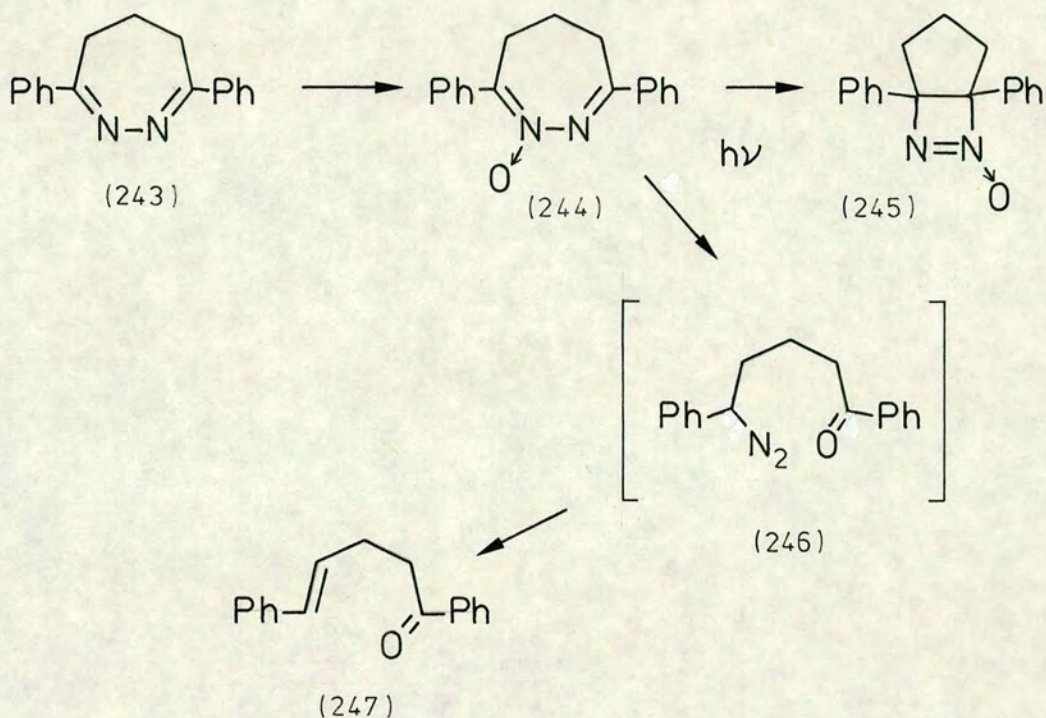
Scheme 80

When there are two different substituents attached to the azo group, more products appear due to oxygen migration¹⁶³ (Scheme 81).



Scheme 81

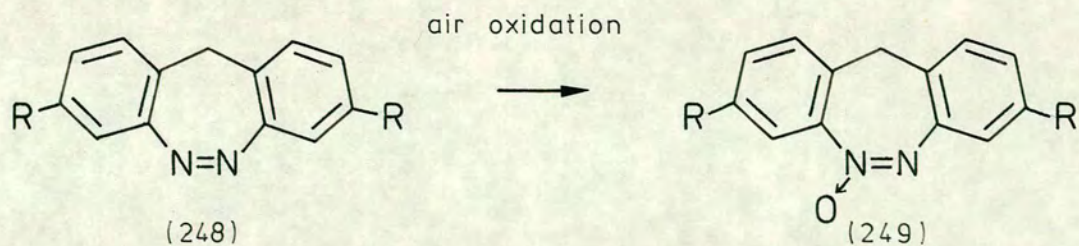
Only two examples of 1,2-diazepine N-oxides are reported. In one treatment of the diazepine (243) with trifluoroacetic acid in the presence of sodium carbonate gave the diazepine N-oxide (244)^{164,165}.



Scheme 82

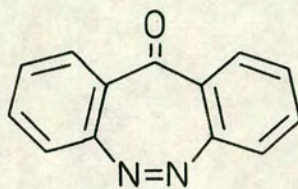
Photolysis of this N-oxide (244) resulted in the formation of the bicyclic compound (245), and the diazoketene (246) which decomposed to give 1,5-diphenylpent-4-en-1-one (247) (Scheme 82).

The other example is a 1905 preparation of the dibenzo 1,2-diazepine N-oxide (249) by air oxidation of the corresponding diazepine (248) as depicted in Scheme 83^{166,167}.



Scheme 83

This early reaction has since been repeated using peracetic acid as the oxidant¹⁶⁸. Chromium oxidation of (248) was found to follow an alternative pathway to give the novel diazepinone (250)¹⁶⁸.



(250)

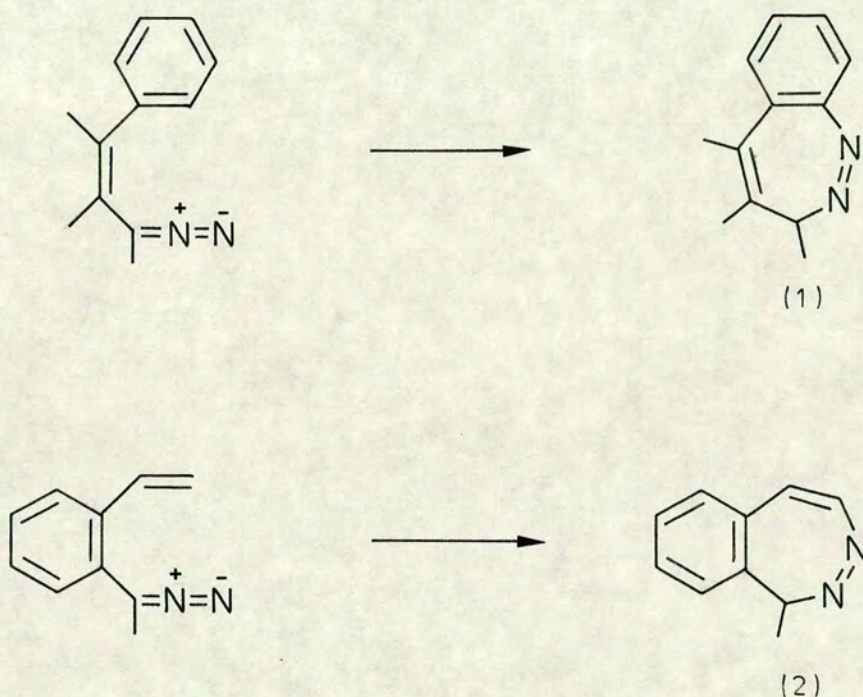
DISCUSSION

Preamble and Programme of Research	84
A. <u>3H-1,2-Diazepines and their rearrangements by rapid [1,5] hydrogen migration</u>	
1. Synthesis	88
2. Structural Assignment	89
3. Mechanism of Formation	93
4. Isomer Interconversion	99
B. <u>Diiron Hexacarbonyl 1,2-Diazepine Complexes</u>	
1. Introduction	116
2. Synthesis and Mechanism of formation	117
3. Characterisation and structural assignment	121
4. The effect of complex formation upon the 3H-1,2-diazepine rearrangement by [1,5] sigmatropic hydrogen migration.	133
C. <u>Reactions of $\alpha\beta,\gamma\delta$-unsaturated carbonyl compounds with hydrazines</u>	
1. Introduction	141
2. Synthesis of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds	148
2.1 Precursors for the 3H-1,2-diazepine and organometallic studies	148
2.2 Precursors for the study of cyclisation reactions to give 2-substituted 3,4- dihydrodiazepines	151

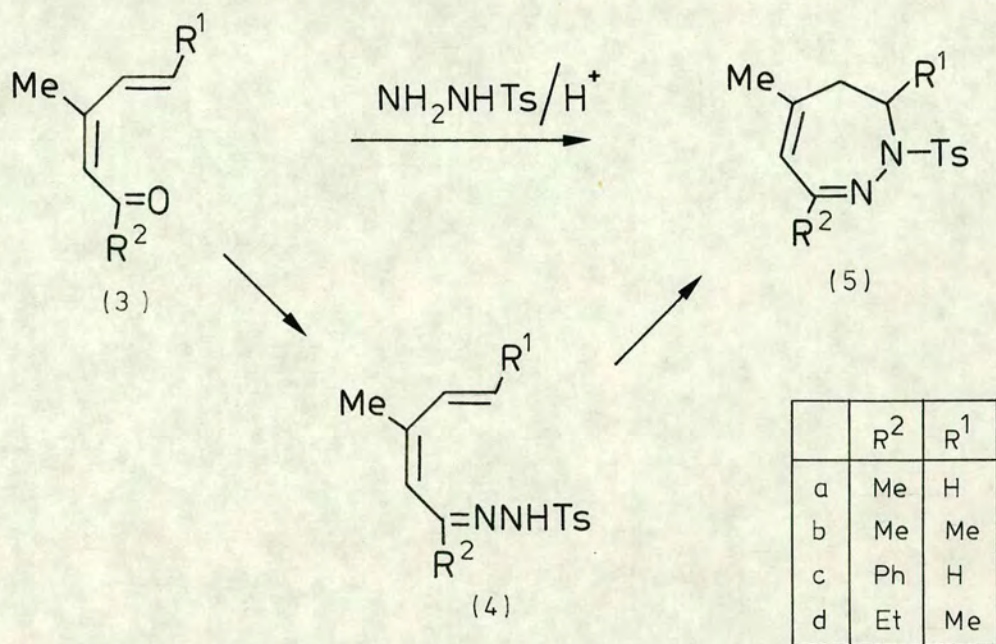
	Page No.
3. Reactions of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds with <i>p</i> -toluenesulphonylhydrazide	159
3.1 To provide 2-tosyldiazepine precursors for the 3 <i>H</i> -1,2-diazepine and organometallic studies	159
3.2 Investigation of the performance of dienals in the cyclisation reaction to give 2-tosyldiazepines.	160
4. Reactions of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds with other hydrazines	164
D. <u>1,2-Diazepine <i>N</i>-Oxides</u>	
1. Introduction	166
2. Oxidation of 4-phenyl-1 <i>H</i> -2,3-benzodiazepine	167
3. Oxidation of 3,5,7-trimethyl-3 <i>H</i> -1,2-diazepine	173

DISCUSSIONPreamble and Programme of Research

Sharp and his co-workers have reported the synthesis of 3*H*-1,2-benzodiazepines⁵⁶ (1) and 1*H*-2,3-benzodiazepines (2)⁶⁴ via 1,7-electrocyclic ring closure of $\alpha\beta,\gamma\delta$ -unsaturated diazo-compounds (scheme 1).

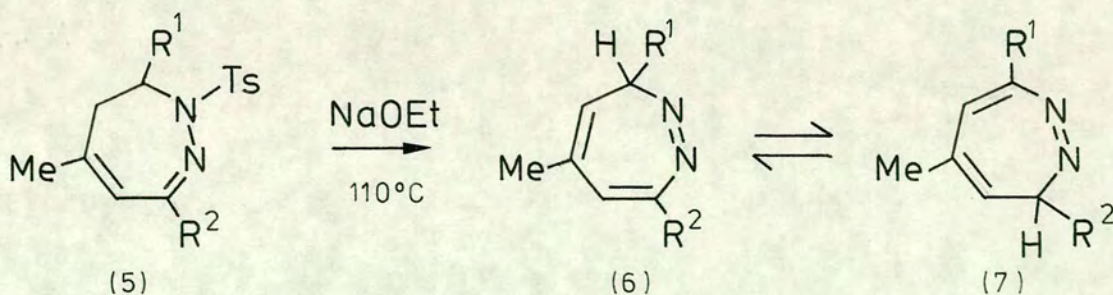
Scheme 1

During an extension of this work to examine dienones (3) having only olefinic unsaturation, an unexpected acid catalysed cyclisation reaction of the precursor tosylhydrazones (4) to give 2-tosyl-3,4-dihydro-1,2-diazepines (5) was discovered³³ (scheme 2).



Scheme 2

These 1-tosyldiazepines (5) are important as precursors in the only known route to the fully unsaturated 3*H*-1,2-diazepine system³⁴ (scheme 3). Another route, via the 1,7-electrocyclisation of $\alpha,\beta,\gamma,\delta$ -unsaturated diazocompounds has been discovered since the conclusion of this work.¹⁶⁹



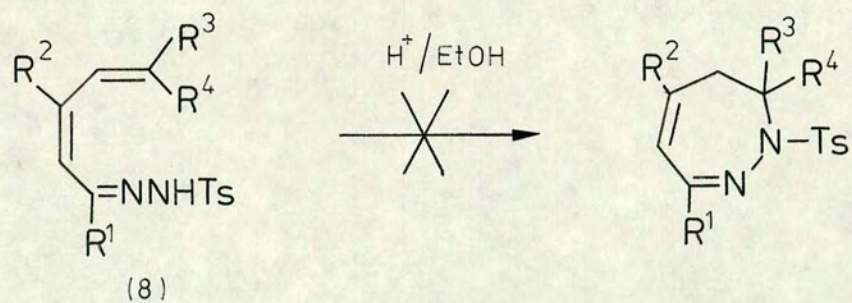
Scheme 3

This system has been shown to have some unique and interesting aspects to its reactivity, for example, the specific

1,5-hydrogen shift which interconverts (6) and (7) is ca. 10^{10} faster than in cycloheptatrienes - the analogous all-carbon ring system. This migration is so rapid at room temperature [$t_{\frac{1}{2}}$ for (6), $R^1=H$, $R^2=Me$, at $0^\circ C$ is ca.30 min] that the isolation of pure samples of each isomer is extremely difficult.

One of the major objectives of this work was the further study of this rapid hydrogen shift and in particular the investigation of ways in which the separation of these isomers (6) and (7) might be achieved so as to facilitate further kinetic studies on the migration reaction. To this end it was intended to study firstly, the preparation and separation of derivatives of (6) and (7) in which it was hoped that the rate of the hydrogen migration would be much reduced, and secondly, their subsequent reconversion to the diazepines. Thus it was planned to work on both the preparation of organometallic derivatives of (6) and (7) and on their conversion to azoxycompounds. Reactions to regenerate the diazepines from these derivatives would also be examined.

In addition to this aspect of the diazepine chemistry the programme also included further work on the synthesis of these systems. The cyclisation reaction of (3) to (5) had worked well in a number of cases but in several others (8a→e) it had not proved possible to cyclise the tosylhydrazones under acid catalysed conditions.³³



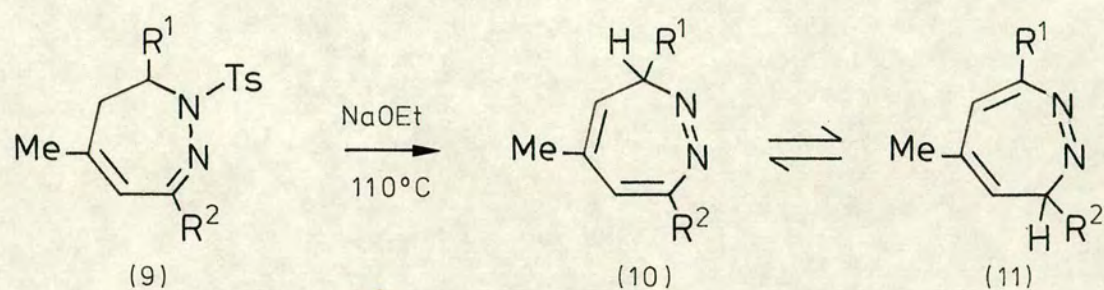
	R ¹	R ²	R ³	R ⁴
a	Me	H	Me	H
b	H	Me	Me	H
c	H	Me	Ph	H
d	Me	Me	Ph	H
e	Me	Me	Ph	Me

It was planned to investigate further the effects of substituents on this cyclisation in the hope of devising ways to extend the range of the synthesis.

A. 3H-1,2-Diazepines and their rearrangements by rapid [1,5] hydrogen migration

1. Synthesis

The 3H-1,2-diazepines (10) and (11) were prepared by the method of Sharp *et al*³⁴; by the base induced elimination of *p*-toluenesulphinic acid from their 3,4-dihydro-2-tosyl-1,2-diazepine precursors (9) shown in scheme 4.



Scheme 4

Compound	R ¹	R ²	Yield %	Ratio (10):(11)
a	Me	Me	81	One isomer formed
b	H	Ph	82	>99:~0
c	H	Me	78	85:15
d	Me	Et	88	52:48
e	Me	<u>i</u> -Pr	74	34:66
f	Me	CH ₂ CH ₂ Ph	93	49:51
g	Me	Ph	84	>99:~0

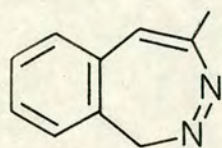
The general method was to heat the tosyldiazepine with a two-fold molar excess of sodium ethoxide in dry toluene, at *ca.* 100° when precipitation of sodium *p*-toluenesulphinate occurred. Heating was continued until inspection by t.l.c. showed that all the starting material had been consumed. After work-up, the 3*H*-1,2-diazepines were isolated as yellow oils, and purified by distillation or recrystallisation.

The synthesis of the precursor 3,4-dihydro-2-tosyl-1,2-diazepines is discussed in detail in section C of this discussion.

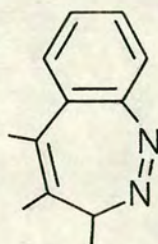
In these reactions the primary product (10) was not always the only compound isolated; in four cases the product was an equilibrium mixture of the two isomers (10) and (11).

2. Structural Assignment

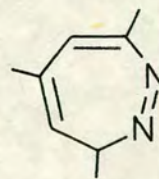
The structures of the 3*H*-1,2-diazepines (14) were inferred mainly by comparison of their properties and spectra with those of the known 3*H*-1,2-(13) and 1*H*-2,3-benzodiazepines (12).



(12)



(13)

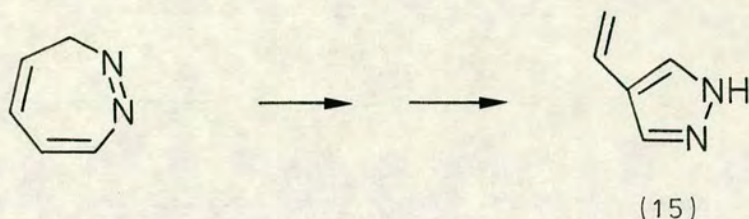


(14)

1*H*-2,3-benzodiazepine 3*H*-1,2-benzodiazepine 3*H*-1,2-diazepine

Like both these known benzodiazepines, the monocyclic 3*H*-1,2-diazepines were yellow, either oils or crystalline solids. They were sufficiently thermally stable to survive rapid

distillation without decomposition, but they decomposed or isomerised to pyrazoles (15) on prolonged heating^{35,36} (scheme 5)



Scheme 5

It was also demonstrated that like 1H-2,3-benzodiazepines they were rapidly photolytically isomerised *via* ring closure of the diazabutadiene unit to give bicyclic compounds of the type (16)³⁷ (scheme 6).

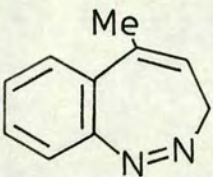
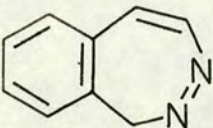
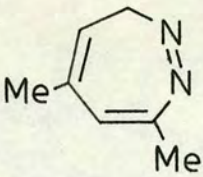


Scheme 6

Examination of the mass spectra of 3H-1,2-diazepines showed pronounced similarities to those of their benzo-annelated analogues; major fragmentation pathways *via* loss of N₂ and methyl fragments being evident.³⁴

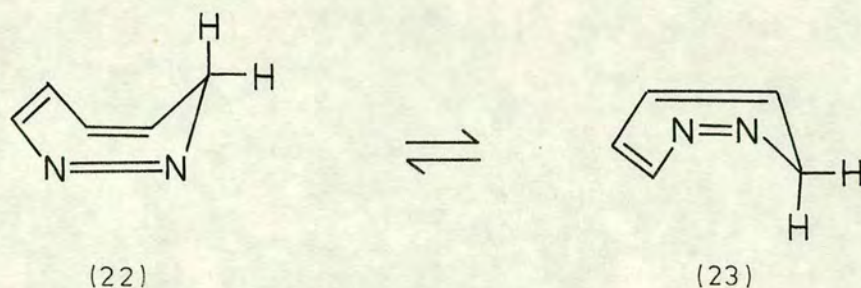
The most important evidence for the structural assignment of 3H-1,2-diazepines however, was derived from their ¹H and ¹³C n.m.r. spectra. The proton spectra of 3H-1,2-diazepines very closely resembled the spectra of similarly substituted 1H-2,3-

Table 1: The coalescence temperatures and free energies of activation for ring inversion of some 1,2-diazepines

Compound	Coalescence Temperature ^o C	ΔG^\ddagger Ring Inversion kJ mol ⁻¹
 (19)	25	59
 (20)	60	63
 (21)	>130	>77

In the case of 3*H*-1,2-diazepines, no coalescence was observed up to 130^oC, when decomposition started, although peak broadening was detected from 70^o onwards. A possible explanation for this alternative behaviour can be provided by examination of the stability of the planar intermediate involved during ring inversion. These heterocycles are normally in the puckered boat configurations (22) and (23), with little delocalisation.

However when they invert, the planar intermediate must be stabilised to some extent by electron delocalisation so lowering the energy barrier to ring inversion. Systems having a fused aromatic ring e.g. the benzodiazepines (19) and (20), would

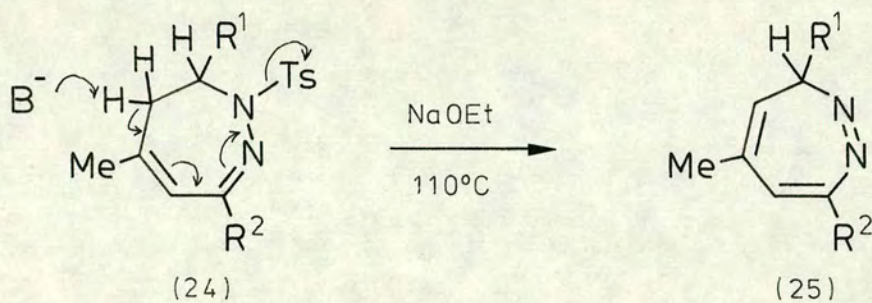


be expected to possess extra stabilisation in the planar transition state due to conjugation with the aromatic ring. This will be absent in the case of the monocyclic system (21) and may account for its higher energy barrier to ring inversion.

^{13}C Spectroscopy further confirmed the structure of the compounds as monocyclic seven membered rings. The C-3 saturated carbon attached to the azo-group is strongly deshielded and absorbs in a range (65-77 ppm) very similar to that observed for analogous benzo-annelated diazepines, see structures (17) and (18). The assignments of ^{13}C signals were confirmed by SFORD proton decoupling and/or the totally proton coupled spectra.

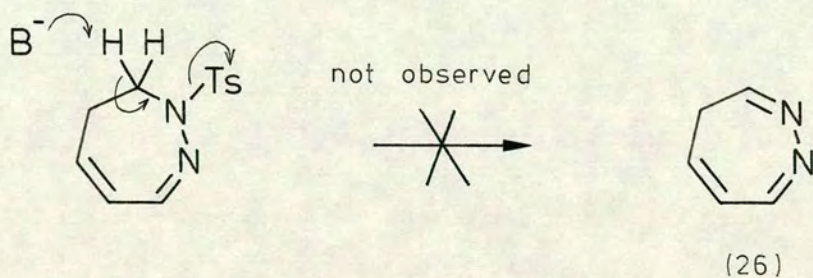
3. Mechanism of Formation

It has been suggested³⁴ that the formation of 3*H*-1,2-diazepines (25) from 3,4-dihydro-2-tosyl-1,2-diazepines (24) occurs *via* either an ElcB or E2 elimination mechanism as depicted in scheme 7.



Scheme 7

It was envisaged that this elimination took place *via* proton abstraction at the C-4 methylene group. It is interesting to consider that the alternative simpler elimination mechanism shown in scheme 8 would have produced a 4H-1,2-diazepine (26) which by comparison with the analogous 1H and 5H-2,3-benzodiazepines would be expected to be the more thermodynamically stable isomer.

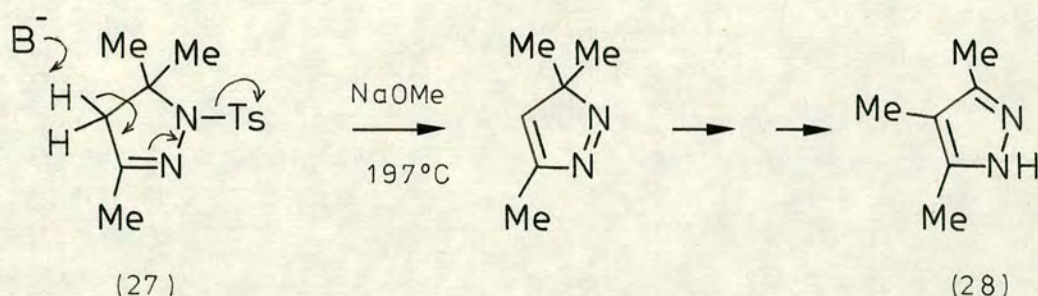


Scheme 8

The preference for the observed reaction could be due to either, the higher acidity of the C-4 than the C-3 protons, or to simply the steric inaccessibility of the antiperiplanar

conformation in (24) which would be required for elimination.

Some precedent for this postulated mechanism of formation for 3*H*-1,2-diazepines is provided by analogous reactions carried out by Bartlett and Stevens¹⁷⁰. They carried out the base-induced conversion of the 1-tosyl pyrazolenine (27) to the 1*H*-pyrazole (28), as shown in scheme 9.



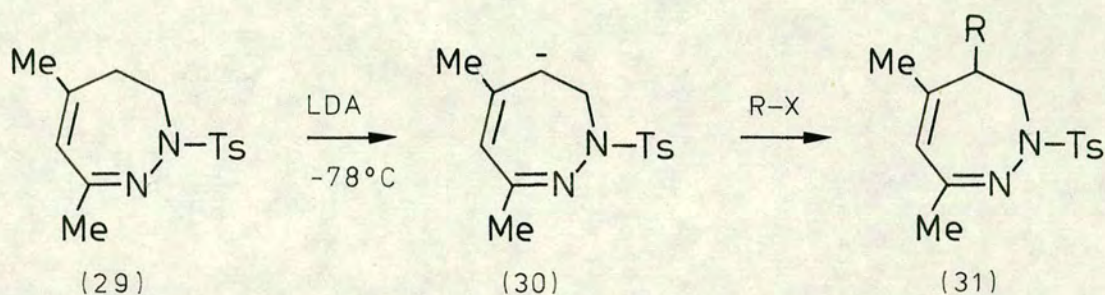
Scheme 9

The pyrazolenine (27) possesses no α -protons and so the elimination reaction must proceed by initial β -hydrogen abstraction,

Thus the mechanism shown in scheme 7 seems a reasonable proposal, however there is no direct evidence for its operation and other reaction pathways from (24) to (25) can be envisaged.

New light was unexpectedly thrown on to the mechanism of the elimination by some work on the functionalisation of the 3,4-dihydro-2-tosyl-1,2-diazepines (29) which was undertaken in the early stages of this project. The original intention was to generate the anion (30) by the low temperature deprotonation

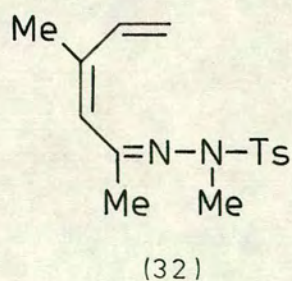
of the tosyl diazepine (29) with lithium diisopropylamide (scheme 10).



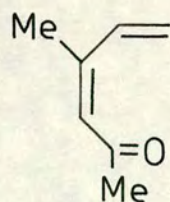
Scheme 10

It was hoped that this anion (30) could be then quenched with electrophiles to yield the 4-substituted diazepines (31).

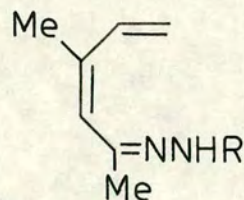
This reaction path was not realised, but instead on quenching with methyl iodide the *N*-methylated tosylhydrazone (32) was isolated.



The structural assignment of this compound was inferred mainly by comparison of its spectra with those of the analogous ketone (33) and hydrazones (34).



(33)



(34)

R = Ts
p-NO₂Ph
2,4-DNP

For example the ¹H n.m.r. spectra contained the characteristic three spin vinylic pattern shown in figure 1.

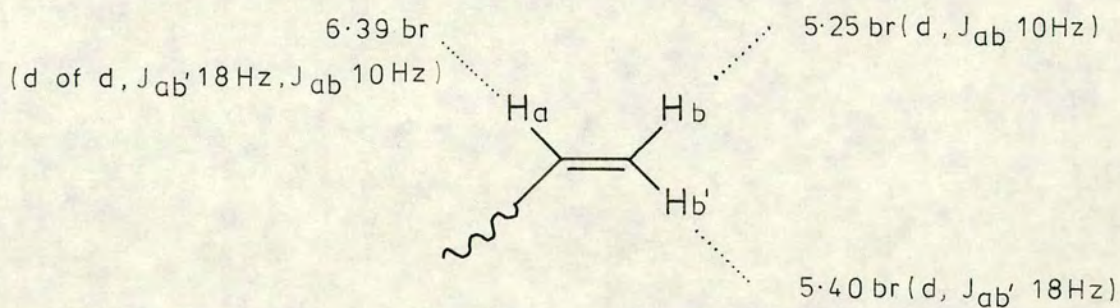
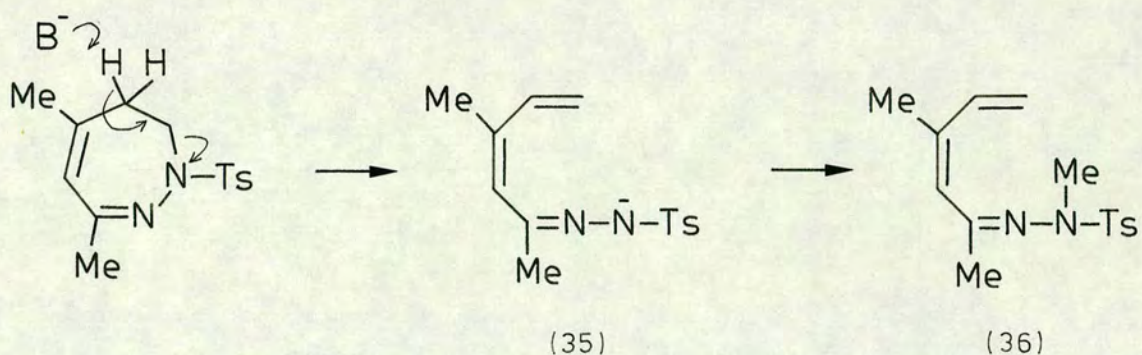


Figure 1

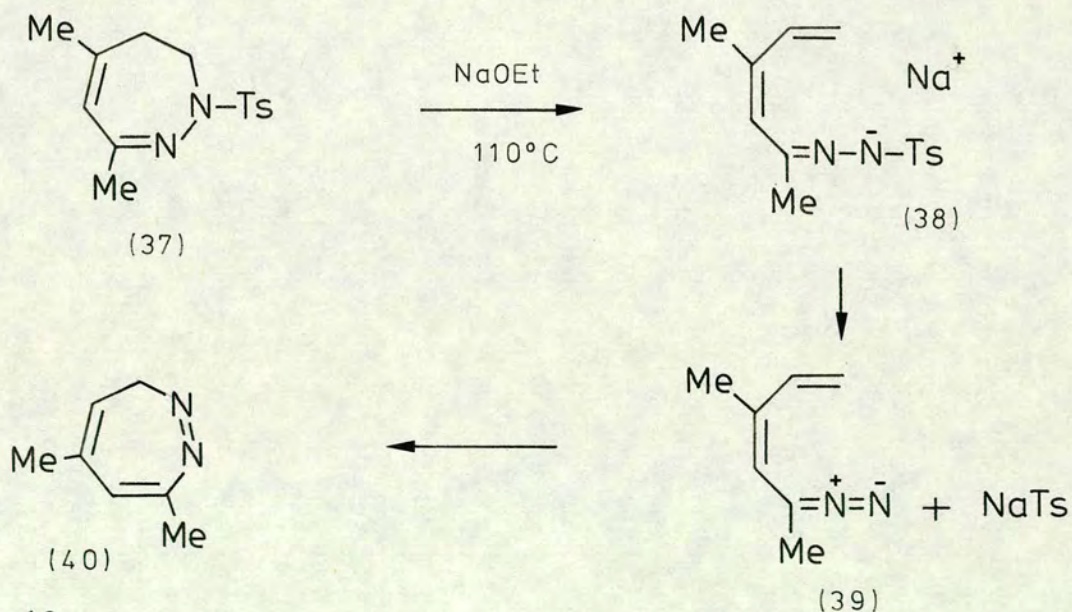
¹³C N.m.r. showed the presence of a deshielded methyl group at 38.7 p.p.m. which was consistent with an *N*-methylated structure. No NH signal was detected by I.R. or proton n.m.r. spectra.

A likely mechanism for the formation of this compound would be *via* C-4 proton abstraction and ring cleavage to give the ring opened anion (35) which was subsequently alkylated with methyl iodide to give the *N*-substituted tosylhydrazone (36) (scheme 11).



Scheme 11

In view of this new experimental data it is now proposed that the mechanism of formation for ^{these} 3H-1,2-diazepines from 3,4-dihydro-2-tosyl-1,2-diazepines follows the path shown in scheme 12.

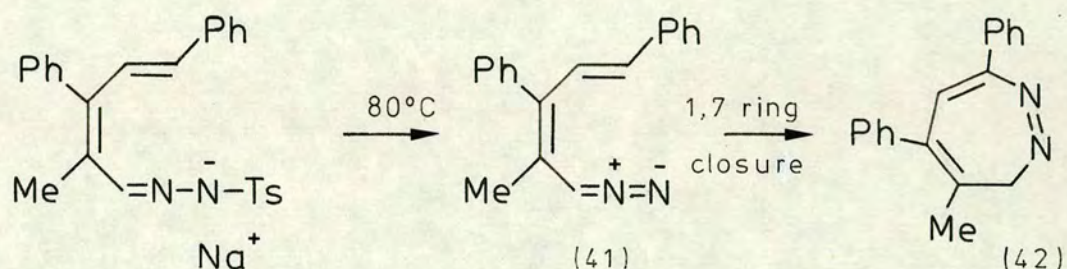


Scheme 12

Treatment of the tosyldiazepine (37) with ethoxide results in the formation of the tosylhydrazone anion (38) which under the elevated temperature conditions, 110^o, decomposes to give

p-toluenesulphinate anion and the diazo compound (39). This diazo compound then undergoes 1,7-electrocyclisation to give the 3*H*-1,2-diazepine (40).

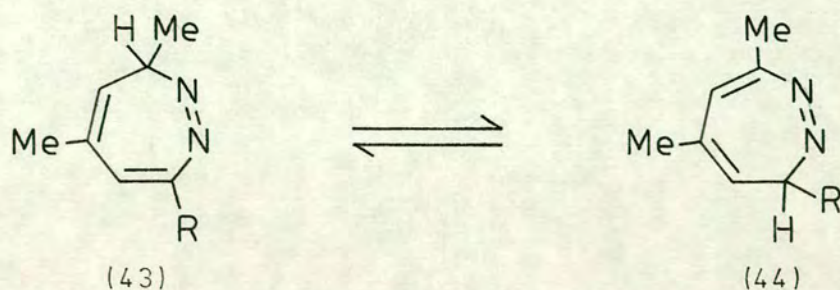
This alternative mechanism is also supported by further work carried out since completion of this project. Sharp and Robertson¹⁶⁹ have recently found that $\alpha\beta,\gamma\delta$ -unsaturated diazo-compounds of the type (41) will ring close by intramolecular 1,7-electrocyclisation to give 3*H*-1,2-diazepines (42) as depicted in scheme 13.



Scheme 13

4. Isomer Interconversion

The formation of two interconverting isomeric diazepines in a number of cases was particularly fascinating (scheme 14).



Scheme 14

Figure 2

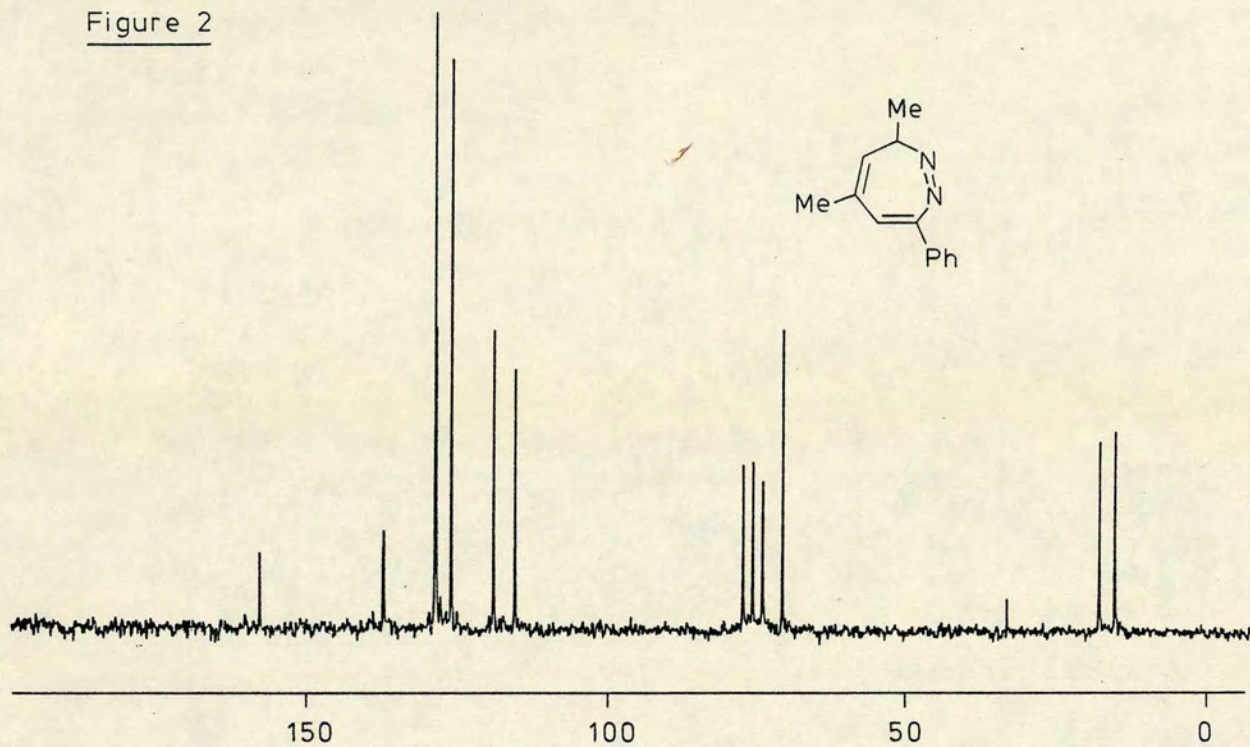
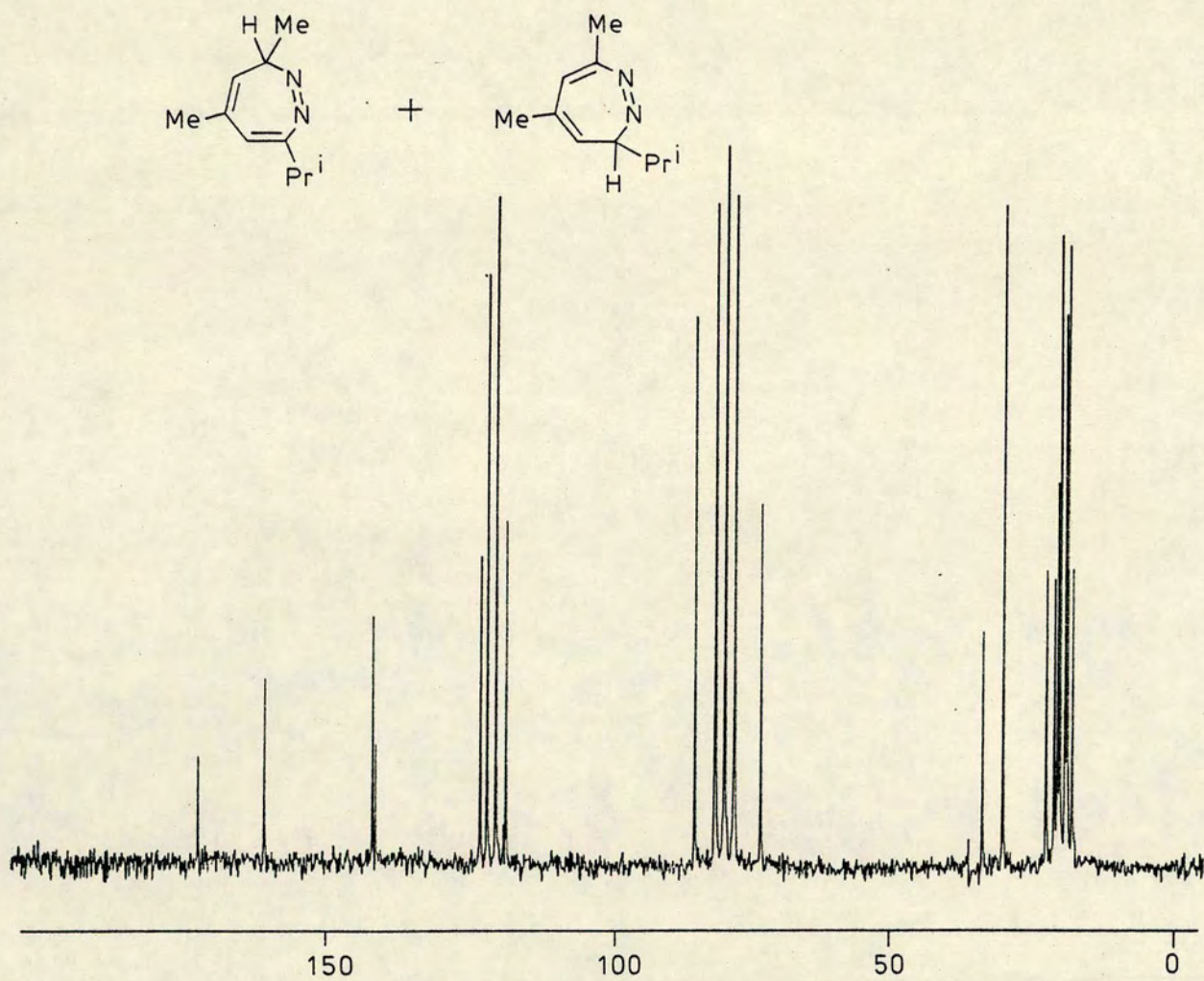


Figure 3



R	Isomer Ratio (43):(44)
H	15:85
Pr ⁱ	34:66
CH ₂ CH ₂ Ph	51:49
Et	52:48
Ph	>99:~0
Me	one isomer formed

Convincing evidence for the existence of the two isomers was provided by n.m.r. spectroscopy and in two cases resolution of the mixture of two isomeric diazepines was achieved by high performance liquid chromatography at low temperature.

Considering first the n.m.r. data, figures (2) and (3) reproduce the ¹³C n.m.r. spectra for 3,5-dimethyl-7-phenyl-3*H*-1,2-diazepine and the 34:66 mixture of 3,5-dimethyl-7-isopropyl and 5,7-dimethyl-3-isopropyl isomeric 3*H*-1,2-diazepines. Examination of these spectra revealed that in the latter example (figure 3) all the expected resonances were present in duplicate. For example in the 65-85 p.p.m. region, characteristic of the saturated C-3 carbon attached to the azo-group, two signals at 70.9 and 82.0 p.p.m. were present. In the C-7 ring carbon region, strongly deshielded at 150-170 p.p.m., two signals at 154 and 165 p.p.m. were present. Similar duplication was observed for the remaining ring carbons and aliphatic substituents.

Proton spectra also exhibited resonances consistent with the presence of two isomeric 3*H*-1,2-diazepines. The resolution

Figure 4

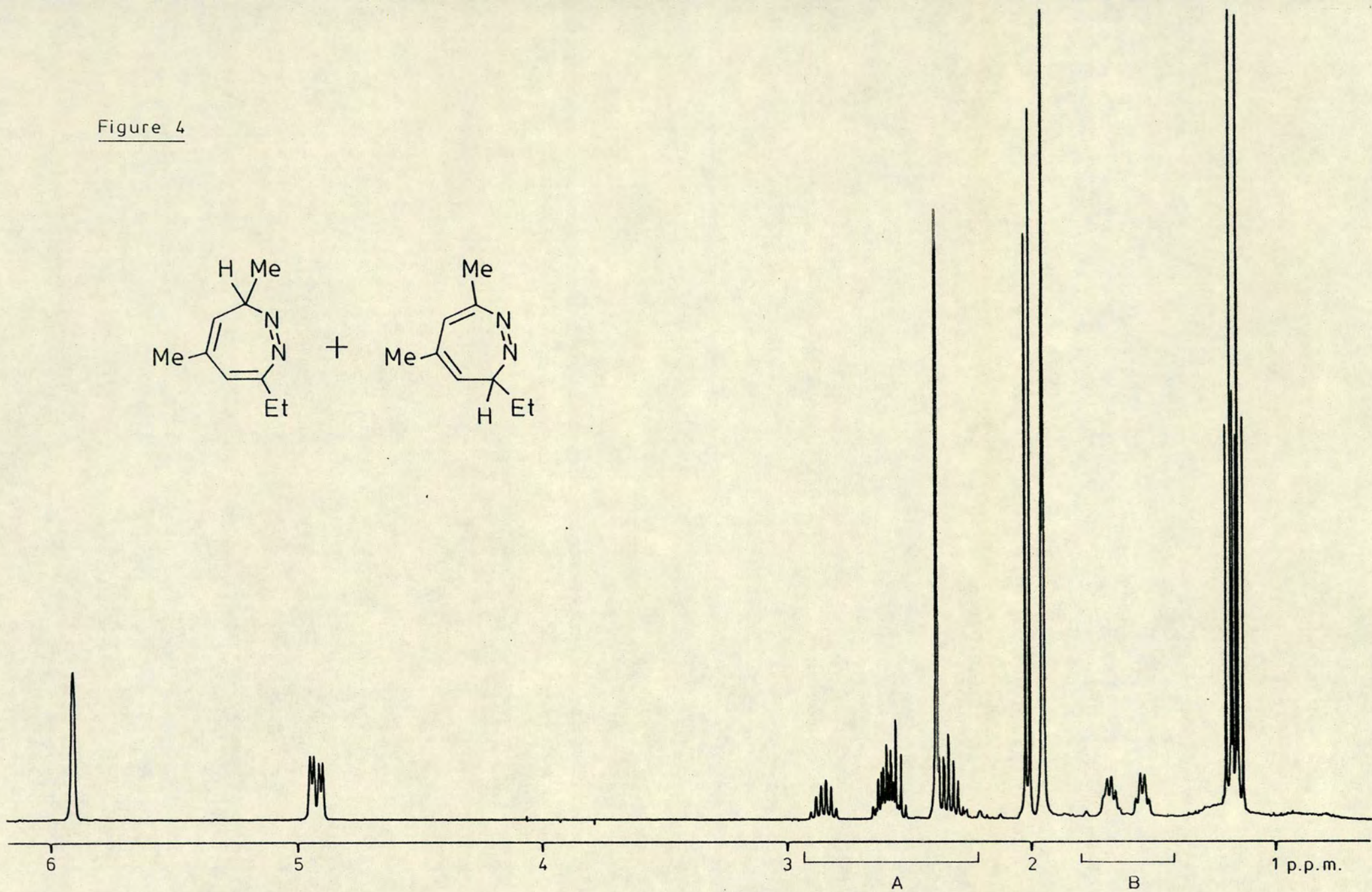
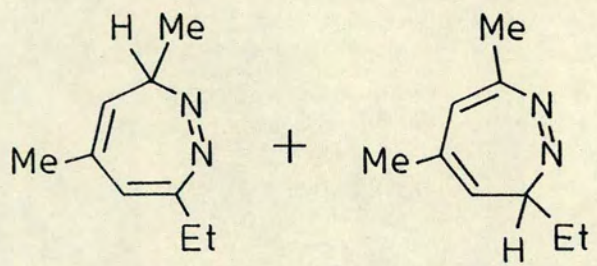
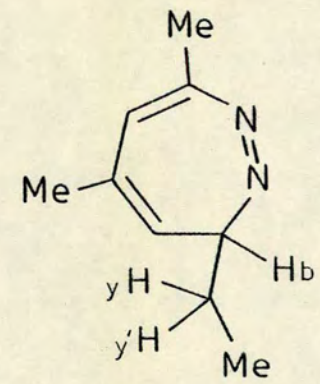
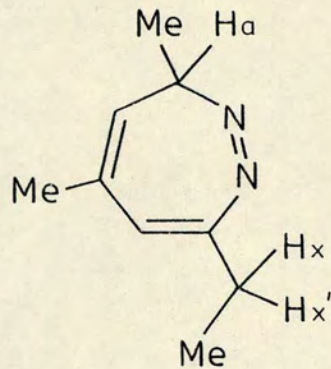
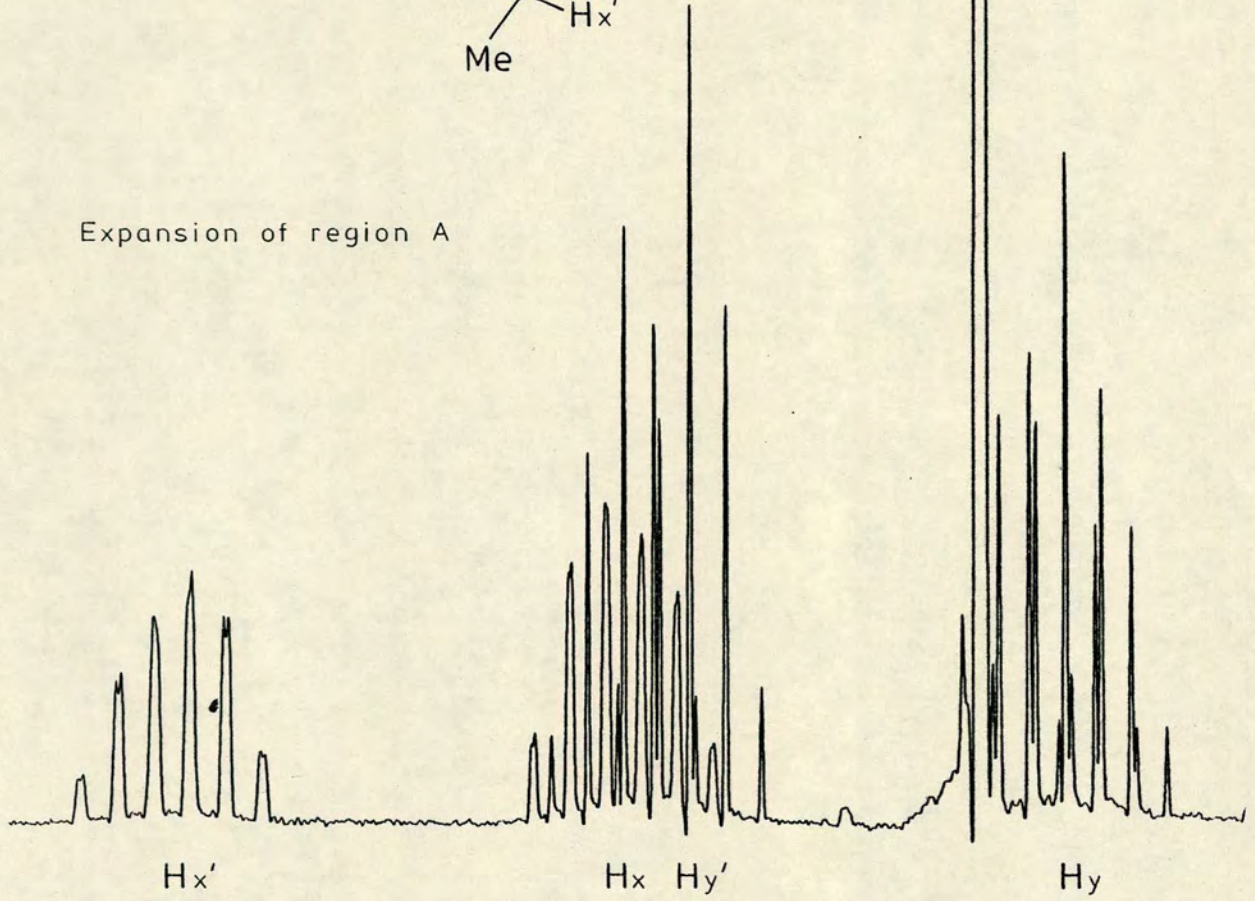


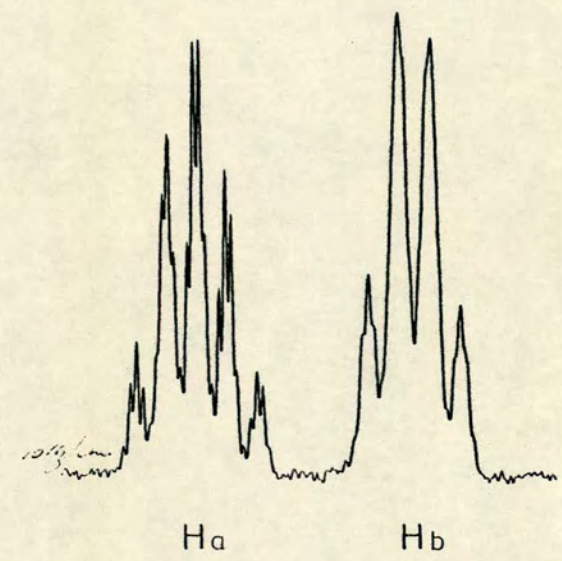
Figure 5



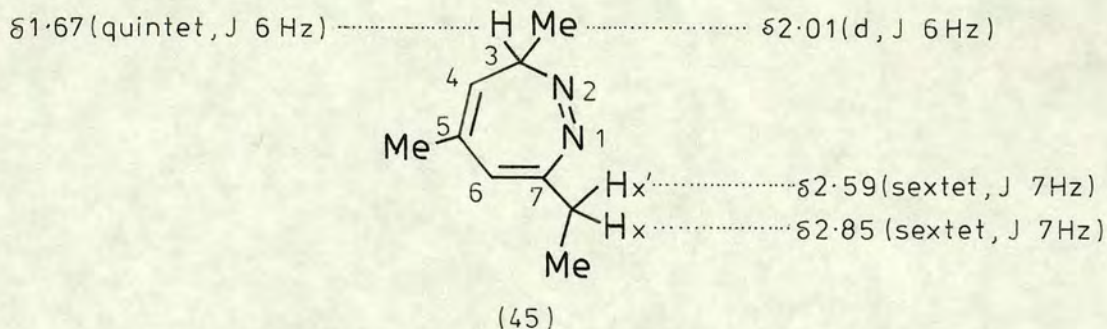
Expansion of region A



Expansion of region B



achieved at 100 MHz was not sufficient to enable unambiguous identification of all the resonances present in the two isomeric diazepines, but this problem was solved when spectra at 360 MHz were obtained. Figures (4) and (5) reproduce the spectra obtained for the 52:48 mixture of 3,5-dimethyl-7-ethyl and 5,7-dimethyl-3-ethyl isomeric 3*H*-1,2-diazepines, the assignments were confirmed by a series of low power decoupling experiments. The key feature of the spectra was the coupling pattern of substituents attached to the C-3 and C-7 ring carbons. Considering the 3,5-dimethyl-7-ethyl isomer (45) first, the 3-Me appeared as doublet with a coupling constant of 6Hz to the adjacent C-3 proton.



This proton on C-3 appeared as a quintet with coupling constant of 6Hz, indicating that coupling to C-3 methyl and C-4 proton were of the same magnitude. The diastereotopic methylene group attached to C-7 appeared as two separate multiplets; overlapping doublets of quartets. With the 5,7-dimethyl-3-ethyl isomer (46) different coupling patterns were observed.

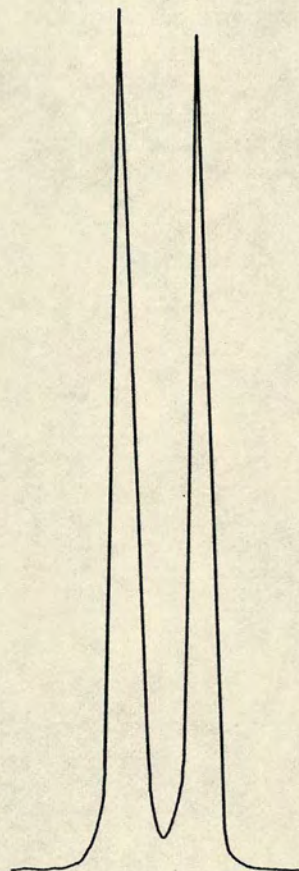
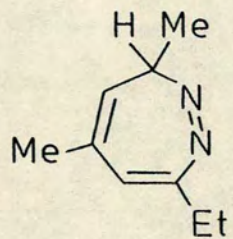


Figure 7

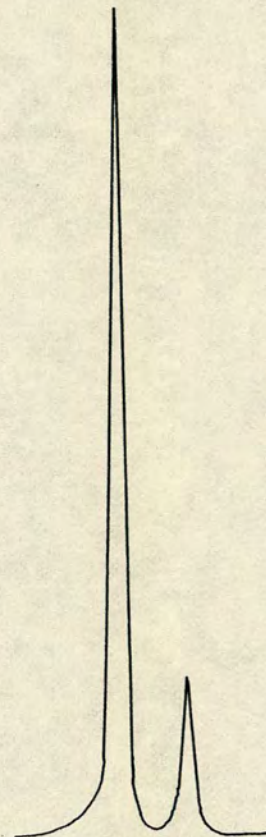
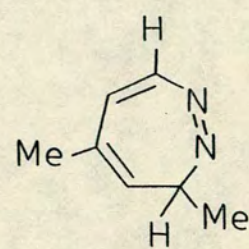
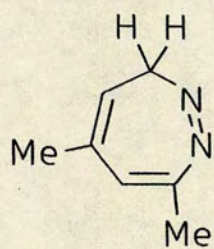
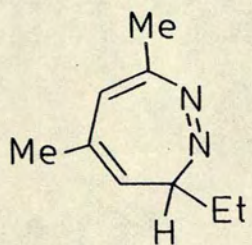
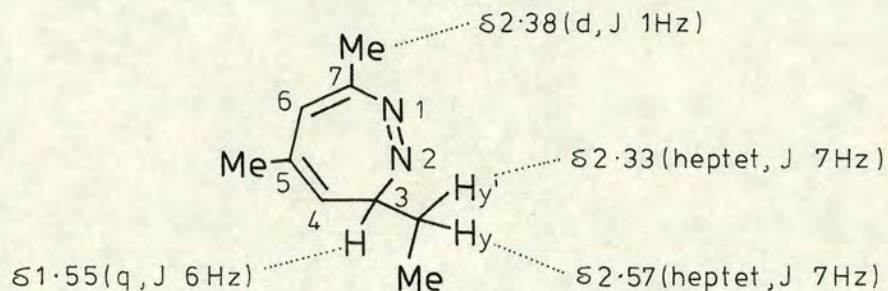


Figure 6



(46)

The C-7 methyl group gave a fine doublet with a small four bond coupling of 1Hz to the C-6 proton. The proton attached to C-3 appeared this time as a quartet with a typical three bond coupling constant of 6Hz. This proton was coupling to the C-4 proton and to the methylene group of the ethyl fragment. The diastereotropic methylene protons of the ethyl group appeared as two separate heptets resulting from an overlapping doublet of doublet quartets.

In two examples, separation of the diazepine isomers on an analytical scale was achieved by high performance liquid chromatography, figures (6) and (7) reproduce the chromatograms obtained. Resolution of the remaining isopropyl and phenethyl substituted diazepine mixtures was not possible although an extensive range of column packing/solvent combinations were examined. Significant peak broadening was detected in a number of cases, and this indicated that some separation on the column must have been taking place.

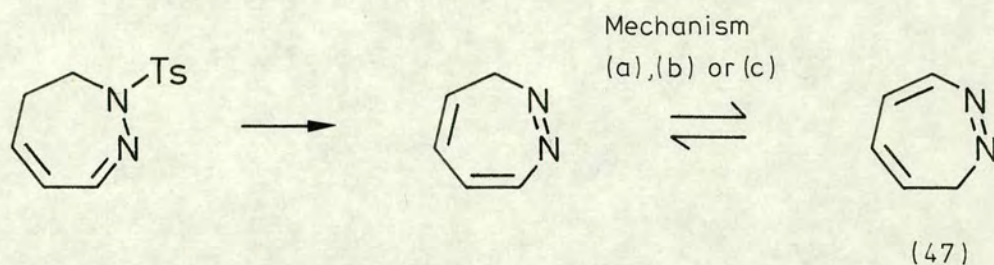
The chromatographic separations were carried out at 0°C because cooling was found to inhibit significantly the isomer interconversion and thus improve peak separation.

The diazepine fractions from the column were collected and stored at -80°C, further analysis of these samples after 3 h by repeat h.p.l.c., showed that greater than 90% isomer

purity was retained.

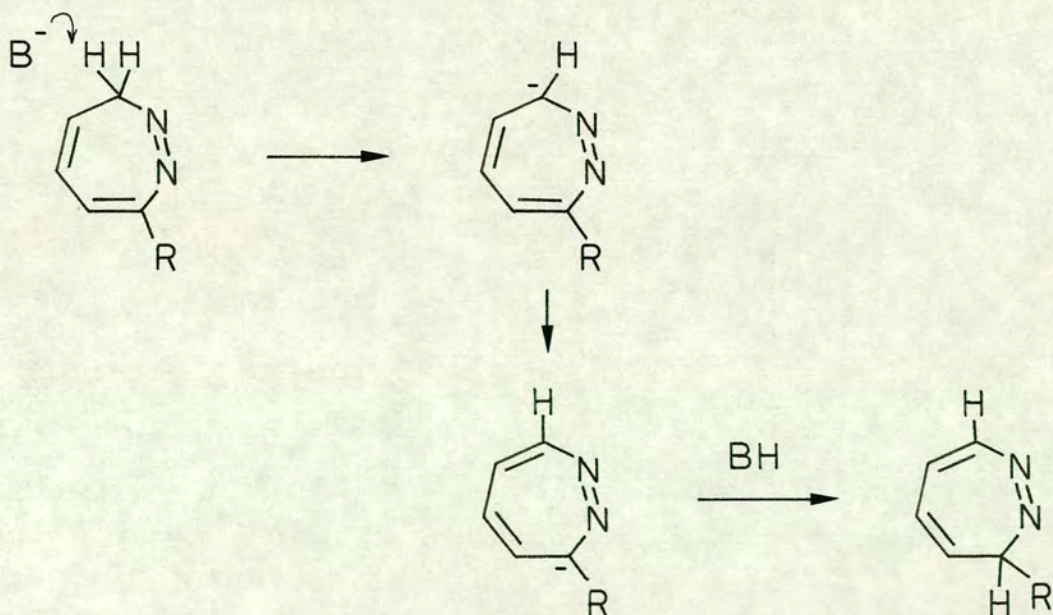
Conversely if the diazepine isomers were stored at room temperature they were found to return rapidly to the previous equilibrium ratio.

These experiments provided significant clues to the nature of the mechanism responsible for the isomer interconversion. *A priori* the formation of the second isomer (47) could be envisaged to occur by three pathways (scheme 15).



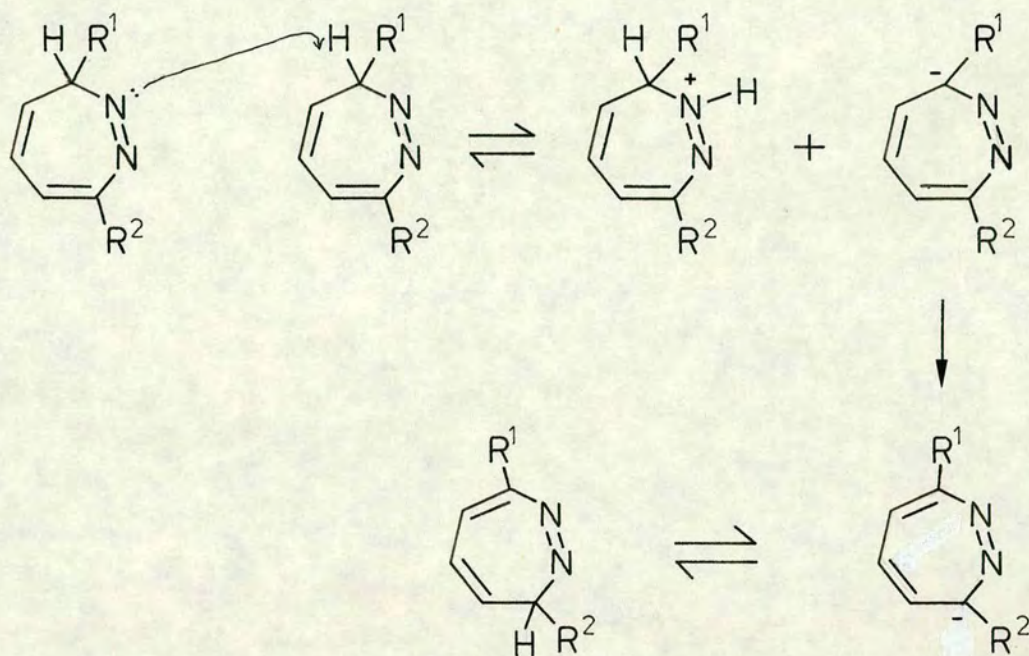
Scheme 15

a) Base catalysed isomerisation, a two-fold excess of ethoxide was used during synthesis (scheme 16).



Scheme 16

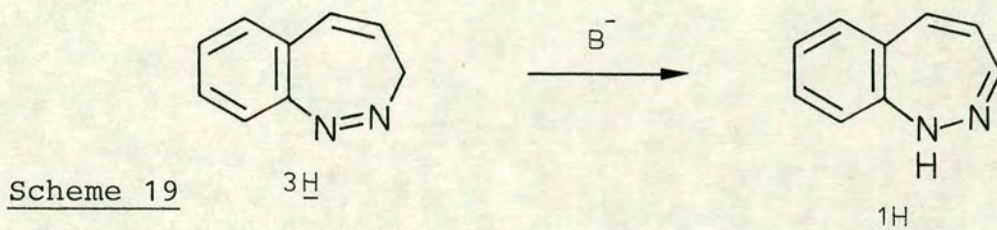
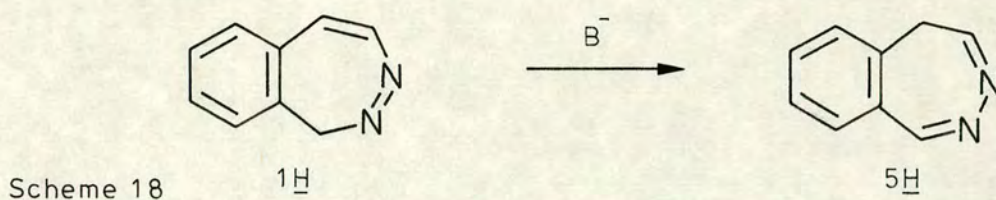
b) Intermolecular isomerisation by the diazepines themselves (scheme 17).



Scheme 17

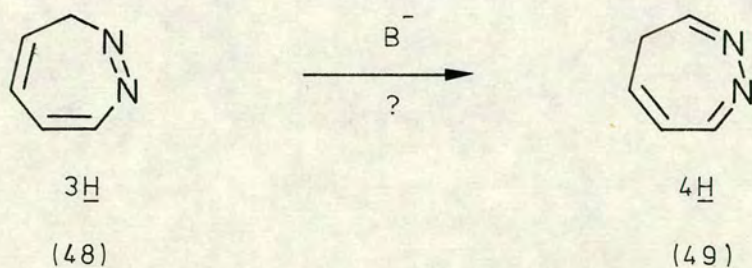
and finally c) intramolecular mechanism, ie [1,5] sigmatropic hydrogen migration.

Option a) can be ruled out because the isomer interconversion still takes place in the absence of base, as demonstrated during h.p.l.c. analysis. Furthermore base catalysed isomerisation would be expected to give the more stable 4H-isomer by comparison with previous benzodiazepine chemistry (schemes 18 and 19).



In these two base-catalysed benzodiazepine isomerisations^{56,64,69}, it is clearly demonstrated that the destabilised azo containing benzodiazepines are readily converted to the thermodynamically preferred 5*H*- and 1*H*-isomers respectively.

By this argument 3*H*-1,2-diazepines (48) would be expected to react with base to give the thermodynamically preferred 4*H*-isomer (49) (scheme 20).

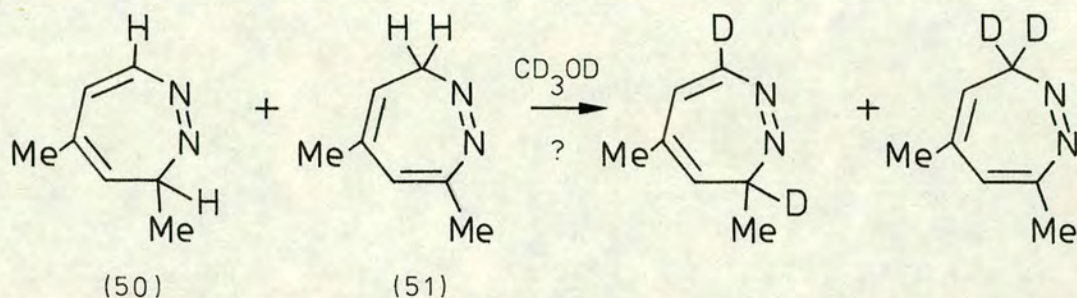


Scheme 20

In fact 3*H*-1,2-diazepines have been shown to react with strong bases but gave no isolable products¹⁷¹.

Option (b) seemed a real possibility since although the nitrogens in an azo-group have very low basic character compared with amines, the hydrogens on C-3 of the diazepine are slightly activated by the electron withdrawing effect of the azo group.

Therefore it was decided to test this option by experiment. If the diazepine mixture, in dynamic equilibrium, was placed in a solvent containing easily abstracted deuterons then on the basis of this mechanism the hydrogens on C-3 should exchange with deuterium atoms in the solvent (scheme 21).



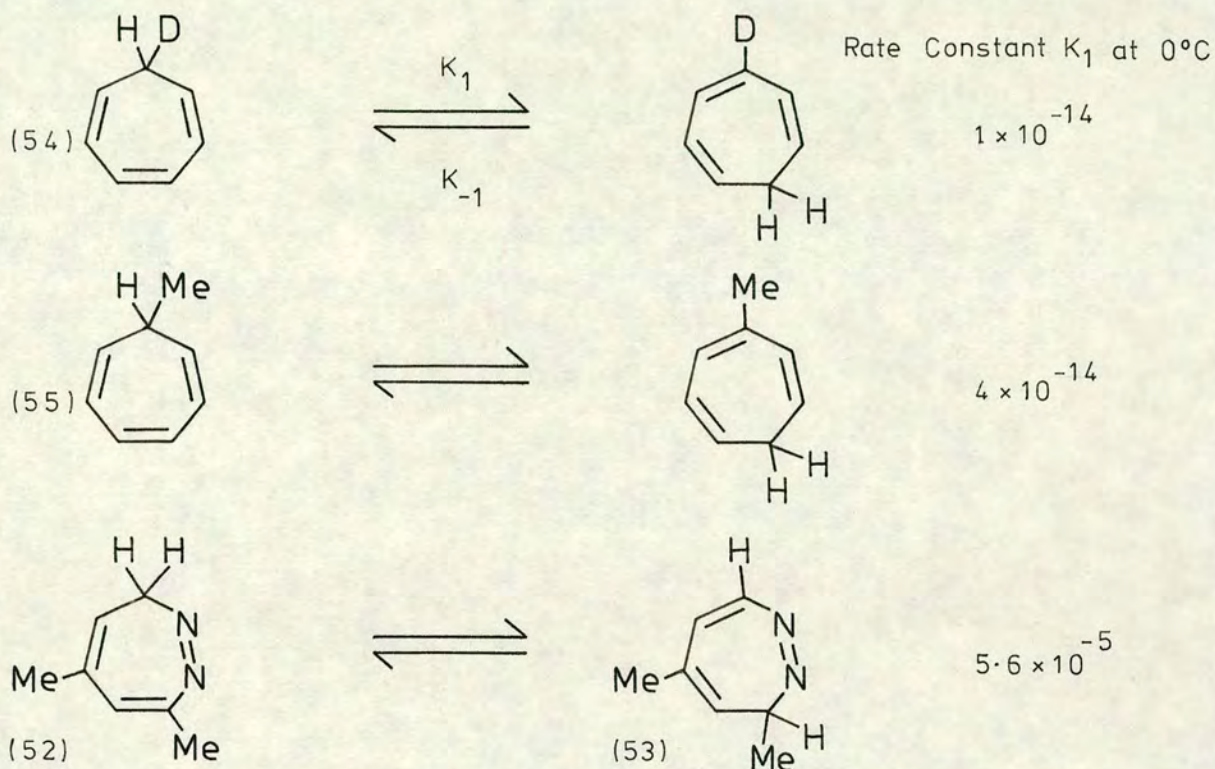
Scheme 21

Thus the 85:15 ratio mixture of 3,5-dimethyl (50) and 5,7-dimethyl (51) 3*H*-1,2-diazepines were dissolved in a five fold molar excess of CD₃OD at room temperature and their proton n.m.r. spectrum was monitored over a period of 24 h. No uptake of deuterium atoms was observed thus ruling out the operation of this mechanism.

This leads to the conclusion that the hydrogen migration is intramolecular, ie a particularly rapid example of [1,5] sigmatropic hydrogen migration.

Sharp has carried out a kinetic study on the isomer inter-conversion utilising the h.p.l.c. separation technique outlined above. He monitored the conversion of (52) into (53) at 0°C over a 90 minute period, from the kinetic data the rate constant

K_1 was calculated to be 0.56×10^{-4} . Comparison with rate constants for analogous cycloheptatrienes (54) and (55) showed that the diazepine [1,5] hydrogen migration was 10^{10} faster.



Typically, [1,5] sigmatropic hydrogen migrations in cycloheptatrienes are only observed at elevated temperatures, $>100^\circ$, whereas this unusual diazepine migration is still rapid at room temperature.

Two explanations for the greatly enhanced rate of migration present in the diazepine system are possible; either that the electronic effect of the azo group is responsible, or that the structural geometry of the diazepine ring is particularly favourable.

Considering the electronic effect first, a molecular orbital description of the transition state for [1,5] sigmatropic hydrogen migration in cycloheptatriene has been recently reported

by Dobbelaere *et al.*¹⁷², and is illustrated in figure 8.

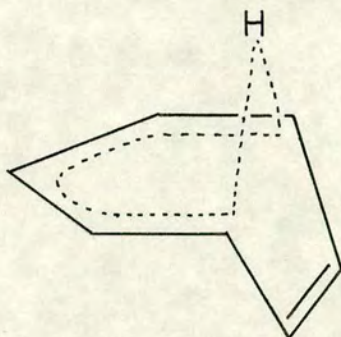
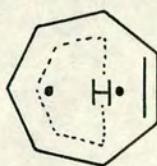


Figure 8

The cycloheptatriene [1,5] sigmatropic hydrogen transition state consists of a planar pentadienyl system perturbed by an out-of-plane olefin bond which is no longer in conjugation. The charge transfer in this system was found to be close to zero; 0.99 electron density on the migrating hydrogen, thus the transition state is essentially a hydrogen atom interacting with a perturbed pentadienyl radical (56).



(56)

According to FMO theory the major stabilising orbital interaction in the transition state for 1,5-suprafacial hydrogen shifts is that between a singly occupied pentadienyl ψ_3 and a singly occupied hydrogen 1s orbital (figure 9) which will be at lower energy¹⁷³.

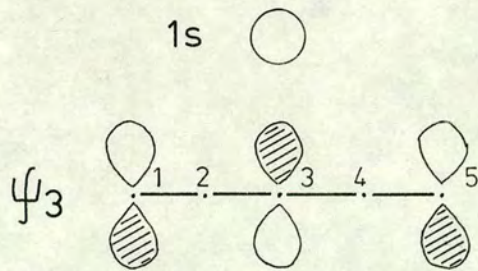


Figure 9

The degree of stabilisation in the transition state contributed by this interaction is related to ϵ (figure 10), which by second order perturbation theory is inversely related to ΔE the energy separation between the interacting orbitals.

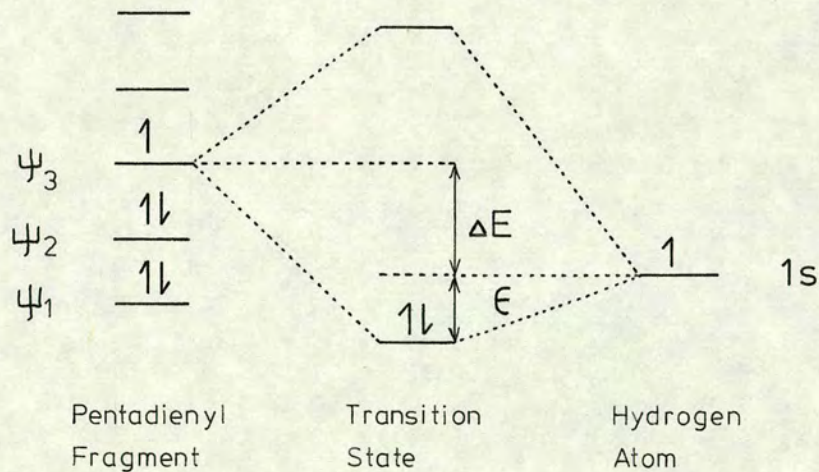


Figure 10

Thus any effect which lowers the energy of ψ_3 , thus reducing ΔE , should stabilise the transition state and lower the activation energy of the reaction.

In figure 11 data¹⁷³ on the effect of C-1 substituents on the frontier orbital energy of butadiene is presented.

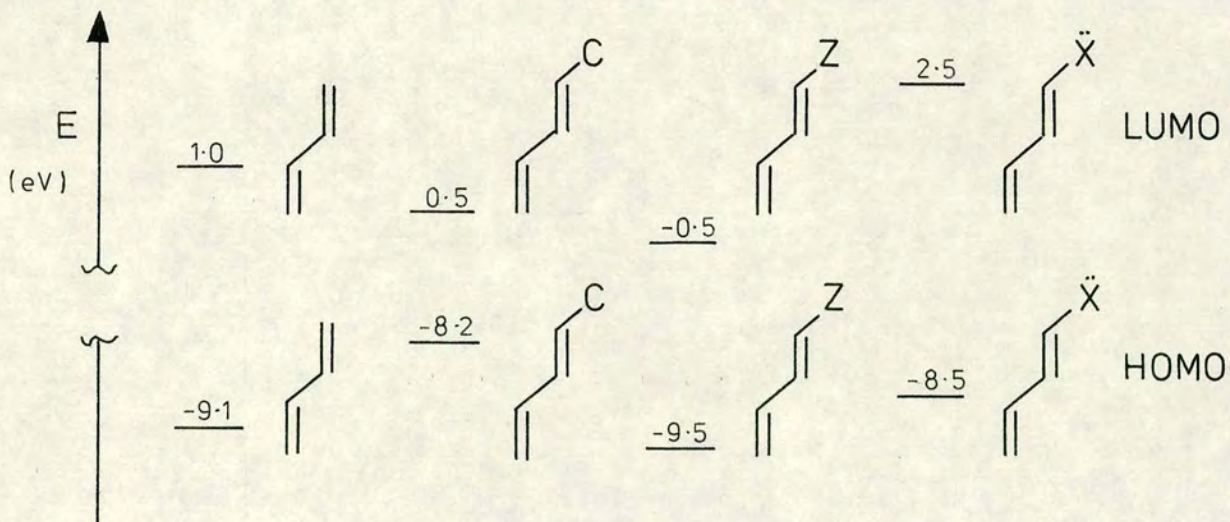


Figure 11

The effect of an electron withdrawing substituent Z, is to lower both the HOMO and the LUMO energy. Thus by analogy the energy of ψ_3 in the 3H-1,2-diazepine (58) would be expected to be lower than that in cycloheptatriene (57) due to the electron withdrawing effect of the azo group attached to both ends of the pentadienyl system (figure 12).

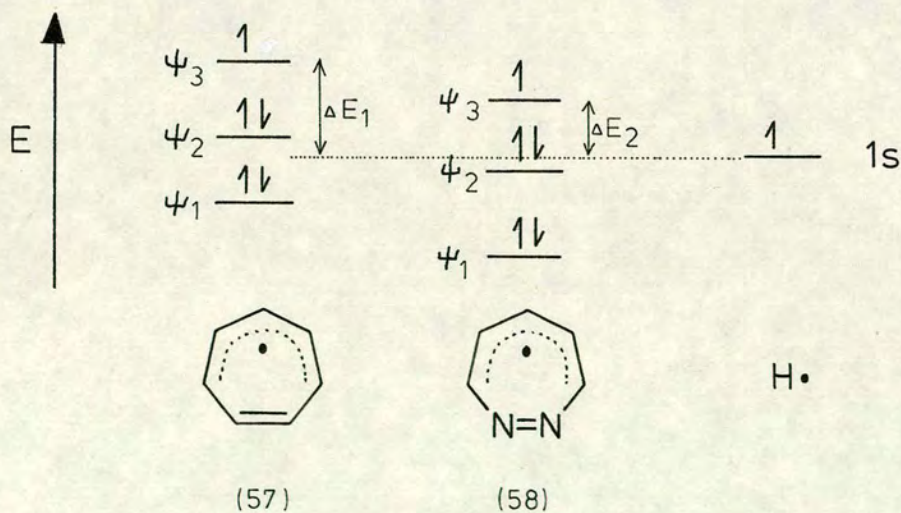
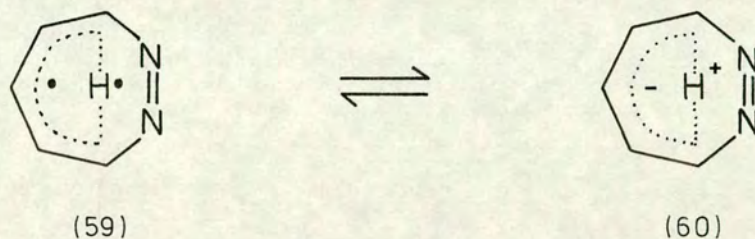


Figure 12

This will promote a better interaction with the hydrogen

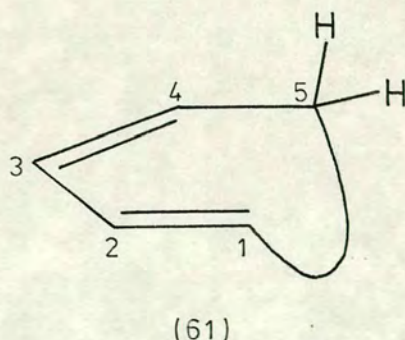
1s orbital and be expected to have a marked rate enhancing effect on the hydrogen shift.

It also seems likely that the transition state will have considerably greater polar character in (58) than in (57); the former could be seen as intermediate between (59) and (60).



In a general configuration interaction treatment of pericyclic reactions some years ago, Epiotis¹⁷⁴ predicted that polar contributions should have a major accelerating effect on [1,5] sigmatropic hydrogen shifts.

Another possible explanation for the enhanced rate of migration is simply a shorter distance of approach of the hydrogen atom to the diene terminus (61).



This distance of approach argument has been put forward previously to account for the differences in rate of [1,5] sigmatropic hydrogen migration encountered in various cyclic dienes¹⁴¹⁻¹⁴³; the authors showed that the distances between migration centres was satisfactorily correlated with the sequence based on decreasing rate of [1,5] sigmatropic hydrogen migration, i.e. $C_5 < C_7 - C_9 \ll C_6$

(see introduction Section D).

When the differences in distance of approach in the diazepine and cycloheptatriene systems are examined they are found to be only marginal compared with the cyclic diene series (Table 2).

Table 2. The distance of approach between migration centres for [1,5] sigmatropic hydrogen migration in some cyclic conjugated dienes

CONJUGATED DIENE	Distance between migration centres Å		Rate of Migration qualitative
	C-C	C-H	
cyclopentadiene	1.5	2.2	Fast
cyclohexa-1,3-diene	2.5	2.9	Slow
cyclohepta-1,3-diene	2.8	2.6	Medium
cyclo-octa-1,3-diene	3.0	2.5	Medium
cycloheptatriene	2.8	2.7	Medium
3H-1,2-diazepine	2.78	2.75	Very fast

From these data it seems unlikely that the distance of approach between migration centres is unusually favourable in the diazepine system. Thus it seems unlikely that steric factors make a major contribution to the accelerated rate of migration encountered in 3H-1,2-diazepines.

A further example of greatly enhanced rate of [1.5] sigmatropic hydrogen migration in a seven membered ring has recently been reported by Japanese workers^{175,176} (scheme 22).



Scheme 22

Although no kinetic data was reported they found that the cyclic lactone (62) readily converts into the isomeric compound (63) at only 4°C. It is interesting to note that in this striking parallel to the diazepine system, the moiety perturbing the pentadienyl unit; the lactone linkage, is also strongly electron withdrawing. Thus the weight of evidence favours the electronic effect as being responsible for the rate enhancement of [1,5] sigmatropic hydrogen migration encountered in 3*H*-1,2-diazepines.

The diazepine equilibrium isomers ratios were found to be very similar to those of hydrocarbon systems which interconverted by [1,5] sigmatropic hydrogen migration¹⁵⁰. The following general features which control the thermodynamic stability of the isomers had been identified;

- i) a lower stability of isomers containing a substituent in the methylene group;
- ii) comparable stability of isomers differing in the position of an alkyl substituent attached to the butadiene unit;
- iii) substituents which lengthen the conjugation in the

1-position are preferred.

The diazepine mixtures agreed with these observations for example in the dimethyl substituted diazepine mixture the isomer containing a methyl substituent in the methylene group (64) was the lower percentage component (figure 13).

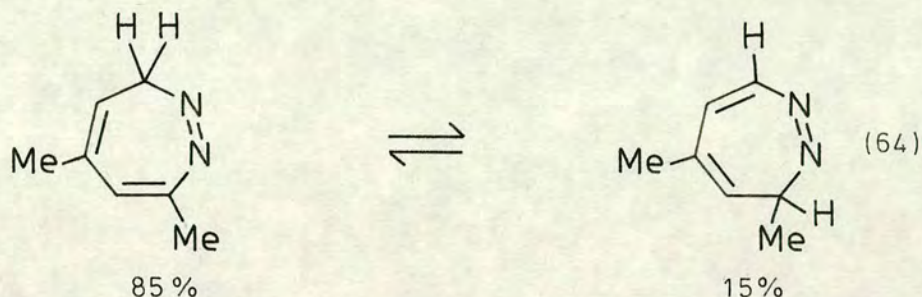


Figure 13

Similarly with the phenyl substituted diazepines only one isomer, the one with extended conjugation (65), was observed (figure 14).

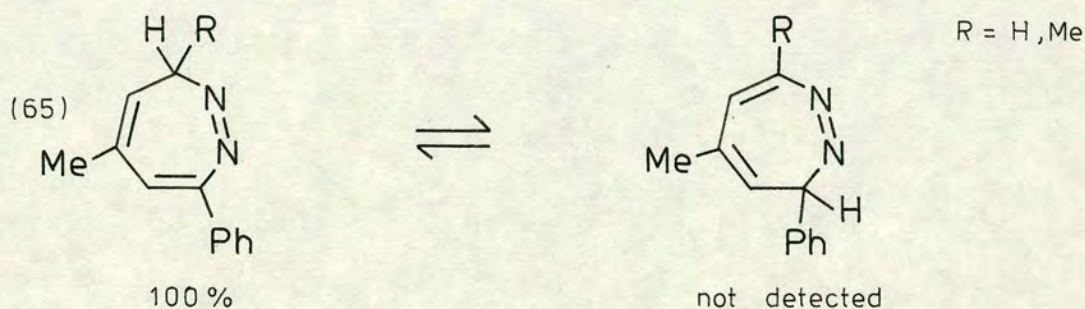
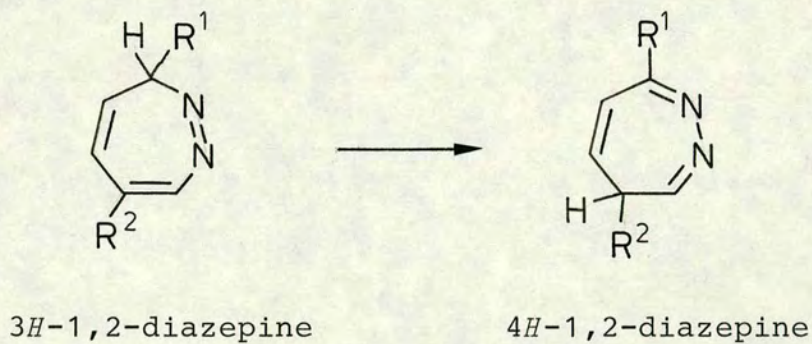


Figure 14

Of the remaining diazepines, those with alkyl substitution at either end of the 1,5-fragment, the isomers were present in approximately equal proportions consistent with observation ii).

Another point of interest about this isomer interconversion is its high specificity, for example there is no leakage via the other possible [1,5] hydrogen shift to give the 4*H*-isomer (scheme 23).



Scheme 23

As previously discussed the 4*H*-isomer which has no azo-group would be expected to be the most thermodynamically preferred isomer - yet is not formed. The transition state (66), must be energetically disfavoured compared with (67).

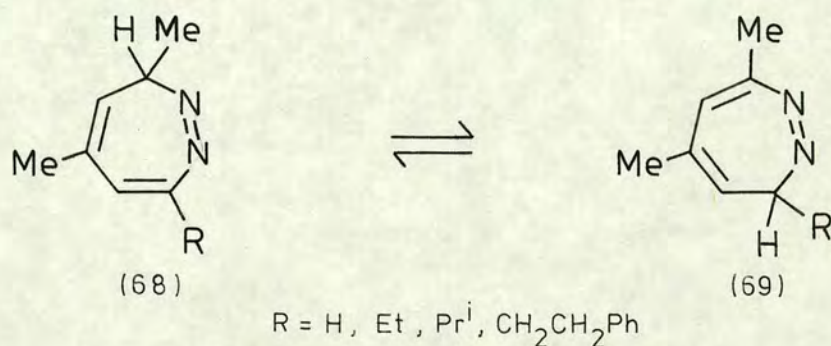


Attempts to induce this alternative [1,5] shift to take place by raising the temperature were thwarted because the diazepine then reacts by other pathways^{35,36} (see Introduction Section A.6.2).

B. Diiron hexacarbonyl 1,2-diazepine complexes

1. Introduction

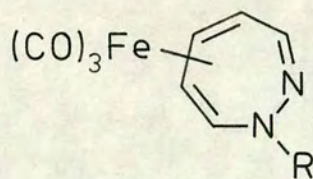
The first synthesis of 3*H*-1,2-diazepines has been recently reported by Sharp *et al.*³⁴ This is an interesting ring system because of the fast [1,5] sigmatropic hydrogen migration which interconverts the two isomers (68) and (69).



This study of metal complex formation by the diazepines was initiated in the hope that complexes could be prepared in which the diazepine ring remained intact but with a much reduced rate for the hydrogen migration. This would enable complexes of the individual isomers to be separated for characterisation, spectroscopic study and possible regeneration of the diazepines.

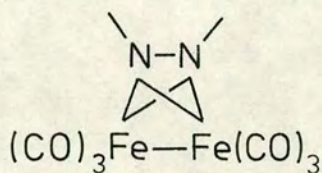
Iron carbonyl adducts were chosen for initial investigation as previous work with 1*H*-1,2-diazepines had shown that complexes were readily formed^{3,75-77}. In that case π -complexes of the type (70) were formed *via* attachment of an iron tricarbonyl moiety to the butadiene unit of the diazepine ring.

An important difference between the structures of the 3*H*- and 1*H*-1,2-diazepines is the presence of the former of an



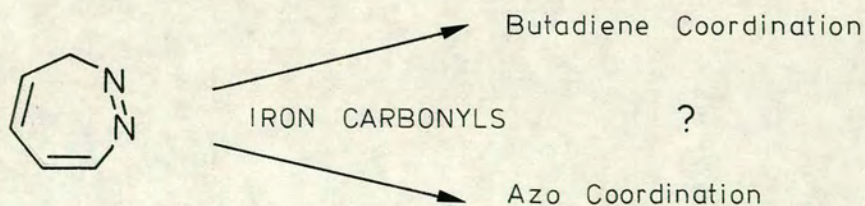
(70)

azo group. Azo groups are also known to react readily with iron carbonyls and give complexes of type (71) with novel tetrahedral Fe_2N_2 structures. Reactions of this type have been reviewed in section C of the introduction.



(71)

It was therefore interesting to see which reaction path the 3H-1,2-diazepines would follow (scheme 23).



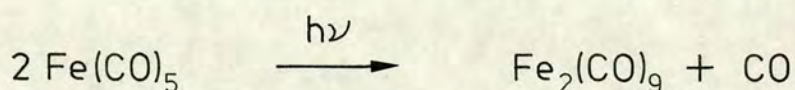
Scheme 23

2. Synthesis and Mechanism of Formation

The complexes were prepared by stirring a solution of the diazepine in benzene with diiron nonacarbonyl until inspection

by t.l.c. showed that the starting material had been consumed.

Diiron nonacarbonyl was chosen as the most convenient reagent since the other two possible carbonyls; iron pentacarbonyl and triiron dodecacarbonyl, are much less reactive and generally require prolonged reflux times and/or ultraviolet irradiation to bring about reaction. This can result in consequent low yields and mixtures of products with thermolabile and ultraviolet sensitive compounds. The diiron nonacarbonyl was prepared by the method of Braye and Hubel¹⁷⁷; by the photolysis of iron pentacarbonyl in acetic acid solution (scheme 24).

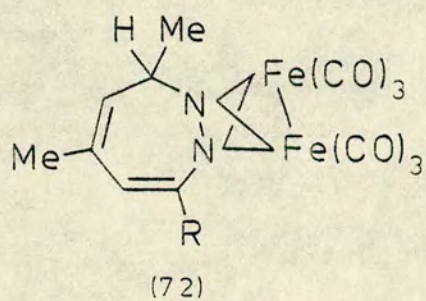


Scheme 24

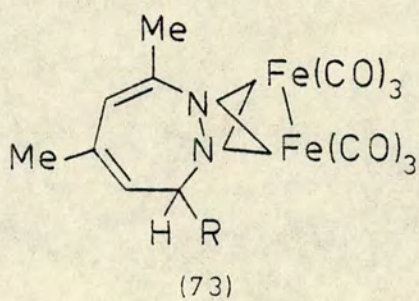
After reaction with the diazepine the reaction mixture was filtered to remove precipitated iron and then the complexes isolated by chromatography as air stable dark red crystalline solids. The complexes were all non-polar, eluting readily with hydrocarbon solvents and readily soluble in them.

The reactivity of 3*H*-1,2-diazepines with diiron nonacarbonyl was found to be quite different from the 1*H*-isomers. The organo-metallic interaction was with the azo group and gave complexes containing the tetrahedral Fe₂N₂ system, similar to those previously reported for some other azo compounds^{97,98}.

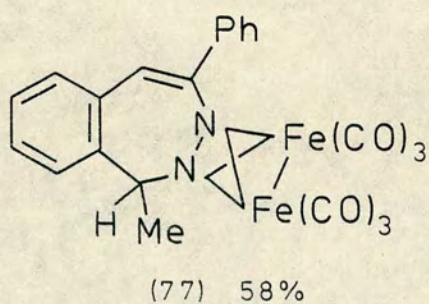
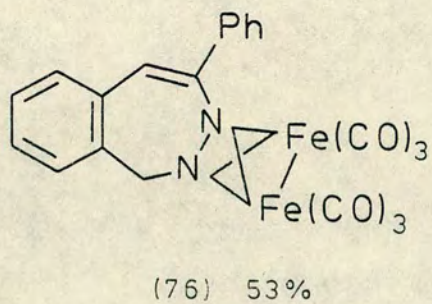
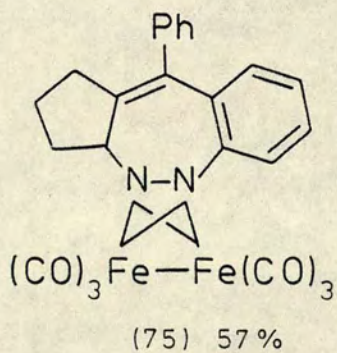
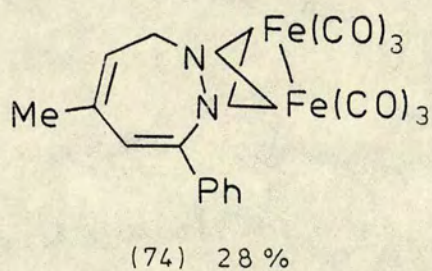
The complexes prepared together with yields are illustrated



+



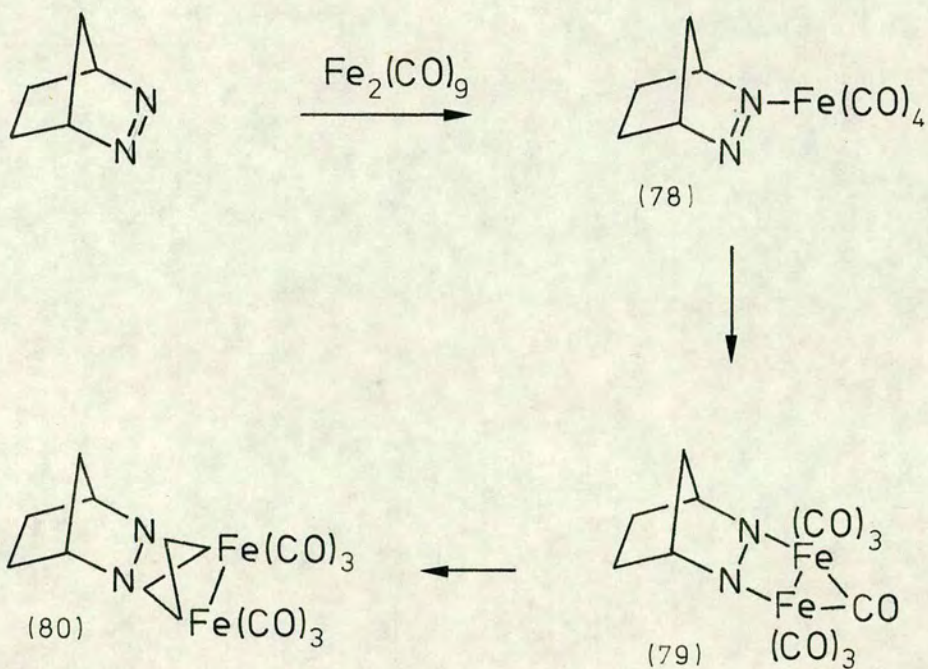
Compound	R	Yield %	Isomer Ratio (72) : (73)
a	H	31	~0 : >99
b	Et	46	60 : 40
c	<u>i</u> -Pr	57	88 : 12
d	CH ₂ CH ₂ Ph	38	72 : 28



in figures (72) to (77). Benzo-annelated diazepine complexes were also prepared in order to confirm the generality of the reaction and further examine the unusual ring inversion properties exhibited by these complexes (discussed in section B.3).

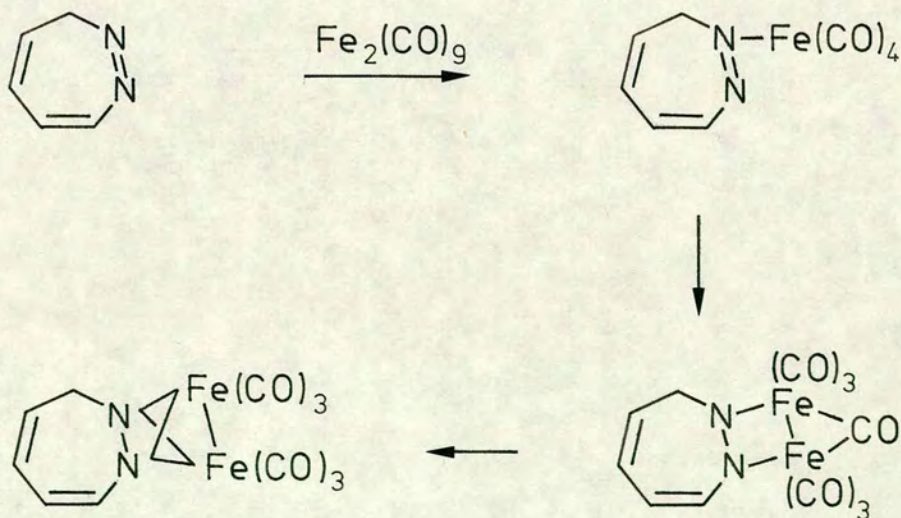
The yields from reaction with the benzodiazepines were all significantly higher than their monocyclic counterparts. An explanation for the lower yields from the monocyclic diazepines might be either that the monocyclic diazepine complexes react further with diiron nonacarbonyl to give unstable products, or the diene fragment of the diazepine also reacts with diiron nonacarbonyl but gives unstable products. The latter explanation seems to be the case since a further reaction of 5,7-dimethyl-3H-1,2-diazepine diiron hexacarbonyl complex with diiron nonacarbonyl gave no new products or evident decomposition.

Interestingly, during the synthesis of these diazepine complexes, a second slower moving purple band was detected in the crude reaction mixture by t.l.c. These compounds were however air unstable and never survived chromatography, despite attempts using degassed solvents and high eluant flow rates. It is possible that these compounds were intermediate complexes of the type that have sometimes been isolated during the synthesis of other azo complexes (see Introduction section C.2.1.1). For example during the preparation of the diazanorbornene diiron hexacarbonyl complex (80), the intermediate iron tetracarbonyl (78) and diiron heptacarbonyl (79) complexes were also identified⁹⁹⁻¹⁰¹ (scheme 25).



Scheme 25

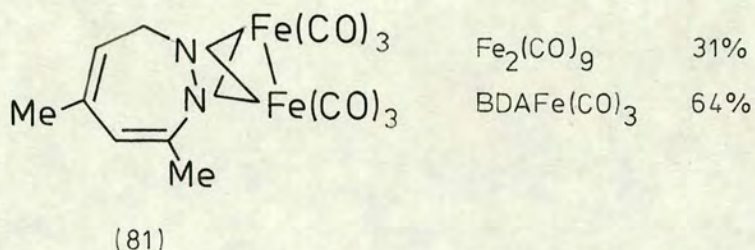
By analogy with this earlier work it seems likely that the mechanism of formation for the diazepine complexes follows the path shown in scheme 26.



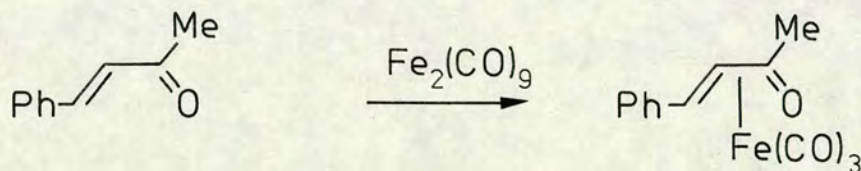
Scheme 26

The yield of monocyclic diazepine complex was much improved by the use of benzylideneacetone iron tricarbonyl as

an alternative reagent for the source of iron carbonyl. For example the yield of complex (81) was increased from 31 to 64% by the use of this reagent.



Benzylideneacetone iron tricarbonyl, prepared by the route shown in scheme 27, has been demonstrated to have synthetic utility as a mild, highly selective reagent for the transfer of the iron tricarbonyl moiety to dienes¹⁷⁸.



Scheme 27

Thus this reagent was also of interest in that it might have allowed alternative butadiene coordination to take place. However, reaction proceeded as before giving the azo-coordinated complex in improved yield.

3. Characterisation and structural assignment

The structures of the complexes; azo-coordination of the diazepine ring to the iron carbonyl residue, were formulated initially on the basis of spectroscopic measurement. This

formulation was subsequently confirmed when an X-ray crystal structure on one of the complexes was obtained.

Elemental analysis and mass spectra showed that all the complexes had the general formula $LFe_2C_6O_6$ where L was the diazepine formula. Mass spectra of the complexes all exhibited parent iron peaks corresponding to this formula. In each case fragmentation of the parent ion occurred *via* consecutive loss of six carbonyl groups yielding the ions LFe_2^+ . Further fragmentation by loss of HCN (LFe_2-27) and prominent signals due to Fe_2^+ (112) and Fe^+ (56) were also evident.

Infrared spectra showed that only terminal carbonyl stretching vibrations ($1900-2150\text{ cm}^{-1}$) were present, no absorptions in the double ($1750-1850\text{ cm}^{-1}$) or triple ($1620-1730\text{ cm}^{-1}$) bridging carbonyl regions were observed. The characteristic three band spectra of diene iron tricarbonyl complexes; a strong band at 2050 cm^{-1} and an intense doublet at 2000 cm^{-1} , were not observed. Instead a multiplet pattern in the $1950-2050\text{ cm}^{-1}$ region, similar to those reported for other azo coordinated complexes was observed^{127,105} (see introduction section C.2.4.2). Examination of the free diazepine and complex spectra in the (N=N) and (C=C) region showed, in cases where resolution permitted, that coordination resulted in the lowering of $150-200\text{ cm}^{-1}$ in the frequency of these bands. This can be interpreted as weaker ring bonding after complexation.

N.m.r. spectra of the complexes provided further evidence that the diazepine ring had remained intact upon complexation. Figures 15 and 16 illustrate the effect of complexation upon the n.m.r. spectra.

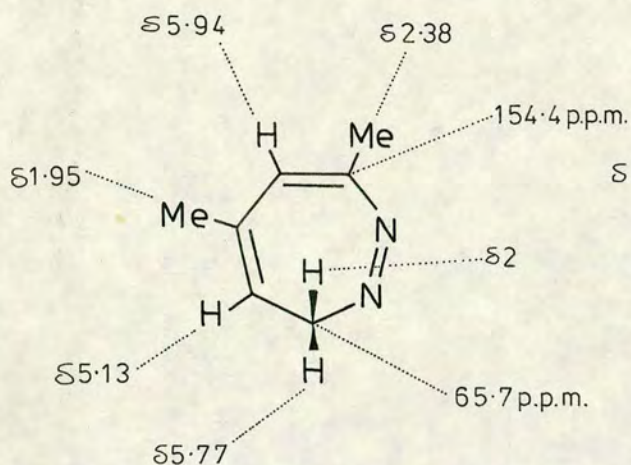


Figure 15

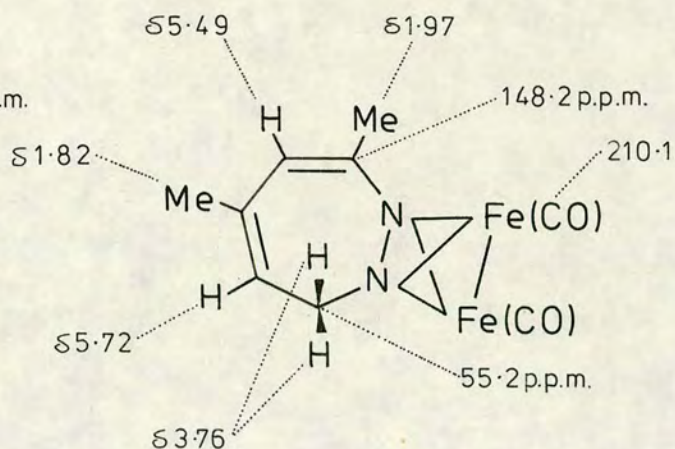


Figure 16

It was found that the essential features of the diazepine spectra were still present, for example the saturated C-3 carbon attached to the azo-group still possessed the characteristically strongly deshielded ^{13}C resonance, absorbing at 55.2 p.p.m. The proton spectra also possessed very similar resonances and splitting patterns confirming that the ring had survived.

The effect of complexation upon 3H-1,2-diazepine proton n.m.r. spectra should be contrasted with that observed for 1H-1,2-diazepine complexes. In these iron tricarbonyl diene coordinated complexes a pronounced shift to lower frequency was observed⁷⁶ (figures 17 and 18).

This shift to lower frequency was attributed to an increase in π -density at the carbon atoms bound to the metal. 179,180.

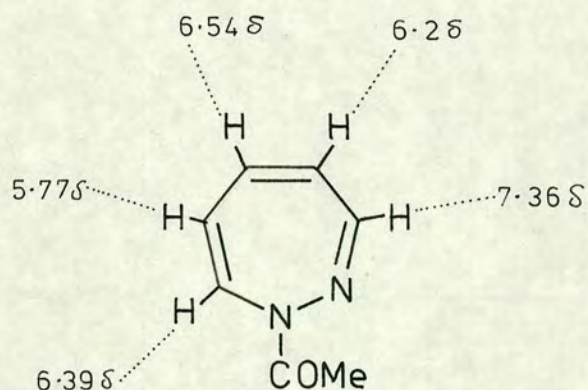


Figure 17

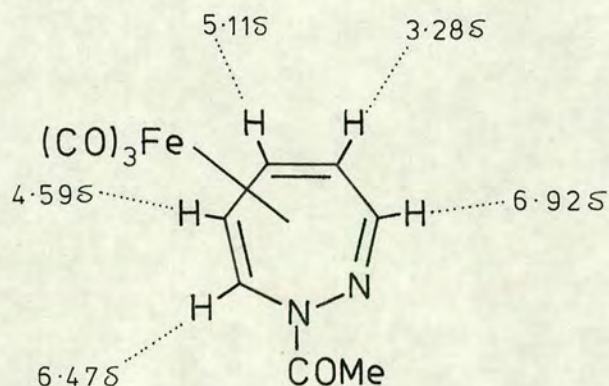
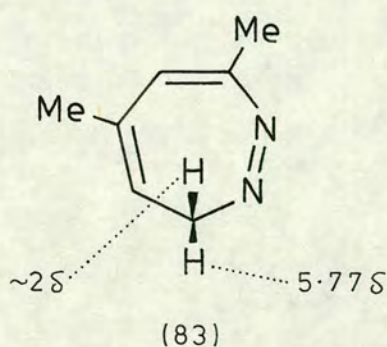
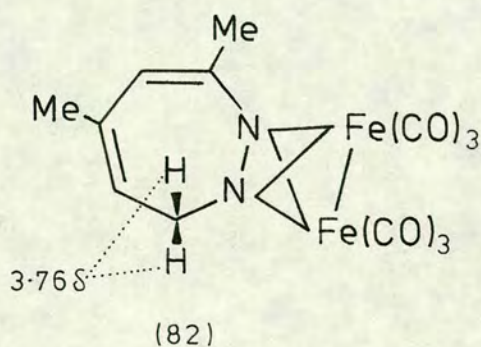


Figure 18

An interesting new feature of the proton n.m.r. spectra of the 3*H*-1,2-diazepine complexes was their temperature dependence for complexes which possessed a C-3 methylene unit. For example in the 5,7-dimethyl-3*H*-1,2-diazepine complex (82) the C-3 protons were now found to be equivalent and absorbed as a doublet at 3.76δ, with a coupling of 6Hz to the adjacent C-4 hydrogen.



In the free diazepine (83) these two protons absorb at widely differing positions, the pseudo equatorial proton, lying in the same plane as the azo group, is strongly deshielded and absorbs at 5.77δ. The pseudo axial proton is not similarly affected and absorbs in the expected aliphatic region at ~2δ.

Figure 19

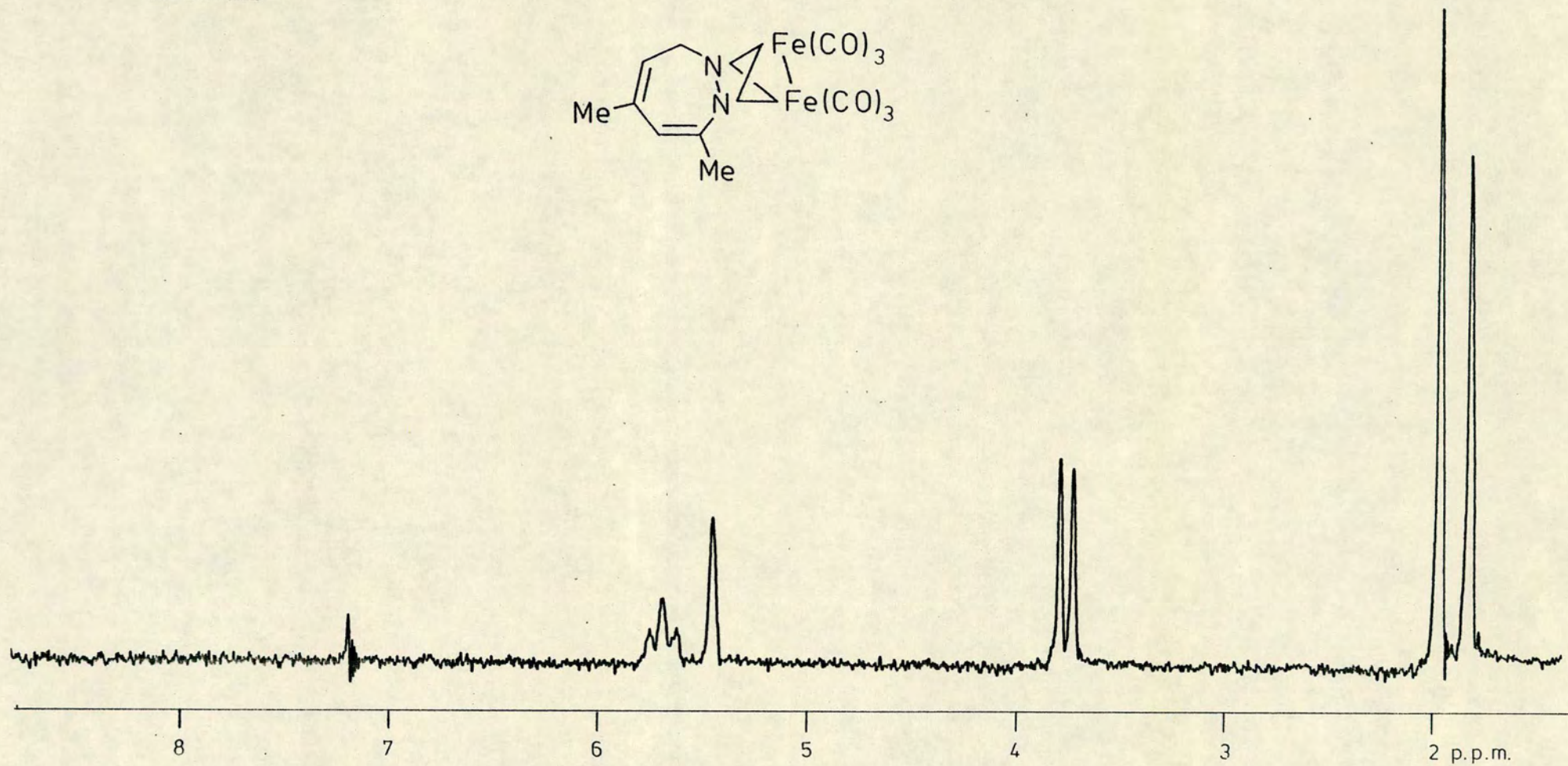
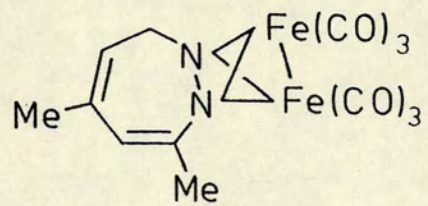
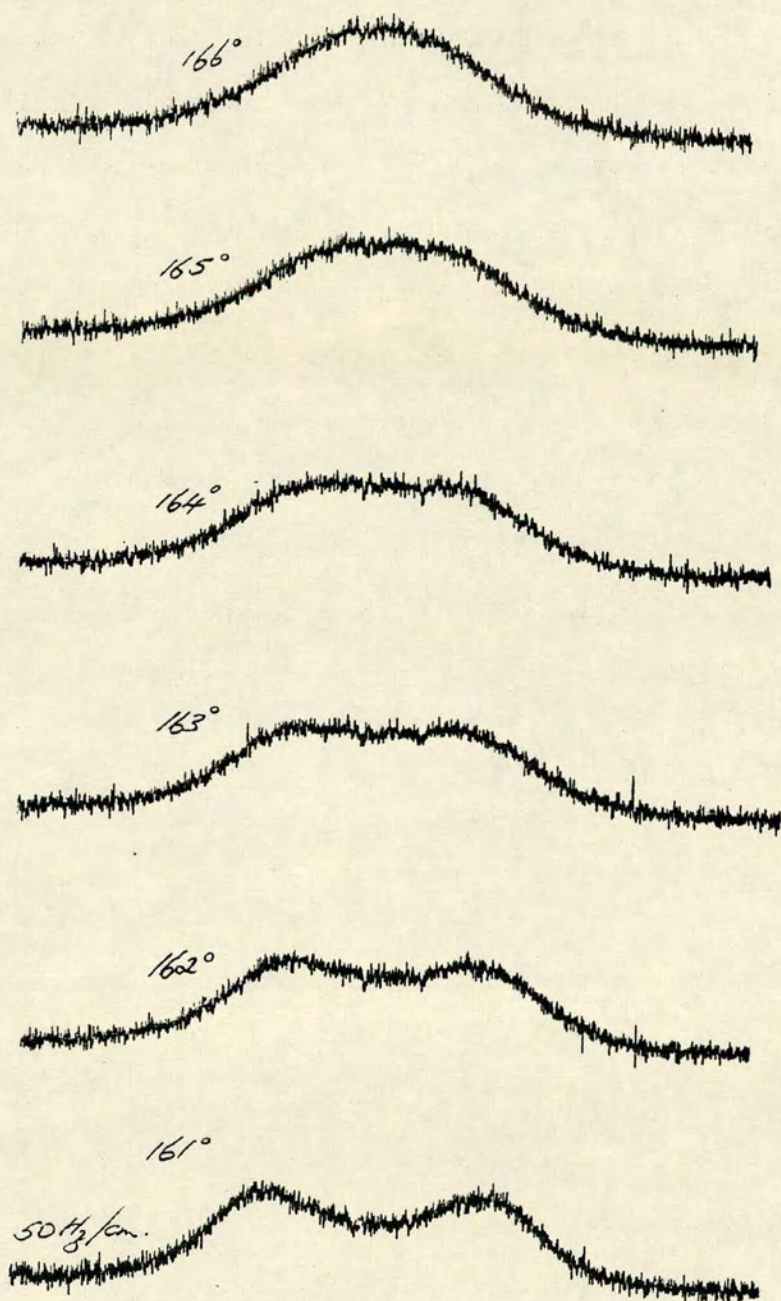
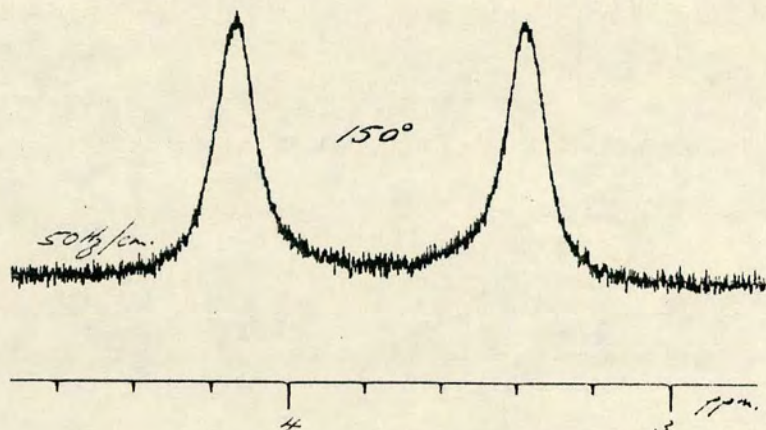


Figure 20 The variable temperature ^1H spectra of the methylene group of 5,7-dimethyl-3H-1,2-diazepine diiron hexacarbonyl complex

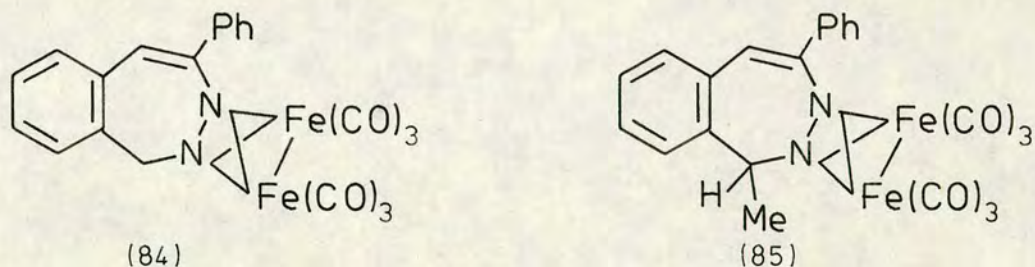


temperature $^\circ\text{Kelvin}$



The demonstration of the temperature dependence of the proton spectra of complex (82) was only possible by the use of a 360 MHz high field instrument and a powerful solvent with very low melting point, arcton CHBrClF . With this combination the coalescence at -109°C , and spectra of the boat conformer at -130°C , were obtained. Figures 19 and 20 reproduce the spectra obtained. The very facile ring inversion exhibited by this complex (82) is in marked contrast to the corresponding free diazepine (83); ring inversion of this compound is slow on the n.m.r. time scale even at $+130^\circ\text{C}$.

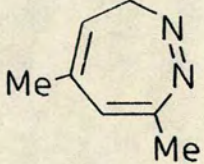
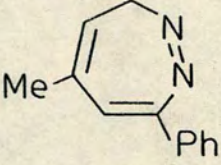
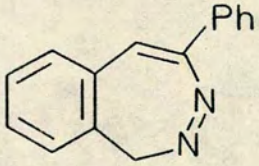
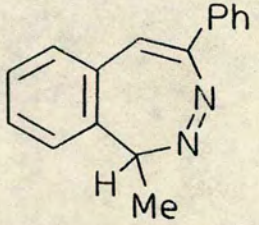
In order to further examine the unusual ring inversion properties exhibited by these complexes, the benzodiazepine diiron hexacarbonyl complexes (84) and (85) were prepared.



These complexes were interesting to study because the uncomplexed free benzodiazepines, unlike their monocyclic counterparts, did exhibit temperature dependent n.m.r. spectra⁶⁴.

The n.m.r. coalescence temperature (T_c) allows calculation of the free energies of activation for ring inversion (ΔG) from the well-developed theory of line broadening¹⁸¹. For the coalescence of an AB-type spectrum, the rate constant K_c of chemical exchange at the coalescence temperature T_c is given¹⁸² by:

Table 3: The n.m.r. coalescence temperatures and ΔG values for some diazepine compounds.

Compound	Diiron Hexacarbonyl Complex		Free Diazepine	
	Coalescence Temp. °C	ΔG K _J mol ⁻¹	Coalescence Temp. °C	ΔG K _J mol ⁻¹
 (86)	-109	30.6	>130	>77
 (87)	-105	31.4	>130	>77
 (88)	-54	44.2	102	72
 (89)	Locked Conformation	-	Locked conformation	-

$$K_c = \pi (\Delta\nu_{AB}^2 + 6J_{AB}^2)^{1/2} / \sqrt{2}$$

where J_{AB} is the coupling constant in Hz between the nuclei A and B. The rate constant of isomerisation is related to ΔG in accordance with the Eyring equation:

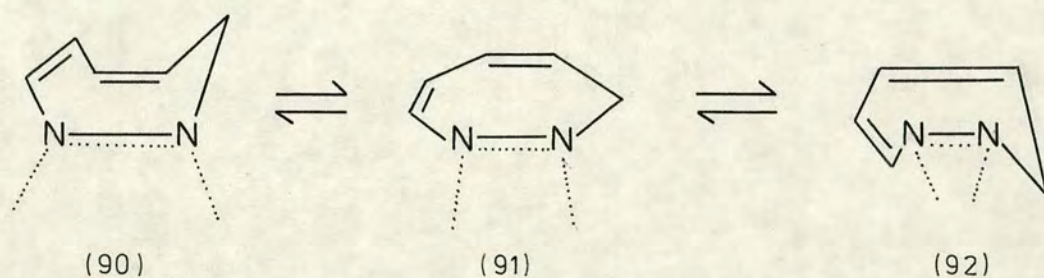
$$K_c = \frac{k_b T_c}{h} e^{-\Delta G / RT_c}$$

k_b = Boltzmann const.
 R = gas const.
 T_c = coalescence temp.
 h = Plank const.

Thus, a value of ΔG can be obtained with high accuracy, since this is dependent on T_c , which can be measured very accurately. The n.m.r. coalescence temperatures and ΔG values for the diazepine diiron hexacarbonyl complexes, together with data for the corresponding free diazepines, are presented in table 3.

An examination of this data showed that complexation of the monocyclic diazepines (86) and (87) had reduced the barrier to ring inversion by at least 45Kj mol^{-1} . Ring inversion for these monocyclic diazepine complexes was now more facile than for the complex counterpart (88). This was a reversal of the situation observed for the uncomplexed ring systems, where the monocyclic diazepine ring inversion was still slow on the n.m.r. time scale at $+130^\circ\text{C}$.

An explanation for the more facile ring inversion of the diazepine iron carbonyl adducts can be provided by an examination of the various conformers involved in the ring inversion. The diazepine ring, whether free or complexed, will normally adopt a puckered boat conformation of the type (90). When undergoing ring inversion the seven membered ring must go through the planar intermediate (91) before passing onto the inverted puckered boat conformer (92).



The angles α and β , which describe the puckering of the ring, will also provide a measure of how far the ring is from the planar ring-inversion intermediate. A comparison of these angles for the free and complexed diazepine structures is informative (figure 21).

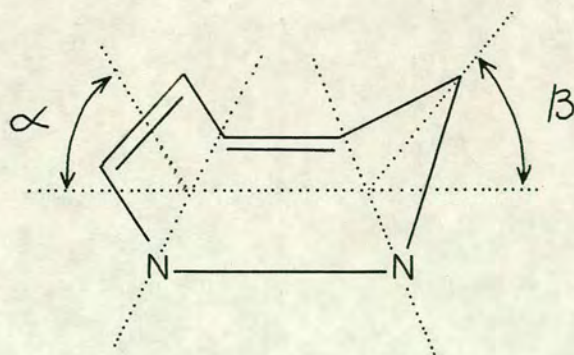
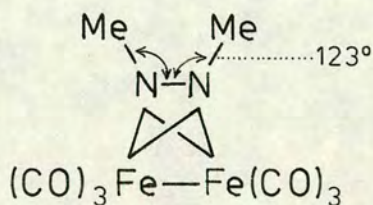


Figure 21

Diazepine Ring	α	β
Free	35°	58°
Complexed	27°	43°

These angle measurements were obtained from the crystal structures of 1-methyl-4-phenyl-1*H*-2,3-benzodiazepine¹⁸³ and 5,7-dimethyl-3*H*-1,2-diazepine diiron hexacarbonyl complex¹⁸⁴. It was found that the complexed diazepine ring adopts a flatter boat conformation than the free diazepine ring, and is therefore closer to the planar ring-conversion intermediate. This flattening of the diazepine ring in the iron carbonyl complex is caused by the larger angle requirement of the diaza-linkage. In the iron carbonyl complex of azo-methane (93)⁹⁷, which is free of any distortions, the angles at nitrogen are 123° .

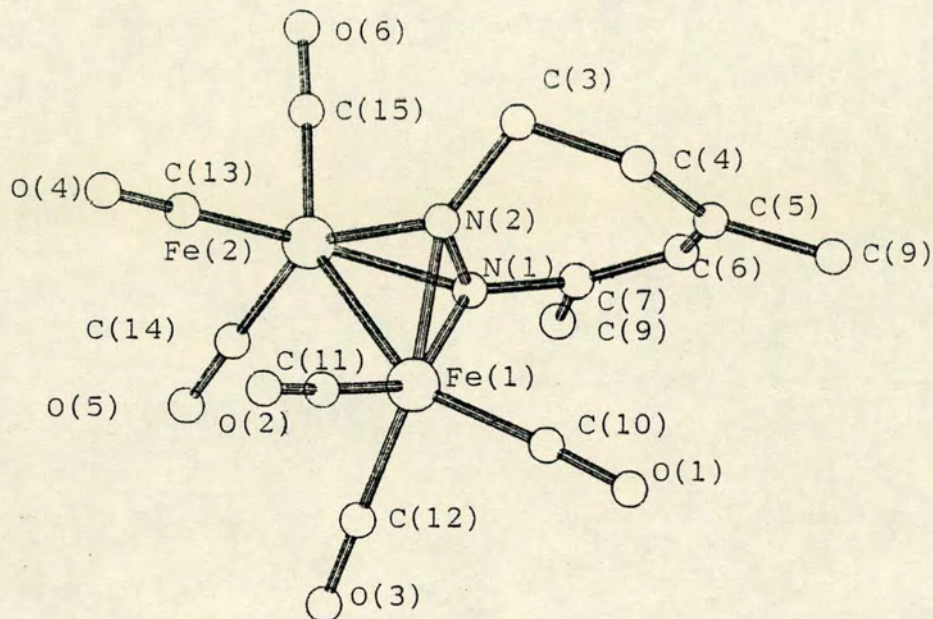


(93)

The ring in the diazepine iron carbonyl complex therefore flattens to accommodate this larger angle requirement. Because of this ring flattening the complexed diazepine ring might therefore be expected to attain the geometry for ring inversion more easily.

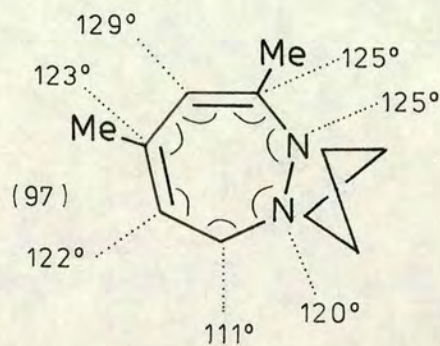
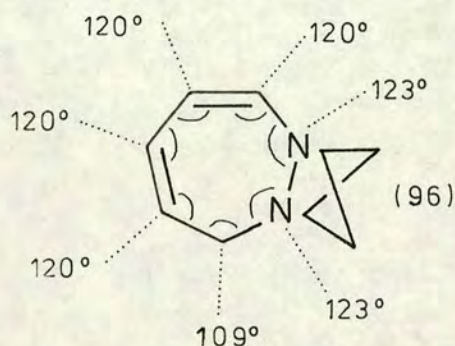
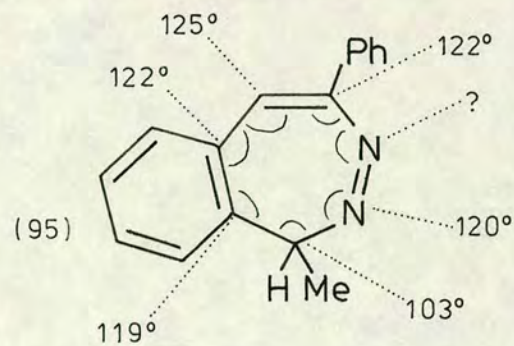
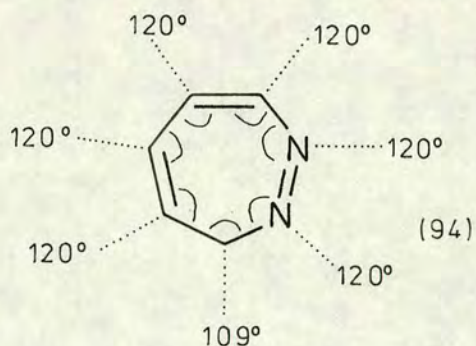
An examination of the change in angle strain in moving from the puckered to planar ring geometries is also informative.

Figure 22 The Crystal Structure of 5,7-Dimethyl-3H-1,2-diazepine diiron hexacarbonyl complex.



<u>Bond Lengths</u> (Å)			
Fe(1)-Fe(2)	2.498(1)	C(10)-O(1)	1.144(5)
Fe(1)-N(1)	1.920(2)	C(11)-O(2)	1.137(5)
Fe(1)-N(2)	1.902(2)	C(12)-O(3)	1.135(4)
Fe(2)-N(1)	1.898(3)	C(13)-O(4)	1.142(5)
Fe(2)-N(2)	1.904(3)	C(14)-O(5)	1.128(5)
		C(15)-O(6)	1.133(5)
Fe(1)-C(10)	1.807(4)	N(1)-N(2)	1.398(3)
Fe(1)-C(11)	1.797(4)	N(1)-C(7)	1.420(5)
Fe(1)-C(12)	1.797(3)	C(7)-C(8)	1.502(6)
Fe(2)-C(13)	1.789(4)	C(7)-C(6)	1.331(6)
Fe(2)-C(14)	1.804(4)	C(6)-C(5)	1.464(5)
Fe(2)-C(15)	1.799(4)	C(5)-C(9)	1.508(8)
		C(5)-C(4)	1.323(6)
		C(4)-C(3)	1.507(6)
		C(3)-N(2)	1.463(4)

Figures (94) to (97) illustrate the idealised and experimentally measured ring angles for the puckered diazepine rings.



The ring angles in the planar ring-inversion intermediate will be $\sim 129^\circ$; thus ring inversion for the complexed diazepine ring will involve a smaller increase in angle strain than that for the diazepine itself and consequently would be expected to undergo ring inversion more easily.

Conformation of the structural assignment of these diazepine iron carbonyl complexes was provided when a crystal structure on the 5,7-dimethyl-3*H*-1,2-diazepine diiron hexacarbonyl complex was obtained. Figure 22 reproduces the crystal structure elucidated by Gould and Walkinshaw¹⁸⁴.

The crystal structure confirmed that both iron atoms had six-fold coordination, each iron atom was bonded to three carbonyl groups with an average Fe-C distance of 1.80 Å. The four Fe-N bonds (1.91 Å), the Fe-Fe bond (2.50 Å) and the N-N bond (1.40 Å) formed a distorted tetrahedron. The carbonyl C-O bonds all had a similar length of 1.14 Å. The

Fe-C-O bond angles were close to linear with an average value of 178° . The two iron atoms showed nearly identical coordination geometry and sat at the apices of two distorted tetrahedron: one with the three carbonyl groups, and the other the shared Fe_2N_2 tetrahedron. The internal angles at the Fe atoms in the Fe_2N_2 tetrahedron were narrow at 47° compared to the wider C-Fe-C angles of the carbonyl tetrahedra of 97° .

All bond lengths and angles in the seven membered were within the expected ranges and confirmed the structure of the 3*H*-1,2-diazepine ring system.

The seven membered ring was found to be in a flattened boat conformation (figure 23).

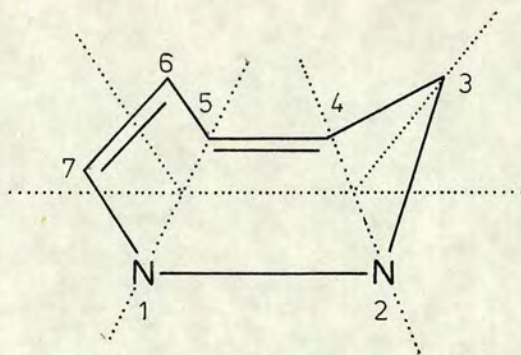


Figure 23

Pseudo-mirror symmetry was observed across the plane lying along the line between C-3 and the midpoint of C-7/C-6 double bond and perpendicular to the line between N-1 and C-5.

The unusual bonding arrangement present in these organo-metallic complexes is worthy of comment. A general characteristic of the d group transition metals is their ability to form complexes with a wide variety of ligands. An uncoordinated transition metal atom will form complexes to complete its normal coordination requirement, ie it will seek to attain the outer

electron configuration of the succeeding noble-gas atom.

In the case of iron its outer electron configuration is $4s^2, 3d^6$ and thus requires a further $10e$ to obtain the noble-gas formalism .

The ligands which provide these extra electrons are of two types; "classical" and π -acceptor.

Examples of "classical" ligands are halide ions F^- , Cl^- , Br^- , I^- , the anions of various oxo acids, such as NO_3^- , NO_2^- , RCO_2^- , SO_4^{2-} and neutral molecules in which the donor atoms are usually N or O, examples being NH_3 , RNH_2 , H_2O , $MeOH$ and R_3PO . These ligands all donate an electron pair to the metal atom.

The nitrogen atom can serve as the donor atom in a wide variety of ligands, some of which are shown in figure 24.

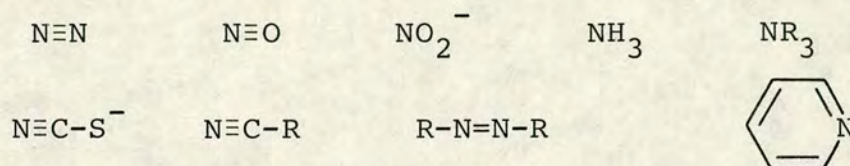
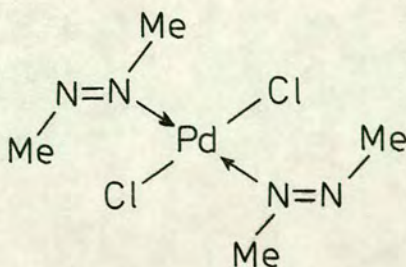


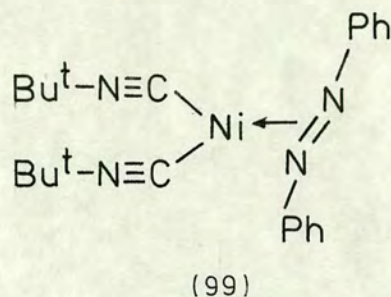
Figure 24

Azo compounds, which have both σ and π electrons available, can serve as a donor ligand in a variety of ways (see Introduction section C). Characteristically they use their σ lone pairs for donation, as in (98)¹⁸⁵.

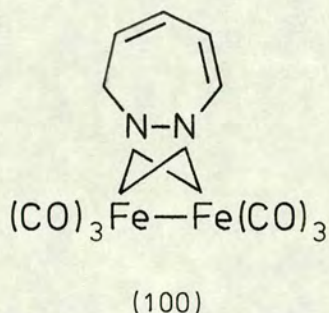


(98)

Coordinating through the π electrons has also been reported¹⁸⁶, compound (99) serves as an example.



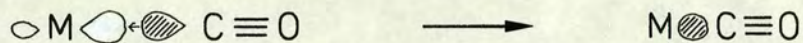
In the 3*H*-1,2-diazepine complexes (100) the azo group is behaving as a donor of six electrons, three to each iron atom.



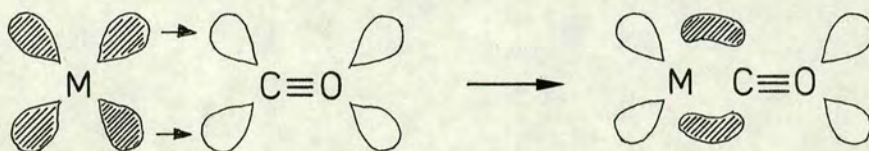
The second type of ligand, the π -acceptors, are molecules which possess delocalized π orbitals. These vacant orbitals accept electron density from filled metal orbitals to form a type of π bonding that supplements the σ bonding arising from lone-pair donation. The high electron density on the metal atom can thus be delocalized onto the ligand.

Examples of π -acceptor ligands are PPX_3 , CN , unsaturated hydrocarbons and the most important example; carbon monoxide.

The molecular orbital description of the bonding between a transition metal atom and a carbonyl group is illustrated in figure 25.



The formation of the carbon to metal σ bond using the unshared electron pair on the C atom.



Formation of the metal to carbon π bond by interaction of the filled metal d orbital with the vacant π^* carbonyl orbital.

Figure 25

An examination of the electron configuration around each iron atom in the complexes shows that 6e are supplied from the three carbonyl groups, 1e from the Fe-Fe bond, and 3e from the azo group, making the total 10e required to achieve the noble-gas arrangement.

4. The Effect of Complex Formation upon the 3H-1,2-diazepine rearrangement by [1,5] sigmatropic hydrogen migration

In most cases where the diazepine existed as an equilibrium mixture of rapidly interconverting isomers (101) and (102), both were converted to the corresponding iron carbonyl complexes (103) and (104).

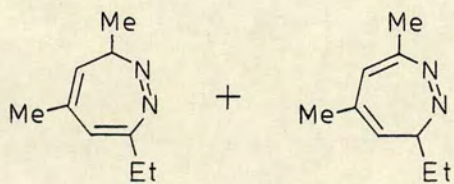


Figure 26

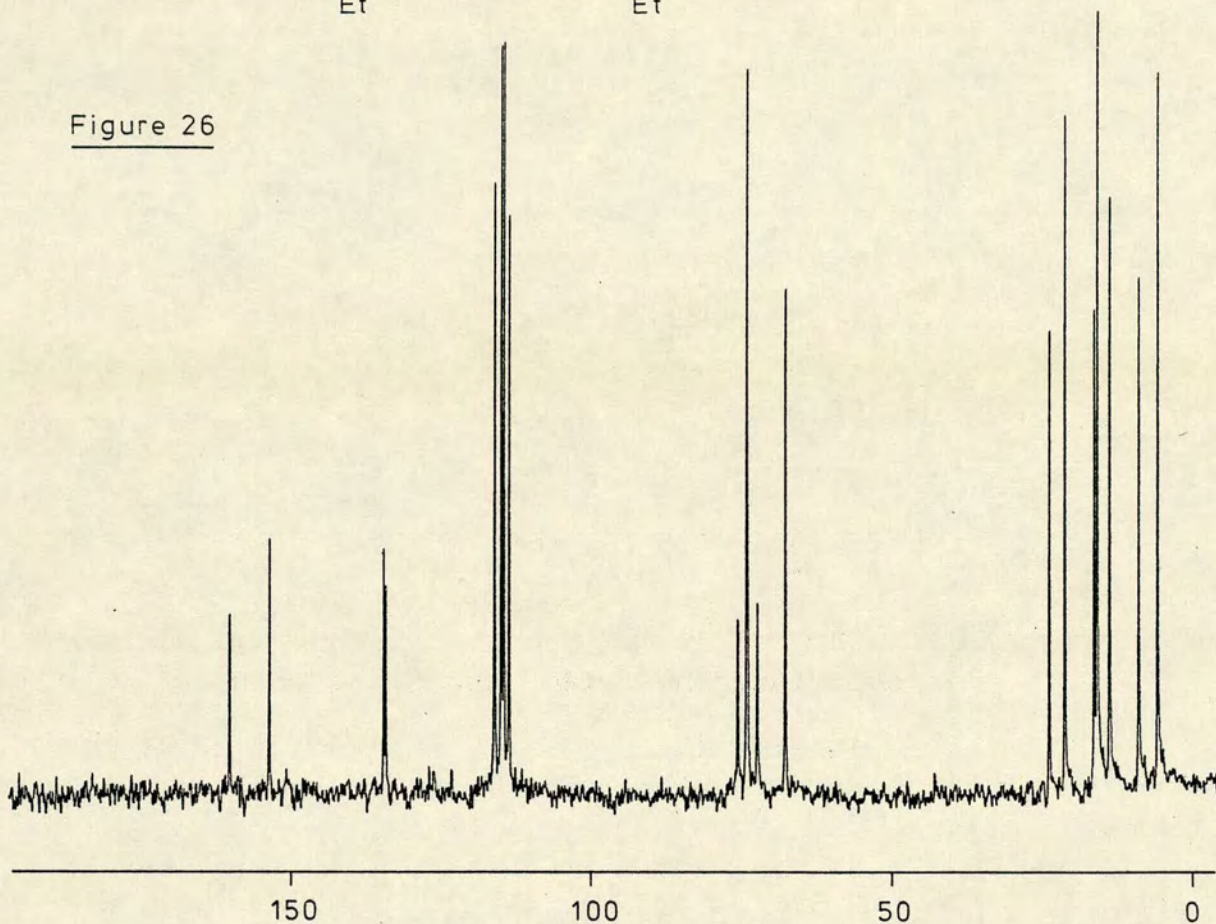
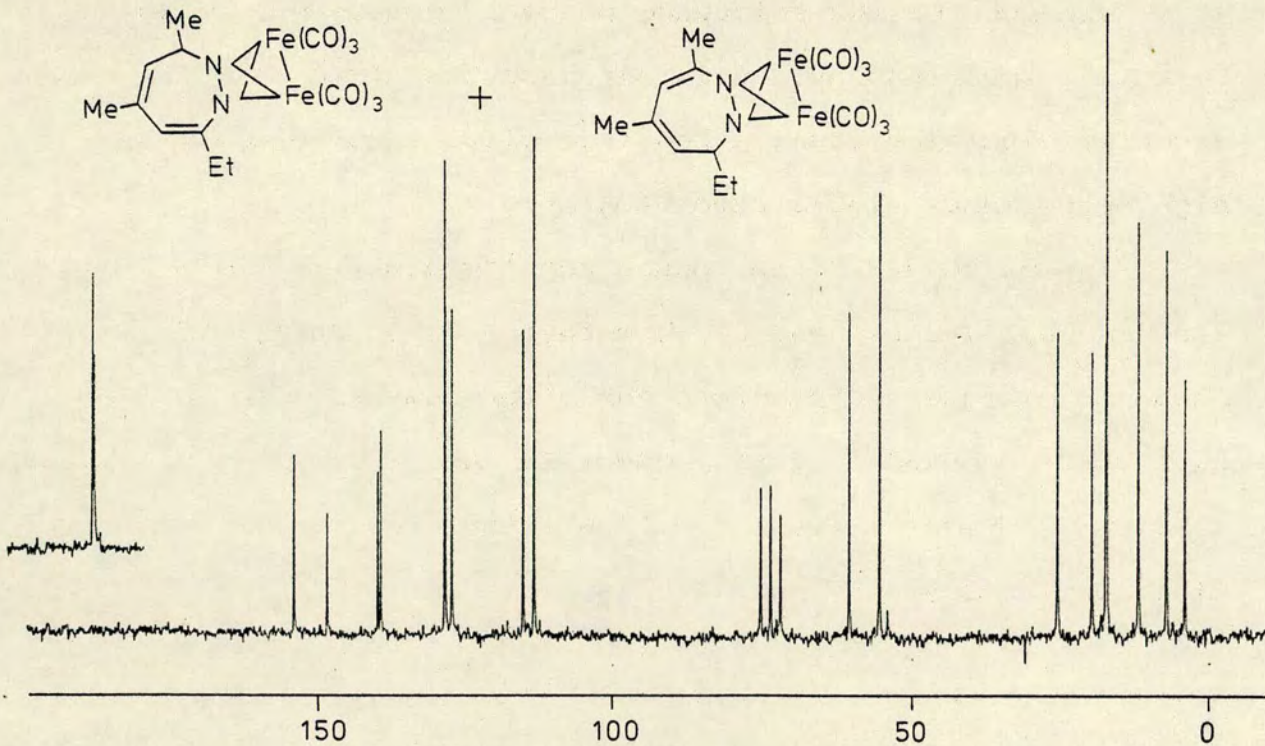
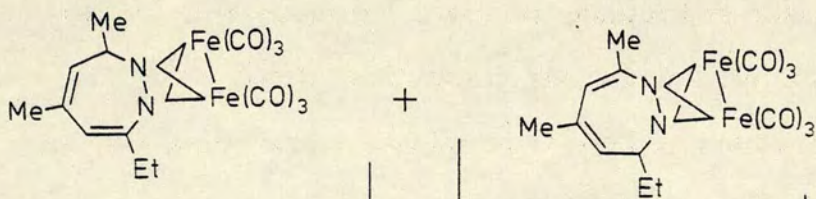
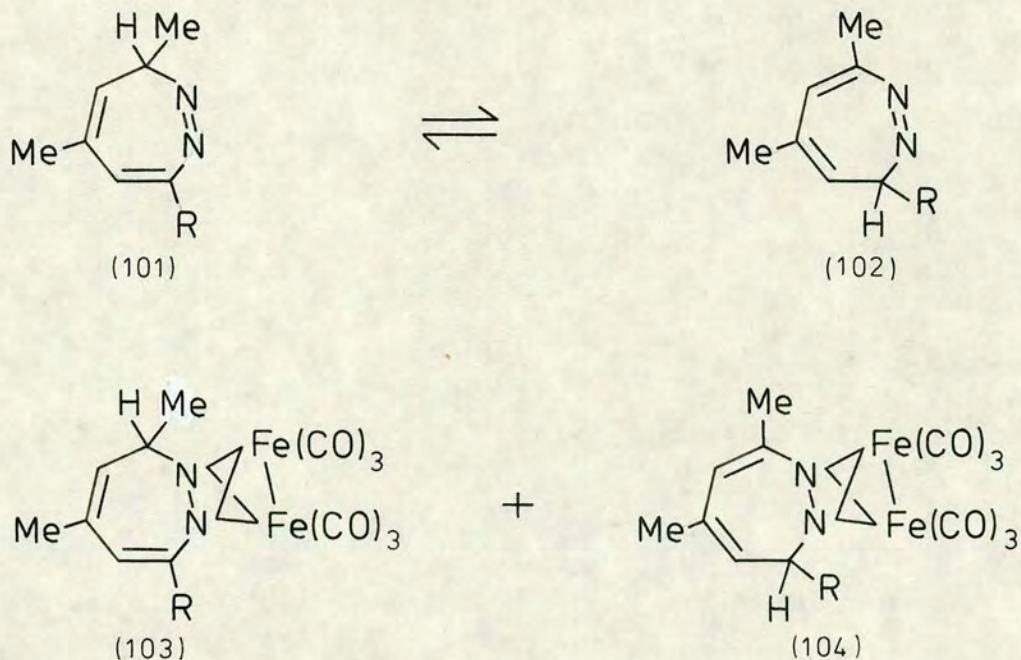


Figure 27



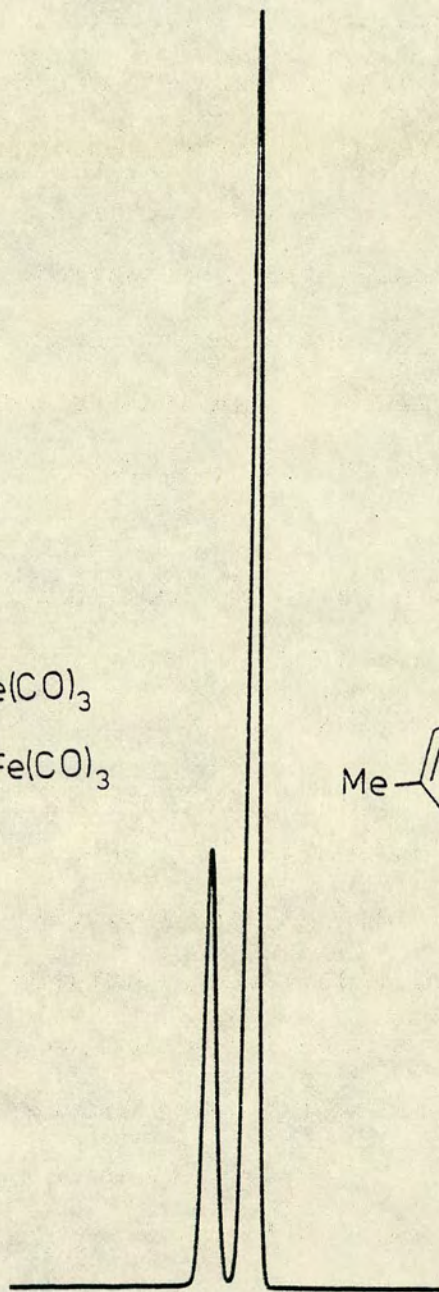
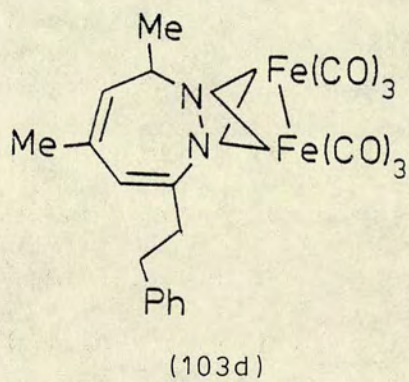
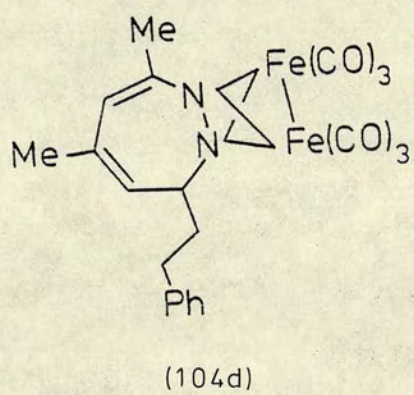


R	Free Diazepine Ratio (101) : (102)	Complexed Diazepine Ratio (103) : (104)
a) H	15 : 85	~0 : >99
b) Et	52 : 48	60 : 40
c) i-Pr	34 : 66	88 : 12
d) CH ₂ CH ₂ Ph	49 : 51	72 : 28

Evidence for the existence of both isomers was provided by n.m.r. spectroscopy and in one case the mixture of the two isomeric diazepine iron carbonyl complexes was resolved by high performance liquid chromatography.

Figures 26 and 27 reproduce the ¹³C n.m.r. spectra for the 3,5-dimethyl-7-ethyl and 5,7-dimethyl-3-ethyl 3*H*-1,2-diazepine isomeric mixture, both before and after complexation. The duplicate resonances still present in the iron carbonyl complex spectrum provide convincing evidence that two isomeric diazepine complexes are present.

Figure 28



High field proton n.m.r. spectra enabled clear identification of all the expected resonances present in the two isomeric diazepine complexes. This was conclusively demonstrated when small samples of the individual complex isomers (103d) and (104d) were obtained by h.p.l.c.

Figure 28 reproduces the analytical chromatogram of the separation. It is interesting to consider why resolution of the mixture of two isomeric complexes only occurred in this case, whereas in the other two mixtures; (103b)/(104b) and (103c)/(104b), no resolution was possible. It seems likely that the longer alkyl substitution present in this case; the phenethyl substituent, proved more satisfactory in binding to the silica surface and thus allowing a chromatographic separation.

Preparative samples of the two isomeric complexes (103d) and (104d) were obtained by 25 injections down the column with the eluant collected in a micro scale fraction collector. The fractions were tested for purity by repeat h.p.l.c. and suitably pure samples combined. After solvent removal under reduced pressure, 6 and 2 mg respectively of the individual complexes (103d) and (104d) were isolated.

This quantity of material proved more than adequate to obtain ^1H n.m.r. spectra (360 MHz Fourier transform instrument), and the assignments of the spectra were thus confirmed. Figures 29 and 30 show the ^1H n.m.r. resonances of the individual complexes.

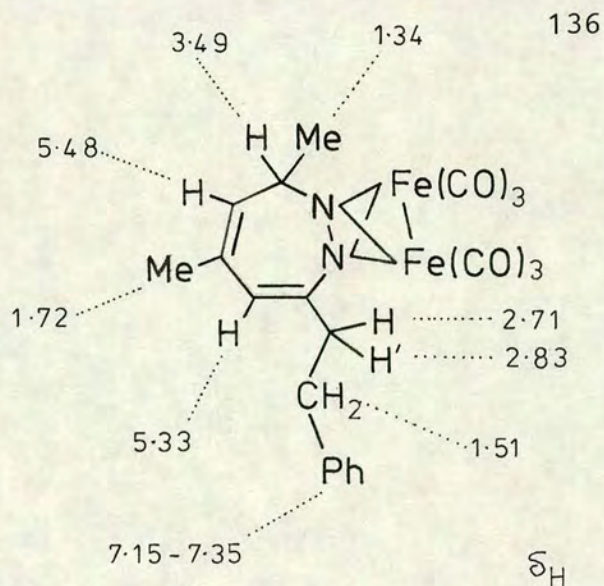


Figure 29

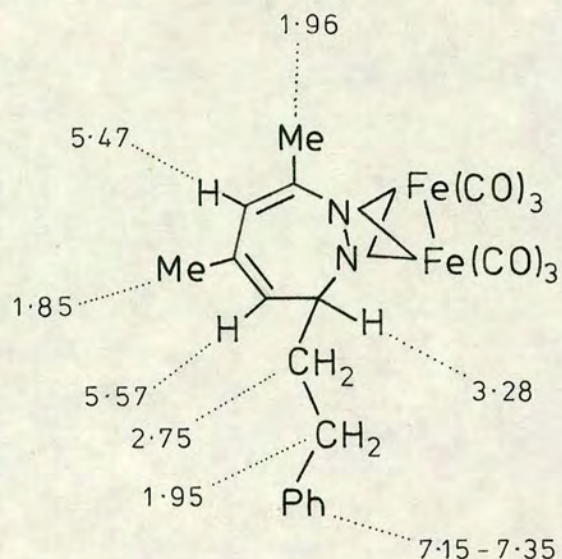


Figure 30

It was evident from the h.p.l.c. separation that complexation of the diazepines had inhibited the rapid [1,5] sigmatropic hydrogen migration which interconverted the two free diazepine isomers. To test if the sigmatropic migration could be regenerated at higher temperatures, a series of thermolysis experiments on the separated complexes (103d) and (104d) were carried out. These experiments were monitored by h.p.l.c. which would detect any appearance of the other possible isomer. It was found that up to 110° no interconversion was observed, at temperatures beyond this value decomposition occurred.

It seems likely that two factors are responsible for the inhibition of the sigmatropic migration, firstly steric; an examination of the crystallographic data for the free¹⁸³ and complexed¹⁸⁴ diazepines showed that the distance of approach between the migration centres C_3/C_7 was larger in the case of the complex (Table 4).

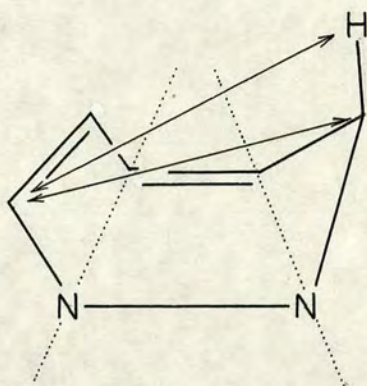


Table 4: The distance between migration centres in 3H-1,2-diazepine and its iron carbonyl complex

Compound	Distance between migration centres Å	
	carbon-carbon	carbon-hydrogen
free diazepine	2.78	2.75
iron carbonyl complex	2.95	2.86

The second factor which would inhibit the sigmatropic migration is the electron withdrawing effect of the diaza-linkage. We have earlier argued that the electron withdrawing nature of the azo group must be largely responsible for the considerable rate enhancement of the migration compared with cycloheptatriene (see discussion section A). An examination of ^{13}C n.m.r. shifts of the carbon atoms adjacent to the diaza-linkage gives a measure of the electron withdrawing strength of that unit. Figures 31 and 32 clearly show that the diaza-linkage of the complex is less electron withdrawing than in the free ring system.

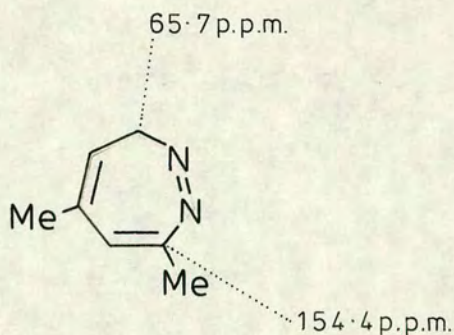


Figure 31

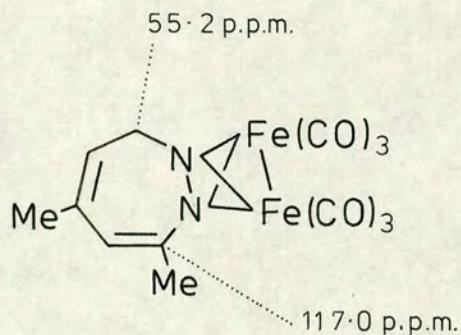
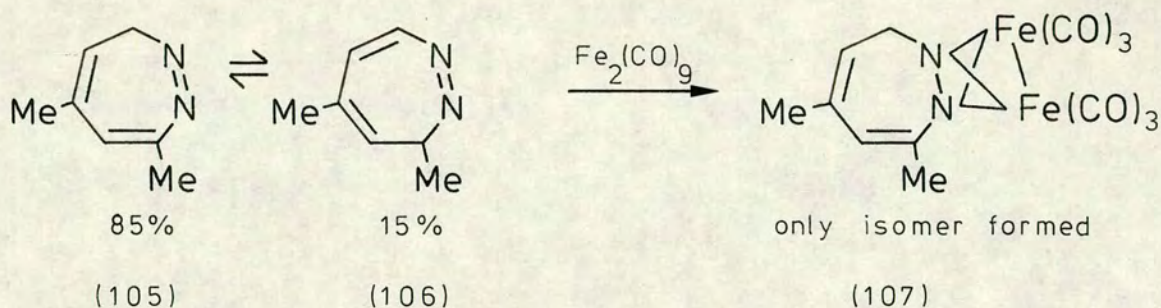


Figure 32

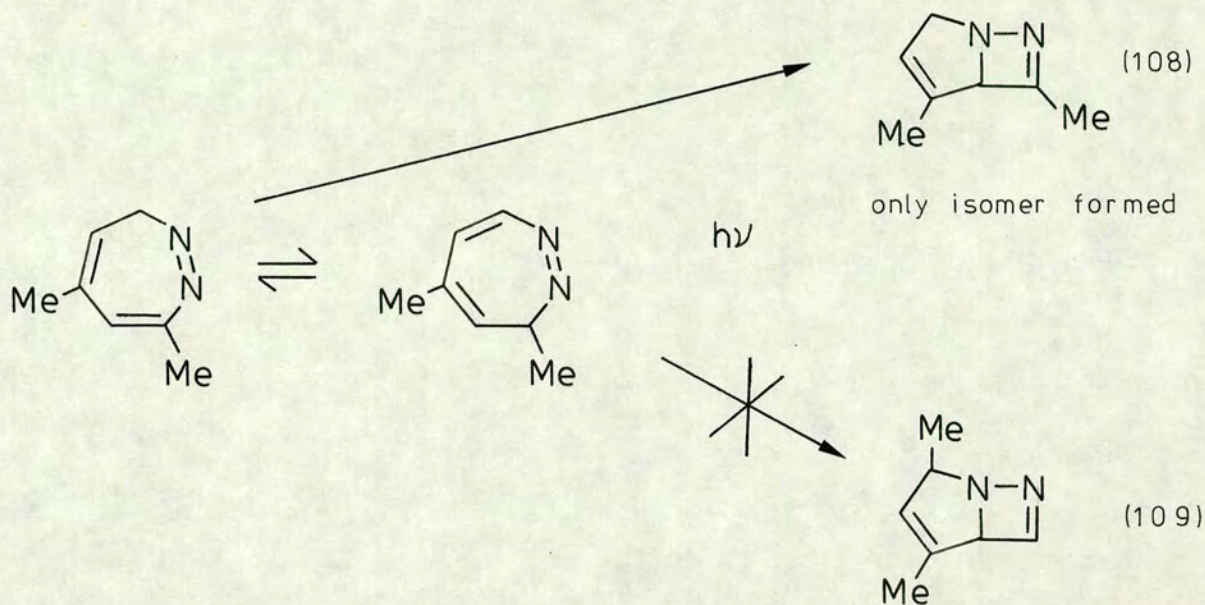
In the case of the dimethyl substituted diazepine mixtures, (105) and (106) only one complex (107) was isolated (scheme 28).



Scheme 28

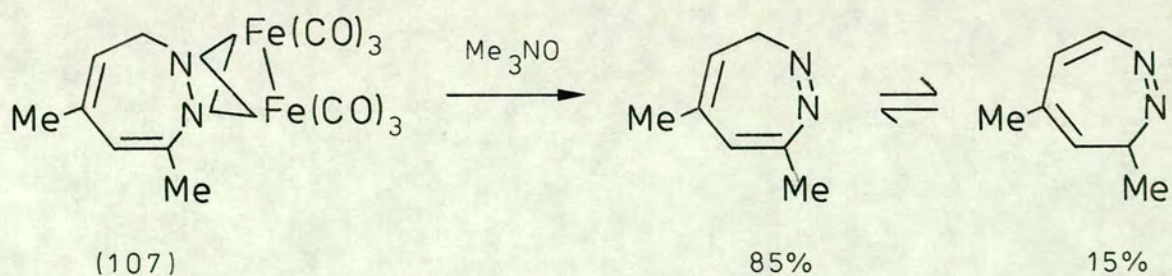
No evidence for the other possible isomer was found despite careful inspection of the crude and purified product by n.m.r. and h.p.l.c. It appears that the diazepine isomer (106) is at least 3x less reactive than its isomer (105). This type of behaviour has also been observed during the photolysis reaction of this diazepine mixture. For example when this

mixture was irradiated, only the photo-adduct (108) was isolated, none of the other possible isomer (109) was detected (scheme 29).



Scheme 29

The dimethyl substituted diazepine complex (107) was successfully disengaged using Shvo's technique⁸¹, this involves mild oxidation with trimethylamine N-oxide (scheme 30).



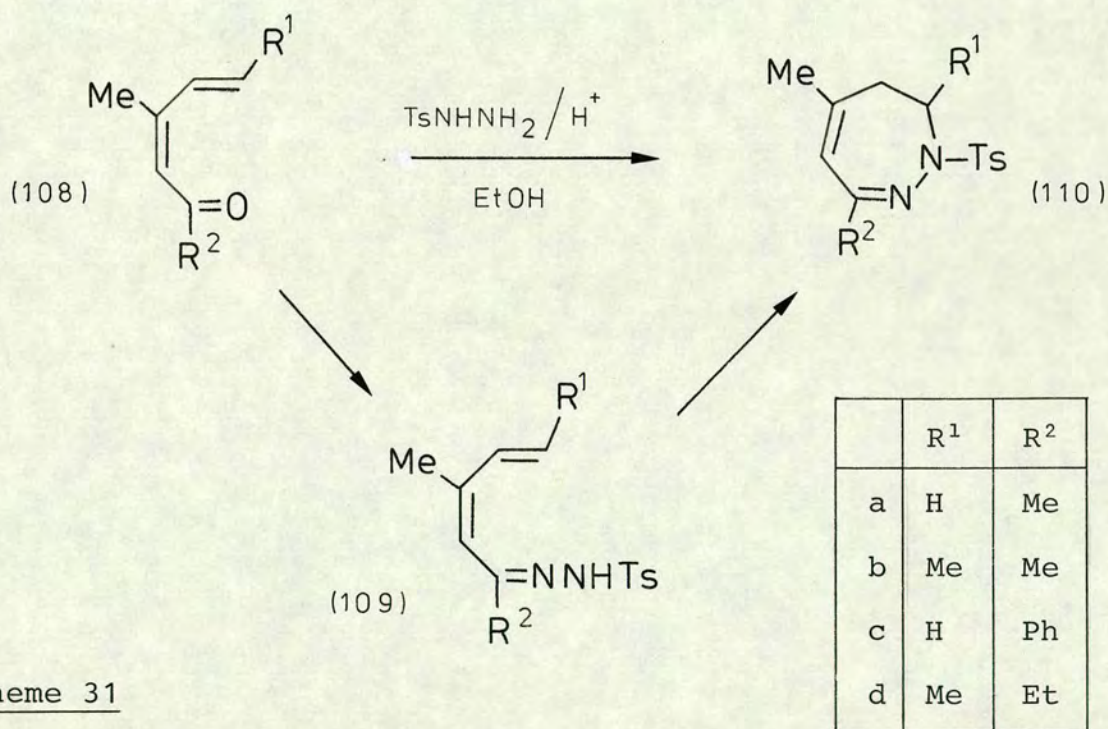
Scheme 30

Significantly, disengagement of this complex at room temperature resulted in the formation of the two isomeric diazepines. This result provides further evidence for the isomer interconversion.

C. Reactions of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds with hydrazines

1. Introduction

The cyclisation reaction to give 2-substituted 3,4-dihydro-1,2-diazepines (110) was discovered when dienones of the type (108) were reacted with tosylhydrazine³³ (scheme 31).

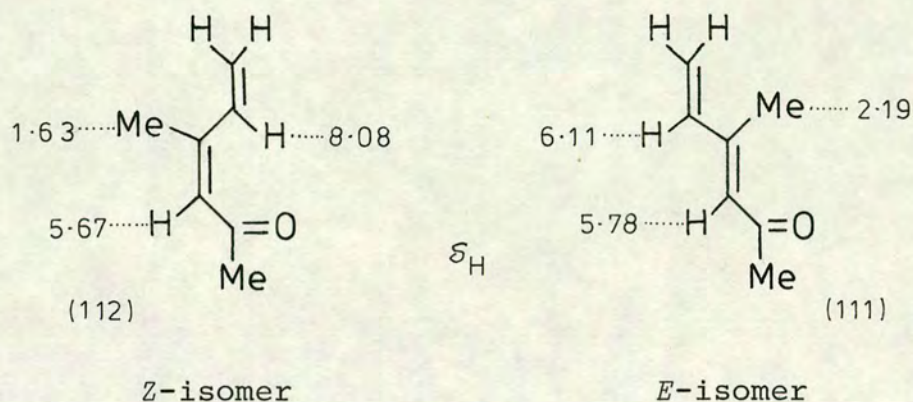


Scheme 31

It was found that these dienones were not converted into the expected tosylhydrazones (109), but rather reacted under acid conditions in ethanol to give the 2-tosyl-3,4-dihydro-1,2-diazepines (110) in yields of 55-77%.

It was noted that both the *E* and *Z* dienones reacted to give diazepines. For example the dienone (108a) had an *E* (111) to *Z* (112) ratio of *ca.* 2.2:1, based on the integral

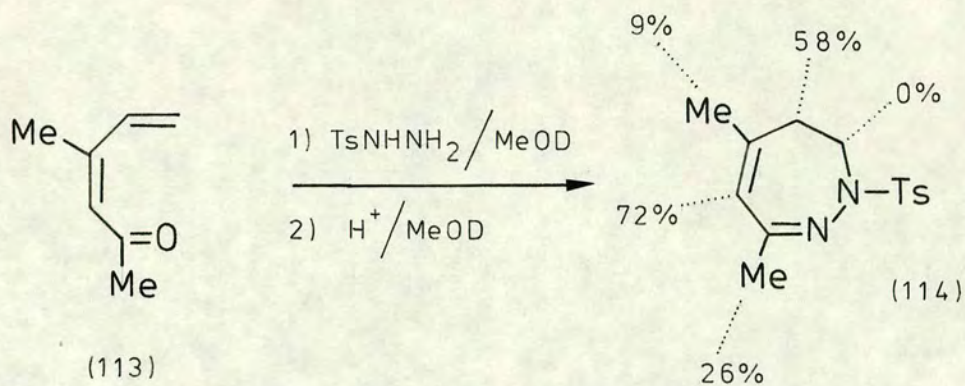
of its ^1H n.m.r. spectrum and gave 69% of the 2-tosyldiazepine.



The tosylhydrazones (109) were demonstrated to be intermediates in the cyclisation reaction by carrying out the reaction of dienone (108a) with tosylhydrazide in the absence of acid. This gave mainly the tosylhydrazone (109a) (mixed *E*- and *Z*-isomers) together with a little (13%) of the diazepine (110a). The tosylhydrazone, dissolved in ethanol could be rapidly converted into the diazepine by the addition of little acid. Thus there appeared to be two mechanisms for diazepine formation: a slow cyclisation of the *Z*-isomer which occurred in the absence of acid, and a fast acid-catalysed reaction in which protonation of the tosylhydrazone allowed *E*→*Z* conversion before ring closure.

Further information about the mechanism of this cyclisation reaction was provided by deuterium incorporation experiments. The cyclisation of (113) with tosylhydrazine in deuteriomethanol was carried out in the presence and absence of acid. (Scheme 32).

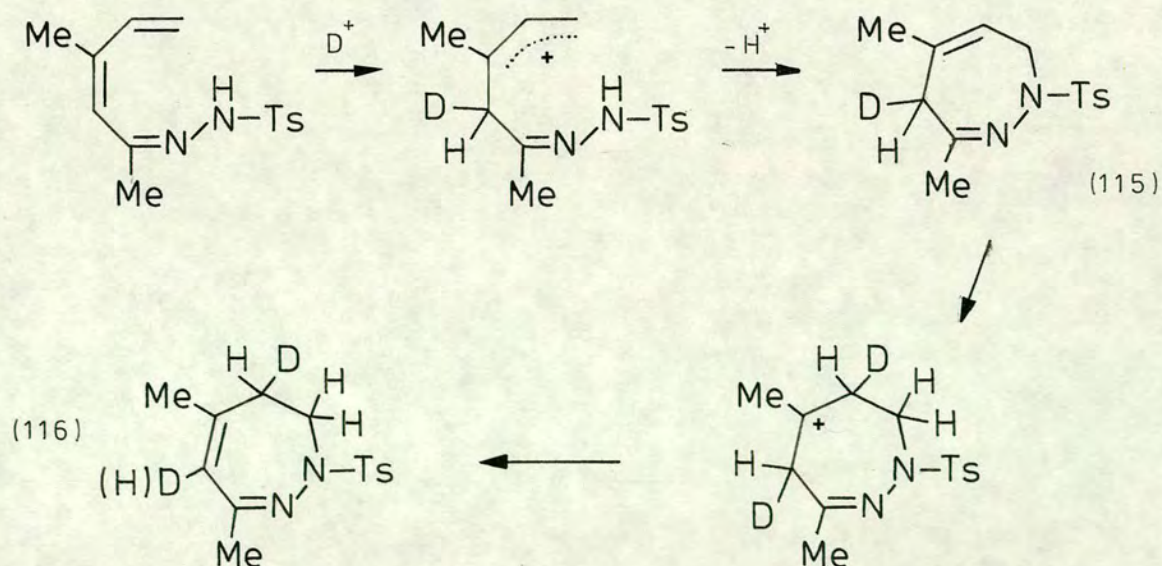
Extensive deuteriation of C-4 and C-6 was observed, together with some deuterium incorporation into the C-5 and C-7



Scheme 32

methyl groups. Control experiments showed that methyl deuterium incorporation could take place by acid-catalysed exchange of the dienone (113), and that the product tosyl-diazepine (114) did not undergo deuterium exchange under the reaction conditions.

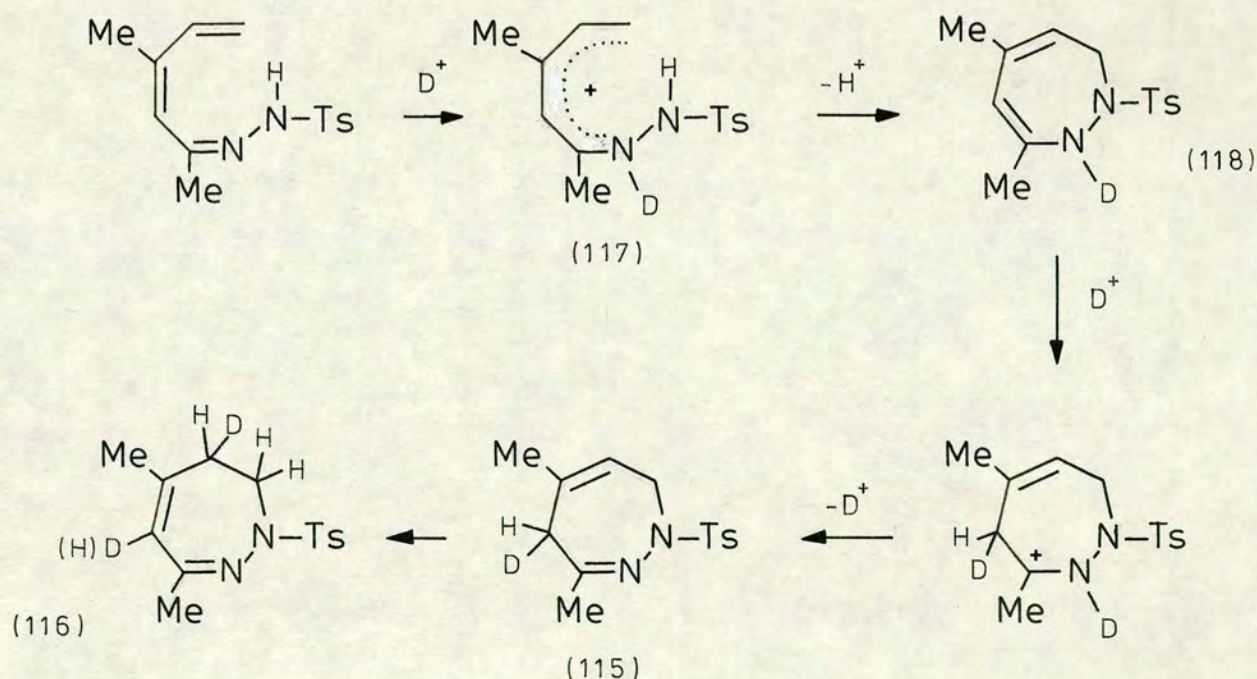
Two possible cyclisation mechanisms are consistent with this deuterium incorporation study and with the formation of the tosyl-diazepine from both *E*- and *Z*-isomers (schemes 33 and 34). The first is the more economical and involves primary



Scheme 33

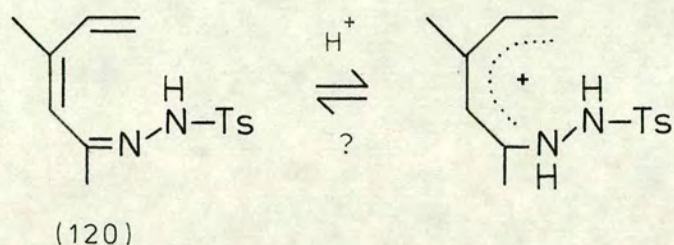
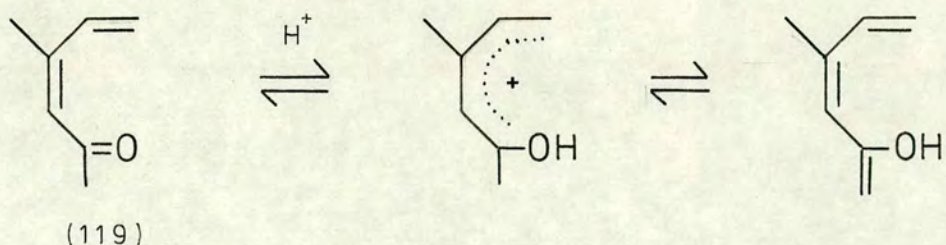
protonation at C-3 of the tosylhydrazone, allowing rotation about the 3-4 bond, followed by ring closure and loss of the proton on the nitrogen to give (115). Further protonation on C-4 of (115) would then allow its isomerisation to the conjugated, and presumably more stable final product (116).

Alternatively, the cyclisation could be initiated by protonation on nitrogen, scheme 34, to give the extensively delocalised carbonium ion (117) which on cyclisation would give (118). This compound, an ene-hydrazine analogue, would be expected to isomerise to the hydrazone (115) and hence to the tosyl diazepine (116).



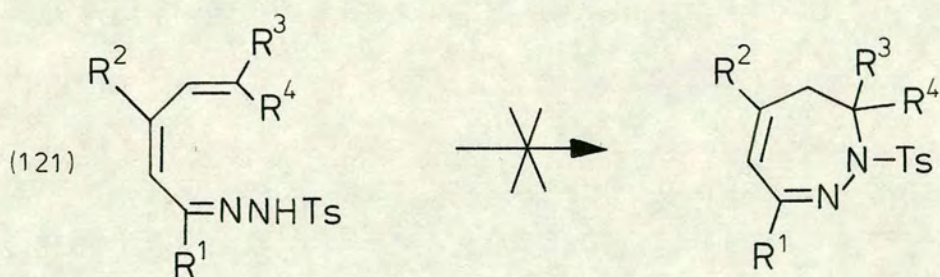
Scheme 34

The deuteriation study did not allow a conclusive differentiation between these two mechanisms but, since the ketone (119) is protonated at oxygen rather than at C-3, it seems likely that (120) will protonate preferentially at nitrogen.



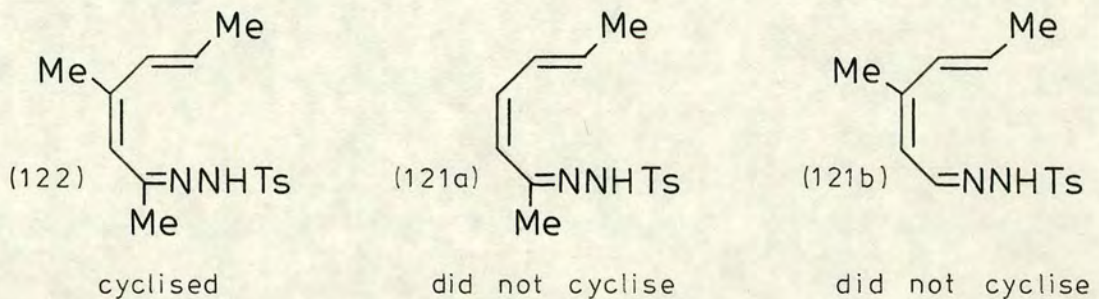
That this does occur is supported by the observation that deuterium is incorporated into both methyl groups via exchange in (117), whereas scheme 33 would lead to deuteration only in the 5-methyl group.

A number of tosylhydrazones (121) did not undergo acid-catalysed cyclisation although a variety of acid/solvent/temperature conditions were tried.



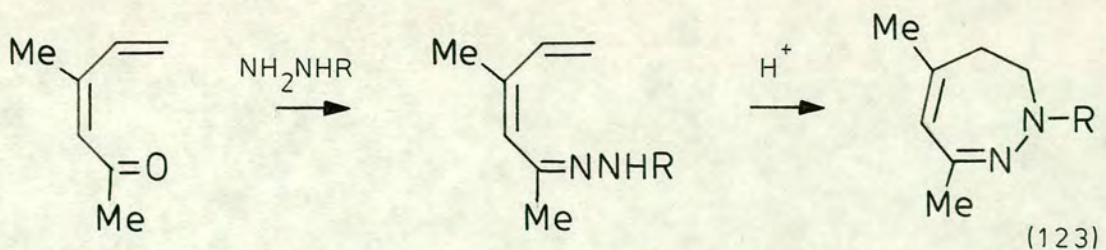
	R ¹	R ²	R ³	R ⁴
a	Me	H	Me	H
b	H	Me	Me	H
c	H	Me	Ph	H
d	Me	Me	Ph	H
e	Me	Me	Ph	Me

The failure of cyclisation must be due to either the inability of the tosylhydrazones (121) to protonate under the reaction conditions or, if protonation did occur, to a charge distribution and/or stereochemistry in the delocalised cation which did not facilitate ring closure. The failure of (121a) and (121b) to cyclise is notable since they differ from (122) only in the absence of methyl groups at C-4 and C-2 respectively.

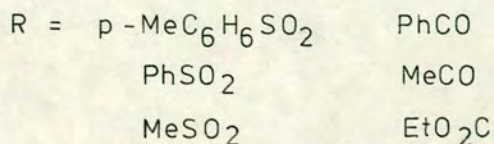


The failure of (121c,d, and e) to cyclise is perhaps less surprising since all have large (phenyl) groups attached to the terminus of the diene. Michael type additions are known to be sensitive to steric hindrance.

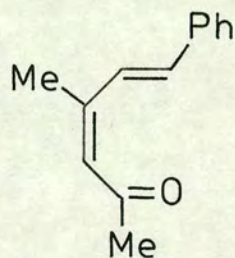
This synthesis of diazepines was extended to other 2-substituted analogues (123) by the use of a variety of hydrazine derivatives (scheme 35).



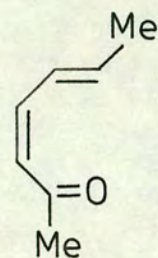
Scheme 35



The limitations on synthesis associated with the 2-tosyldiazepines were also observed for this series of substituted hydrazine analogues. For example dienones of the type (124) and (125) were found to be still resistant to cyclisation.



(124)



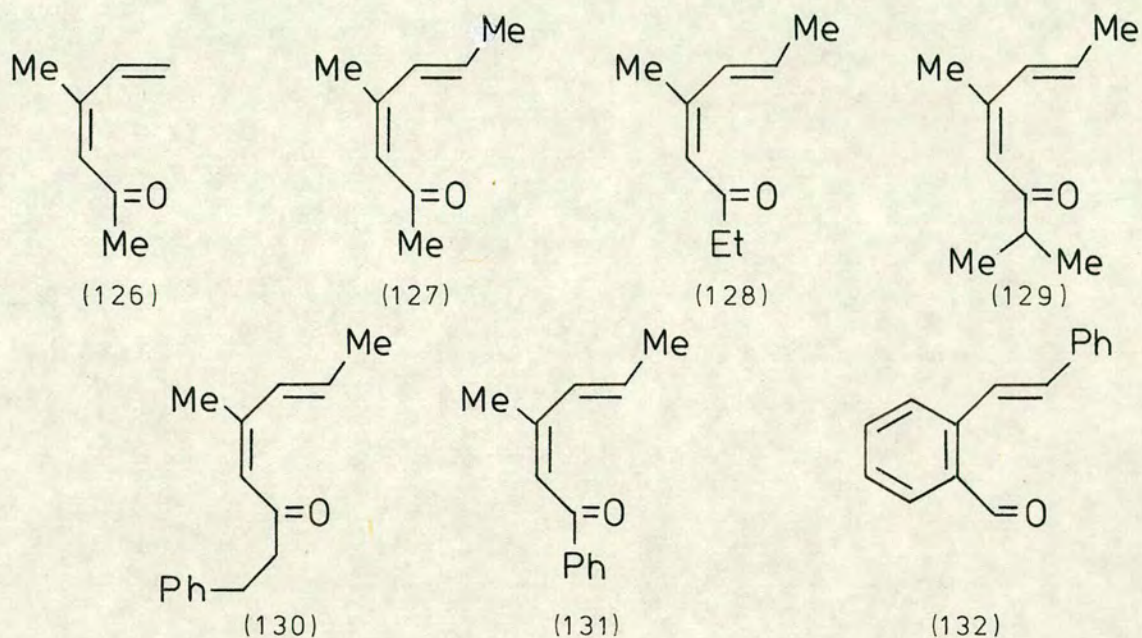
(125)

The objective of the following section of work was two-fold:

i) to synthesise suitable precursors for the 3*H*-1,2-diazepine sigmatropic migration and organometallic studies; and ii) to provide a further range of substituted $\alpha\beta,\gamma\delta$ -olefinic unsaturated carbonyl compounds with which to understand better the limitations of the cyclisation reaction to give 2-substituted-3,4-dihydrodiazepines. In particular the cyclising ability of dienals would be investigated.

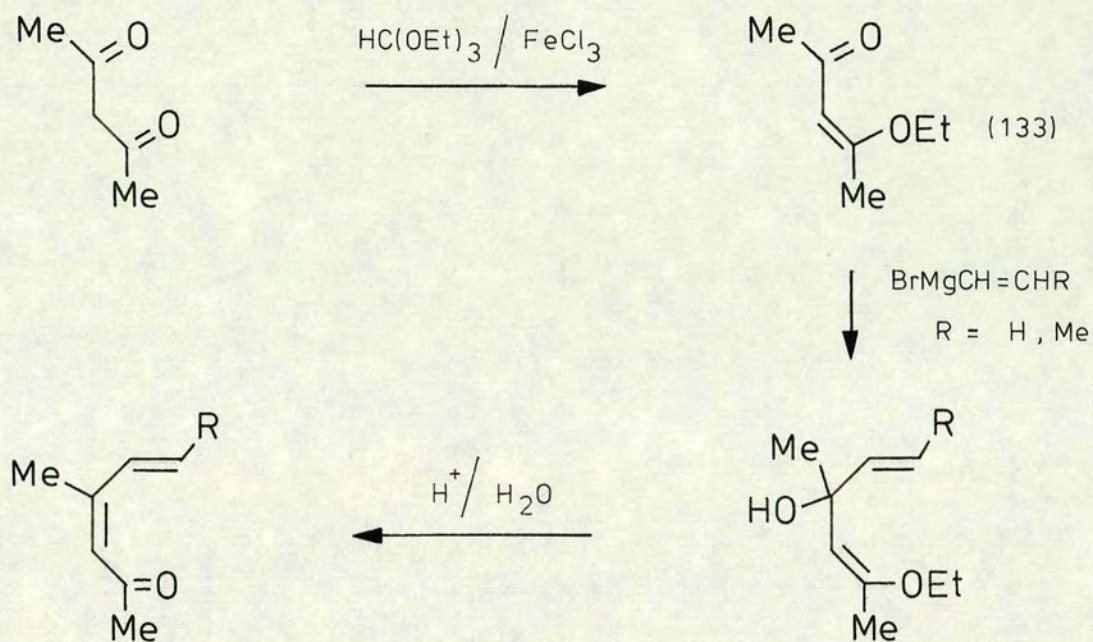
2. Synthesis of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds

2.1 Precursors for the 3H-1,2-diazepine and organometallic studies



The $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds (126 \rightarrow 132) were prepared by several different routes, with no one method proving general enough to allow synthesis of them all.

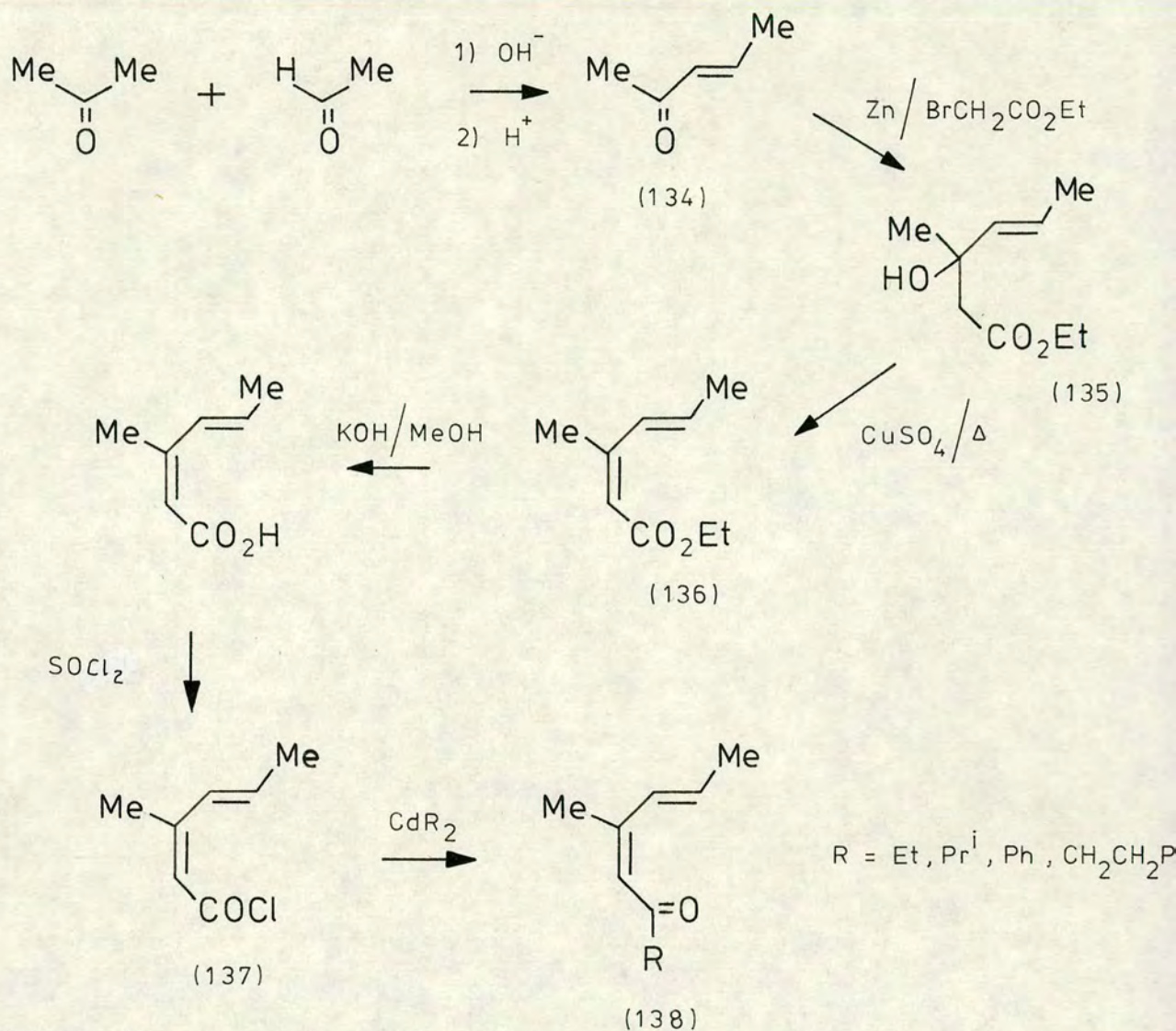
4-Methylhexa-3,5-dien-2-one (126) and 4-methylhepta-3,5-dien-2-one (127) were prepared using Normant's Grignard method¹⁸⁷ as shown in scheme 36.



Scheme 36

The mono-protected ketone 4-ethoxypent-4-en-2-one (133) was prepared by the reaction of acetylacetone, triethyl orthoformate and ferric chloride catalyst in ethanol. Reaction of this compound with either vinyl or propenyl magnesium bromide, followed by acidic work-up, gave the required dienone.

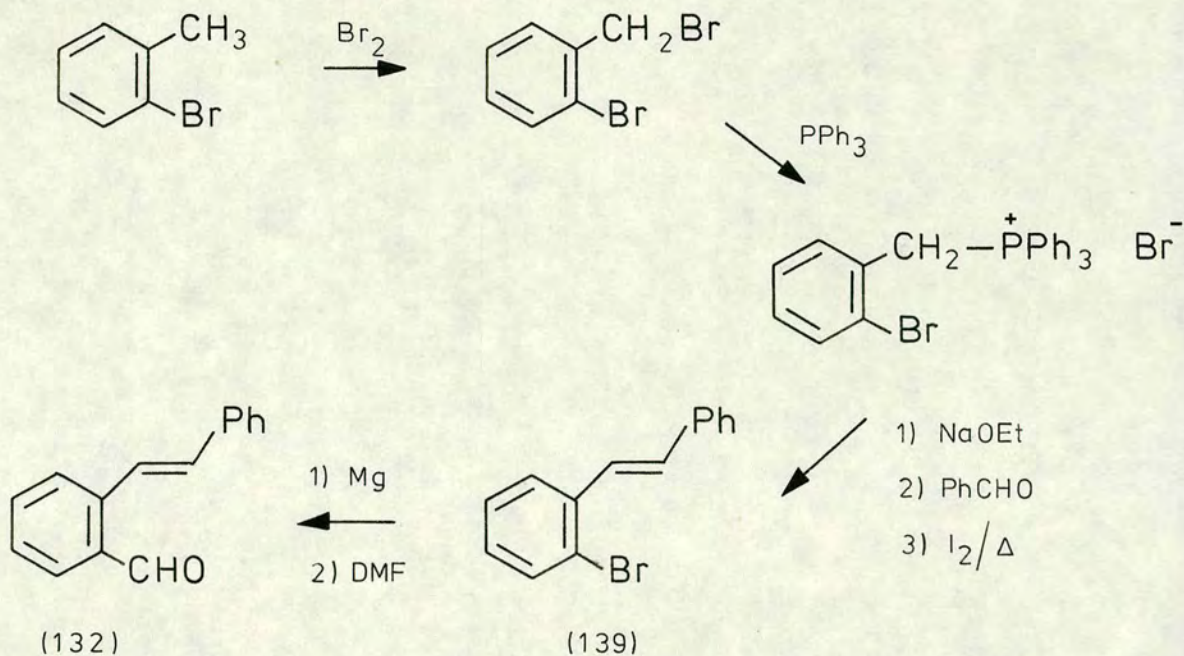
Dienones (128→131) required Cologne and Varagnats'¹⁸⁸ more lengthy synthetic route shown in Scheme 37.



Scheme 37

Pent-3-en-2-one (134) was prepared from the aldol reaction of acetaldehyde, acetone and sodium hydroxide. A Reformatsky reaction between ethyl α -bromoacetate and pent-3-en-2-one gave the hydroxy ester (135), this was dehydrated by slow distillation from anhydrous copper sulphate to give the diene ester (136). Hydrolysis to the acid followed by treatment with thionyl chloride gave the acid chloride (137) which was converted to the ketone (138) by reaction with the appropriate dialkyl cadmium reagent.

E-2-Formylstilbene (132), was prepared by the route developed by Sharp *et al.*⁶⁴ shown in scheme 38.

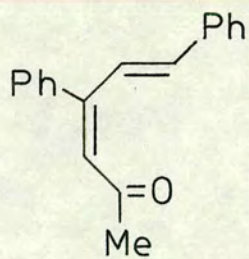


Scheme 38

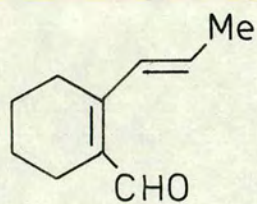
o-Bromotoluene was brominated to give *o*-bromobenzyl bromide, from which a phosphonium salt was prepared by reaction with triphenylphosphine. A Wittig reaction with benzaldehyde followed by isomerisation with iodine gave *E*-2-bromostilbene (139). Functional group interconversion of formyl for bromo was achieved by a Grignard reaction.

2.2 Precursors for the study of cyclisation reactions to give 2-substituted-3,4-dihydrodiazepines

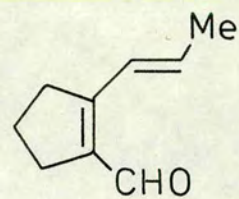
Once again these conjugated carbonyl compounds (140→144) were prepared by several routes.



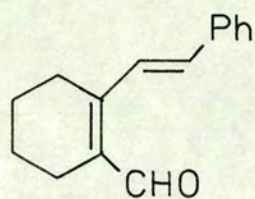
(140)



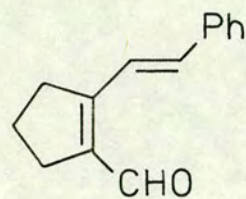
(141)



(142)

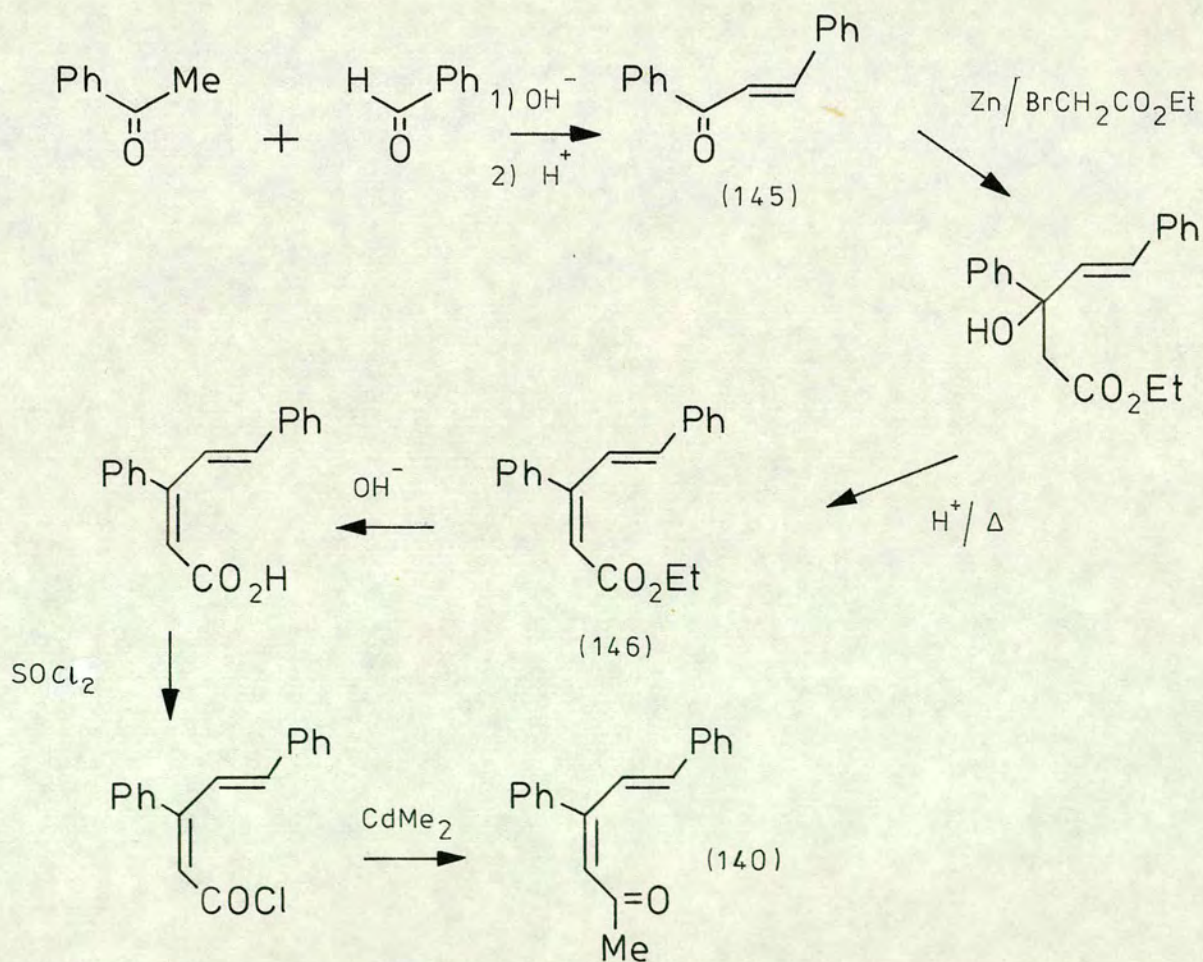


(143)



(144)

4,6-Diphenylhexa-3,5-dien-2-one (140) was prepared by the route shown in scheme 39.



Scheme 39

Benzylideneacetophenone (145) was prepared by the aldol reaction of acetaldehyde, acetophenone and sodium hydroxide. A Reformatsky reaction with ethyl α -bromoacetate followed by dehydration and hydrolysis gave the $\alpha\beta,\gamma\delta$ -insaturated acid (146). Conversion to the acid chloride and reaction with dimethyl cadmium gave the required dienone (140).

Because hydrazone derivatives of this carbonyl compound could not be prepared, the evidence for the structural assignment of this compound as the dienone (140) will be discussed in detail.

Elemental analysis together with accurate mass measurement of the parent ion confirmed that the molecular formula was $C_{18}H_{16}O$. The infrared spectrum showed the presence of a conjugated carbonyl group at 1672 cm^{-1} and an olefinic absorption at 1612 cm^{-1} . The ^1H n.m.r. spectra showed the presence of E,E and Z,E isomers in the ratio $ca.4:1$, the resonance assignments are shown in figures 33 and 34.

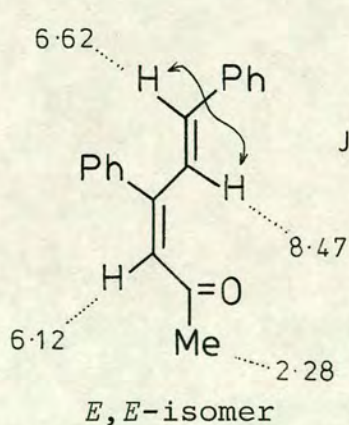


Figure 33

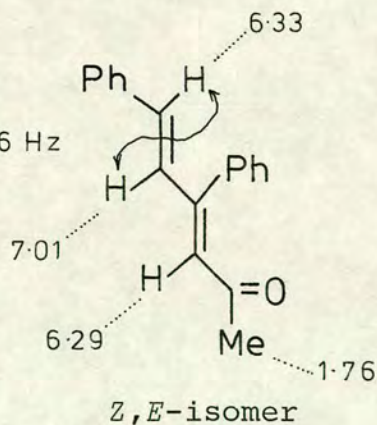
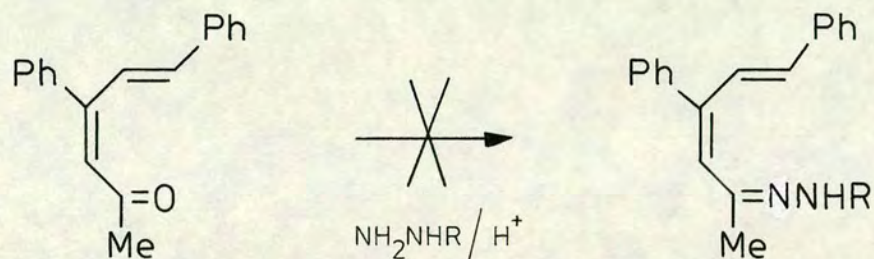


Figure 34

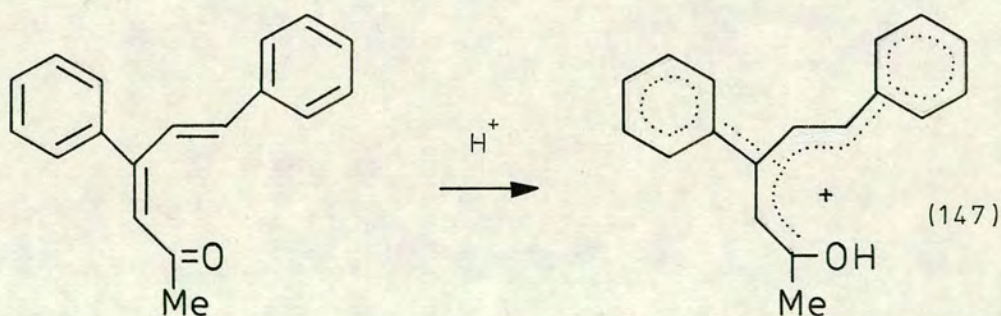
The strongly deshielded olefinic C-5 proton of the E,E isomer was highly characteristic of such dienones³³.

Reaction of this dienone with several hydrazines under a variety of acid catalysed conditions (see experimental section D.4) did not yield the expected hydrazone derivatives (scheme 40).



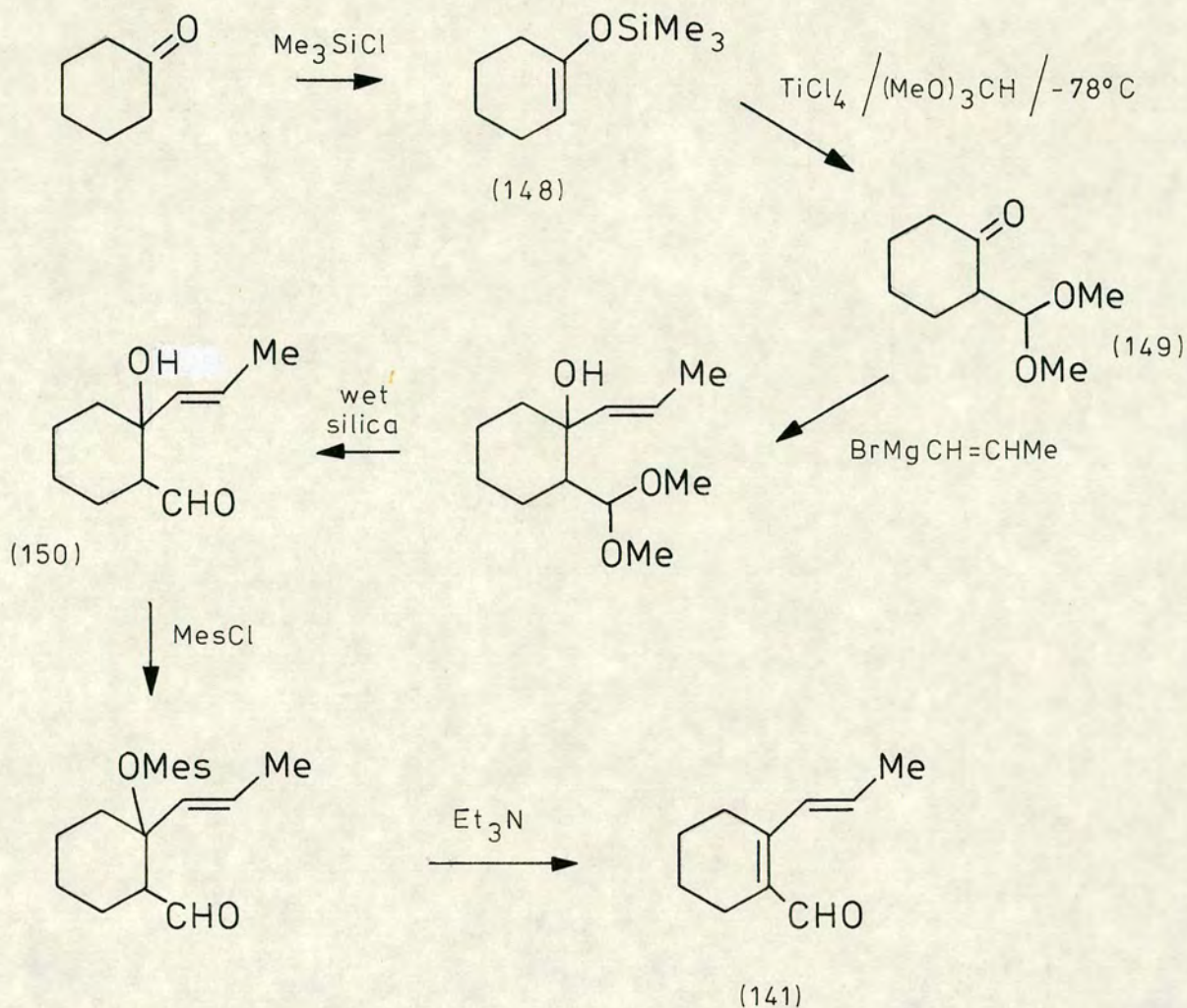
Scheme 40

In these reactions the starting dienone was consumed, evidently by polymerisation pathways. It was also noted that the addition of acid catalyst to dienone/hydrazine solution resulted in a rapid yellow colouration indicating that protonation had occurred. It seems likely that this dienone protonates readily to form a highly resonance stabilised cation of the type (147).



This species apparently then reacts by polymerisation pathways more rapidly than the expected reaction with hydrazines to form hydrazone derivatives.

2-Propenyl-1-cyclohexene-1-carboxaldehyde (141) was synthesised as shown in scheme 41.



Scheme 41

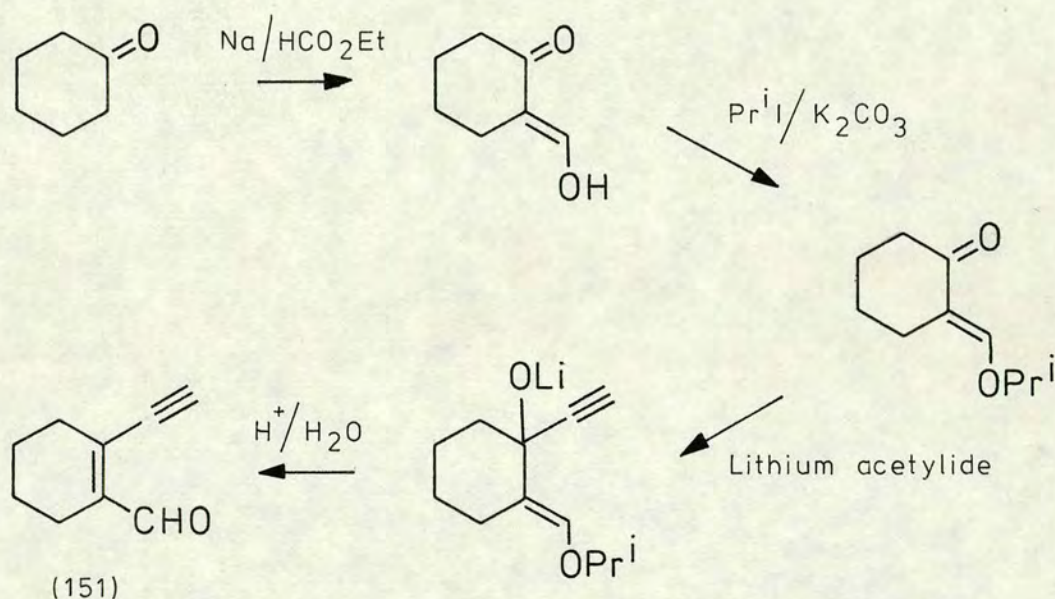
Cyclohexanone was reacted with trimethyl silyl chloride to give the trimethylsilyl enol ether (148), which was converted to the β -keto acetal (149) by treatment with titanium tetrachloride and trimethylorthoformate in dichloromethane solution at -78° .

Reaction with propenyl magnesium bromide followed by hydrolysis of the acetal group gave the formyl compound (150). The final dehydration step to give (141) was carried out using the technique described by Corey¹⁸⁹; by conversion of the alcohol to the mesylate followed by treatment with triethylamine.

Interestingly, this elimination reaction gave exclusively

the fully conjugated isomer (141), none of the other possible elimination product was detected.

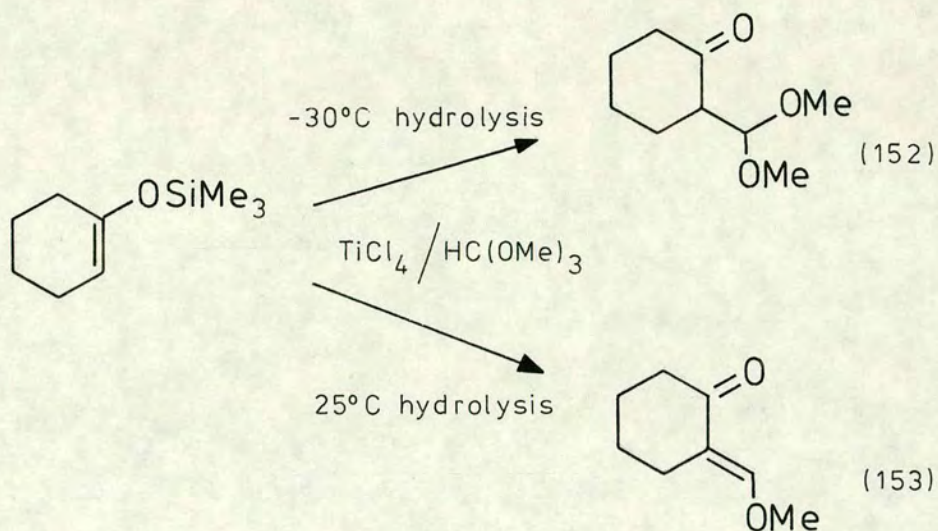
2-Propenyl-1-cyclopentene-1-carboxaldehyde (142) was prepared using an alternative synthetic strategy. In his work examining fully conjugated macrocyclic polyenynes, Sondheimer¹⁹⁰ reported the synthesis of compound (151) by the route shown in scheme 42.



Scheme 42

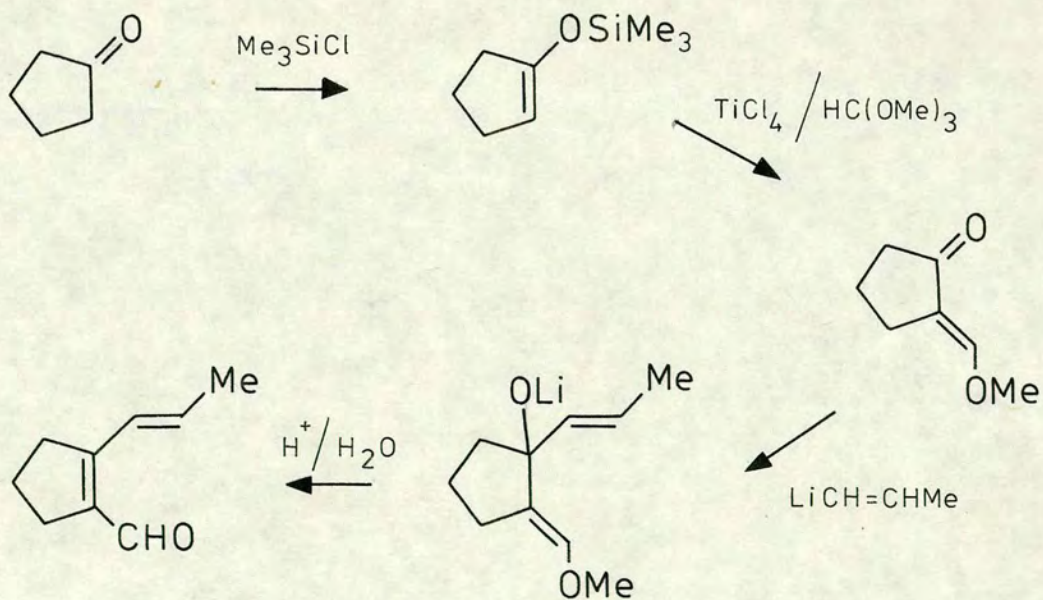
It seemed feasible that our target molecule (142) could be prepared by this route if propenyl lithium was substituted for lithium acetylide.

It was fortuitously discovered earlier during the preparation of the β -keto acetal (152), that 2-methoxymethylene-cyclohexanone (153) could be isolated as an alternative product if the hydrolysis step was carried out at room temperature instead of at -30°C (scheme 43).



Scheme 43

Thus, utilizing these two observations, 2-propenyl-1-cyclopentene-1-carboxaldehyde (142) was prepared by the route shown in scheme 44.

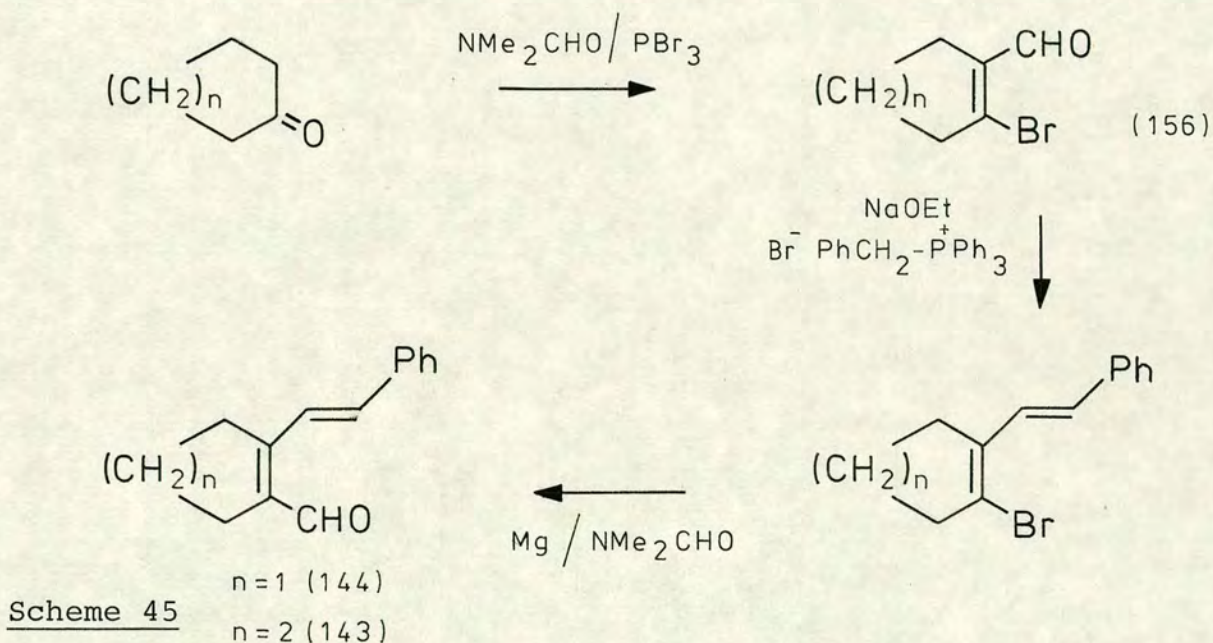


Scheme 44

Cyclopentanone was converted into the enol ether (154) by reaction with trimethylsilyl chloride. Reaction with titanium tetrachloride and trimethyl orthoformate at -78°C followed by hydrolysis at room temperature gave 2-methoxy-

methylenecyclopentanone (155). Treatment of this compound with propenyl lithium followed by acid hydrolysis gave the required $\alpha\beta,\gamma\delta$ -olefinic unsaturated aldehyde (142).

The dienals (143) and (144) were prepared by a further synthetic route shown in scheme 45. This route proved the most satisfactory both in terms of overall yield and economy of steps.

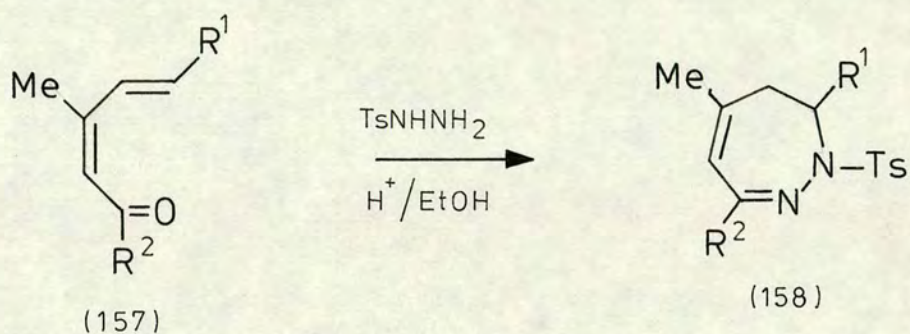


The 1-formyl-2-bromo compound (156) was obtained by treatment of the carbonyl compound with dimethylformamide and phosphorus tribromide. The styryl fragment was introduced by a Wittig reaction using benzytriphenylphosphonium bromide. The conversion of the vinyl bromine atom to the formyl group was achieved by the preparation of the Grignard reagent followed by reaction with dimethylformamide and hydrolysis to give the dienal (143,144).

3. Reactions of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds with *p*-toluenesulphonylhydrazide

3.1 To provide 2-tosyldiazepine precursors for the 3*H*-1,2-diazepine and organometallic studies

The dienones (157a→f) reacted with *p*-toluenesulphonylhydrazide in ethanol containing a catalytic amount of mineral acid to give the corresponding 2-tosyldiazepines (158a→f) as shown in scheme 46.

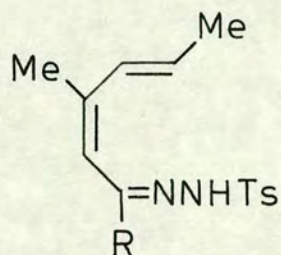


Scheme 46

Compound	R ¹	R ²	Yield %
a	H	Me	69
b	Me	Me	45
c	Me	Et	18 (+41 hydrazone)
d	Me	Pr ⁱ	27 (+11 hydrazone)
e	Me	CH ₂ CH ₂ Ph	63
f	Me	Ph	59

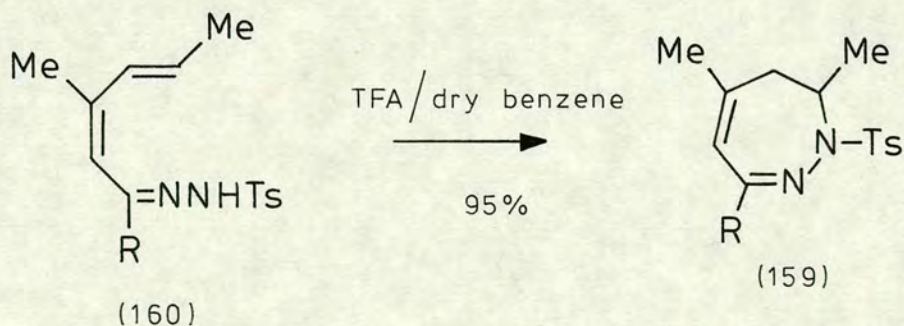
Dienones (157d→f) were new examples of the series and were found to undergo cyclisation just as readily. Thus variation in the substituent attached to the carbonyl group did not seem to affect the cyclisation step to dihydrodiazepine.

In two cases (c and d) the intermediate hydrazones (160) were also isolated from the reaction.



(160) R = Et, Prⁱ

This was probably due to an insufficient quantity of mineral acid catalyst being added to the reaction. Cyclisation of these intermediate tosylhydrazones (160) to diazepines (159) was carried out using an alternative acid catalyst system; trifluoroacetic acid in dry benzene. This system was found to be highly effective and quantitatively converted the hydrazones to the corresponding 2-tosyldiazepines (scheme 47).

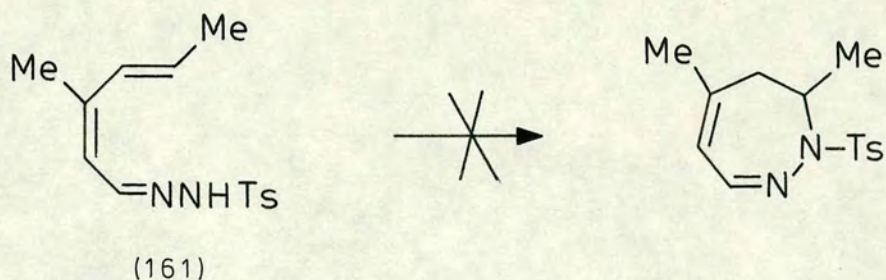


Scheme 47

R = Et, Prⁱ

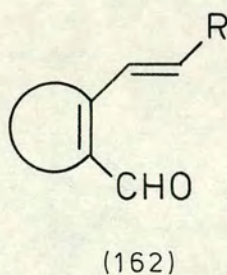
3.2 Investigation of the performance of dienals in the cyclisation reaction to give 2-tosyldiazepines

It had earlier been observed that the tosylhydrazones of $\alpha\beta,\gamma\delta$ -unsaturated aldehydes of the type (161) did not undergo cyclisation to give 2-tosyldiazepines³³ (scheme 48).

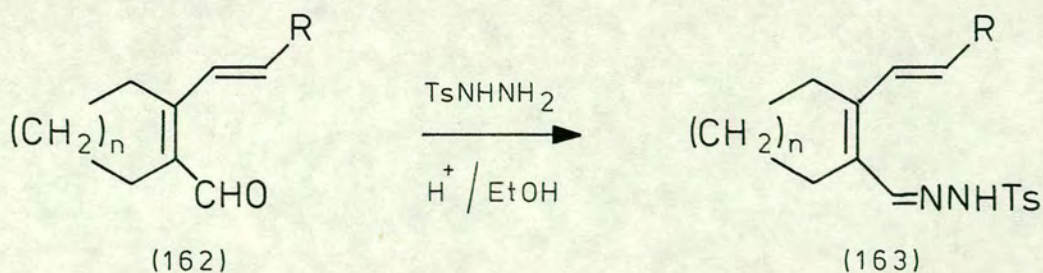


Scheme 48

The object of this present work was to investigate the reaction of aldehydes of the type (162), where the fused ring now holds the diene fragment in the favoured *cis* configuration for cyclisation.



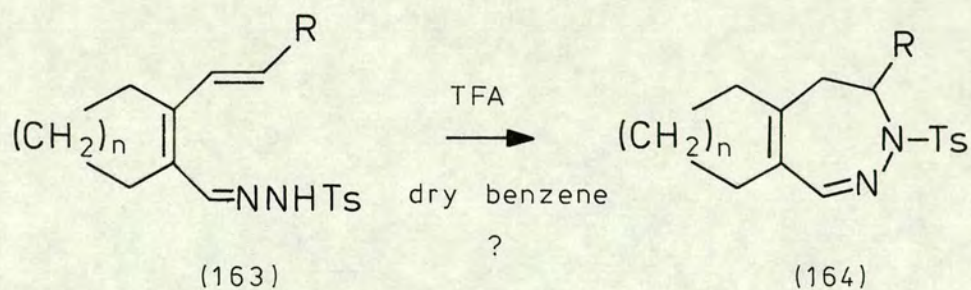
The tosylhydrazones (163) were isolated in good yield by reaction of the dienals (162) with *p*-toluenesulphonylhydrazide in ethanol with a minimum quantity of acid catalyst (scheme 49).



Scheme 49

Compound	n	R	Yield of tosylhydrazone %
a	1	Me	54
b	1	Ph	58
c	2	Me	67
d	2	Ph	92

Cyclisation experiments on these tosylhydrazones were carried out using the effective trifluoroacetic acid/dry benzene catalyst system, and the results are summarised in scheme 50.



Scheme 50

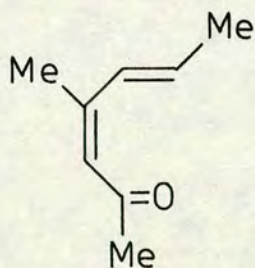
Compound	n	R	Cyclisation to 2-tosyldiazepine
a	1	Me	Yes, readily 54%
b	1	Ph	No, hydrazone recovered
c	2	Me	Yes, slowly 16% after 60 h
d	2	Ph	No, hydrazone recovered

It was found that the two propenyl substituted tosylhydrazones (163a and c) did undergo cyclisation, the cyclopentyl

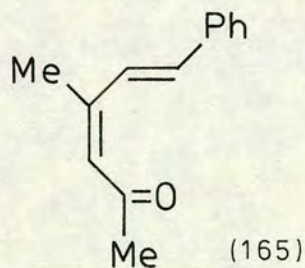
system cyclising more readily.

It is not easy to rationalise why the cyclopentyl system should cyclise so much more readily than the cyclohexyl and analogous acyclic systems. In general the tosylhydrazones of dienals will protonate on nitrogen to give less stable cations than those from the analogous methyl ketones. In the cyclopentyl case however, the approximate planarity of the five membered ring will enhance the delocalisation of the positive charge and hence the stability of the cation and thus may affect the ease of cyclisation.

The failure of the phenyl substituted dienals (163b and d) to undergo cyclisation requires further explanation. It has been earlier shown that phenyl substituted dienones of the type (165) do not undergo cyclisation³³.

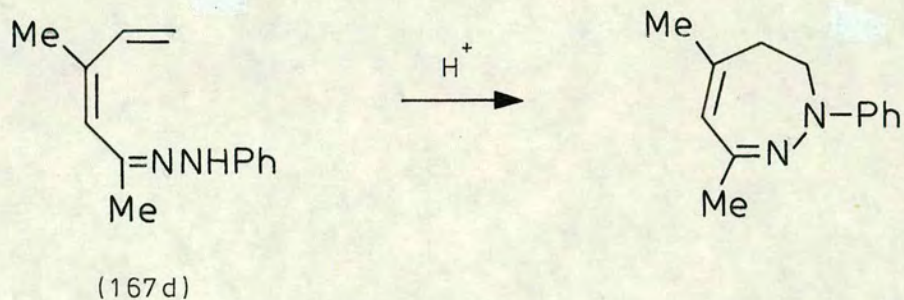


cyclises



does not cyclise

It seems that their failure to cyclise must be due to the steric hindrance and/or the electronic effect of the phenyl group at the diene terminus. Clarification of this point, ie. distinction between the conjugating effect and steric requirement of the phenyl group, would require synthesis of systems with a terminus substituent which has a large steric requirement but without an electronic effect, for example cyclohexyl or *t*-butyl groups.

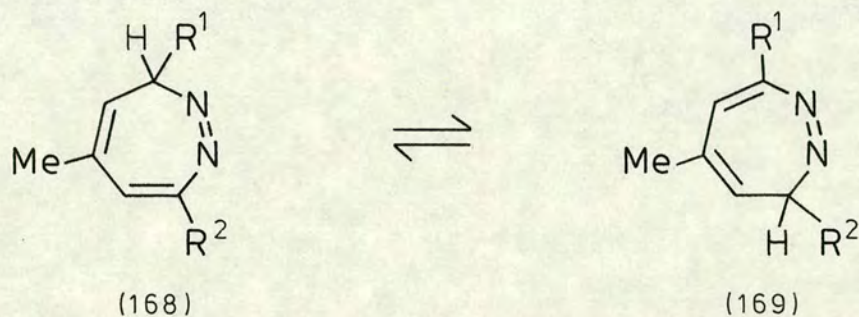


This is a somewhat surprising result since the previous examples which successfully cyclised were hydrazone derivatives of hydrazines which possessed an electron withdrawing substituent. The phenyl substituent would be expected to be a departure from the series, yet still underwent cyclisation.

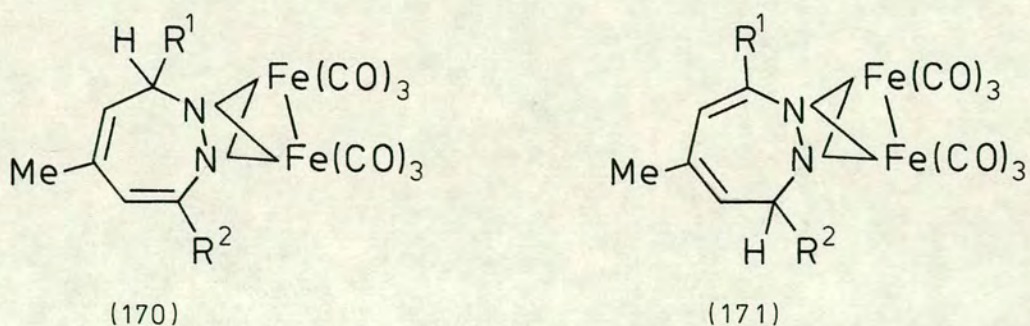
The failure of the nitro benzene hydrazone derivatives (167a→c) presents a further problem, these compounds appeared to meet all the criteria required for successful cyclisation; ie favourable stereochemistry and an electron withdrawing substituted hydrazine, yet are resistant to cyclisation.

D. 1,2-Diazepine N-Oxides1. Introduction

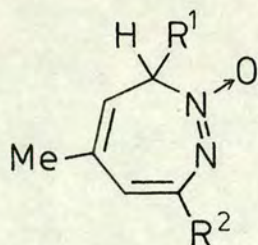
The investigation of N-oxide formation by 1,2-diazepines was a further strategy to isolate the individual isomers (168) and (169) which interconvert by rapid [1,5] sigmatropic hydrogen migration (scheme 52).

Scheme 52

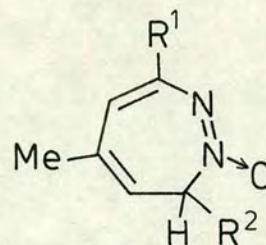
This separation of isomers had been successfully achieved by conversion of the diazepines into their corresponding diiron hexacarbonyl complexes (170) and (171), see discussion section B.



It was hoped by analogy, that conversion of the diazepines into their N-oxide derivatives (172) and (173), a similar separation of isomers would prove possible.



(172)



(173)

If so, it was expected that the isomers would be susceptible to deoxygenation under mild conditions, eg. by the use of a trivalent phosphorus reagent, to regenerate the diazepines themselves.

N-Oxide formation by a benzodiazepine was initially investigated since this system contained only one isomer, the compounds are crystalline solids, apparently chemically more stable than the monocyclic diazepines, and so were expected to provide more easily handled products.

2. Oxidation of 4-phenyl-1*H*-2,3-benzodiazepine

A survey of azoxy compound literature (see introduction section E) had revealed that the most popular and convenient reagents for the oxidation of azo compounds to their corresponding *N*-oxide derivatives were peracids. An initial reaction of 4-phenyl-1*H*-2,3-benzodiazepine with peracetic acid resulted in rapid decomposition of the diazepine with no isolable products.

A further reaction using an alternative milder reagent, *m*-chloroperbenzoic acid, was much more successful; stirring the diazepine with a molar equivalent of the peracid for 12 h resulted in the formation of a single product. Purification by column chromatography on alumina gave a pale yellow

Figure 35

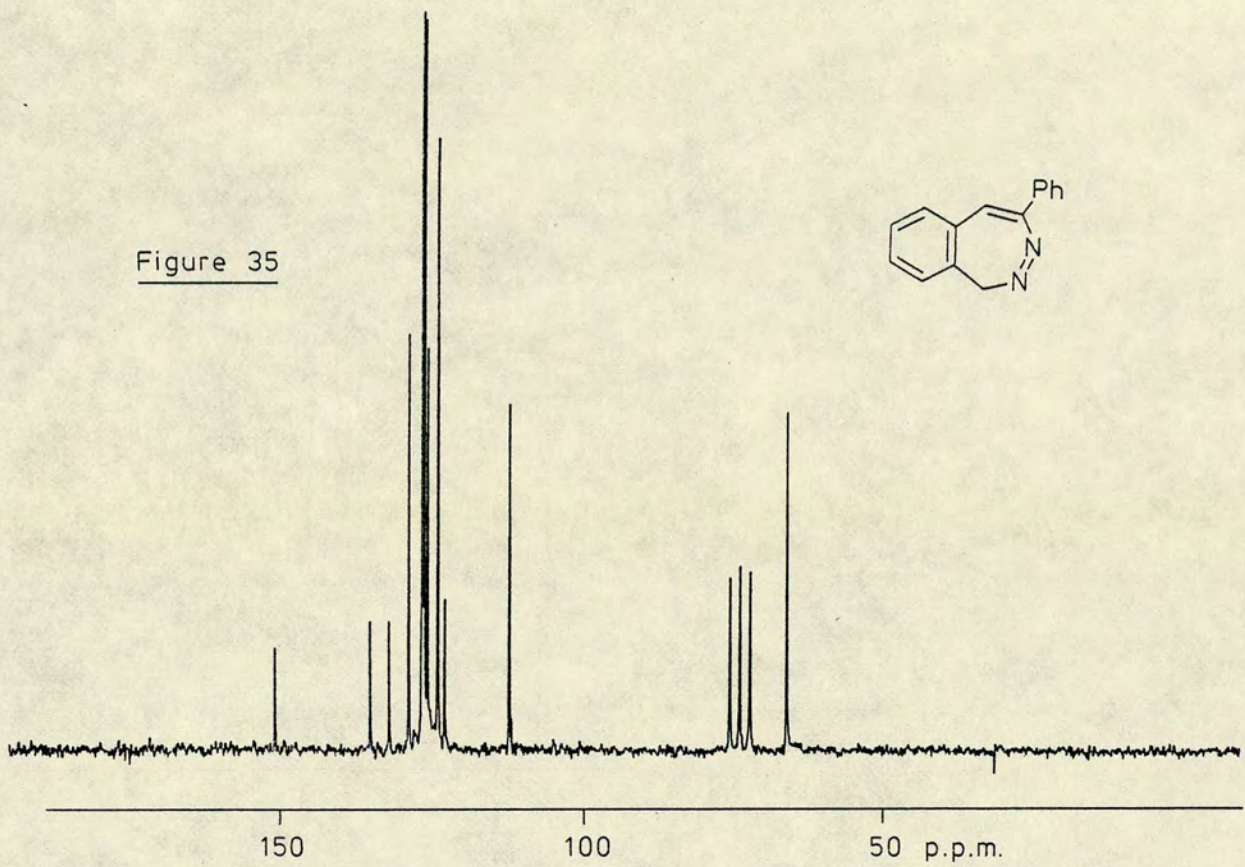
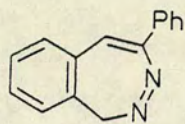
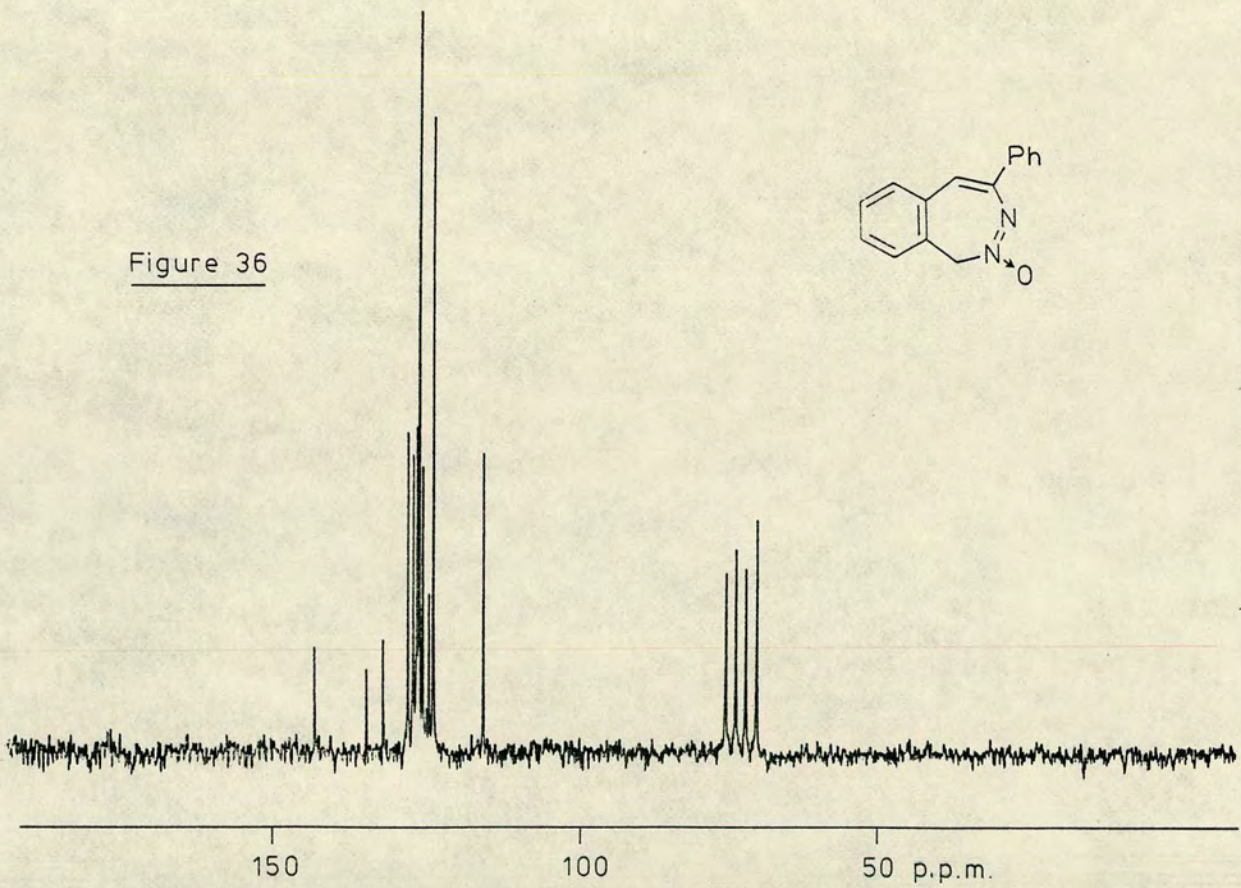
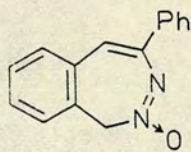
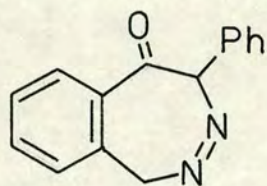


Figure 36

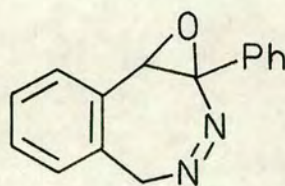


crystalline compound in high yield. Elemental analysis together with exact mass measurement of the parent ion showed that the molecular formula of this compound was that of the original diazepine plus one oxygen atom. The ^1H and ^{13}C n.m.r. spectra of the compound showed that the essential features of the diazepine ring were still intact, figures 35 and 36 reproduce the ^{13}C n.m.r. of 4-phenyl-1*H*-2,3-benzodiazepine before and after oxidation, and similarities of the spectra are apparent.

Utilising this evidence four possible oxidised diazepine structures (174-177) could be envisaged as the product from this reaction.

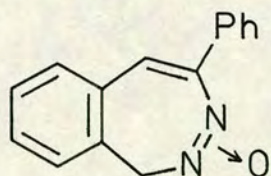


(174)

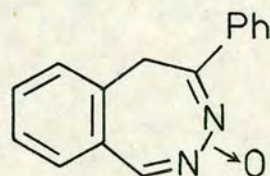


(175)

The oxidised nitrogen in (176)&(177) is not specified



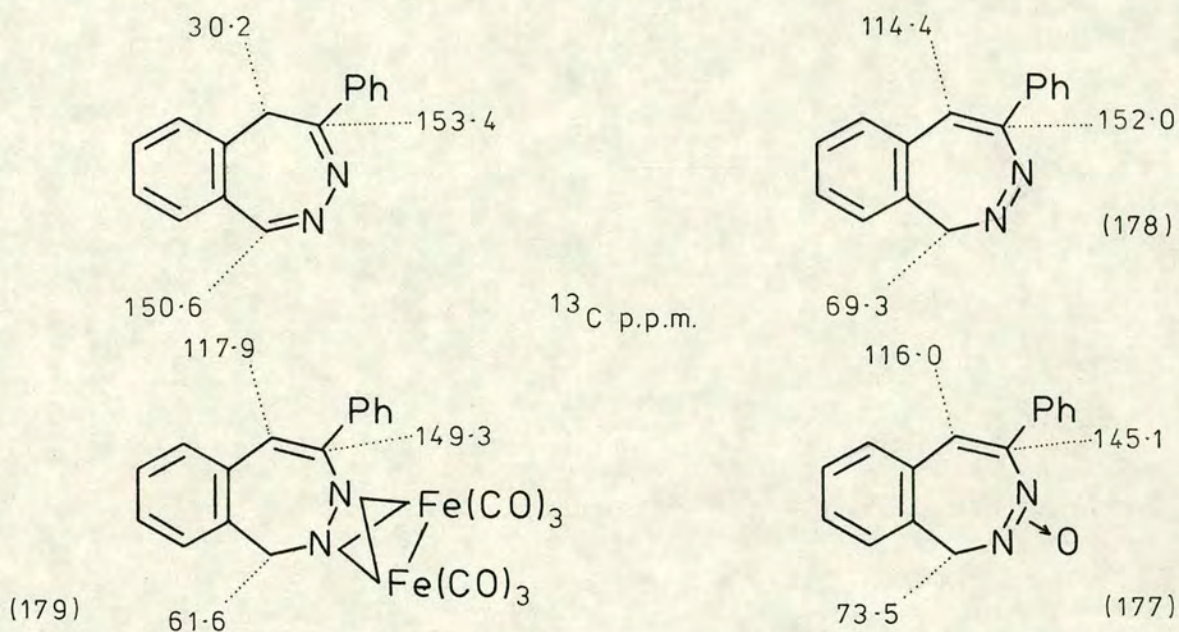
(177)



(176)

Structure (174) could be discounted because of the absence of a carbonyl absorption in the infrared spectrum. The epoxide structure (175) could also be ruled out because the ^{13}C n.m.r. spectra did not contain the characteristic oxirane signals, nor was the expected singlet epoxide proton observed in the ^1H spectrum.

Of the two remaining structures the 1*H*-2,3-benzodiazepine structure (177) was selected because of the similarity of ^{13}C signals of the carbons attached to the diaza-linkage compared with the corresponding carbon atoms in the parent benzodiazepine (178) and iron carbonyl complex (179).



The final piece of structural information required for full characterisation of this compound was which of the nitrogen atoms was oxidised. This was deduced by comparison of the diazepine n.m.r. spectra before and after oxidation. The effect of azo group oxidation on the chemical shifts of substituents directly attached to the azo group has previously been reported and explained¹⁵⁸ (table 5).

For example, the methyl protons of azomethane resonate at δ 3.68 and are more deshielded than the corresponding signal in alkenes (δ 1.7), methyl ketones (δ 2.1) and methyl cyanide (δ 1.97). This difference is accounted for by the high electronegativity of the nitrogen bonded to the methyl group.

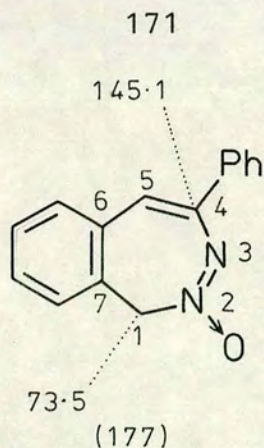
Table 5: N.m.r. chemical shifts in aliphatic azoxy and azo compounds

Compound	p.p.m. from TMS
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{Me-N=N-Me} \end{array}$	4.05
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{Me-N=N-Me} \end{array}$	3.07
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{Me-N=N-Me} \end{array}$	3.68
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{Ph-N=N-Me} \end{array}$	3.40
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{Ph-N=N-Me} \end{array}$	4.15
$\begin{array}{c} \text{O} \\ \uparrow \\ \text{Ph-N=N-Me} \end{array}$	3.90

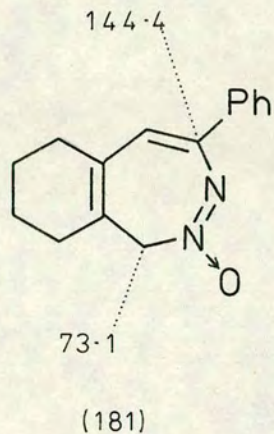
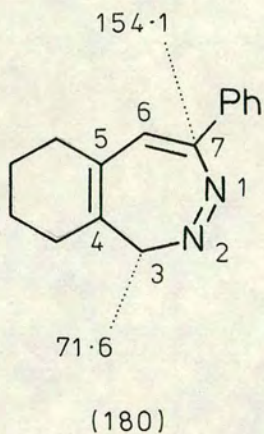
The spectra of azoxymethane shows two signals at 4.05 and 3.07, the methyl adjacent to the oxidised nitrogen atom is more deshielded than the parent azo compound, whereas the other methyl is less deshielded. This deshielding behaviour is duplicated in other azoxy compounds¹⁵⁸.

Extending this analysis to our oxidised benzodiazepine (177), we would predict that the oxygen is attached to N-2 since C-1 is more deshielded compared with the parent compound (178), and C-4 is less deshielded.

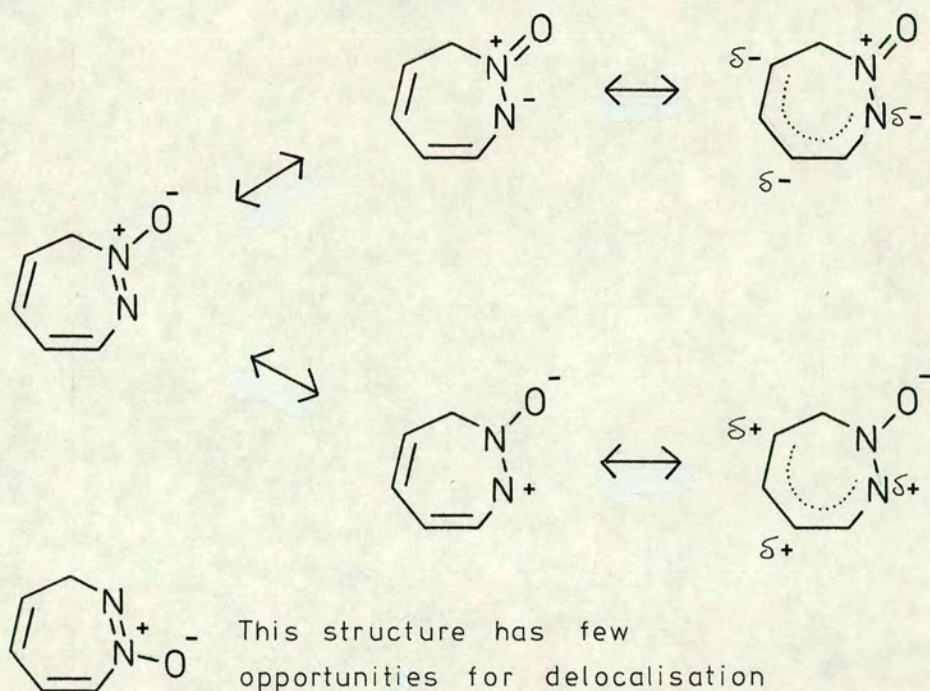
This assignment has been confirmed by work carried out since completion of this project, Sharp *et al.*¹⁶⁹ have synthesised the 3*H*-1,2-diazepine (180) and its *N*-oxide derivative (181).



An X-ray crystal structure on the latter has shown that the oxygen atom is located on N-2. The deshielding effect on C-3 and C-7 followed the expected pattern described above; C-3 is more deshielded and C-7 is less deshielded.



In both these diazepine *N*-oxides (177) and (181), oxidation occurred on the nitrogen atom adjacent to the saturated carbon atom. Thus the oxidation reaction seems to follow thermodynamic control since these product structures are the more delocalised systems in terms resonance hybrids (scheme 53).



Scheme 53

An interesting feature of the benzodiazepine *N*-oxide (177) was its rapid ring inversion (table 6).

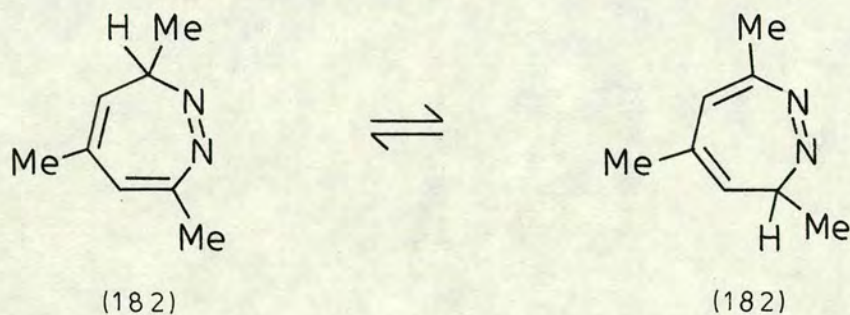
Table 6: The coalescence temperatures and ΔG (ring inversion) values for 4-phenyl-1*H*-2,3-benzodiazepine and its iron carbonyl and *N*-oxide derivatives

Compound	Coalescence Temperature $^{\circ}\text{C}$	ΔG (ring inversion) $\text{K}_J \text{ mol}^{-1}$
	+102	72
	-54	44
	+21	59

This is a further example of how chemical modification of the diaza-linkage has produced a marked lowering of the activation energy for the ring inversion. The possible explanations responsible for this enhanced rate of ring inversion have been described in detail in section B of this discussion.

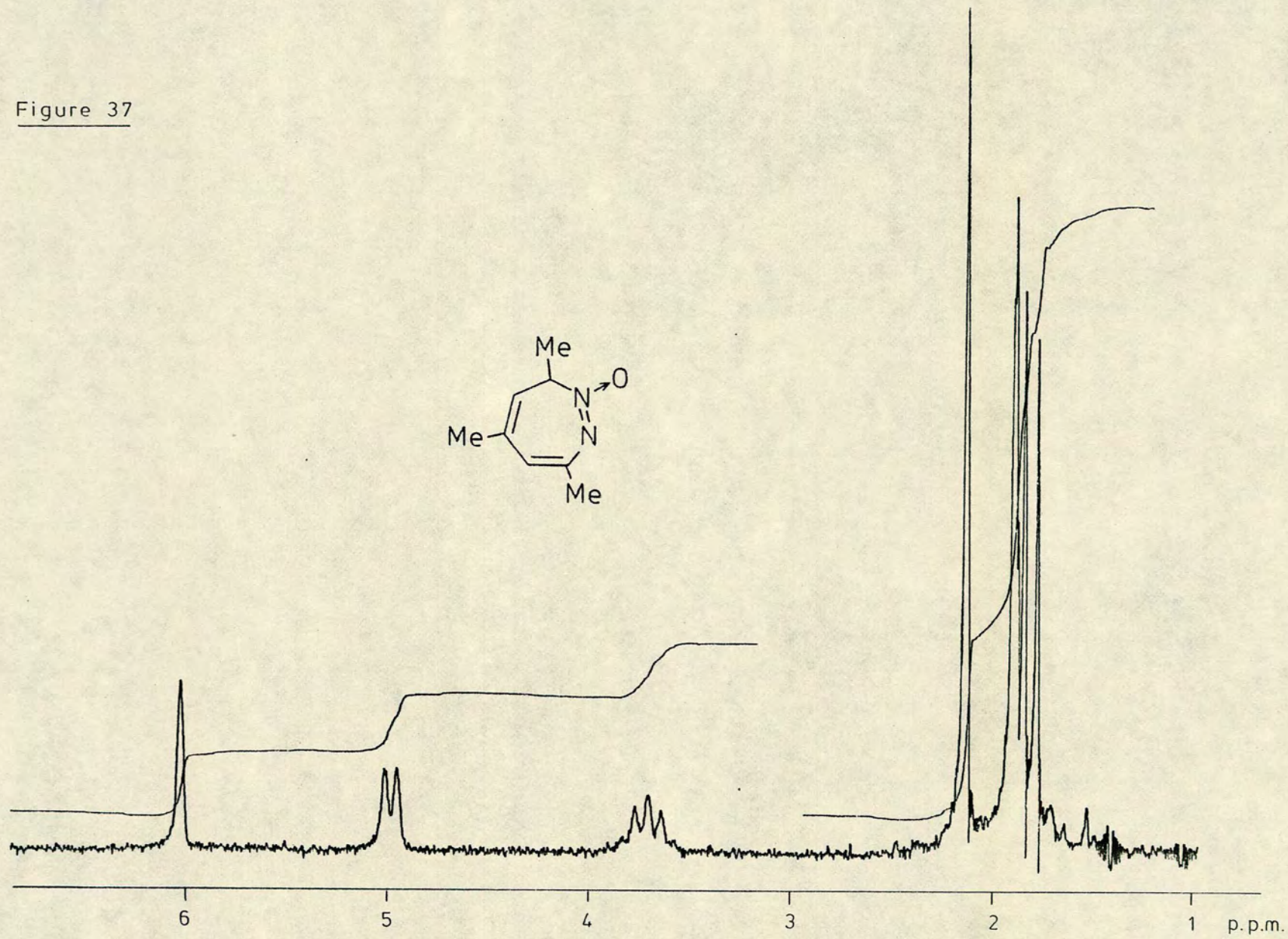
3. Oxidation of 3,5,7-trimethyl-3*H*-1,2-diazepine

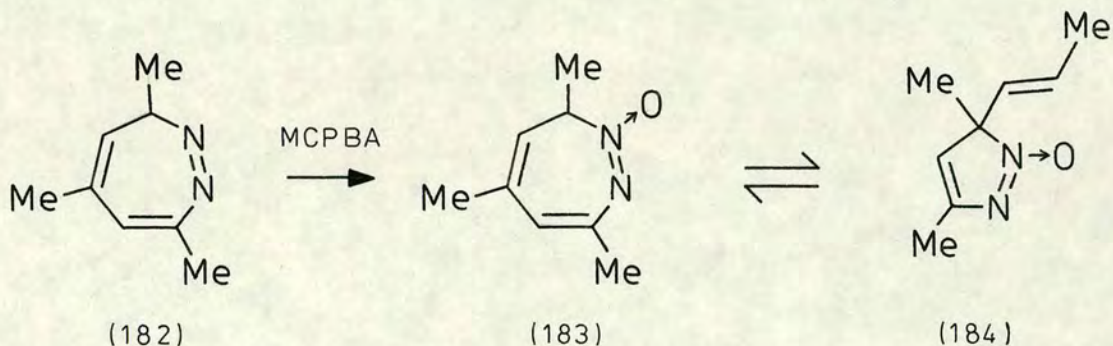
Having successfully achieved oxidation of a benzodiazepine we next turned our attention to the monocyclic 3*H*-1,2-diazepine series. The trimethyl substituted compound (182) was chosen for initial investigation because in this case the two interconverting isomers were identical, and thus should provide a simple system in terms of a single expected product.



Oxidation of 3,5,7-trimethyl-3*H*-1,2-diazepine with *m*-chloroperbenzoic acid resulted in the formation of a 1:1 mixture of two compounds formulated as the diazepine *N*-oxide (183) and the vinylpyrazole *N*-oxide (184) as shown in scheme 54.

Figure 37





Scheme 54

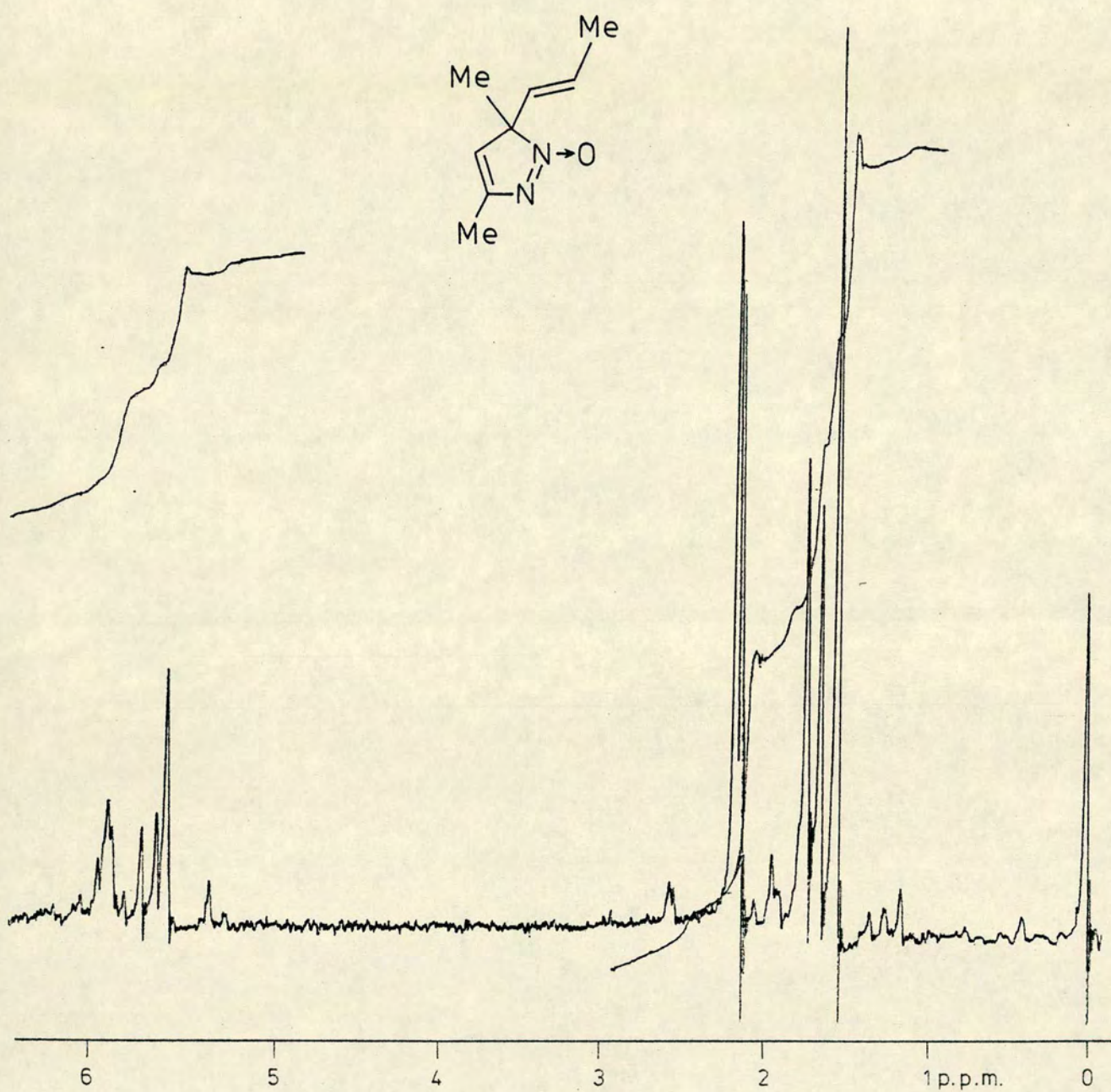
The 1:1 product mixture of (183) and (184) could be separated by preparative t.l.c., but each of the separated pure compounds was found to slowly isomerise back to the 1:1 mixture on standing at room temperature. This interconversion could however be prevented by storing the purified samples at below -30°C .

The structures of these two compounds were assigned on the basis of their ^1H and ^{13}C n.m.r. spectra, having first established that the molecular formula for these compounds was the original diazepine plus one oxygen atom from elemental analysis and exact parent ion mass measurements.

Figure 37 reproduces the ^1H n.m.r. spectrum of the diazepine *N*-oxide. Figures 38 and 39 detail the key n.m.r. assignments of the monocyclic diazepine before and after oxidation, the similarity of the chemical shifts and splitting patterns is apparent.

The location of the oxygen atom is assigned to N-2 on the basis of the shielding/deshielding effects on the carbon atoms C-3 and C-7 directly attached to the azo-linkage, as discussed earlier.

Figure 40



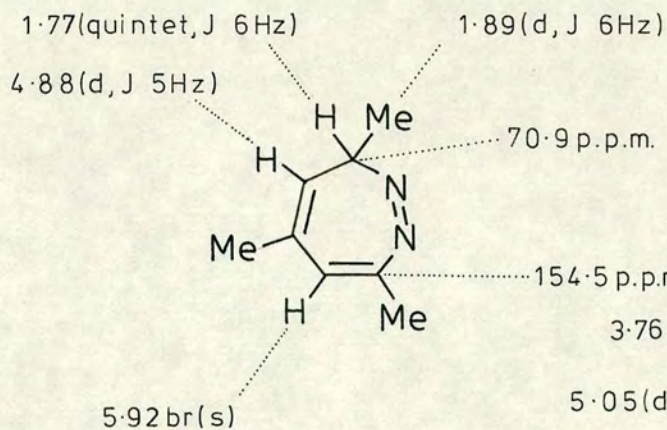


Figure 38

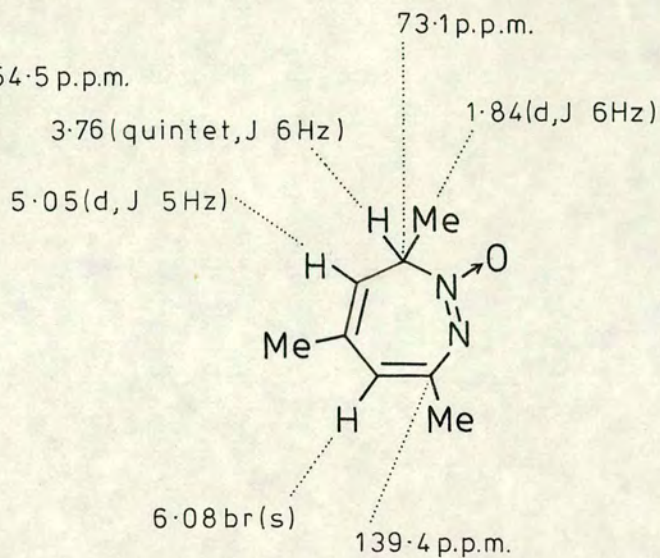
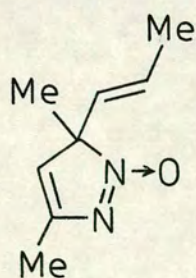
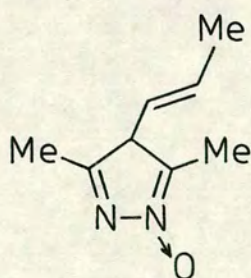


Figure 39

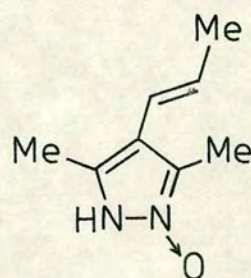
The structural assignment of the pyrazole *N*-oxide was more difficult, figure 40 reproduces its ^1H n.m.r. spectrum. A propenyl fragment together with a broad olefinic proton were identified, this enabled formulation of the compound as (184).



(184)



(185)

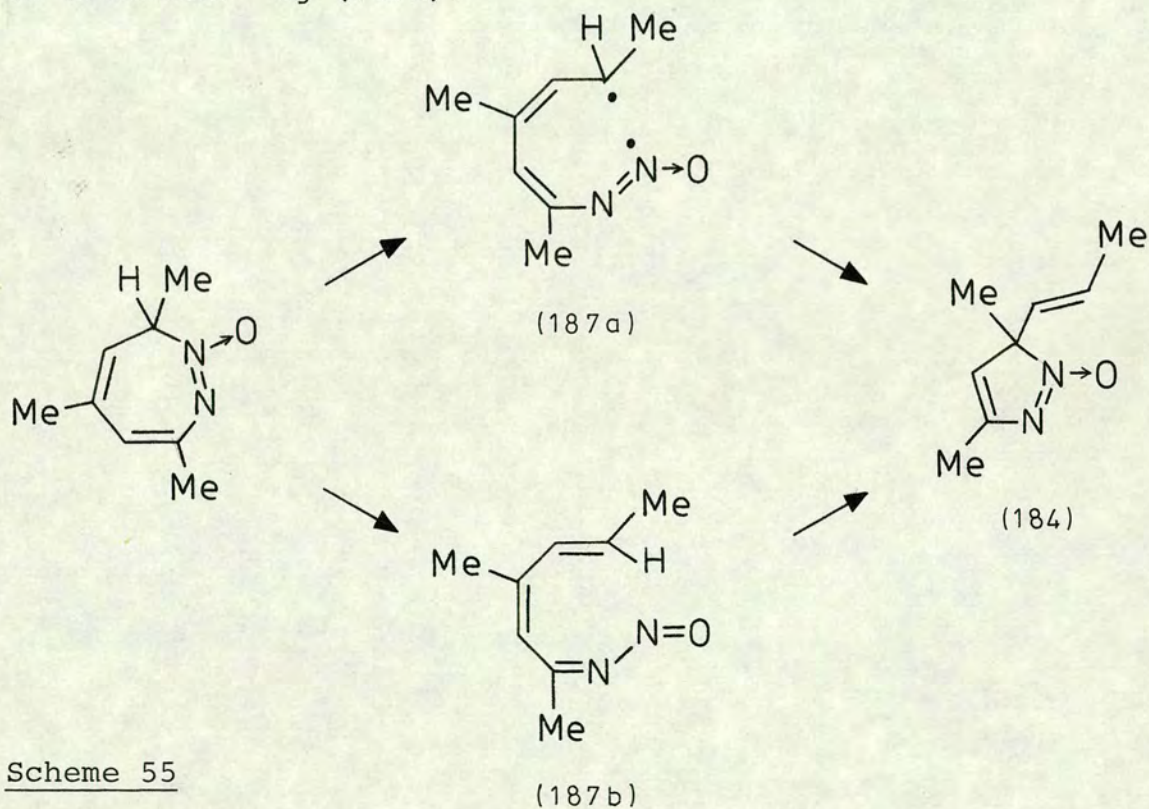


(186)

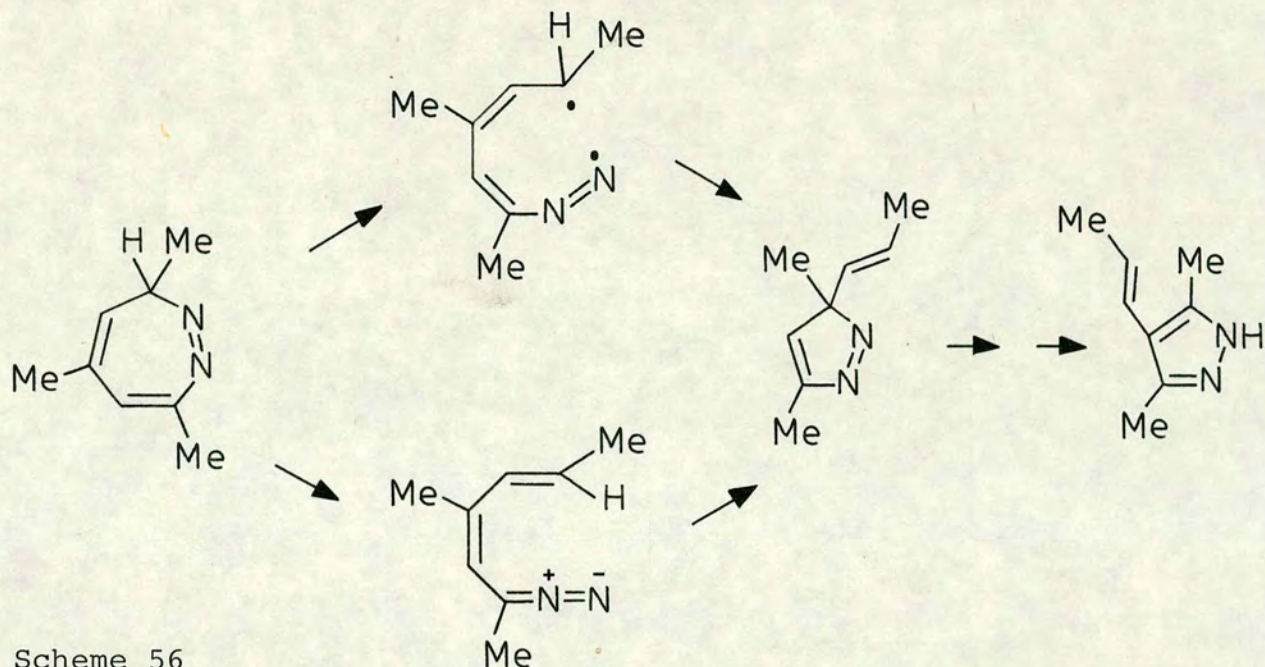
Possible structures (185) and (186) could be discounted because they possessed only two olefinic protons instead of the three observed.

It seems likely that this rearrangement follows the

mechanism shown below (scheme 55) involving firstly ring cleavage between N-2 and C-3 to generate an intermediate (187a or b) followed by cyclisation to give the pyrazole (184). The primary cleavage could take place *via* an electrocyclic ring opening to give the conjugated *N*-nitrosamine (187b) directly or it could be envisaged as an homolytic or heterolytic process giving an intermediate formulated as a dipole or diradical eg (187a).

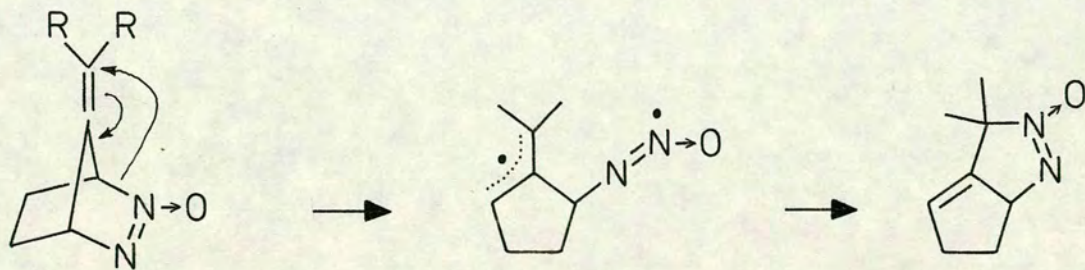


This isomerisation parallels a similar reaction of the diazepine itself, (Scheme 56), the major difference being that the diazepine requires a temperature of $>100^{\circ}\text{C}$ to induce reaction while its oxide isomerises quite quickly at room temperature.



Scheme 56

It is again not certain whether the bond cleavage step is *via* electrocyclic ring opening or homolytic scission. Another example of a formal 1,3-migration of the azoxy-group was published while the above work was in progress^{191,192} (Scheme 57).

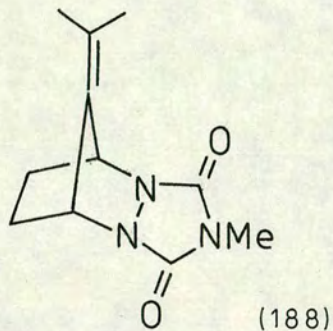


Scheme 57

In this case the authors favoured a diradical mechanism on the basis of the following experimental evidence;

- i) the insensitivity of the reaction to solvent polarity,
ie ionic species improbable

- ii) a positive entropy of activation
- iii) the reaction rates were similar to the free radical reactions of the triazolidinedione (188).



However the relative rates of reaction of schemes 55 and 56 make it unlikely that their isomerisations follow a similar radical route since it is well known that homolytic cleavage α to an azoxy group is much slower than that α to an azo group¹⁵⁸.

EXPERIMENTAL

	Page No
A. SYMBOLS AND ABBREVIATIONS	185
B. INSTRUMENTATION AND GENERAL TECHNIQUES	186
C. PREPARATION OF STARTING MATERIALS	
1. Diiron nonacarbonyl	188
2. Benzylideneacetone iron tricarbonyl	188
3. 2-Bromobenzylbromide	188
4. 2-Bromobenzyltriphenylphosphonium bromide	189
5. <i>E</i> -2-Bromostilbene	189
6. <i>E</i> -2-Formylstilbene	190
7. <i>E</i> -2-Formylstilbene tosylhydrazone	190
8. 4-Ethoxypent-3-en-2-one	190
9. 4-Methylhexa-3,5-dien-2-one	191
10. 4-Methylhepta-3,5-dien-2-one	191
11. Pent-3-en-2-one	191
12. Ethyl 3-hydroxy-3-methylhexa-4-enoate	192
13. Ethyl 3-methylhexa-2,4-dienoate	192
14. 3-Methylhexa-2,4-dienoic acid	192
15. 3-Methylhexa-2,4-dienoic acid chloride	193
16. 5-Methylocta-4,6-dien-3-one	193
17. 2,5-Dimethylocta-4,6-dien-3-one	194
18. 1-Phenyl-5-methylocta-4,6-dien-3-one	194
19. 1-Phenyl-3-methylhexa-2,4-dien-1-one	195
20. Benzylideneacetophenone	196
21. Ethyl 3-hydroxy-3,5-diphenylpenta-4-enoate	196

	Page No
22. Ethyl 3,5-diphenylpenta-2,4-dienoate	196
23. 3,5-Diphenylpenta-2,4-dienoic acid	197
24. 3,5-Diphenylpenta-2,4-dienoic acid chloride	197
25. 4,6-Diphenylhexa-3,5-dien-2-one	198
26. Cyclohexanone trimethylsilyl enol ether	198
27. 2-Methoxymethylenecyclohexanone	199
28. 2-Dimethoxymethylcyclohexanone	199
29. 2-Hydroxy-2-propenylcyclohexane-1-carboxaldehyde dimethyl acetal	200
30. 2-Hydroxy-2-propenylcyclohexane-1-carboxaldehyde	201
31. 2-Propenyl-1-cyclohexene-1-carboxaldehyde	202
32. Cyclopentanone trimethylsilyl enol ether	203
33. 2-Methoxymethylenecyclopentanone	203
34. 2-Propenyl-1-cyclopentene-1-carboxaldehyde	204
35. 2-Bromo-1-cyclohexene-1-carboxaldehyde	205
36. 1-Bromo-2-styryl-1-cyclohexene	205
37. 2-Styryl-1-cyclohexene-1-carboxaldehyde	206
38. 2-Bromo-1-cyclopentene-1-carboxaldehyde	206
39. 1-Bromo-2-styryl-1-cyclopentene	207
40. 2-Styryl-1-cyclopentene-1-carboxaldehyde	208

D. REACTIONS OF $\alpha\beta,\gamma\delta$ -UNSATURATED CARBONYL COMPOUNDS WITH SUBSTITUTED HYDRAZINES

1. To give 2-substituted-3,4-dihydro-1,2-diazepines
 - 1.1 4-Methylhexa-3,5-dien-2-one with *p*-toluene-sulphonylhydrazide 209

1.2	4-Methylhexa-3,5-dien-2-one with phenyl- hydrazine	209
1.3	4-Methylhepta-3,5-dien-2-one with <i>p</i> -toluenesulphonylhydrazide	210
1,4	5-Methylocta-4,6-dien-3-one with <i>p</i> -toluenesulphonylhydrazide	210
1.5	2,5-Dimethylocta-4,6-dien-3-one with <i>p</i> -toluenesulphonylhydrazide	211
1.6	1-Phenyl-5-methylocta-4,6-dien-3-one with <i>p</i> -toluenesulphonylhydrazide	212
1.7	1-Phenyl-3-methylhexa-2,4-dien-1-one with <i>p</i> -toluenesulphonylhydrazide	212
1.8	2-Propenyl-1-cyclopentene-1-carboxaldehyde with <i>p</i> -toluenesulphonylhydrazide	213
1.9	2-Propenyl-1-cyclohexene-1-carboxaldehyde with <i>p</i> -toluenesulphonylhydrazide	213
2.	<u>To give only hydrazones</u>	
2.1	4-Methylhexa-3,5-dien-2-one with 2,4-dinitro- phenylhydrazine	214
2.2	4-Methylhepta-3,5-dien-2-one with 2,4-dinitro- phenylhydrazine	215
2.3	4-Methylhexa-3,5-dien-2-one with 4-nitrophenyl- hydrazine	215
2.4	2-Styryl-1-cyclopentene-1-carboxaldehyde with <i>p</i> -toluenesulphonylhydrazide	216
2.5	2-Styryl-1-cyclohexene-1-carboxaldehyde with <i>p</i> -toluenesulphonylhydrazide	216
2.6	4-Methyl-6-phenylhexa-3,5-dien-2-one	217

3.	<u>Attempted acid-catalysed cyclisations of hydrazones of $\alpha\beta,\gamma\delta$-unsaturated carbonyl compounds</u>	
3.1	Control experiments	217
3.2	Experiments	217
4.	<u>Anomalous reactivity of 4,6-diphenylhexa-3,5-dien-2-one</u>	219
5.	<u>Reaction of 3,4-dihydro-5,7-dimethyl-2-tosyl-1,2-diazepine with lithium diisopropylamide followed by treatment with methyl iodide</u>	220
E.	SYNTHESIS OF DIAZEPINES	
1.	<u>2,3-Benzodiazepines</u>	
1.1	4-Phenyl-1 H -2,3-benzodiazepine	221
1.2	1-Methyl-4-phenyl-1 H -2,3-benzodiazepine	221
1.3	1,2,3,3a-Tetrahydro-10-phenylbenzo-[c]cyclopenta-[f][1,2]diazepine	221
2.	<u>1,2-Diazepines</u>	
2.1	3,5-Dimethyl-3 H -1,2-diazepine and 5,7-dimethyl-3 H -1,2-diazepine	222
2.1.1	Synthesis	222
2.1.2	Isomerisation study	223
2.1.3	Deuterium incorporation study	223
2.1.4	Photolysis study	224

	Page No	
2.2	3,5-Dimethyl-7-ethyl-3 <i>H</i> -1,2-diazepine and 5,7-dimethyl-3-ethyl-3 <i>H</i> -1,2-diazepine	225
2.2.1	Synthesis	225
2.2.2	Isomerisation study	225
2.3	3,5-Dimethyl-7-isopropyl-3 <i>H</i> -1,2-diazepine and 5,7-dimethyl-3-isopropyl-3 <i>H</i> -1,2- diazepine	226
2.4	3,5-Dimethyl-7-phenethyl-3 <i>H</i> -1,2-diazepine and 5,7-dimethyl-3-phenethyl-3 <i>H</i> -1,2- diazepine	227
2.5	3,5,7-Trimethyl-3 <i>H</i> -1,2-diazepine	227
2.6	3,5-Dimethyl-7-phenyl-3 <i>H</i> -1,2-diazepine	229
2.7	5-Methyl-7-phenyl-3 <i>H</i> -1,2-diazepine	229
F.	CONVERSION OF 1,2-DIAZEPINES INTO DIIRON HEXACARBONYL COMPLEXES	
1.	4-Phenyl-1 <i>H</i> -2,3-benzodiazepine	230
2.	1-Methyl-4-phenyl-1 <i>H</i> -2,3-benzodiazepine	230
3.	1,2,3,3a-Tetrahydro-10-phenylbenzo-[c]cyclo- penta[f][1,2]diazepine	231
4.	5-Methyl-7-phenyl-3 <i>H</i> -1,2-diazepine	231
5.	3,5-Dimethyl-3 <i>H</i> -1,2-diazepine and 5,7- dimethyl-3 <i>H</i> -1,2-diazepine	232
5.1	Reaction with diiron nonacarbonyl	232
5.2	Reaction with benzylideneacetone iron tri- carbonyl	233
5.3	Thermolysis study	233

6.	3,5-Dimethyl-7-ethyl-3 <i>H</i> -1,2-diazepine and 5,7-dimethyl-3-ethyl-3 <i>H</i> -1,2-diazepine	234
7.	3,5-Dimethyl-7-isopropyl-3 <i>H</i> -1,2-diazepine and 5,7-dimethyl-3-isopropyl-3 <i>H</i> -1,2-diazepine	235
8.	3,5-Dimethyl-7-phenethyl-3 <i>H</i> -1,2-diazepine and 5,7-dimethyl-3-phenethyl-3 <i>H</i> -1,2-diazepine	236
8.1	Synthesis	237
8.2	H.p.l.c. separation	237
8.3	Thermolysis study	238
G.	DISENGAGEMENT OF DIAZEPINE DIIRON HEXA- CARBONYL COMPLEXES	
1.	4-Phenyl-1 <i>H</i> -2,3-benzodiazepine diiron hexacarbonyl complex	239
2.	5,7-Dimethyl-3 <i>H</i> -1,2-diazepine diiron hexa- carbonyl complex	239
H.	OXIDATION OF 1,2-DIAZEPINES	
1.	4-Phenyl-1 <i>H</i> -2,3-benzodiazepine	240
2.	3,5,7-Trimethyl-3 <i>H</i> -1,2-diazepine	240

EXPERIMENTALA. Symbols and Abbreviations

b.p.	boiling point
m.p.	melting point
t.l.c.	thin-layer chromatography
g.l.c.	gas liquid chromatography
h.p.l.c.	high pressure liquid chromatography
n.m.r.	nuclear magnetic resonance
s; d; t;	singlet; doublet; triplet;
q; m	quartet; multiplet
J	coupling constant
δ	chemical shift
I.R.	infra-red
ν	wavenumber (cm^{-1})
M^+	mass of molecular ion
m/e	mass to charge ratio
h; min;	hours; minutes;
s;	seconds
p.p.m.	parts per million
mol;	moles
mmol	millimoles

B. Instrumentation and General Techniques

Melting Points. Melting points of new compounds were obtained on a Kofler hot-stage apparatus. All others were obtained using capillary tubes and Gallenkamp apparatus.

Nuclear Magnetic Resonance Spectroscopy. Routine ^1H n.m.r. spectra were recorded on a Varian EM360 spectrometer. 100MHz spectra of new compounds were obtained using a Varian HA100 spectrometer operated by Mr. J. Millar. 360MHz spectra were recorded by Dr. I.H. Sadler using a Bruker WH360 spectrometer. Chemical shifts (δ_{H}) are measured in parts per million relative to tetramethylsilane (T.M.S.) as standard ($\delta = 0.0$).

^{13}C N.m.r. spectra were generally recorded on a Varian CFT20 spectrometer operated by Mr. J. Millar, and in a few cases, on a Varian XL100 spectrometer operated by Mr. L. Bell. Chemical shifts (δ_{C}) were measured in p.p.m. relative to tetramethylsilane ($\delta = 0.0$).

All samples were dissolved in deuteriochloroform unless otherwise stated.

Infra-red Spectroscopy. I.R. spectra were recorded on a Perkin-Elmer 157G Grating Spectrophotometer. Liquid samples were recorded as thin films, and solid samples as nujol mulls or in solution in chloroform.

Mass Spectroscopy. Mass spectra and exact masses were obtained on an AEI MS902 mass spectrometer operated by Mr. D. Thomas.

Elemental Analysis. Microanalyses of all new compounds were obtained using a Perkin-Elmer model 240 analyser operated by Mr. J. Grunbaum.

Gas-liquid Chromatography. Qualitative g.l.c. analysis was carried out using a Pye Series 104 chromatograph with a flame ionisation detector.

Medium Pressure Liquid Chromatography. Preparative chromatography using pressurised eluants was carried out using glass columns and fittings supplied by Jobling, and 50 micron silica as the column packing. A U.V. detector was used to monitor the eluant from the column to the fraction collector.

Thin-layer Chromatography. Chromatograms were developed on 0.33 mm layers of alumina (Merck, Aluminium Oxide G) or silica gel (Merck, Silica Gel G) containing Woelm fluorescent green indicator (0.5%). Components of the chromatogram were detected by their quenching of fluorescence under U.V. light, or by their absorption of iodine.

Preparative t.l.c. was performed on 20x20 cm plates coated with a 1 mm layer of alumina or silica.

Column Chromatography. Alumina was Laporte Industries, grade H, 100/200 mesh, 6% deactivated with water.

High Pressure Liquid Chromatography.

H.p.l.c. analyses utilised a 25x0.5 cm column packed with Spherisorb (S5Y) silica (10,700 plates), used with an ARL constant pressure pump and an L.D.C.1205 ultraviolet monitor operated at 254 nm.

C. Preparation of Starting materials

1. Diiron nonacarbonyl

This was prepared by the method of Braye and Hubel¹⁷⁷. A photolysis apparatus was charged with iron pentacarbonyl (73 g, 0.20 mole) in glacial acetic acid (200 ml). The reaction mixture was irradiated for 4 h at room temperature, under nitrogen (Applied photo-physics 400W Medium-pressure arc tube, with a quartz water-cooling jacket). The precipitated diiron nonacarbonyl was filtered from solution, washed with water, ethanol and finally ether (49.6 g, 73%) m.p. 100-120°C (decomp.) (lit.,¹⁷⁷ 100-120°C).

2. Benzylideneacetone iron tricarbonyl

This was prepared by the method of Domingos et al.¹⁷⁸ Benzylideneacetone (8.48 g, 58 mmol) and diiron nonacarbonyl (21.2 g, 58 mmol) were heated in toluene (100 ml) under nitrogen for 5 h at 60°C. After the removal of the solvent under reduced pressure, the residue was dissolved in 10% ethylacetate/toluene (30 ml) filtered through celite and chromatographed on alumina. This gave benzylideneacetone iron tricarbonyl as red-orange crystals (3.9 g, 25%) m.p. 88-89°C (lit.,¹⁷⁸ 88-89°C), δ_{H} 2.5 (s, Me), 3.1 and 6.02 (d, J 6Hz, olefinic), 7.57 (m, phenyl).

3. 2-Bromobenzyl bromide

This was prepared by the method of Shoesmith and Slater¹⁹³ from 2-bromotoluene (200 g, 1.17 mole) and bromine (184.8 g, 2.31 mole). The product was distilled from the crude oil as

a pale yellow liquid (260 g, 89%) b.p. 68-73°C at 0.6 mmHg (lit.,¹⁹³ 129°C at 19 mmHg).

4. 2-Bromobenzyltriphenylphosphonium bromide

This was prepared by the reaction of 2-bromobenzyl bromide (260 g, 1.04 mole) with triphenylphosphine (356 g, 1.36 mole) in boiling benzene (600 ml). After 1.5 h the product was filtered off and washed with petrol 40/60 (535 g, 98%) m.p. 196-198°C (lit.,¹⁹⁴ 197-199°C).

5. E-2-Bromostilbene

A solution of sodium ethoxide, prepared from sodium (6.73 g, 0.293 mole) in "super-dry" ethanol (150 ml) was dripped into a stirred solution containing 2-bromobenzyltriphenylphosphonium bromide (150 g, 0.293 mole) and freshly distilled benzaldehyde (31.1 g, 0.293 mole) in dry ethanol (300 ml). After 24 h the precipitate of sodium bromide was filtered off and the solvent was evaporated under reduced pressure to give a brown oil. Triphenylphosphine oxide was removed by gravity chromatography on alumina, eluting with petrol 40/60. This gave a clear oil (73.2 g) containing both *E* and *Z* isomers. Isomerization to the *E* isomer was carried out by boiling the mixture under reflux in *n*-heptane (300 ml) for 60 h in the presence of a few crystals of iodine. Analysis of g.l.c. (2½% OVI, 185°C) showed greater than 95% of the *E* isomer. The solution was washed with 5% sodium thio-sulphate (2x250 ml), dried and the solvent removed in vacuo. *E*-2-Bromostilbene was distilled from the crude oil as a pale yellow liquid (49.2 g, 65%) b.p.144-146°C at 0.6 mmHg (lit.,¹⁹⁵ 145°C at 0.55 mmHg).

6. E-2-Formylstilbene

This was prepared by the method of Smith and Bayliss¹⁹⁶ using the Grignard reaction of *E*-2-bromostilbene (49.2 g, 0.190 mole) and magnesium (4.62 g, 0.190 mole) in dry T.H.F. (200 ml) and dry dimethylformamide (20.9 g, 0.285 mole). The product was distilled from the crude material as a yellow liquid (24.5 g, 62%) b.p. 147-150°C at 0.6 mmHg, m.p. 80-82°C (lit.,¹⁹⁷ 83°C), ν_{\max} (film) 1690 cm⁻¹ (C=O), δ_{H} 10.35 (s, aldehyde), 6.85-8.25 (m, 11H, aromatic and olefinic).

7. E-2-Formylstilbene tosylhydrazone

E-2-Formylstilbene (11.3 g, 54.1 mmol) and *p*-toluene-sulphonylhydrazide (10.1 g, 54.1 mmol) were dissolved separately in ethanol (60 ml) and warmed to 50°C. These two solutions were mixed and concentrated hydrochloric acid (0.5 ml) added. On cooling a white precipitate was deposited which was recrystallized from ethanol to give *E*-2-formylstilbene tosylhydrazone (13.7 g, 72%) as white crystals m.p. 141-143°C (lit.,⁶⁴ 145-146.5°C), ν_{\max} (Nujol) 3210 cm⁻¹ (N-H), δ_{H} 2.37 (s, tosyl Me), 6.7-8.0 (m, 15H, aromatic plus olefinic), 8.19 (s, CH=N), 8.3 br (s, NH).

8. 4-Ethoxypent-3-en-2-one

This was prepared by Claisen's method¹⁹⁸ from acetylacetone, triethyl orthoformate and ferric chloride in ethanol. The reaction was monitored by g.l.c. (2% CAR 20M, 90°C). 4-Ethoxypent-3-en-2-one was distilled as a pale yellow liquid in 27% yield, b.p. 74-75°C at 16 mmHg (lit.,¹⁹⁹ 71-72°C at 15 mmHg) ν_{\max} (film) 1675 cm⁻¹ (C=O), δ_{H} 1.35 (t, J 7Hz, ethyl Me),

2.15 (s, Me), 2.27 (s, Me), 3.83 (q, J 7Hz, ethyl CH₂), 5.4 (s, olefinic).

9. 4-Methylhexa-3,5-dien-2-one

This was prepared by the method of Crisan and Normant¹⁸⁷ from vinylmagnesium bromide and 4-ethoxypent-3-en-2-one. Distillation of the crude oil afforded the dienone as a pale yellow liquid in 47% yield, b.p.58-60°C at 20 mmHg (lit.,¹⁸⁷ 55-56°C at 15 mmHg) ν_{\max} (film) 1670 cm⁻¹ (C=O) δ_{H} 1.63 and 2.19 (d, J 1.5Hz, 4-Me), 1.84 (s, Me), 4.9-5.5 (m, 6-H₂), 5.78 and 5.67 br (s, 3-H), 6.11 and 8.18 (dd, J 17.5Hz, J' 10.5Hz, 5-H); *E* to *Z* ratio ca. 2:1.

10. 4-Methylhepta-3,5-dien-2-one

This was prepared by the method of Crisan and Normant¹⁸⁷ from the reaction of the Grignard reagent of 1-bromoprop-1-ene and 4-ethoxypent-3-en-2-one. The dienone was distilled from the crude material as a pale yellow liquid in 53% yield, b.p. 78-80°C at 15 mmHg (lit.,¹⁸⁷ 79-80°C at 16 mmHg) ν_{\max} (film) 1640 cm⁻¹ and 1685 cm⁻¹ (C=O), δ_{H} 1.35 and 1.81 (m, 6-Me), 1.94 and 2.16 (d, J 1.5Hz, 4-Me), 2.2 (m, 2-Me), 5.6-6.3 (m, 3H, olefinic), 7.52 (d, J 16Hz, 6-H, *EE* isomer); estimated *E,E* to *E,Z* ratio ca. 1.5:1.

11. Pent-3-en-2-one

This was prepared by the method of Wilds and Djerassi²⁰⁰ from the aldol reaction of acetaldehyde, acetone and sodium hydroxide (18%), b.p.120-124°C at 760 mmHg (lit.,²⁰⁰ 121-122.5°C at 760 mmHg).

12. Ethyl 3-hydroxy-3-methylhexa-4-enoate

This was prepared in 71% yield using the method of Cologne and Varagnat¹⁸⁸, by the Reformatsky reaction of ethyl bromoacetate, zinc and pent-3-en-2-one. The hydroxyester was distilled from the crude material as a colourless oil, b.p. 87-90°C at 10 mmHg (lit.,¹⁸⁸ 93°C at 15 mmHg), ν_{\max} (film) 3500 cm^{-1} (O-H), 1620 cm^{-1} (C=O) δ_{H} 1.28 (t, J 7Hz, ethyl Me), 1.3 (s, 3-Me), 1.69 (d, J 6Hz, =CHMe), 2.57 (s, CH₂), 3.44 br (s, OH), 4.22 (q, J 7Hz, ethyl CH₂), 5.67 (m, 2H, olefinic).

13. Ethyl 3-methylhexa-2,4-dienoate

This was obtained by slow distillation from ethyl 3-hydroxy-3-methylhexa-4-enoate with anhydrous copper sulphate according to the method of Cologne and Varagnat¹⁸⁸. The ester was redistilled, after drying, as a colourless liquid (73%), b.p. 83-85°C at 14 mmHg (lit.,¹⁸⁸ 85°C at 15 mmHg), ν_{\max} (film) 1610 cm^{-1} (C=O).

14. 3-Methylhexa-2,4-dienoic acid

This was prepared using Burton and Ingold's method²⁰¹ by stirring ethyl 3-methylhexa-2,4-dienoate with 10% methanolic potassium hydroxide solution. This gave the acid as a white solid (84%) which was recrystallized from ethanol, m.p. 118-120°C (lit.,²⁰¹ 120°C), ν_{\max} (Nujol) 2700 cm^{-1} (acidic OH), 1680 cm^{-1} (C=O), δ_{H} 1.86 (d, J 5Hz, =CHMe), 2.27 (s, 3-Me), 5.71 br (s, 2-H), 6.19 (m, 4-H and 5-H), 10.91 br (s, acid H).

15. 3-Methylhexa-2,4-dienoic acid chloride

This was prepared according to Burton and Ingold's method²⁰¹ by the addition of thionyl chloride to 3-methylhexa-2,4-dienoic acid in benzene. The acid chloride was distilled as a pale yellow liquid in 77% yield, b.p.100°C at 20 mmHg (lit.,²⁰¹ 94-95°C at 15 mmHg), ν_{\max} (film) 1750 cm^{-1} (C=O).

16. 5-Methylocta-4,6-dien-3-one

This was prepared using a method based on that of Heilbron et al.²⁰² A Grignard reagent was prepared from ethyl bromide (14.3 g, 131 mmol) and magnesium (3.16 g, 131 mmol) in dry ether (60 ml). This was cooled to 0°C in ice, an anhydrous cadmium chloride (11.9 g, 65.4 mmol) was added in one batch with vigorous mechanical stirring. Dry benzene (100 ml) was added and the ether was removed by distillation. After 30 min at room temperature 3-methylhexa-2,4-dienoic acid (7.54 g, 52.3 mmol) in benzene (25 ml) was dripped in at 0°C. The reaction mixture was boiled under reflux for 20 min, cooled to 0°C and carefully hydrolysed with ammonium chloride solution (10%, 100 ml). The aqueous layer was washed with ether (3x50 ml), the ether extracts combined with the organic phase, dried over magnesium sulphate and the solvent evaporated under reduced pressure to leave a yellow oil. Short-path distillation from this gave 5-methylocta-4,6-dien-3-one as a clear yellow oil (3.6 g, 50%) b.p.80°C at 10 mmHg (lit.,¹⁹⁴ 77-79°C at 10 mmHg); ν_{\max} (film) 1680 cm^{-1} (C=O); δ_{H} 1.06 (t, J 7.5Hz, ethyl Me), 1.84 (d, J 5Hz, 8+H₃), 1.96 and 2.23 (d, J 1.5Hz, 5-Me), 2.44 and 2.46 (overlapping q, J 7.5Hz, ethyl CH₂), 5.95 and 6.03 br (s, 4-H), 7.6 br (d, J 16Hz) and 6.1-6.4 (m,

6-H and 7-H); *E,E* to *Z,E* ratio 2.3:1.

17. 2,5-Dimethylocta-4,6-dien-3-one

This was prepared using the adapted Heilbron method described above²⁰². A Grignard reagent was prepared from isopropyl bromide (17.1 g, 0.139 mole) and magnesium (3.38 g, 0.139 mole) in dry ether (80 ml). This was cooled to 0°C and anhydrous cadmium chloride (12.7 g, 0.070 mole) added in one batch, under nitrogen. After rapid mechanical stirring for 30 min, 3-methylhexa-2,4-dienoic acid chloride (8.0 g, 0.056 mole) in ether (30 ml) was dripped in. The mixture was boiled under reflux for 2 h, cooled to 0°C and carefully hydrolysed with ammonium chloride solution (10%, 120 ml). The reaction mixture was then extracted with ether (3x50 ml), the organic phase dried, and the solvent was evaporated under reduced pressure to give a yellow oil. Short-path distillation from this gave 2,5-dimethylocta-4,6-dien-3-one as a yellow oil (2.88 g, 33%), b.p.95-100°C at 10 mmHg (Found: M^+ , 152.119333 $C_{10}H_{16}O$ requires m/e , 152.120109); ν_{max} (film) 1680 cm^{-1} (C=O); δ_H 1.08 (d, J 7Hz, isopropyl Me), 1.84 (d, J 5Hz, 8-H₃), 1.98 and 2.22 (d, J 1.5Hz, 5-Me), 2.62 (heptet, J 7Hz, 2-H), 7.57 (d, J 16Hz) and 5.9-6.35 (m, 3H, olefinic) *E,E* to *Z,E* ratio ca.2:1. The 2,4-dinitrophenylhydrazone derivative had m.p. 137-138°C (Found: C, 57.6; H, 6.0; N, 16.8. $C_{16}H_{20}N_4O_4$ requires C, 57.8; H, 6.1; N, 16.9%).

18. 1-Phenyl-5-methylocta-4,6-dien-3-one

This was prepared using the adapted Heilbron method described above²⁰². A Grignard reagent was prepared from

phenethyl bromide (25.7 g, 0.139 mole) and magnesium (3.38 g, 0.139 mole) in dry ether (100 ml). This was cooled to 0°C and anhydrous cadmium chloride (12.7 g, 0.070 mole) added in one batch, under nitrogen. After rapid mechanical stirring for 30 min, 3-methylhexa-2,4-dienoic acid chloride (8.0 g, 0.056 mole) in ether (30 ml) was dripped in. This mixture was boiled under reflux for 2 h, cooled to 0°C and carefully hydrolysed with ammonium chloride solution (10%, 120 ml). The reaction mixture was extracted with ether (3x50 ml), the organic phase dried, and the solvent evaporated under reduced pressure to leave a yellow oil. Short-path distillation from the afforded 1-phenyl-5-methylocta-4,6-diene-3-one (7.1 g, 60%) as a yellow oil, b.p.140-145°C at 0.05 mmHg (Found: M^+ , 214.133658 $C_{15}H_{18}O$ requires m/e, 214.135758; ν_{max} (film) 1685 cm^{-1} (C=O); δ_H 1.85 (d, J 4Hz, 8-H₃), 1.95 and 2.23 (d, J 1.5Hz, 5-Me), 2.85 (m, CH₂CH₂), 7.58 (d, J 16Hz) and 5.8-6.3 (m, 3H, olefinic), 7.05-7.3 (m, 5H, phenyl); *E,E* to *Z,E* ratio ca.4:1. The 2,4-dinitrophenylhydrazone derivative had m.p.163-164°C (Found: C, 63.7; H, 5.6; N, 14.1. $C_{21}H_{22}N_4O_4$ requires C, 64.0; H, 5.6; N, 14.2%).

19. 1-Phenyl-3-methylhexa-2,4-dien-1-one.

This was prepared using the adapted Heilbron method 202.
 A Grignard reagent was prepared from bromobenzene (21.8 g, 0.139 mole) and magnesium (3.38 g, 0.139 mole) in dry ether (100 ml). This was cooled to 0°C and anhydrous cadmium chloride (12.7 g, 0.070 mole) added in one batch, under nitrogen. After rapid mechanical stirring for 30 min, 3-methylhexa-2,4-dienoic acid chloride (8.0 g, 0.056 mole) in ether (30 ml) was dripped in. The mixture was boiled under reflux for 2 h,

cooled to 0°C and carefully hydrolysed with ammonium chloride (10%, 120 ml). The reaction mixture was extracted with ether (3x50 ml), the organic phase dried, and the solvent evaporated under reduced pressure to leave a yellow oil. Short-path distillation afforded 1-phenyl-3-methylhexa-2,4-dien-1-one (6.4 g, 62%) as a yellow oil, b.p.110°C at 0.1 mmHg (Found: C, 83.9; H, 7.4. $C_{13}H_{14}O$ requires C, 83.8; H, 7.6), ν_{\max} (film) 1680 cm^{-1} (C=O); δ_H 1.45 and 1.9 (d, J 4Hz, 6-Me), 2.13 and 2.3 (d, J 1.5Hz, 3-Me), 6.1-6.3 (m, 2H, olefinic), 6.62 and 6.73 br (s, 2-H), 7.2-7.95 (m, 5H, phenyl); *E,E* to *Z,E* ratio ca.3:1.

20. Benzylideneacetophenone

This was prepared by the method of Vogel²⁰³ from the reaction between benzaldehyde, acetophenone and sodium hydroxide (53%) m.p.56-57°C (lit.,²⁰³ 56-57°C).

21. Ethyl 3-hydroxy-3,5-diphenylpenta-4-enoate

This was prepared by the method of Ingold and Bloom²⁰⁴ from the Reformatsky reaction of ethyl bromoacetate, benzylideneacetophenone and zinc in dry benzene (65%) m.p.91-92°C (lit.,²⁰⁴ 93°C), ν_{\max} (Nujol) 3500 cm^{-1} (OH), δ_H 1.22 (t, J 7Hz, ethyl Me), 3.09 br (s, CH₂), 4.19 (q, J 7Hz, ethyl CH₂), 4.87 br (s, OH), 6.64 (m, olefinic), 7.2-7.75 (m, 10H, aromatic).

22. Ethyl 3,5-diphenylpenta-2,4-dienoate

This was prepared by heating ethyl 3-hydroxy-3,5-diphenylpenta-4-enoate and *p*-toluenesulphonic acid (catalyst) in dry benzene under reflux in an apparatus fitted with a Dean and

Stark trap. Ethyl 3,5-diphenylpenta-2,4-dienoate was distilled from the crude material as a yellow liquid (64%), b.p. 160-165°C at 0.6 mmHg (lit.,²⁰⁵ 156-164°C at 0.6 mmHg), δ_H showed the presence of *E* and *Z* isomers, in the ratio ca.2:1, 1.07 and 1.33 (t, J 7Hz, ethyl Me), 4.01 and 4.28 (q, J 7Hz, ethyl CH₂), 5.86 and 6.09 br (s, 2-H), 6.2-7.0 and 8.5-8.8 (m, 2H, 4-H and 5-H), 7.2-8.0 (m, 10H, aromatic).

23. 3,5-Diphenylpenta-2,4-dienoic acid

This was prepared using Bergmann and Solomonovici's method²⁰⁵ by refluxing ethyl 3,5-diphenylpenta-2,4-dienoate with 10% aqueous ethanolic sodium hydroxide. This gave the acid as a white solid which was recrystallized from ethanol (66%) m.p. 143-145°C (lit.,²⁰⁶ 145°C) ν_{\max} (Nujol) 2800 cm⁻¹ (acidic OH), δ_H 5.89 br (s, 2-H), 6.68 and 8.57 (d, J 16Hz, 4-H and 5-H), 7.2-7.7 (m, 10H, aromatic), 10.3 br (s, acidic H).

24. 3,5-Diphenylpenta-2,4-dienoic acid chloride

This was prepared using Burton and Ingold's method²⁰¹. 3,5-Diphenylpenta-2,4-dienoic acid (10.0 g, 0.04 mole) and thionyl chloride (23.8 g, 0.20 mole) in dry benzene (100 ml) were stirred at room temperature overnight and then boiled under reflux for 10 minutes. The benzene and excess thionyl chloride were evaporated off under reduced pressure to leave a brown oil. Short-path distillation afforded 3,5-diphenylpenta-2,4-dienoic acid chloride as a yellow oil (5.2 g, 48%), b.p. 195°C at 0.05 mmHg, δ_H 6.19 (s, 2-H), 6.87 and 8.29 (AB, J 16Hz, 4-H and 5-H), 7.2-7.8 (m, 10H, aromatic), *E,E* to *E,Z* ratio greater than 10:1.

25. 4,6-Diphenylhexa-3,5-dien-2-one.

This was prepared using the adapted Heilbron method²⁰². A Grignard reagent was prepared from methyl iodide (6.04 g, 42.5 mmol) and magnesium (1.02 g, 42.5 mmol) in dry ether (50 ml). This was cooled to 0° and anhydrous cadmium chloride (3.88 g, 21.3 mmol) added in one batch under nitrogen. After rapid mechanical stirring for 30 min, 3,5-diphenylpenta-2,4-dienoic acid chloride (4.6 g, 17 mmol) in ether (20 ml) was dripped in. The mixture was boiled under reflux for 2 h, cooled to 0°C and carefully hydrolysed with ammonium chloride (10%, 60 ml). The reaction mixture was extracted with ether (3x25 ml), the organic phase dried, and the solvent evaporated under reduced pressure to leave a yellow oil. Short-path distillation afforded 4,6-diphenylhexa-3,5-dien-2-one (2.47 g, 59%) b.p.185°C at 0.7 mmHg. (Found: C, 86.8; H, 6.7. C₁₈H₁₆O requires C, 87.1; H, 6.5) (Found: M⁺, 248.121288 C₁₈H₁₆O requires m/e, 248.120109), ν_{\max} (film) 1670 cm⁻¹ (C=O); δ_{H} 7.1-7.6 (m, 10H, aromatic), 8.45 (d, J 16Hz) and 6.1-6.9 (m, 3H, olefinic), 2.29 and 1.84 (s, Me); *E,E* to *Z,E* ratio ca.4:1. Despite numerous attempts a 2,4-dinitrophenylhydrazone derivative could not be isolated.

26. Cyclohexanone trimethylsilyl enol ether

This was prepared by the method of House et al.²⁰⁷ from the reaction of trimethylsilyl chloride, triethylamine, dimethylformamide and cyclohexanone in 80% yield, b.p.60-61°C at 12 mmHg (lit.,²⁰⁷ 74-75°C at 20 mmHg), δ_{H} (CCl₄); 0.9 (s, SiMe₃), 2.1-3.1 (m, cyclohexyl), 5.43 br (m, olefinic).

27. 2-Methoxymethylenecyclohexanone

This was prepared by an adaption of Mukaiyama and Hayashi's method²⁰⁸. Titanium tetrachloride (17.7 g, 93 mmol), trimethylorthoformate (9.4 g, 88 mmol) and cyclohexanone trimethylsilyl enol ether (15 g, 88 mmol) were stirred in dry methylene chloride (80 ml) at -78°C for 3 h. The mixture was allowed to warm to room temperature and stirred for a further 2 h. Hydrolysis was carried out by adding the mixture dropwise to a rapidly stirred solution of sodium carbonate (10%, 1 l). The aqueous layer was washed with ether (3x150 ml) and the ether extracts combined with the organic layer, dried over magnesium sulphate, and evaporated under reduced pressure to give a brown oil. Rapid distillation under nitrogen through a short Vigreux column afforded 2-methoxymethylenecyclohexanone as a clear liquid (6.3 g, 51%), b.p. $78-80^{\circ}\text{C}$ at 0.4 mmHg (lit.,²⁰⁹ 85°C at 3.2 mmHg). (Found: M^+ , 140.083248 $\text{C}_8\text{H}_{12}\text{O}_2$ requires m/e, 140.083724), ν_{max} (film) 1675 cm^{-1} (C=O), δ_{H} 1.55-1.95 and 2.2-2.3 (m, 8H, cyclohexyl), 3.81 (s, OMe), 7.23 (t, J 1.5Hz, olefinic).

28. 2-Dimethoxymethylcyclohexanone

This was prepared by the method of Mukaiyama and Hayashi²⁰⁸. Titanium tetrachloride (35.2 g, 0.185 mole), trimethyl orthoformate (18.7 g, 0.176 mole) and cyclohexanone trimethylsilyl enol ether (30 g, 0.176 mole) were stirred in dry methylene chloride (150 ml) at -78°C for 3 h. Hydrolysis was carried out by injecting the mixture (below -30°C) into a rapidly stirred sodium carbonate solution (10%, 2 l). The aqueous layer was washed with ether (3x300 ml), the ether extracts

combined with the organic layer, dried over magnesium sulphate, and evaporated under reduced pressure to give a brown oil. Distillation of this afforded 2-dimethoxymethylcyclohexanone as a colourless liquid (15.1 g, 53%), b.p. 66-68°C at 0.1 mmHg (lit.,^{202,210,211} not quoted) (Found: M^+ , 172.110020 $C_9H_{16}O_3$ requires 172.109937) ν_{\max} (film) 1670 cm^{-1} (C=O) δ_H 4.72 (d, J 6Hz, CH-(OMe)₂), 3.42 (s, OMe), 2.60 (m, CH-CH-(OMe)₂), 1.5-2.4 (m, 8H, cyclohexyl).

29. 2-Hydroxy-2-propenylcyclohexane-1-carboxaldehyde dimethyl acetal.

A Grignard reagent was prepared from 1-bromopropene (24.7 g, 0.204 mole) and magnesium (4.96 g, 0.204 mole) in dry T.H.F. (100 ml). This was cooled to 0°C in ice and 2-dimethoxymethylcyclohexanone (28 g, 0.163 mole) in T.H.F. (50 ml) was dripped in. The reaction mixture was stirred at room temperature for a further 12 h. The Grignard complex was decomposed by the careful addition of saturated ammonium chloride (100 ml) at 0°C. The aqueous layer was washed with ether (3x50 ml), the ether extracts combined with the organic layer, dried over magnesium sulphate and the solvent removed under reduced pressure to give yellow oil. This was distilled to give 2-hydroxy-2-propenylcyclohexane-1-carboxaldehyde dimethylacetal (21.9 g, 63%) as yellow oil b.p. 89-91°C at 0.3 mmHg (Found: C, 67.3; H, 9.95. $C_{12}H_{20}O_2$ requires C, 67.3; H, 10.3%) ν_{\max} (film) 3500 cm^{-1} (OH), δ_H 1.1-1.9 (m, 9H, cyclohexyl), 1.86 (d, J 7Hz, =CHMe), 2.2 br (s, OH), 3.32 and 3.38 (s, 6H, OMe), 4.46 br (s, CH-(OMe)₂), 5.15-5.55 (m, 2H, olefinic).

30, 2-Hydroxy-2-propenylcyclohexane-1-carboxaldehyde

The acetal was hydrolysed by the method of Conia et al.²¹²

An aqueous solution of oxalic acid (10%, 6 ml) was added to a stirred suspension of silica gel (60 g, Merck; silica gel 60, 230-400 mesh) in dichloromethane (200 ml). After 2-3 min the water phase disappeared due to adsorption on the silica gel surface. 2-Hydroxy-2-propenylcyclohexane-1-carboxaldehyde dimethylacetal (10 g, 47 mmol) dissolved in dichloromethane (25 ml) was dripped in and the mixture stirred for a further 12 h. Sodium hydrogen carbonate (2.0 g) was added, the mixture stirred for 5 min and the solid phase then separated by suction filtration. Evaporation of the solvent under reduced pressure gave a yellow oil which when separated by medium pressure liquid chromatography (silica, ether:petrol 40/60, 1:4) gave 2-hydroxy-2-propenylcyclohexane-1-carboxaldehyde as a yellow oil (5.3 g, 68%) (Found: M^+ , 168.114801 $C_{10}H_{16}O_2$ requires m/e , 168.115023) ν_{max} (film) 3500 cm^{-1} (OH), 1710 cm^{-1} (C=O) δ_H showed the presence of *E* and *Z* isomers in the ratio ca. 1:1, 9.7 and 9.73 (d, *J* 2Hz, aldehyde), 5.3-5.9 (m, 2H, olefinic), 2.83 br (s, 1H, OH), 2.28 (m, 1H, CH-CHO), 1.86 and 1.66 (d, *J* 5Hz, Me), 1.17-2.1 (m, 8H, cyclohexyl). The 2,4-dinitrophenylhydrazone derivative had m.p. 133-134°C (Found: C, 55.4; H, 5.9; N, 16.1. $C_{16}H_{20}N_4O_5$ requires C, 55.2; H, 5.8; N, 16.1%), δ_H 10.98 br (s, NH), 9.06 (d, *J*, 2Hz, *m*-ArH), 8.28 (dd, *J* 10Hz, *J'* 2Hz, *m'*-ArH), 7.86 (d, *J* 10Hz, *o*-ArH), 7.66 (d, *J* 5Hz, CH=N), 5.48 (m, 2H, olefinic), 2.55 (m, 1H, CH-CH=N), 1.87 (d, *J* 5Hz, Me), 1.5-2.1 (m, 9H, cyclohexyl including OH).

31. 2-Propenyl-1-cyclohexene-1-carboxaldehyde

This was prepared by the dehydration technique outlined by Corey and Enders¹⁸⁹. Freshly distilled methanesulphonyl chloride (4.01 g, 35 mmol) was added dropwise to a stirred solution of triethylamine (10.1 g, 0.10 mole) and 2-hydroxy-2-propenylcyclohexane-1-carboxaldehyde (5.2 g, 31 mmol) in dry methylene chloride (50 ml) at 0°C under nitrogen and in the dark. Almost immediately a white precipitate of triethylamine hydrochloride was observed. The reaction mixture was stirred for 30 h and then the organic phase was washed with dilute hydrochloric acid (2x20 ml), sodium bicarbonate solution (10%, 1x20 ml) and finally with water (1x20 ml). The organic phase was dried over magnesium sulphate and the solvent removed under reduced pressure to leave a yellow oil. This oil was separated by medium pressure chromatography (silica, ether: petrol 40/60, 1:1) to give recovered 2-hydroxy-2-propenylcyclohexane-1-carboxaldehyde (2.08 g, 40% recovery) and 2-propenylcyclohex-1-ene-1-carboxaldehyde (1.91 g, 68% based on consumed starting material) as a clear liquid (Found: M^+ , 150.104006 $C_{10}H_{14}O$ requires m/e , 150.104459), ν_{max} (film) 1715 cm^{-1} (C=O), δ_H showed the presence of *E* and *Z* isomers in the ratio ca.1:1, *Z* isomer; 9.73 (s, aldehyde), 6.01 (d, J 12Hz, CH=CHMe), 5.9 (dq, J 12Hz, J'5Hz, CH=CHMe), 2.05-2.35 and 1.5-1.85 (m, cyclohexyl including Me), *E* isomer; 10.25 (s, aldehyde), 6.98 (d, J 16Hz, CH=CHMe), 6.0 (dq, J 16Hz, J' 6Hz, CH=CHMe), 1.87 (d, J 6Hz, Me), 2.1-2.35 and 1.5-1.8 (m, cyclohexyl). The 2,4-dinitrophenylhydrazone derivative had m.p.147-148°C (Found: C, 57.9; H, 5.6; N, 17.0 $C_{16}H_{18}N_4O_4$ requires C, 58.2; H, 5.5; N, 17.0%).

32. Cyclopentanone trimethylsilyl enol ether*

This was prepared by the method of House et al.²⁰⁷ from the reaction of trimethylsilyl chloride, triethylamine, dimethylformamide and cyclopentanone in 67% yield, b.p. 154-155°C at 760 mmHg (lit., 158-159°C at 760 mmHg) δ_H (CCl₄); 1.0 (s, SiMe₃), 2.45-3.2 (m, cyclopentyl), 5.42 br (s, olefinic).

33. 2-Methoxymethylenecyclopentanone*

This was prepared by an adaption of Mukaiyama and Hayashi's method²⁰⁸. Titanium tetrachloride (24.3 g, 0.128 mole), trimethylorthoformate (12.7 g, 0.120 mole) and cyclopentanone trimethylsilyl enol ether (19.2 g, 0.120 mole) were stirred in dry methylene chloride (120 ml) at -78°C for 3 h. The mixture was allowed to warm to room temperature and stirred for a further 2 h. Hydrolysis was carried out by adding the mixture dropwise to a rapidly stirred solution of sodium carbonate (10%, 1 l). The aqueous layer was extracted with ether (3x150 ml), the ether extracts were combined with the organic layer, dried over magnesium sulphate, and the solvent removed under reduced pressure to give a black oil. Rapid distillation under nitrogen through a short Vigreux column afforded 2-methoxymethylenecyclopentanone as a clear liquid (8.5 g, 56%) b.p. 76-78°C at 2.5 mmHg (lit.,²¹⁰ 54-56°C at 0.1 mmHg) (Found: M⁺, 126.068277 C₇H₁₀O₂ requires m/e, 126.068075) ν_{\max} (film) 1695 cm⁻¹ (C=O) δ_H 1.8-2.1 (m, 4-H₂), 2.15-2.35 (m, 3-H₂), 2.4-2.6 (m, 5-H₂), 3.8 (s, OMe), 7.2 br (s, olefinic). The 2,4-dinitrophenylhydrazone derivative had

* Prepared in collaboration with Mr. I.R. Robertson.

This applies throughout

m.p. 222-224°C (Found: C, 50.8; H, 4.7; N, 18.2. $C_{13}H_{14}N_4O_5$ requires C, 51.0; H, 4.6; N, 18.3%).

34. *E*-2-Propenyl-1-cyclopentene-1-carboxaldehyde*

This was prepared using the adapted method of Dreiding and Nickel²¹³. A lithium reagent was prepared from 1-bromopropene (5.33 g, 44 mmol) and lithium (0.616 g, 88 mmol) in dry ether (50 ml). The lithium reagent was decanted and then added dropwise to a rapidly stirred solution of 2-methoxymethyl-enecyclopentanone (3.7 g, 30 mmol) in dry ether (50 ml) at -50°C. After the addition was complete the reaction was allowed to warm to room temperature and stirred for a further 12 h. Hydrolysis was carried out by the careful addition of hydrochloric acid (10%, 100 ml) at 0°C, after the addition the reaction mixture was stirred for a further 8 h. The aqueous layer was washed with ether (3x30 ml), the ether extracts were combined with the organic layer, dried over magnesium sulphate and the solvent evaporated under reduced pressure to give a brown oil. This oil was separated by medium pressure chromatography (silica, ether:petrol 40/60, 1:4) to give *E*-2-propenylcyclopent-1-ene-1-carboxaldehyde as a colourless liquid (1.27 g, 31.8%), b.p. 83-84°C at 1.5 mmHg (Found: M^+ , 136.087861 $C_9H_{12}O$ requires m/e, 136.088810) ν_{max} (film) 1710 cm^{-1} (C=O), δ_H 1.7-2.1 and 2.5-2.9 (m, 9H, cyclopentyl including Me at 1.91, d, J 6Hz), 6.1 (dq, J 16Hz, J' 6Hz, CH=CHMe), 7.0 (d, J 16Hz, CH=CHMe), 10.17 (s, aldehyde). The 2,4-dinitrophenylhydrazone derivative had m.p. 187-188°C (Found: C, 57.2; H, 5.0; N, 17.8. $C_{15}H_{16}N_4O_4$ requires C, 57.0; H, 5.10; N, 17.7%).

35. 2-Bromo-1-cyclohexene-1-carboxaldehyde

This was prepared using the method of Arnold et al.²¹⁴ by the reaction between dimethylformamide (110 g, 1.5 mole), phosphorus tribromide (340 g, 1.25 mole) and cyclohexanone (49 g, 0.50 mole). 2-Bromocyclohex-1-ene-1-carboxaldehyde was distilled from the crude material as a colourless liquid (26 g, 27%), b.p. 60-62°C at 0.8 mmHg (lit.,²¹⁴ 51°C at 0.7 mmHg), ν_{\max} (film) 1695 cm^{-1} (C=O), δ_{H} 1.45-2.85 (m, 8H, cyclohexyl), 10.1 (s, aldehyde).

36. 1-Bromo-2-styryl-1-cyclohexene

A solution of sodium ethoxide, prepared from sodium (3.17 g, 0.138 mole) in "super-dry" ethanol (100 ml) was dripped into a stirred suspension of 2-bromobenzyltriphenylphosphonium bromide (59.8 g, 0.138 mole) in ethanol (200 ml). This mixture was stirred for 1 h at room temperature and the 2-bromocyclohex-1-ene-1-carboxaldehyde (26 g, 0.138 mole) was dripped into the mixture at 0°C. The reaction mixture was stirred at room temperature for 12 h and then boiled under reflux for 5 min. The precipitate of sodium bromide was filtered off and the solvent removed under reduced pressure to give a brown oil. Triphenylphosphine oxide was removed by gravity chromatography on alumina eluting with petrol 40/60 and 1-bromo-2-styryl-1-cyclohexene was isolated as a clear oil (30.6 g, 84%) (Found: M^+ , 262.036093 $\text{C}_{14}\text{H}_{15}^{79}\text{Br}$ requires m/e, 262.035760) δ_{H} showed the presence of *E* and *Z* isomers, in the ratio ca.2:1, *E* isomer; 1.5-1.85 and 2.1-2.7 (m, 8H, cyclohexyl), 6.51 (d, J 16Hz, 1H, olefinic), 7.05-7.5 (m, 6H, aromatic plus one olefinic); *Z* isomer, 1.4-1.85 and 2.2-2.75 (m, 8H, cyclohexyl), 6.16 and 6.43 (AB, J 12Hz, olefinic, 7.1-7.5

(m, 5H, aromatic).

37. 2-Styryl-1-cyclohexene-1-carboxaldehyde

A Grignard reagent was prepared from 1-bromo-2-styryl-1-cyclohexene (28.5 g, 0.108 mole) and magnesium (2.62 g, 0.108 mole) in dry T.H.F. (100 ml). This was cooled to 0°C in ice and dry dimethylformamide (11.8 g, 0.162 mole) in T.H.F. (50 ml) was dripped in. The mixture was then allowed to stir at room temperature for 12 h. The Grignard complex was decomposed by the careful addition of saturated ammonium chloride (100 ml) at 0°C. The aqueous layer was washed with ether (3x50 ml) and the ether extracts combined with the organic layer, dried over magnesium sulphate, and the solvent evaporated under reduced pressure to give a dark yellow oil. Purification of this oil by medium pressure chromatography (silica, ether: petrol 40/60, 1:3) gave 2-styryl-1-cyclohexene-1-carboxaldehyde as a yellow solid (14.0 g, 61%) which recrystallized from ethanol m.p. 82-83°C (Found: M^+ , 212.120366 $C_{15}H_{16}O$ requires m/e, 212.120109) ν_{max} (Nujol) 1645 cm^{-1} (C=O), δ_H showed the presence of *E* and *Z* isomers in the ratio ca. 9:1, *E* isomer; 1.5-1.85 and 2.25-2.65 (m, 8H, cyclohexyl), 6.81 and 7.72 (AB, J 16Hz, 2H, olefinic), 7.2-7.55 (m, 5H, aromatic), 10.38 (s, aldehyde). The 2,4-dinitrophenylhydrazone derivative had m.p. 215-218°C (Found: C, 64.1; H, 5.05; N, 14.0. $C_{21}H_{20}N_4O_4$ requires C, 64.3; H, 5.1; N, 14.3%).

38. 2-Bromo-1-cyclopentene-1-carboxaldehyde*

This was prepared using the method of Arnold et al.²¹⁴ by the reaction between dimethylformamide (110 g, 1.5 mole),

phosphorus tribromide (340 g, 1.25 mole) and cyclopentanone (42 g, 0.50 mole). 2-Bromo-1-cyclopentene-1-carboxaldehyde was distilled from the crude material as a colourless liquid (47.2 g, 54%) b.p. 45°C at 0.8 mmHg (lit.²¹⁴ 45-47°C at 1.5 mmHg) ν_{\max} (film) 1695 cm^{-1} (C=O) δ_{H} 1.8-3.1 (m, 6H, cyclopentyl), 9.93 (s, aldehyde).

39. 1-Bromo-2-styryl-1-cyclopentene*

A solution of sodium ethoxide, prepared from sodium (0.95 g, 41.4 mmol) in "super-dry" ethanol (50 ml) was dripped into a stirred suspension of 2-bromobenzyltriphenylphosphonium bromide (17.9 g, 41.4 mmol) in dry ethanol (200 ml). This mixture was stirred for 1 h at room temperature and then 2-bromo-1-cyclopentene-1-carboxaldehyde (7.24 g, 41.4 mmol) dripped into the mixture at 0°C. The reaction mixture was stirred at room temperature for 12 h and then boiled under reflux for 5 min. The precipitate of sodium bromide was removed by filtration and the solvent removed under reduced pressure to leave a brown oil. Triphenylphosphine oxide was removed by gravity chromatography on alumina eluting with petrol 40/60. 1-Bromo-2-styryl-1-cyclopentene was isolated as a yellow oil (7.68 g, 74%) (Found: C, 62.85; H, 5.3. $\text{C}_{13}\text{H}_{13}\text{Br}$ requires C, 62.7; H, 5.3) δ_{H} showed the presence of *E* and *Z* isomers, in the ratio ca.2:1, *E* isomer; 1.7-2.95 (m, cyclopentyl), 6.51 and 7.09 (AB, J 16Hz, 2H, olefinic), 7.15-7.65 (m, 5H, phenyl), *Z* isomer; 1.6-2.3 and 2.5-2.75 (m, cyclopentyl), 6.34 and 6.64 (AB, J 12Hz, olefinic), 7.05-7.4 (m, phenyl).

40. 2-Styryl-1-cyclopentene-1-carboxaldehyde*

A Grignard reagent was prepared from 1-bromo-2-styryl-cyclopent-1-ene (1.4 g, 5.62 mmol) and magnesium (0.13 g, 5.62 mmol) in dry T.H.F. (60 ml). This was cooled to 0°C in ice and dry dimethylformamide (0.62 g, 8.4 mmol) in T.H.F. (20 ml) was dripped in. The mixture was then allowed to stir at room temperature for 12 h. The Grignard complex was decomposed by the careful addition of saturated ammonium chloride (50 ml) at 0°C. The aqueous layer was washed with ether (3x50 ml), the ether extracts combined with the organic layer, dried over magnesium sulphate and the solvent evaporated under reduced pressure to give dark orange oil. This oil was separated by gravity chromatography on alumina (eluant; ether:petrol 40/60, 1:3) to give 2-styryl-1-cyclopentene-1-carboxaldehyde as an orange solid (0.69 g, 62%) which was recrystallized from ethanol, m.p. 103-104°C (Found: C, 84.6; H, 7.25 C₁₄H₁₄O requires C, 84.8; H, 7.1%) ν_{\max} (Nujol) 1640 cm⁻¹ (C=O), δ_{H} showed the presence of *E* and *Z* isomers, in the ratio ca.5:1, 1.75-2.1 and 2.55-2.95 (m, cyclopentyl), 6.80 and 7.62 (AB, J 16Hz, olefinic *E* isomer), 7.2-7.6 (m, 5H, phenyl), 10.31 (s, aldehyde *E* isomer), 9.92 (s, aldehyde *Z* isomer).

D. Reaction of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds with substituted hydrazines

1 To give 2-substituted-3,4-dihydro-1,2-diazepines

1.1 4-Methylhexa-3,5-dien-2-one with *p*-toluenesulphonylhydrazide

This reaction was carried out by the method of Sharp et al.³³ *p*-Toluenesulphonylhydrazide (5.08 g, 26.2 mmol) and 4-methylhexa-3,5-dien-2-one (3.0 g, 26.2 mmol) were stirred in ethanol (30 ml) containing concentrated hydrochloric acid (1.5 ml) under nitrogen and in the dark for 12 h. Recrystallisation of the deposited white precipitate from ethyl acetate gave 3,4-dihydro-5,7-dimethyl-2-tosyl-1,2-diazepine as colourless needles (5.03 g, 69%), m.p. 185°C (lit.,¹⁹⁴ 185°C) δ_{H} 1.89 br (s, 5-Me), 2.00 (s, 7-Me), 2.41 (s, tosyl Me), 2.61 br (t, 4-H₂), 3.38 (t, J 5Hz, 3-H₂), 5.64 br (s, 6-H), 7.30 and 7.86 (AB, J 8Hz, ArH).

1.2 4-Methylhexa-3,5-dien-2-one with phenylhydrazine

This reaction was carried out using the method of Vogel et al.²⁰³ The ketone (0.20 g, 1.82 mmol) was added to a solution of phenylhydrazine hydrochloride (0.524 g, 3.64 mmol) and sodium acetate (0.79 g) in water (10 ml) and the mixture was stirred for 12 h at room temperature in the dark and under nitrogen. The mixture was extracted with ether (3x10 ml), the ether solution was dried and evaporated under reduced pressure and the residue was chromatographed on alumina to give 3,4-dihydro-5,7-dimethyl-2-phenyl-1,2-diazepine (0.078 g, 21%) as a colourless oil (Found: M⁺, 200.131290 C₁₃H₁₆N₂)

requires m/e , 200.131342). Spectral data see appendix 2.1, and 4-methylhexa-3,5-dien-2-one phenylhydrazone (0.166 g, 46%) as a colourless oil, readily oxidised in air (Found: M^+ , 200.130162, $C_{13}H_{16}N_2$ requires m/e , 200.131342).

Spectral data see appendix 1.1.

1.3 4-Methylhepta-3,5-dien-2-one with *p*-toluenesulphonyl hydrazide

p-Toluenesulphonylhydrazide (1.6 g, 8.3 mmol) and 4-methylhepta-3,5-dien-2-one (1.0 g, 8.3 mmol) were stirred in ethanol (30 ml) containing concentrated hydrochloric acid (0.5 ml) under nitrogen and in the dark for 12 h. The white solid obtained by filtration was recrystallized from ethanol to give 3,4-dihydro-3,5,7-trimethyl-2-tosyl-1,2-diazepine as white needles 1.1 g, 45%), m.p. 164-166°C (lit.,¹⁹⁴ 164-166°C) δ_H 0.48 (d, J 7Hz, 3-Me), 1.87 br (s, 5-Me), 2.06 (s, 7-Me), 2.41 (s, tosyl Me), 2.18 (d of d, J 19Hz, J' 2Hz, 4-H_a), 2.95 br (d of d, J 19Hz, J' 7Hz, 4-H_b), 4.68 (quintet of d, J 7Hz, J' 2Hz, 3-H), 5.69 br (s, 6-H), 7.28 and 7.68 (A_2M_2 , J 8Hz, ArH).

1.4 5-Methylocta-4,6-dien-3-one with *p*-toluenesulphonylhydrazide

5-Methylocta-4,6-dien-3-one (3.6 g, 26.1 mmol) was stirred in ethanol (75 ml) with *p*-toluenesulphonylhydrazide (4.85 g, 26.1 mmol) and concentrated hydrochloric acid (0.5 ml). After stirring for 12 h a white precipitate of 5-methylocta-4,6-dien-3-one tosylhydrazone (3.26 g, 41%) was filtered off and recrystallized from ethanol, m.p. 129-130°C (Found: C, 62.4; H, 7.0; N, 9.1 $C_{16}H_{22}N_2O_2S$ requires C, 62.7; H, 7.2;

N, 9.1%). Spectral data see appendix 1.2. Addition of further concentrated hydrochloric acid (1.5 ml) to the mother liquors and stirring for 12 h resulted in the formation of another white precipitate of 3,4-dihydro-3,5-dimethyl-7-ethyl-2-tosyl-1,2-diazepine (1.4 g, 17.6%) which recrystallized from ethanol m.p. 125-126°C (lit., ¹⁹⁴ 126°C) δ_{H} 0.47 (d, J 7Hz, 3-Me), 1.08 (t, J 8Hz, ethyl Me), 1.88 br (s, 5-Me), 2.2-2.5 (m, ethyl CH₂), 2.40 (s, tosyl Me), 2.0-2.4 (m, overlapping with ethyl CH₂, 4-H_a), 2.96 br (d of d, J 18, J' 7Hz, 4-H_b), 4.70 (quintet of d, J 7, J' 2Hz, 3-H), 5.69 br (s, 6-H), 7.26 and 7.87 (A₂M₂, J 8Hz, ArH).

1.5 2,5-Dimethylocta-4,6-dien-3-one with *p*-toluenesulphonylhydrazide

The ketone (2.50 g, 16.4 mmol) was stirred in ethanol (50 ml) with *p*-toluenesulphonylhydrazide (3.05 g, 16.4 mmol) and concentrated hydrochloric acid (1 ml) for 12 h. The reaction mixture was neutralised with sodium bicarbonate and the solvent removed under reduced pressure to give a brown oil. This was then separated by medium pressure chromatography (silica, ether:petrol 40/60, 1:4) to give 3,4-dihydro-3,5-dimethyl-7-isopropyl-2-tosyl-1,2-diazepine (1.42 g, 27%) which was recrystallized from ethanol m.p. 86-87°C (Found: C, 63.8; H, 7.6; N, 9.0 C₁₇H₂₄N₂O₂S requires C, 63.7; H, 7.6; N, 8.7%). Spectral data see appendix 2.2, and 2,5-dimethylocta-4,6-dien-3-one tosylhydrazone (0.57 g, 11%) which was recrystallized from ethanol, m.p. 130-131°C (Found: C, 63.4; H, 7.4; N, 8.7 C₁₇H₂₄N₂O₂S requires C, 63.7; H, 7.6; N, 8.7%) spectral data see appendix 1.3.

1.6 1-Phenyl-5-methylocta-4,6-dien-3-one with *p*-toluenesulphonylhydrazide

p-Toluenesulphonylhydrazide (4.0 g, 21.5 mmol) and 1-phenyl-5-methylocta-4,6-dien-3-one (4.6 g, 21.5 mmol) were stirred for 12 h in ethanol (50 ml) containing concentrated hydrochloric acid (3 ml). The reaction mixture was neutralised with sodium bicarbonate, dried over magnesium sulphate, and the solvent removed under reduced pressure to give a brown oil. This oil was separated by gravity chromatography (alumina, ether:petrol 40/60, 1:4) to give 3,4-dihydro-3,5-dimethyl-7-phenethyl-2-tosyl-1,2-diazepine as a white solid (5.20 g, 63%) which was recrystallized from ethanol m.p. 131-132°C (Found: C, 68.8; H, 6.8; N, 7.2. $C_{22}H_{26}N_2O_2S$ requires C, 69.0; H, 6.8; N, 7.3%) spectral data see appendix 2.3.

1.7 1-Phenyl-3-methylhexa-2,4-dien-1-one with *p*-toluenesulphonylhydrazide

1-Phenyl-3-methylhexa-2,4-dien-1-one (3.80 g, 20.4 mmol) and *p*-toluenesulphonylhydrazide (3.80 g, 20.4 mmol) were stirred for 12 h in ethanol (30 ml) containing concentrated hydrochloric acid (3 ml). The white solid obtained by filtration was recrystallized from ethanol to give 3,4-dihydro-3,5-dimethyl-7-phenyl-2-tosyl-1,2-diazepine as white crystals (4.30 g, 59%) m.p. 168-169°C (Found: C, 67.9; H, 6.2; N, 8.0. $C_{20}H_{22}N_2O_2S$ requires C, 67.8; H, 6.3; N, 7.9%) spectral data see appendix 2.4.

1.8 2-Propenyl-1-cyclopentene-1-carboxaldehyde with
p-toluenesulphonylhydrazide

The aldehyde (0.22 g, 1.62 mmol) and p-toluenesulphonylhydrazide (0.30 g, 1.62 mmol) were stirred in ethanol (10 ml) containing concentrated hydrochloric acid (1 drop) for 12 h. The reaction mixture was neutralised by the addition of solid sodium bicarbonate, dried over magnesium sulphate, and the solvent removed under reduced pressure to give a brown oil. This oil was separated by medium pressure chromatography (silica, ether:petrol 40/60, 1:4) to give 2-propenyl-1-cyclopentene-1-carboxaldehyde tosylhydrazone as a white solid (0.266 g, 54%) which was recrystallized from ethanol, m.p. 111-113°C (Found: C, 63.1; H, 6.8; N, 9.3. $C_{16}H_{20}N_2O_2S$ requires C, 63.1; H, 6.6; N, 9.2) spectral data see appendix 1.7.

Cyclisation was carried out by stirring the tosylhydrazone (1.0 g, 3.3 mmol) in dry benzene (20 ml) containing trifluoroacetic acid (5 drops) under nitrogen and in the dark for 24 h. The solution was washed with sodium bicarbonate solution (10%, 20 ml), dried over magnesium sulphate, and the solvent removed under reduced pressure to give a brown oil. This oil was separated by medium pressure chromatography (silica, ether:petrol 40/60, 1:4) to give 4-methyl-4,5,6,7,8-pentahydro-3-tosylcyclopenta [d]-[1,2] diazepine (0.57 g, 57%) which was recrystallized from ethanol, m.p. 131-132°C (Found: C, 63.4; H, 6.5; N, 9.0. $C_{16}H_{20}N_2O_2S$ requires C, 63.1; H, 6.6; N, 9.2%) spectral data see appendix 2.5.

1.9 2-Propenyl-1-cyclohexene-1-carboxaldehyde with p-toluene-
sulphonylhydrazide

The aldehyde (1.80 g, 12 mmol) and *p*-toluenesulphonylhydrazide (2.23 g, 12 mmol) were stirred in ethanol (30 ml) containing concentrated hydrochloric acid (1 drop). After stirring for 1 h, inspection by t.l.c. (alumina, ether:petrol 40/60, 1:1) showed that the reaction had gone to completion. The deposited white precipitate of 2-propenyl-1-cyclohexene-1-carboxaldehyde tosylhydrazone was filtered off (2.55 g, 67%) and was recrystallized from ethanol, m.p. 126-127°C (Found: C, 64.0; H, 7.2; N, 8.7. $C_{17}H_{22}N_2O_2S$ requires C, 64.1; H, 7.0; N, 8.8%) spectral data see appendix 1.8.

Cyclisation was carried out by stirring 2-propenyl-1-cyclohexene-1-carboxaldehyde tosylhydrazone (0.65 g, 2.04 mmol) in dry benzene (20 ml) containing trifluoroacetic acid (5 drops) for 60 h in the dark and under nitrogen. The reaction mixture was then washed with sodium bicarbonate solution (10%, 10 ml), dried over magnesium sulphate, and the solvent removed under reduced pressure to give a brown oil. This oil was separated by medium pressure chromatography (silica, ether:petrol 40/60, 1:4) to give 4-methyl-4,5,6,7,8,9-hexahydro-3-tosyl-cyclohexa-[d]-[1,2]diazepine as a white solid (0.104 g, 16%) which was recrystallized from ethanol m.p. 126-127°C (Found: C, 64.0; H, 6.9; N, 8.8. $C_{17}H_{22}N_2O_2S$ requires C, 64.1; H, 7.0; N, 8.8%) spectral data see appendix 2.6.

2. To give only hydrazones

2.1 4-Methylhexa-3,5-dien-2-one with 2,4-dinitrophenylhydrazide

The reaction was carried out using the method of Vogel.²⁰³ 2,4-Dinitrophenylhydrazine (300 mg, 1.5 mmol) in methanol (5 ml) was dissolved by the careful addition of concentrated sulphuric

acid (1.0 ml). The solution was filtered, and 4-methylhexa-3,5-dien-2-one (0.11 g, 1 mmol) dissolved in ether (1 ml) was added dropwise. An immediate red precipitate of the hydrazone was deposited, which was filtered off and washed with methanol followed by n-pentane. Attempts to recrystallise the solid from refluxing solvents such as ethanol and ethyl acetate resulted in decomposition. Purification was carried out by dissolving the solid in a small volume of chloroform (3 ml) and adding n-pentane (6 ml). After standing overnight 4-methylhexa-3,5-dien-2-one 2,4-dinitrophenylhydrazone was isolated as bright red needles (123 mg, 42%) m.p. 159-160°C (Found: C, 53.8; H, 4.9; N, 19.2. $C_{13}H_{14}N_4O_4$ requires C, 53.8; H, 4.9; N, 19.3%). Spectral data see appendix 1.4.

2.2 4-Methylhepta-3,5-dien-2-one with 2,4-dinitrophenylhydrazone

A similar reaction between 2,4-dinitrophenylhydrazine (300 mg, 1.5 mmol) and 4-methylhepta-3,5-dien-2-one (124 mg, 1 mmol) gave 4-methylhepta-3,5-dien-2-one 2,4-dinitrophenylhydrazone as a red solid (225 mg, 74%) which was recrystallized from a chloroform/n-pentane solvent mixture, m.p. 169-170°C (Found: C, 55.5; H, 5.2; N, 18.4. $C_{14}H_{16}N_4O_4$ requires C, 55.3; H, 5.3; N, 18.4%). Spectral data see appendix 1.5.

2.3 4-Methylhexa-3,5-dien-2-one with 4-nitrophenylhydrazine

A similar reaction gave 4-methylhex-3,5-dien-2-one-4-nitrophenylhydrazone as an orange solid (85 mg, 35%) which was recrystallized from a chloroform/n-pentane solvent mixture m.p. 135-136°C (Found: M^+ , 245.117089 $C_{13}H_{15}N_3O_2$ requires

m/e, 245.116419) spectral data see appendix 2.5.

2.4 2-Styryl-1-cyclopentene-1-carboxaldehyde with *p*-toluene-sulphonylhydrazide

2-Styryl-1-cyclopentene-1-carboxaldehyde (2.25 g, 11.4 mmol) and *p*-toluenesulphonylhydrazide (2.12 g, 11.4 mmol) were dissolved separately in ethanol (20 ml) and warmed to 35°C. These two solutions were then mixed and concentrated hydrochloric acid (1 drop) was added. On cooling a white solid was deposited which was recrystallized from ethanol to give 2-styryl-1-cyclopentene-1-carboxaldehyde tosylhydrazone as white needles (2.43 g, 58%) m.p. 147°C (Found: C, 68.6; H, 6.2; N, 7.5. $C_{21}H_{23}N_2O_2S$ requires C, 68.8; H, 6.05; N, 7.6%) Spectral data see appendix 1.9.

2.5 2-Styryl-1-cyclohexene-1-carboxaldehyde with *p*-toluene-sulphonylhydrazide

2-Styryl-1-cyclohexene-1-carboxaldehyde (10.0 g, 47.2 mmol) and *p*-toluenesulphonylhydrazide (8.78 g, 47.2 mmol) were dissolved separately in ethanol (100 ml) and warmed to 35°C. These two solutions were then mixed and concentrated hydrochloric acid (0.5 ml) was added. On cooling a white precipitate was deposited (9.59 g) and concentration of the mother liquors followed by purification by medium pressure chromatography (silica, petrol 40/60 : methylene chloride : ether, 2:2:1) yielded a further 6.81 g. Recrystallization of this white solid from ethanol gave 2-styryl-1-cyclohexene-1-carboxaldehyde tosylhydrazone as white needles (16.4 g, 92%) m.p. 125-126°C (Found: C, 69.2; H, 6.2; N, 7.1 $C_{22}H_{24}N_2O_2S$ requires C, 69.4; H, 6.4; N, 7.4%) Spectral data see appendix 1.10.

2.6 4-Methyl-6-phenylhexa-3,5-dien-2-one p-tosylhydrazone

Sample provided by Dr.J.T.Sharp.

3. Attempted acid-catalysed cyclisations of hydrazones of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compounds

3.1 Control experiments

A number of experiments were performed to establish the effectiveness of the cyclising reaction conditions. Thus a range of tosylhydrazones were successfully cyclised to the corresponding tosyldiazepines by using various acidic conditions, the results are summarised in the table below.

<i>p</i> -Tosylhydrazone	Conditions
5-Methylocta-4,6-dien-3-one	H ⁺ /EtOH and CF ₃ CO ₂ H/benzene
2,5-Dimethylocta-4,6-dien-3-one	H ⁺ /EtOH and CF ₃ CO ₂ H/benzene
2-Propenyl-1-cyclopentene-1-carboxaldehyde	H ⁺ /EtOH and CF ₃ CO ₂ H/benzene
2-Propenyl-1-cyclohexene-1-carboxaldehyde	CF ₃ CO ₂ H/benzene

3.2 Experiments

The following hydrazones failed to cyclise despite reaction

3.2 continued; Table of experimental conditions

Hydrazone	Conditions	Result
4-Methylhex-3,5-dien-2-one 2,4-dinitrophenylhydrazone	H^+ /EtOH, CF_3CO_2H /benzene	No reaction, recovered starting material
4-Methylhepta-3,5-dien-2-one 2,4-dinitrophenylhydrazone	H^+ /EtOH, CF_3CO_2H /benzene	No reaction, recovered starting material
4-Methylhexa-3,5-dien-2-one 4-nitrophenylhydrazone	H^+ /EtOH, CF_3CO_2H /benzene	No reaction, recovered starting material
-Styryl-1-cyclopentene-1-carboxaldehyde <i>p</i> -tosylhydrazone	CF_3CO_2H /benzene	No reaction, recovered starting material
2-Styryl-1-cyclohexene-1-carboxaldehyde <i>p</i> -tosylhydrazone	CF_3CO_2H /benzene	No reaction, recovered starting material
4-Methyl-6-phenylhex-3,5-dien-2-one <i>p</i> -tosylhydrazone	CF_3CO_2H /benzene	Starting material consumed, extensive decomposition
<i>E</i> -2-Formystilbene tosylhydrazone	CF_3CO_2H /benzene	No reaction, recovered starting material

under proven, effective $\text{CF}_3\text{CO}_2\text{H}$ /benzene conditions. Treatment with very high concentrations of acid resulted in decomposition, presumably by polymerisation pathways. The results of the attempted cyclisations are summarised in the table below.

4. Anomalous reactivity of 4,6-diphenylhexa-3,5-dien-2-one

Despite using a variety of substituted hydrazines and a range of mild, gentle acidic conditions, hydrazone derivatives of this ketone could not be obtained. The reaction conditions examined are summarised in the table below.

Substituted hydrazine	Conditions
<i>p</i> -Toluenesulphonylhydrazide	i) H^+ /EtOH at room temperature ii) H^+ /EtOH at 0°C iii) Without acid/EtOH, room temp.
2,4-Dinitrophenylhydrazine	Vogel method
Benzoyl hydrazide	H^+ /EtOH, room temperature

T.l.c. inspection of all reactions showed the loss of the starting material. Chromatography (both alumina and silica, eluant; petrol 40/60 with increasing amounts of ether) yielded only small recoveries of unidentified material. Most of the material was irreversibly adsorbed on the stationary phase.

5. Reaction of 3,4-dihydro-5,7-dimethyl-2-tosyl-1,2-diazepine with lithium diisopropylamide followed by treatment with methyl iodide.

To a solution of lithium diisopropylamide [4.4 mmol prepared from diisopropylamine (0.62 ml, 444 mg, 4.4 mmol) and n-butyl lithium (3 ml of a 1.6N solution in hexane) stirred at 0°C for 30 min] and dry tetramethylethylenediamine (0.72 ml, 4.4 mmol) cooled to -78°C was added the tosyl diazepine (556 mg, 2 mmol) dissolved in dry tetrahydrofuran (10 ml) with vigorous stirring. On addition of the tosyl diazepine the solution was observed to turn orange. The solution was allowed to warm slowly to 0°C and stirred for a further 30 min, methyl iodide (3 ml, large excess) was then added. After stirring for 2 h at room temperature the mixture was quenched with ice-cold water (20 ml), neutralised with dilute hydrochloric acid and extracted with dichloromethane. The organic phase was dried over MgSO₄ and the solvent evaporated under reduced pressure to give a brown oil. This oil was separated by medium pressure chromatography (silica, ether : petrol 40/60, 1:1) to give 4-methylhexa-3,5-dien-2-one N-methyltosylhydrazone as a white solid (294 mg, 50%) which was recrystallised from an ether/petrol 40/60 solvent mixture m.p.98-100°C (Found: C, 61.9; H, 6.8; N, 9.8. C₁₅H₂₀N₂O₂S requires C, 61.7; H, 6.9; N, 9.6%) spectral data see appendix 1.11. Unreacted tosyl diazepine (63 mg, 11%) was also isolated from the separated reaction product.

E. Synthesis of 1,2-diazepines1. 2,3-Benzodiazepines1.1 4-Phenyl-1H-2,3-benzodiazepine

To a solution of sodium ethoxide, prepared from sodium (0.586 g, 25.5 mmol) dissolved in "super-dry" ethanol (50 ml) was added *E*-2-formystilbene tosylhydrazone (10 g, 26.6 mmol). The mixture was stirred for 30 min, then the solvent was removed on a pre-dried rotary evaporator. The residual sodium salt was dried overnight in the reaction flask, under high vacuum over phosphorus pentoxide. Dry d.m.e. (150 ml) was then added and the mixture heated to reflux for 30 min when t.l.c. (alumina, eluant ether:petrol 40/60 1:1) showed no starting material remaining. After cooling, the solution was filtered through celite and the precipitate washed thoroughly with d.m.e. The solvent was then evaporated under reduced pressure to give a red solid. This was purified by gravity column chromatography (alumina, eluant 10% ether in petrol 40/60) followed by recrystallization from ethanol to give the 1H-benzodiazepine (3.65, 64%) as yellow crystals m.p.130-132°C (lit., ⁶⁴ 132-133°C). δ_{H} 3.02 (d, J 9Hz, axial methylene, 6.35 (d, J 9Hz, equatorial methylene), 6.98 (s, 5-H), 7.1-8.1 (m, 9H, aromatic).

1.2 1-Methyl-4-phenyl-1H-2,3-benzodiazepine

Sample kindly provided by Dr. J.T.Sharp.

1.3 1,2,3,3a-Tetrahydro-10-phenylbenzo-[c]cyclopenta[f]-[1,2]diazepine

Sample kindly provided by Dr. J.T.Sharp.

2. 1,2-Diazepines

These were prepared by the method of Sharp *et al.*³⁴

The general method was to heat the 3,4-dihydro-2-tosyl-1,2-diazepine with a two-fold molar excess of sodium ethoxide in dry toluene. At ca.100°C precipitation of sodium *p*-toluene-sulphinate occurred, and heating was continued until t.l.c. showed that all the starting material had been consumed. The mixture was then filtered, washed with water, dried, and the solvent evaporated under reduced pressure to leave the crude product which was then purified by chromatography followed by distillation or recrystallisation.

2.1 3,5-Dimethyl-3*H*-1,2-diazepine and 5,7-dimethyl-3*H*-1,2-diazepine.

2.1.1 Synthesis

Sodium (1.66 g, 72 mmol) was dissolved in "super-dry" ethanol (100 ml) and 5,7-dimethyl-3,4-dihydro-2-tosyl-1,2-diazepine (10.0 g, 36 mmol) added. The ethanol was removed on a dry rotary evaporator with bath temperature not exceeding 35°C. The residual salt was dried in the flask, at ca.0.1 mmHg in a desiccator over phosphorus pentoxide overnight. Dry toluene (200 ml) was then added and the mixture boiled under reflux for 15 min. The precipitate of sodium *p*-toluene-sulphinate was filtered off and the filtrate washed with water (2x100 ml), dried, and the solvent removed under reduced pressure to leave a yellow oil. The last traces of toluene were removed by gravity column chromatography (Alumina, ether: petrol 40/60, 1:4) and the resultant oil was distilled to give a yellow liquid (3.1 g, 70%), b.p. 85°C at 16 mmHg (lit.,³⁴

80°C at 12 mmHg) which consisted of a mixture of 5,7-dimethyl-3H-1,2-diazepine and 3,5-dimethyl-3H-1,2-diazepine. δ_{H} 5,7-Dimethyl isomer; 5.94 br (s, 6-H), 5.77 (d of d, J geminal 8.5Hz, J vicinal 7.5Hz, 3-H, quasi equatorial), 5.13 br (t, J ca.7-8Hz, 4-H), 2.38 br (s, 7-Me), 1.95 (m, 5-Me) superimposed on 1.8-2.2 (m, 3-H quasi axial), 3,5-dimethyl isomer; 8.1 (d, J 9Hz, 7-H), 6.08 (d, J 9Hz, 6-H), 5.0 br (d, J 8Hz, 4-H), the absorptions for 5-Me, 3-Me, and 3-H are all under the 1.8-2.2 multiplet. H.p.l.c. analysis (25x0.5 cm, 5 μm silica, 10,700 plates) with the column at 0°C and using a mixture of dry diethyl ether (10% vol) and 50% water-saturated hexane (90% vol) as eluant at a flow rate of 2.5 ml min⁻¹ gave the 5,7-dimethyl to 3,5-dimethyl isomer ratio of 85:15.

2.1.2² Isomerisation study

The isomers were separated using the column conditions described above using 2 μl injections of a ca.0.05 molar solution of the mixture. About 0.5-1 ml of the eluant was collected in a sample vial around each peak maximum and the vials were closed with Suba-seals and immediately cooled to -80°C. For H.p.l.c. analysis of the solutions kept at -80°C for 3 h showed greater than 90% isomeric purity. The solutions of each isomer were then kept at room temperature for 1 h when h.p.l.c. analysis showed that the isomer ratio had returned to the 85:15 ratio.

2.1.3 Deuterium incorporation study

An n.m.r. sample of the mixture of the two isomeric diazepines (133 mg, 1.1 mmol) in deuteriochloroform was prepared.

A molar equivalent of deuteromethanol (36 mg, 1.03 mmol) was added and the ^1H n.m.r. spectrum run at $t = 5$ and 40 min after the addition. No deuterium incorporation was observed, the deuteromethanol was increased to five fold excess (182 mg, 5.06 mmol) and the ^1H n.m.r. spectrum run after 24 h. This still showed no incorporation.

2.1.4 Photolysis study

The mixture of the two isomeric diazepines (0.50 g, 4.1 mmol) dissolved in acetonitrile (175 ml) were irradiated for 30 min with a Hanovia 100W medium-pressure lamp to give 4,6a-dihydro-1,6-dimethyl[1,2]diazeto[1,4-a]pyrrole (0.466 g, 93%) after removal of solvent. Distillation accompanied by losses by polymerisation, gave the product as a pale yellow oil (0.25 g, 50%), b.p. 85°C at 50 mmHg (lit., 85°C at 50 mmHg) δ_{H} 1.82 (m, 6-Me), 2.00 (s, 1-Me), 3.83 br (s, 4- CH_2), 5.11 (m, 5-H), and 5.35 (m, 6a-H).

Monitoring of the reaction by h.p.l.c. [15 x 0.5 cm, Spherisorb S5Y silica at 0°C using a mixture (1:9 v/v) of dry ether and 50% v/v water-saturated hexane as eluant at a flow rate of 2.5 ml min^{-1}] showed that the ratio of the 5,7-dimethyl to 3,5-dimethyl isomer remained at ca. 6:1 throughout as they were consumed but only a single product peak was detected although a variety of solvent combinations were used as eluant (eg 100% ether and mixtures of hexane and dioxan ranging from 1:3 to 1:1).

2.2 3,5-Dimethyl-7-ethyl-3H-1,2-diazepine and 5,7-dimethyl-3-ethyl-3H-1,2-diazepine

2.2.1 Synthesis

A similar reaction (5 min) of 3,4-dihydro-7-ethyl-3,5-dimethyl-2-tosyl-1,2-diazepine (2.52 g, 8.24 mmol) gave after distillation a yellow oil (1.09 g, 88%) b.p. 100°C at 10 mmHg (lit.,³⁴ 94-96°C at 10 mmHg) which consisted of a mixture of the two isomeric diazepines; 3,5-dimethyl-7-ethyl and 5,7-dimethyl-3-ethyl-3H-1,2-diazepines. Spectral data see appendix 3.1.

H.p.l.c. analysis (25x0.5 cm, 5 µm silica, 10,700 plates) with the column at 0°C and using a mixture of dry diethyl ether (4 vol %) at 50% water-saturated hexane (96%) as eluant at a flow rate of 2.0 ml min⁻¹ gave a peak ratio of 51:49 which compares with the 3,5-dimethyl-7-ethyl to 5,7-dimethyl-3-ethyl isomer ratio of 52:48 obtained from the integral of the 360MHz proton n.m.r. spectrum.

2.2.2 Isomerisation study

The isomers were separated using the column conditions described above using 2 µl injections of a ca.0.05 molar solution of the mixture. About 1 ml of the eluant was collected in a sample vial around each peak maximum and the vials were closed with Suba-seals and immediately cooled to -80°C. H.p.l.c. analysis of the solutions kept at -80°C for 3 h

showed greater than 90% isomeric purity. The solutions of each isomer were then kept at room temperature for 1 h when h.p.l.c. analysis showed that the isomer ratio had returned to 52:48.

2.3 3,5-Dimethyl-7-isopropyl-3H-1,2-diazepine and 5,7-dimethyl-3-isopropyl-3H-1,2-diazepine

A similar reaction (5 min) of 3,4-dihydro-3,5-dimethyl-7-isopropyl-2-tosyl-1,2-diazepine (0.670 g, 2.1 mmol) gave after distillation a yellow oil (0.256 g, 74%) b.p. 90°C at 0.2 mmHg which consisted of a mixture of the two isomeric diazepines (Found: M^+ , 164.130303 $C_{10}H_{16}N_2$ requires m/e, 164.131342) spectral data see appendix 3.2.

H.p.l.c. analysis (25x0.5 cm, 5 μ m silica, 10,700 plates) with the column at 0°C and using a variety of solvent combinations (mixtures of dry diethyl ether, 0 to 5% volume in 0.5% increments, and 50% water-saturated hexane, 95 to 100% volume) did not resolve the two isomer components, only a single product peak was detected. Measurement of the column efficiency using this product peak showed a considerable loss of theoretical plates, suggesting that some separation on the column must have been taking place.

The 3,5-dimethyl-7-isopropyl to 5,7-dimethyl-3-isopropyl isomer ratio was calculated as 34:66 from the integral of the 360MHz proton n.m.r. spectrum of the mixture.

2.4 3,5-Dimethyl-7-phenethyl-3H-1,2-diazepine and 5,7-dimethyl-3-phenethyl-3H-1,2-diazepine

A similar reaction (5 min) of 3,4-dihydro-3,5-dimethyl-7-phenethyl-2-tosyl-1,2-diazepine (3.15 g, 8.25 mmol) gave after distillation a yellow oil (1.73 g, 93%) b.p.150°C at 0.01 mmHg (Found: C, 79.7; H, 8.1; N, 12.3. $C_{15}H_{18}N_2$ requires C, 79.7; H, 8.0; N, 12.4) which consisted of a mixture of the two isomeric diazepines (Found: M^+ , 226.146231 $C_{15}H_{18}N_2$ requires 226.146991) spectral data see appendix 3.3.

The mixture of the two isomeric diazepines was subjected to extensive analysis by h.p.l.c. using a variety of column packings and solvent combinations. The conditions examined are summarised in the following table.

No resolution of the two isomers was achieved. However measurement of the column efficiency using the peak obtained, indicated that in a number of cases a loss of theoretical plates. This suggested that some separation on the column must have been taking place. All h.p.l.c. conditions examined successfully resolved the dimethyl substituted diazepine mixture.

The 3,5-dimethyl-7-phenethyl to 5,7-dimethyl-3-phenethyl isomer ratio was calculated as 49:51 from the integral of the 360MHz proton n.m.r. spectrum.

2.5 3,5,7-Trimethyl-3H-1,2-diazepine

A similar reaction (15 min) of 3,4-dihydro-3,5,7-trimethyl-2-tosyl-1,2-diazepine (5.83 g, 20 mmol) gave the crude product as a yellow oil. This was purified by gravity column

2.5 continued; Table h.p.l.c. conditions

RESOLUTION OF ISOMERIC DIAZEPINES

COLUMN	SOLVENT SYSTEM	Dimethyl substituted mixture	Dimethyl phenethyl substituted mixture
25x0.5 cm, 5 μ m SiO ₂ , 10,700 plates	mixtures of 50% water-saturated hexane with 1. 0→10% vol % ether 2. 0.5 vol % ethanol 3. 0.25 vol % ethanol	✓ ✓ ✓	X X X
"	mixtures of 25% water-saturated hexane with 1. 0→10 vol % ether 2. 0.5 vol % ethanol 3. 0.25 vol % ethanol	✓ ✓ ✓	X X X
"	mixtures of 50% water-saturated hexane with 1-5 vol % dioxan 1 vol % acetonitrile	✓ ✓ ✓	X X X
"	totally activated column 9:10 vol % dry hexane/ether	✓	X
15x0.5 cm, 10 μ m AlO ₃ , 4,100 plates	90:10 vol % of water-saturated hexane/ether at 0, -10 & -20°C	✓	X
25x0.5 cm, 10 μ m reverse phase ODS, 8,100 plates	methanol/water mixtures 1:1 to 9:1	X	X

chromatography (alumina, ether:petrol 40/60, 1:9) to remove the last traces of toluene, and followed by distillation to give 3,5,7-trimethyl-3*H*-1,2-diazepine as a yellow oil (2.2 g, 81%), b.p. 78-80°C at 12 mmHg (lit.,³⁴ 75-78°C at 10 mmHg) δ_{H} 1.73 br (quintet, *J* 6Hz, 3-H), 1.94 (m, 5-Me), 1.99 (d, *J* 6Hz, 3-Me), 2.36 (s, 7-Me), 4.88 br (d, *J* 5Hz, 4-H), 5.92 br (s, 6-H), δ_{C} ; C-3, 70.9; C-4 and C-6, 117.4, 118.1; C-5, 135.9; C-7, 154.5; 3-Me, 5-Me and 7-Me, 21.0, 20.4, 18.5.

2.6 3,5-Dimethyl-7-phenyl-3*H*-1,2-diazepine

A similar reaction (5 min) of 3,4-dihydro-3,5-dimethyl-7-phenyl-2-tosyl-1,2-diazepine (2.27 g, 6.41 mmol) gave after distillation 3,5-dimethyl-7-phenyl-3*H*-1,2-diazepine as a yellow oil (1.07 g, 84%) b.p. 145°C at 0.2 mmHg. This was recrystallised at ca. -30°C from light petroleum as yellow prisms, m.p. 45-46°C (Found: C, 79.0; H, 7.2; N, 14.0 C₁₃H₁₄N₂ requires C, 78.8; H, 7.1; N, 14.1%) spectral data see appendix 3.4.

2.7 5-Methyl-7-phenyl-3*H*-1,2-diazepine

Sample (prepared to C.D. Anderson) provided by Dr. J.T.Sharp.

F. Conversion of 1,2-diazepines into diiron hexacarbonyl complexes

The complexes were prepared by stirring a solution of the diazepine under nitrogen in dry degassed benzene with a two-fold excess of diiron nonacarbonyl for 24 h. The resulting residue was chromatographed on alumina to give the complex in moderate yield as air stable crystalline solids.

1. 4-Phenyl-1H-2,3-benzodiazepine

4-Phenyl-1H-2,3-benzodiazepine (1.5 g, 6.8 mmol) was dissolved in dry, degassed benzene (20 ml) and diiron nonacarbonyl (5.0 g, 13.7 mmol) was added. The suspension was stirred in the dark under nitrogen at room temperature for 24 h. Inspection by t.l.c. (alumina, ether:petrol 40/60, 1:1) showed all the starting material to be consumed. The reaction mixture was filtered through celite and the precipitate washed thoroughly with benzene. Removal of the solvent under reduced pressure gave a red oil. This was separated by gravity column chromatography (alumina, petrol 40/60) to give 4-phenyl-1H-2,3-benzodiazepine diiron hexacarbonyl complex as a red solid (1.18 g, 53%) which was recrystallised from n-hexane, m.p.158-162°C (decomposes) (Found: C, 50.5; H, 2.4; N, 5.7 C₂₁H₁₂N₂O₆Fe₂ requires C, 50.4; H, 2.4; N, 5.6%) ν_{\max} (chloroform solution) $\sim 2000\text{ cm}^{-1}$ intense multiplet (terminal C=O) Spectral data see appendix 4.1.

2. 1-Methyl-4-phenyl-1H-2,3-benzodiazepine

A similar reaction (12 h) of 1-methyl-4-phenyl-1H-2,3-benzodiazepine (317 mg, 1.35 mmol) gave after chromatography a red solid which was recrystallised from n-hexane to give

1-methyl-4-phenyl-1*H*-2,3-benzodiazepine diiron hexacarbonyl complex as red needles (406 mg, 58%) m.p. 165-168°C (decomposes) (Found: C, 51.7; H, 2.7; N, 5.6. $C_{22}H_{14}N_2O_6Fe_2$ requires C, 51.4; H, 2.7; N, 5.5%) ν_{max} (chloroform solution) $\sim 2000\text{ cm}^{-1}$ intense multiplet (terminal C=O). Spectral data see appendix 4.2.

3. 1,2,3,3a-Tetrahydro-10-phenylbenzo-[c]cyclopenta[f][1,2]-diazepine

A similar reaction (24 h) of 1,2,3,3a-tetrahydro-10-phenylbenzo-[c]cyclopenta[f][1,2]diazepine diiron hexacarbonyl (192 mg, 0.74 mmol) gave after chromatography 1,2,3,3a-tetrahydro-10-phenylbenzo-[c]cyclopenta[f][1,2]diazepine diiron hexacarbonyl complex as a red solid (229 mg, 57%) which was recrystallised from n-pentane, m.p. 164-166°C. (Found: C, 53.2; H, 3.0; N, 5.0 $C_{24}H_{16}N_2O_6Fe_2$ requires C, 53.4; H, 3.0; N, 5.2%) ν_{max} (chloroform solution) $\sim 2000\text{ cm}^{-1}$ intense multiplet (terminal C=O). Spectral data see appendix 4.3.

4. 5-Methyl-7-phenyl-3*H*-1,2-diazepine

A similar reaction (24 h) of 5-methyl-7-phenyl-3*H*-1,2-diazepine (786 mg, 2.16 mmol) gave after chromatography 5-methyl-7-phenyl-3*H*-1,2-diazepine diiron hexacarbonyl as a red solid (141 mg, 28%) which was recrystallised from n-pentane as red needles, m.p. 119-120°C (Found: C, 46.7; H, 2.6; N, 6.1 $C_{18}H_{12}N_2O_6Fe_2$ requires C, 46.6; H, 2.6; N, 6.0%), ν_{max} (chloroform solution) $\sim 2000\text{ cm}^{-1}$ intense multiplet (terminal C=O). Spectral data see appendix 4.4.

5. 3,5-Dimethyl-3H-1,2-diazepine and 5,7-dimethyl-3H-1,2-diazepine

5.1 Reaction with diiron nonacarbonyl

A mixture of the two isomeric diazepines (1.5 g, 12.3 mmol), ratio of 3,5-dimethyl to 5,7-dimethyl isomer of 15:85, was dissolved in dry benzene (30 ml) and diiron nonacarbonyl (8.96 g, 24.6 mmol) added. The suspension was stirred in the dark under nitrogen at room temperature for 24 h. Inspection by t.l.c. (alumina, ether:petrol 40/60; 1:1) showed all the starting material to be consumed and the emergence of fast moving product spot (red). The reaction mixture was filtered through celite and the fine precipitate washed thoroughly with benzene. Removal of the solvent under reduced pressure gave a red oil. This was separated by gravity column chromatography (alumina, petrol 40/60) to give a red solid, which was recrystallised from n-hexane to give 5,7-dimethyl-3H-1,2-diazepine diiron hexacarbonyl complex as red prisms (1.51 g, 31%) m.p. 122-123°C (Found: C, 38.7; H, 2.4; N, 6.7 C₁₃H₁₀N₂O₆Fe₂ requires C, 38.8; H, 2.5; N, 7.0%) ν_{\max} (chloroform solution) $\sim 2000\text{ cm}^{-1}$ intense multiplet (terminal C=O). Spectral data see appendix 4.5. No signals of the other possible isomer in the ¹H and ¹³C n.m.r. spectra were detected. In view of this anomaly the reaction was repeated and the crude product (both before and after chromatography) was examined very carefully by both n.m.r. spectroscopy and h.p.l.c., but no evidence of the other possible isomer was found. The h.p.l.c. conditions examined are summarised in the following table.

Column	Eluant
25x0.5 cm, 5 μ m SiO ₂ , 10,700 plates	Water-saturated hexane/dry hexane mixtures ranging from 1:1 to 0:1
15x0.5 cm, 10 μ m AlO ₃ , 4,100 plates	
25x0.5 cm, 10 μ m reverse phase 00S, 8,100 plates	Methanol/water mixtures ranging from 7:3 to 9:1

5.2 Reaction with benzylideneacetone iron tricarbonyl

A mixture of the two isomeric diazepines (200 mg, 1.6 mmol) and benzylideneacetone iron tricarbonyl (500 mg, 1.7 mmol) were dissolved in dry degassed benzene (20 ml). The solution was heated to 55-60°C for 48 h, removal of the solvent under reduced pressure and gravity chromatography of the residue on alumina (eluant; petrol 40/60) afforded 5,7-dimethyl-3*H*-1,2-diazepine diiron hexacarbonyl complex (206 mg, 64%, based on benzylideneacetone iron tricarbonyl).

5.3 Thermolysis study

5,7-Dimethyl-3*H*-1,2-diazepine diiron hexacarbonyl was heated in dry organic solvents and the reaction monitored by h.p.l.c. (for conditions see 5.1) and n.m.r. spectroscopy, no isomerisation to the other possible isomer by a thermal 1,5-sigmatropic shift was detected. The thermolysis conditions are summarised in the table below.

Solvent	Temperature	Time interval
toluene	90 ^o	1.5 h
toluene	110 ^o C (reflux)	0.5 h
toluene	110 ^o C (reflux)	2.0 h
xylene	150 ^o C	2.0 h (extensive decomposition)

6. 3,5-Dimethyl-7-ethyl-3H-1,2-diazepine and 5,7-dimethyl-3-ethyl-3H-1,2-diazepine

A mixture of the two isomeric diazepines (1.01 g, 6.73 mmol), ratio of 3,5-dimethyl-7-ethyl to 5,7-dimethyl-3-ethyl isomer ratio of 51:49, was dissolved in dry benzene (20 ml) and diiron nonacarbonyl (4.89 g, 13.5 mmol) added. The suspension was stirred in the dark under nitrogen at room temperature for 24 h. The usual work-up gave a red oil, which when separated by gravity column chromatography (alumina, petrol 40/60) gave a red solid. Recrystallisation of this solid from n-pentane gave red needles which were identified as the two isomeric complexes; 3,5-dimethyl-7-ethyl-3H-1,2-diazepines diiron hexacarbonyl and 5,7-dimethyl-3-ethyl-3H-1,2-diazepine diiron hexacarbonyl complexes, (1.34 g, 46%), m.p. 72-73^oC (Found: C, 42.0; H, 3.2; N, 6.5 C₁₅H₁₄N₂O₆Fe₂ requires C, 41.9; H, 3.3; N, 6.5%) ν_{\max} (chloroform solution) ~ 2000 cm⁻¹ intense multiplet (terminal C=O). Spectral data see appendix 4.6. The ratio of 3,5-dimethyl-7-ethyl to 5,7-dimethyl-3-ethyl isomer ratio was calculated as 60:40 from the integral of the 36MHz proton n.m.r. spectrum, and from the ¹³C n.m.r. spectrum

peak height (assuming that corresponding C-atoms in each isomer would have very similar relaxation times and nuclear Overhauser effects).

The isomer mixture was extensively examined by h.p.l.c. but no resolution of the components was obtained. The h.p.l.c. conditions examined are summarised in the table below.

Column	Eluant
25x0.5cm, 5 μ m SiO ₂ , 10,700 plates	Water-saturated hexane/dry hexane mixtures ranging from 1:1 to 0.1 (totally activated column)
15x0.5cm, 10 μ m AlO ₃ , 4,100 plates	
25x0.5cm, 10 μ m reverse phase ODS, 8,100 plates	methanol/water mixtures ranging from 7:3 to 9:1

7. 3,5-Dimethyl-7-isopropyl-3H-1,2-diazepine and 5,7-dimethyl-3-isopropyl-3H-1,2-diazepine

A mixture of the two diazepines (165 mg, 1.0 mmol), ratio of 3,5-dimethyl-7-isopropyl to 5,7-dimethyl-3-isopropyl isomer ratio of 34:66, was dissolved in dry benzene (10 ml) and diiron nonacarbonyl (0.730 g, 2.0 mmol) added. The suspension was stirred in the dark under nitrogen at room temperature for 48 h. The usual work-up gave a red oil, which when separated by gravity column chromatography (alumina, petrol 40/60) gave a red solid. Recrystallisation of this solid from n-pentane gave red needles which were identified as the two isomeric

complexes; 3,5-dimethyl-7-isopropyl-3*H*-1,2-diazepine diiron hexacarbonyl and 5,7-dimethyl-3-isopropyl-3*H*-1,2-diazepine diiron hexacarbonyl (253 mg, 57%), m.p. 64-65°C (Found: C, 43.2; H, 3.7; N, 6.3 $C_{16}H_{16}N_2O_6Fe_2$ requires C, 43.3; H, 3.6; N, 6.3%) ν_{max} (chloroform solution) $\sim 2000\text{ cm}^{-1}$ intense multiplet (terminal C=O). Spectral data see appendix 4.7. The ratio of 3,5-dimethyl-7-isopropyl to 5,7-dimethyl-3-isopropyl isomer ratio was calculated as 88:12 from the integral of the 360MHz proton n.m.r. spectrum and from the peak heights in the ^{13}C n.m.r. spectrum (assuming that corresponding C-atoms in each complex will have very similar relaxation times and nuclear Overhauser effects).

The isomer mixture was extensively examined by h.p.l.c. but no resolution of the components was obtained, although significant peak broadening was observed. The h.p.l.c. conditions examined are summarised in the table below.

Column	Eluant
25x0.5cm, 5 μ m SiO ₂ , 10,700 plates	Water-saturated hexane/dry hexane mixtures from 1:1 to 0.1 (totally activate column)
15x0.5cm, 10 μ m AlO ₃ , 4,100 plates	
25x0.5cm, 10 μ m reverse phase ODS, 8,100 plates	methanol/water mixture ranging from 7:3 to 9:1

8. 3,5-Dimethyl-7-phenethyl-3*H*-1,2-diazepine and 5,7-dimethyl-3-phenethyl-3*H*-1,2-diazepine

8.1 Synthesis

A mixture of the two isomeric diazepines (600 mg, 2.65 mmol), ratio of 3,5-dimethyl-7-phenethyl to 5,7-dimethyl-3-phenethyl isomer ratio of 49:51, was stirred in dry benzene (20 ml) with diiron nonacarbonyl (1.57 g, 4.3 mmol) for 7 days. The usual work-up gave a red oil, which was purified by gravity chromatography (alumina, eluant petrol 40/60) to give a red solid. Recrystallisation from n-hexane gave a mixture of the two isomeric complexes, 3,5-dimethyl-7-phenethyl-3*H*-1,2-diazepine and 5,7-dimethyl-3-phenethyl-3*H*-1,2-diazepine diiron hexacarbonyl complex, as red needles (0.514 g, 38%), m.p. 64-65°C (Found: C, 49.6; H, 3.6; N, 5.5 $C_{21}H_{18}N_2Fe_2O_6$ requires C, 49.8; H, 3.6; N, 5.5%) ν_{max} (chloroform solution) $\sim 2000\text{ cm}^{-1}$ intense multiplet (terminal C=O), spectral data see appendix 4.8.

8.2 H.p.l.c. separation

H.p.l.c. analysis (25x0.5 cm, 5 μm SiO_2 , 10,700 plates) using 50% water-saturated hexane as eluant at a flow rate of 2.5 ml min^{-1} , successfully resolved the two components and gave the 3,5-dimethyl-7-phenethyl-3*H*-1,2-diazepine to 5,7-dimethyl-3-phenethyl-3*H*-1,2-diazepine diiron hexacarbonyl complex isomer ratio as 72:28.

The isomers were separated preparatively on a small scale with a larger column (25x0.7 cm, 5 μm SiO_2 , $\sim 9,000$ plates, 3.5 ml min^{-1} flow rate) using 5 μl injections of a ca. 0.2 molar solution of the mixture. 25 Injections enabled 6 mg of the 3,5-dimethyl-7-phenethyl and 2 mg of the 5,7-dimethyl-3-

phenethyl to be isolated. Proton n.m.r. spectra were successfully obtained using a 360MHz instrument.

8.3 Thermolysis Study

3,5-Dimethyl-7-phenethyl-3*H*-1,2-diazepine diiron hexacarbonyl complex (1 mg) was dissolved in dry toluene (2 ml) and slowly heated to reflux (110°C). Samples were withdrawn at various temperatures and analysed by h.p.l.c. (25x0.5 cm, 5 µm SiO₂, 10,700 plates), no interconversion to the 5,7-dimethyl-7-phenethyl isomer was observed. The experiment was repeated for the 5,7-dimethyl-7-phenethyl isomer, again no interconversion was observed. The conditions examined are summarised in the following table.

Thermolysis Conditions	H.p.l.c. Analysis
15 mins at 50°C	no isomer interconversion
15 mins at 65°C	
15 mins at 80°C	
15 mins at 85°C	
2 h at 110°C	decomposition occurring

G. Disengagement of diazepine diiron hexacarbonyl complexes

1. 4-Phenyl-1*H*-2,3-benzodiazepine diiron hexacarbonyl complex

This was carried out by the method of Shvo et al.⁸¹ The diiron hexacarbonyl complex (645 mg, 1.29 mmol) was stirred in anhydrous benzene (20 ml) with a 20-fold molar excess of freshly sublimed trimethylamine *N*-oxide²¹⁵ (1.78 g, 25.8 mmol) at room temperature for 12 h. Removal of the solvent under reduced pressure followed by chromatography (alumina, ether:petrol 40/60, 1:9) afforded 4-phenyl-1*H*-2,3-benzodiazepine (120 mg, 42%) as a yellow solid, which was recrystallized from ethanol, m.p. 130-132°C (lit.,⁶⁴ 132-133°C).

2. 5,7-Dimethyl-3*H*-1,2-diazepine diiron hexacarbonyl complex

The diiron hexacarbonyl complex (1.51 g, 3.76 mmol) was stirred in anhydrous benzene (20 ml) with freshly sublimed trimethylamine *N*-oxide (5.2 g, 75.2 mmol) at room temperature for 12 h. Removal of the solvent under reduced pressure followed by chromatography (alumina, ether:petrol 40/60, 1:1) afforded the two isomeric diazepines; 3,5-dimethyl-3*H*-1,2-diazepine and 5,7-dimethyl-3*H*-1,2-diazepine, as a yellow oil (0.179 mg, 39%) b.p. 85°C at 16 mmHg (lit.,³⁴ 80°C at 12 mmHg). H.p.l.c. analysis with the column at 0°C and using a mixture of diethyl ether (10% vol) and 50% water-saturated hexane (90% vol) as eluant at a flow rate of 2.5 ml min⁻¹ gave the 3,5-dimethyl to 5,7-dimethyl isomer ratio of 15:85.

H. Oxidation of Diazepines

1. 4-Phenyl-1*H*-2,3-benzodiazepine

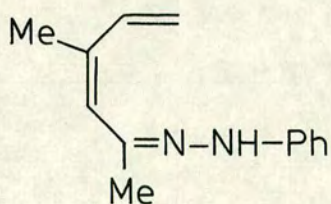
4-Phenyl-1*H*-2,3-benzodiazepine (0.50 g, 2.3 mmol) was dissolved in dry methylene chloride (20 ml) and a solution of *m*-chloro-perbenzoic acid (85%, 0.42 g, 2.3 mmol) in methylene chloride (20 ml) dripped in. The reaction was stirred under nitrogen, in the dark for 12 h. Removal of the solvent under reduced pressure gave a yellow solid which was purified by chromatography (alumina, petrol 40/60:ether, 1:1) to give 4-phenyl-1*H*-2,3-benzodiazepine *N*-oxide as a yellow solid (0.441 g, 81%) which was recrystallized from ethanol, m.p. 122-123^o (Found: C, 76.3; H, 5.2; N, 11.8 C₁₅H₁₂N₂O requires C, 76.2; H, 5.2; N, 11.9%) spectral data see appendix 5.1.

2. 3,5,7-Trimethyl-3*H*-1,2-diazepines

3,5,7-Trimethyl-3*H*-1,2-diazepine (0.50 g, 4.63 mmol) was dissolved in dry methylene chloride (20 ml) and a solution of *m*-chloro-perbenzoic acid (85%, 0.85 g, 4.63 mmol) in methylene chloride (20 ml) dripped in. The reaction was stirred under nitrogen, in the dark, at room temperature for 12 h. The reaction mixture was then washed with sodium bicarbonate solution (10%, 20 ml), dried over magnesium sulphate, and the solvent removed under reduced pressure to give a yellow oil. This oil was then separated by gravity column chromatography (alumina, ether:petrol 40/60, 1:1) to give a mixture of 3,5,7-trimethyl-3*H*-1,2-diazepine *N*-oxide and 3,5-dimethyl-3-propenyl-3*H*-pyrazole *N*-oxide as a pale yellow oil (268 mg, 47%) b.p. 80^oC at 0.1 mmHg (Found: M⁺, 152.094738 C₈H₁₂N₂O requires

m/e, 152.094958) Spectral data see appendix 5.2. The ratio of diazepine to pyrazole was calculated to be 50:50 from n.m.r. integral data. Pure samples of each isomer were obtained by preparative t.l.c. (alumina, ether:petrol 40/60, 1:1). These pure samples isomerised to the equilibrium mixture when left standing overnight in chloroform solution at room temperature. This interconversion could be prevented by storing freshly purified samples at below -30°C .

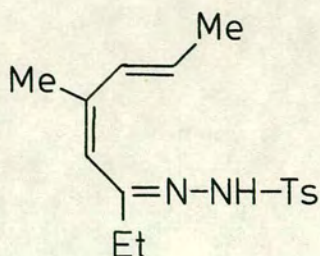
Appendix 1: Spectral data of hydrazones of $\alpha\beta,\gamma\delta$ -unsaturated ketones



1.1 4-Methylhexa-3,5-dien-2-one phenylhydrazone

δ_{H} : 1.99 (s, Me), 2.23 (s, Me), 5.13 br (d, J 11Hz, 6-H), 5.32 br (d, J 17Hz, 6-H'), 5.95 br (s, 3-H), 6.49 (d of d, J 17Hz, J' 11Hz, 5-H), 6.75-7.5 (m, 5H, phenyl).

m/e: 39 (42), 41 (43), 42 (47), 51 (40), 65 (60), 77 (93), 92 (67), 93 (87), 108 (100), 173 (44), 185 (73), 200 (53).

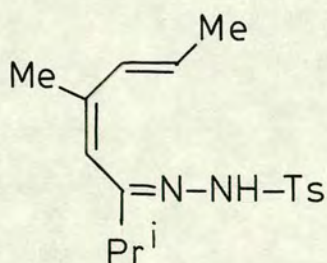


1.2 5-Methylocta-4,6-dien-3-one tosylhydrazone

δ_{H} : 0.99 (t, J 7Hz, ethyl Me), 1.56 br (s, 5-Me),
1.81 (d, J 5Hz, 7-Me), 2.24 (q, J 7Hz, ethyl
CH₂), 2.39 (s, tosyl Me), 5.37 br (s, 4-H),
5.82 (d of q, J 16Hz, J' 5Hz, 7-H), 6.08 (d,
J 16Hz, 6-H), 7.25 and 7.79 (AB, J 8Hz, aromatic),
7.43 br (s, NH).

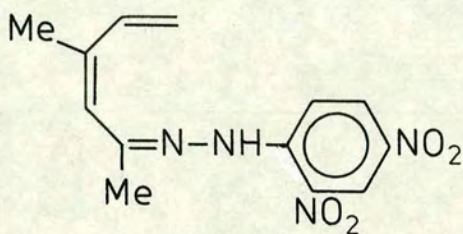
δ_{C} : C₃, 157.2; aromatic and olefinic, 118.1, 127.8,
129.0, 129.3, 133.1, 135.7, 142.3, 143.6;
ethyl CH₂, 30.2; 2-Me, 5-Me, 7-Me and tosyl Me,
10.5, 14.9, 18.1, 21.4.

m/e: 39 (24), 41 (51), 53 (15), 55 (12), 65 (24),
77 (21), 79 (18), 91 (54), 107 (22), 123 (25),
136 (16), 151 (100), 291 (40), 306 (less than 1).

1.3 2,5-Dimethylocta-4,6-dien-3-one tosylhydrazone

δ_{H} : 0.97 (d, J 6Hz, isopropyl Me), 1.53 (t, J 0.5Hz,
5-Me), 1.8 (d, J 5Hz, 7-Me), 2.38 (s, tosyl Me),
2.41 (heptet, J 6Hz, isopropyl CH), 5.36 br (s,
4-H), 5.83 (d of q, J 15Hz, J' 5Hz, 7-H), 6.1
(d, J 15Hz, 6-H), 7.25 and 7.77 (AB, J 8Hz, ArH),
7.41 br (s, NH).

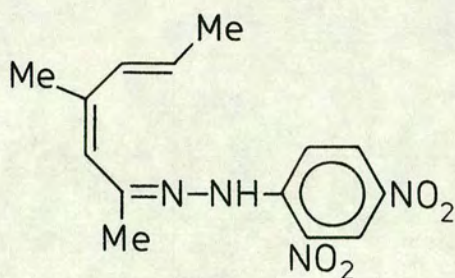
m/e: 39 (11), 41 (28), 43 (20), 53 (6), 55 (8), 65 (9), 77 (11), 79 (10), 91 (30), 95 (12), 105 (5), 123 (85), 165 (100), 305 (18), 320 (less than 1).



1.4 4-Methylhexa-3,5-dien-2-one 2,4-dinitrophenylhydrazone

δ_{H} : 2.18 (s, 2-Me), 2.22 br (s, 4-Me), 5.27 (d, J 10Hz, 6-H), 5.48 (d, J 16Hz, 6-H'), 5.99 br (s, 3-H), 6.47 (d of d, J 16Hz, J 10Hz, 5-H), 7.88 (d, J 8Hz, *o*-ArH), 8.29 (d of d, J 8Hz, J' 2Hz, *m*-ArH), 9.10 (d, J 2Hz, *m'*-ArH), 11.2 br (s, NH).

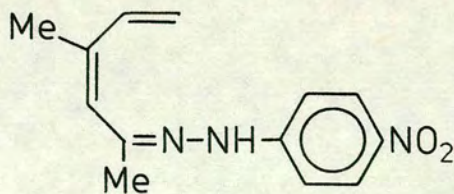
m/e: 39 (22), 41 (35), 51 (10), 53 (12), 65 (13), 67 (17), 77 (25), 79 (13), 91 (12), 107 (92), 108 (100), 242 (13), 273 (19), 289 (17), 290 (42).



1.5 4-Methylhepta-3,5-dien-2-one 2,4-dinitrophenylhydrazone

δ_{H} : 1.88 (d, J 5Hz, 6-Me), 2.19 (s, 2-Me), 2.23 br (s, 4-Me), 5.87 br (s, 3-H), 5.9-6.3 (m, 2H, 5-H and 6-H), 7.89 (d, J 8Hz, *o*-ArH), 8.33 (d of d, J 8Hz, J' 2Hz, *m*-ArH), 9.12 (d, J 2Hz, *m'*-ArH), 11.3 br (s, NH).

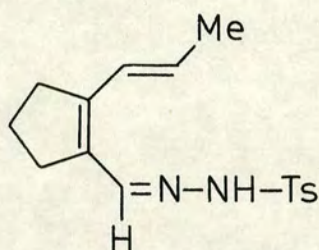
m/e: 39 (9), 41 (15), 53 (10), 77 (10), 79 (10), 107 (26), 111 (10), 112 (9), 289 (100), 304 (16).



1.6 4-Methylhexa-3,5-dien-2-one p-nitrophenylhydrazone

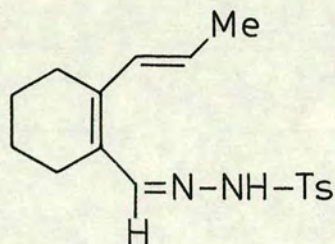
δ_{H} : 2.04 (s, 2-Me), 2.19 br (s, 4-Me), 5.19 (d, J 10Hz, 6-H), 5.39 (d, J 16Hz, 6-H'), 5.91 br (s, 3-H), 6.42 (d of d, J 16Hz, J' 10Hz, 6-H'), 7.05 and 8.09 (AB, J 9Hz, ArH), 7.8 br (s, NH).

m/e: 39 (15), 41 (31), 65 (14), 67 (15), 77 (8), 79 (9), 92 (9), 108 (100), 184 (5), 198 (7), 230 (8), 244 (22), 245 (29).

1.7 2-Propenyl-1-cyclopentene-1-carboxaldehyde tosylhydrazone

δ_{H} : 1.65-2.0 and 2.4-2.7 (m, 6H, cyclopentyl ring), 2.38 (s, tosyl Me), 5.74 (d of q, J 16Hz, J' 7Hz, CHMe), 6.44 (d, J 16Hz, CH=CHMe), 7.24 (d, J 6.5Hz, 2H, ArH), 7.7-8.0 (m, 3H, 2 aromatic and CH=N), 8.2 br (s, NH).

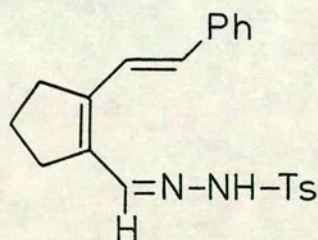
m/e: 39 (29), 41 (26), 55 (21), 65 (38), 77 (32), 79 (41), 91 (100), 105 (24), 121 (56), 132 (34), 139 (38), 149 (88), 156 (25), 278 (12), 304 (13).



1.8 2-Propenyl-1-cyclohexene-1-carboxaldehyde tosylhydrazone

δ_{H} : 1.5-1.75 and 2.1-2.35 (m, 8H, cyclohexyl ring),
 1.81 (d, J 6Hz, CHMe), 2.39 (s, tosyl Me), 2.83
 br (s, NH), 5.76 (d of q, J 16Hz, J' 6Hz, CHMe),
 6.54 (d, J 16Hz, CH=CHMe), 7.26 and 7.77 (AB,
 J 8Hz, ArH), 8.21 (s, CH=N).

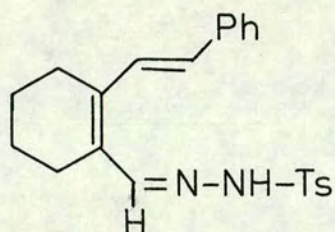
m/e: 39 (25), 41 (13), 51 (14), 63 (15), 65 (38),
 77 (17), 79 (16), 91 (100), 107 (19), 119 (19),
 139 (29), 146 (42), 156 (40), 163 (56), 318 (16).



1.9 2-Styryl-1-cyclopentene-1-carboxaldehyde tosylhydrazone

δ_{H} : 1.7-2.0 and 2.5-2.8 (m, 6H, cyclopentyl ring),
 2.33 (s, tosyl Me), 6.51 (d, J 16Hz, 1H, olefinic),
 7.05-7.5 (m, 8H, aromatic + olefinic), 7.82 (d,
 J 8H, ArH), 8.06 (s, CH=N), 8.35 br (s, NH).

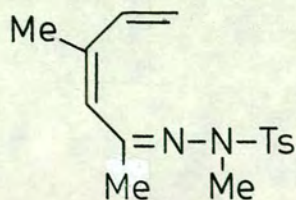
m/e (180°C) 39 (9), 44 (10), 51 (9), 65 (14), 77 (13), 91 (43),
115 (12), 128 (8), 141 (52), 183 (100),
338 (1).



1.10 2-Styryl-1-cyclohexene-1-carboxaldehyde tosylhydrazone

δ_H : 1.45-1.8 and 2.2-2.5 (m, 8H, cyclohexyl ring),
2.37 (s, tosyl Me), 3.0 br (s, NH), 6.58 (one
half an AB system, J 16Hz, olefinic), 7.1-7.5
(m, 8H, aromatic plus one olefinic), 7.79 (one
half an AB system, J 8Hz, tosyl ArH), 8.42 (s,
CH=N).

m/e (160°C): 39 (32), 41 (31), 51 (25), 65 (54), 77 (45),
91 (100), 115 (39), 129 (34), 141 (41),
155 (42), 197 (99), 208 (95), 352 (15).



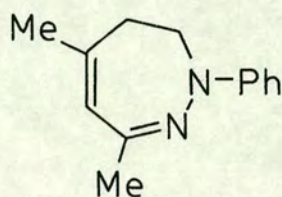
1.11 4-Methylhexa-3,5-dien-2-one N-methyltosylhydrazone

δ_{H} : 2.08 (s, Me), 2.26 (s, Me), 2.41 (s, tosyl Me), 2.73 (s, N-Me), 5.25 br (d, J 10Hz, 6-H), 5.40 br (d, J 18Hz, 6-H'), 5.92 br (s, 3-H), 6.39 (d of d, J 18Hz, J' 10Hz, 5-H), 7.28 and 7.74 (AB, J 8Hz, aromatic).

δ_{C} : C₂, 170.8; aromatic and olefinic, 116.3, 125.2, 129.0, 131.0, 140.3, 140.7, 143.8; N-Me, 38.7; 2-Me, 4-Me and tosyl Me, 14.4, 21.4, 24.2.

m/e: 42(7), 56(6), 65(6), 77(7), 91(18), 107(7), 122(8), 137(100), 155(3), 185(2), 292(3).

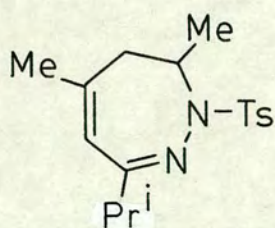
Appendix 2. Spectral data of 2-substituted 3,4-dihydro-1,2-diazepines



2.1 3,4-Dihydro-5,7-dimethyl-2-phenyl-1,2-diazepine

δ_{H} : 1.91 (s, 5-Me), 2.14 (s, 7-Me), 2.61 (t, J 6Hz, 4-H₂), 3.68 (t, J 6Hz, 3-H₂), 5.74 (m, 6H), 6.65-7.35 (m, 5H, phenyl).

m/e: 39 (18), 41 (12), 51 (14), 65 (8), 77 (37), 91 (11), 104 (18), 105 (21), 159 (25), 171 (7), 185 (15), 200 (100).



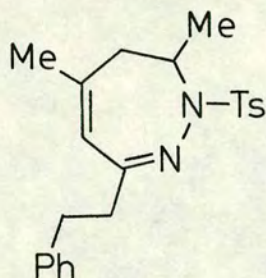
2.2 3,4-Dihydro-7-isopropyl-3,5-dimethyl-2-tosyl-1,2-diazepine

δ_{H} : 0.48 (d, J 8Hz, 3-Me), 1.04 (d, J 7Hz, isopropyl Me), 1.11 (d, J 7Hz, isopropyl Me), 1.88 br (s,

5-Me), 2.18 and 2.98 (AB, J 18Hz, 4-H₂), 2.4 (s, tosyl Me), 2.53 (heptet, J 7Hz, isopropyl CH), 4.7 (quintet of d, J 6Hz, J' 2Hz, 3-H), 5.7 br (s, 6-H), 7.24 and 7.86 (AB, J 8Hz, ArH).

δ_C : C-3, 51.3; C-4, 44.6; C-5, 134.7; C-6, 120.0; C-7, 160.6; aromatic, 149.7 (tert.), 143.4 (tert.), 128.8, 128.6; CHMe₂, 37.2; 3-Me, 5-Me, tosyl Me and isopropyl Me, 12.6, 20.2, 21.4, 26.8.

m/e: 39 (18), 41 (55), 42 (32), 53 (14), 55 (22), 65 (14), 67 (13), 77 (11), 79 (15), 91 (39), 95 (13), 107 (11), 123 (69), 165 (100), 320 (15).

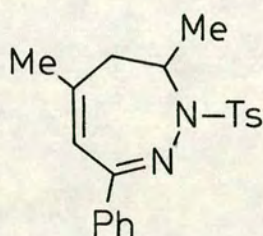


2.3 3,4-Dihydro-3,5-dimethyl-7-phenethyl-2-tosyl-1,2-diazepine

δ_H : 0.46 (d, J 8Hz, 3-Me), 1.86 br (s, 5-Me), 2.18 and 2.92 (AB, J 18Hz, 4-H₂), 2.4 (s, tosyl Me), 2.78 (m, CH₂CH₂), 4.74 (quintet of d, J 6Hz, J' 2Hz, 3-H), 5.71 br (s, 6-H), 7.15 br (s, 5H, phenyl), 7.25 and 8.85 [AB, J 8Hz, ArH (tosyl)].

δ_C : C-3, 51.5; C-4 and CH₂, 33.0, 40.0, 44.4;
C-5, 134.5; C-6, 120.6, C-7, 154.9; aromatic,
149.8 (tert.), 143.2 (tert.), 141.0 (tert.),
128.8, 128.2, 128.0, 127.9, 125.4; 3-Me, 5-Me and
Tosyl Me, 12.5, 21.1, 26.5.

m/e: 39 (7), 41 (12), 51 (4), 53 (5), 65 (11), 77 (8),
79 (6), 91 (45), 105 (11), 136 (5), 185 (4),
227 (100), 38 (12).

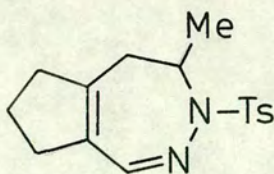


2.4 3,4-Dihydro-3,5-dimethyl-7-phenyl-2-tosyl-1,2-diazepine

δ_H : 0.6 (d, J 7Hz, 3-Me), 1.98 br (s, 5-Me), 3.18 and
2.4 (AB, J 18Hz, 4-H₂), 2.4 (s, tosyl Me), 4.84
(quintet of d, J 6Hz, J' 2Hz), 6.23 br (s, 6-H),
7.15-7.7 (m, 7H, ArH), 7.88 (d, J 8Hz, 2H, ArH).

δ_C : C-3, 52.9; C-4, 44.6; C-5, 134.3; C-6, 119.4,
C-7 and phenyl quaternary, 152.9, 151.3, aromatic,
143.6 (tert.), 139.2 (tert.), 134.5 (tert), 129.1,
128.7, 128.6, 128.0, 127.1, 3-Me, 5-Me and tosyl
Me, 13.4, 21.3, 27.1.

m/e: 39 (14), 41 (27), 51 (10), 65 (18), 77 (22),
91 (50), 102 (8), 115 (14), 128 (23), 141 (12),
158 (15), 171 (15), 199 (100), 354 (26).

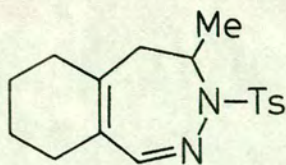


2.5 4-Methyl-4,5,6,7,8-pentahydro-3-tosyl-cyclopenta-
[d][1,2]diazepine

δ_{H} : 1.52 (d, J 7Hz, 4-Me), 1.85 (quintet, J 7Hz, 7-H₂), 2.2-3.1 (m, 6H, 6-H₂, 8-H₂ and 5-H₂), 2.39 (s, tosyl Me), 4.88 (quintet of d, J 6Hz, J' 2Hz, 4-H), 7.18 (s, 1-H), 7.24 and 7.87 (AB, J 8Hz, ArH).

δ_{C} : C-4, 51.1; C-5, 39.6; C-6, C-7, C-8, 4-Me and tosyl Me, 12.7, 21.3, 21.8, 35.8; C-1, 144.9; aromatic and olefinic, 150.6 (tert.), 143.6 (tert.), 134.8 (tert.), 129.2, 128.5, 128.2.

m/e: 39 (10), 41 (13), 55 (14), 65 (11), 67 (12), 77 (15), 79 (19), 91 (18), 149 (100), 304 (18).

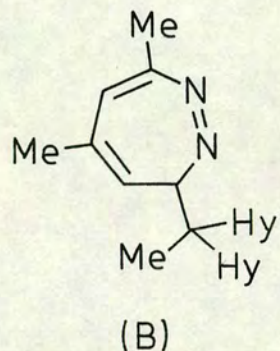
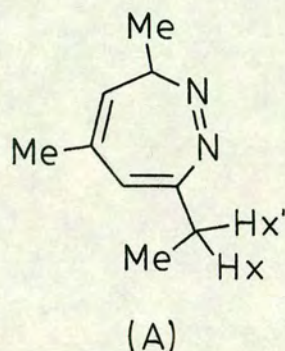


2.6 4-Methyl-4,5,6,7,8,9-hexahydro-3-tosyl-cyclohexa-
[d][1,2]diazepine

δ_{H} : 0.69 (d, J 8Hz, 4-Me), 1.4-2.3 (m, 9H, cyclohexyl ring and 5-H), 2.39 (s, tosyl Me), 2.78 (one half an AB system, J 20Hz, 5-H'), 4.89 (nontuplet, J 2Hz, 4-H), 6.83 (s, 1-H), 7.27 and 7.83 (AB, J 8Hz, ArH).

m/e: 39 (42), 41 (68), 57 (33), 65 (49), 77 (48), 79 (41), 91 (97), 105 (15), 121 (38), 135 (16), 163 (100), 164 (66), 212 (10), 318 (17).

Appendix 3: Spectral data of 3H-1,2-diazepines



3.1 7-Ethyl-3,5-dimethyl-3H-1,2-diazepine (A) and 3-Ethyl-5,7-dimethyl-3H-1,2-diazepine (B)

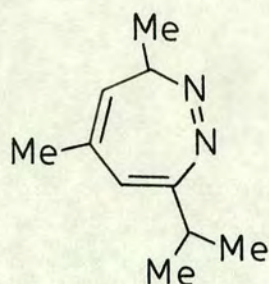
δ_{H}^* (A): 1.18 (t, J 7Hz, ethyl Me), 1.67 (quintet, J 6Hz, 3-H), 1.95 (t, J 1Hz, 5-Me), 2.01 (d, J 6Hz, 3-Me), 2.59 (sextet, J 7Hz, Hx), 2.85 (sextet, J 7Hz, Hx'), 4.91 (d, J 6Hz, 4-H), 5.91 br (s, 6-H).

δ_{H} (B): 1.15 (t, J 7Hz, ethyl Me), 1.55 (q, J 6Hz, 3-H), 1.94 (t, J 1Hz, 5-Me), 2.33 (heptet, J 7Hz, Hy), 2.38 (d, J 1Hz, 7-Me), 2.57 (heptet, J 7Hz, Hy'), 4.94 (d, J 6Hz, 4-H), 5.91 br (s, 6-H).

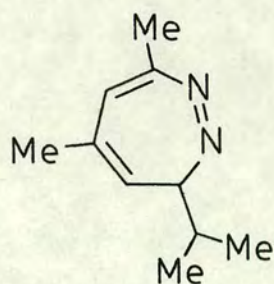
δ_{C} (A+B) C-3, 71.2, 77.4; C-4 and C-6, 118.4, 117.3, 116.9, 116.0; C-5, 136.3; C-7, 154.5, 160.8; CH_2 , 28.5, 26.0, 3-Me, 5-Me, 7-Me and ethyl Me, 21.1, 20.6, 18.6, 13.8, 10.7.

m/e(A+B) 39 (18), 41 (13), 53 (12), 77 (55), 79 (100), 80 (13), 91 (24), 93 (25), 94 (53), 95 (11), 106 (11), 122 (14).

* recorded at 360MHz



(A)



(B)

3.2 3,5-Dimethyl-7-isopropyl-3H-1,2-diazepine (A) and
5,7-Dimethyl-3-isopropyl-3H-1,2-diazepine (B)

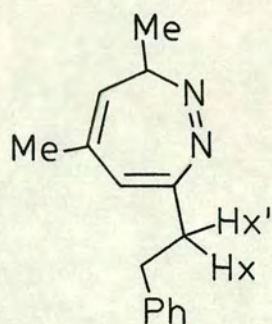
δ_{H}^* (A): 1.12 (d, J 7Hz, isopropyl Me), 1.26 (d, J 7Hz, isopropyl Me), 1.63 (quintet, J 6.5Hz, 3-H), 1.96 br (s, 5-Me), 2.01 (d, J 6.5Hz, 3-Me), 2.97 (quintet, J 7Hz, isopropyl CH), 4.90 (d, J 5.5Hz, 4-H), 5.90 br (s, 6-H).

δ_{H}^* (B): 1.16 (d, J 7Hz, isopropyl Me), 1.23 (d, J 7Hz, isopropyl Me), 1.15-1.25 (unresolved, 3-H), 1.96 br (s, 5-Me), 2.39 (s, 7-Me), 2.73 (sextet, J 6.5Hz, isopropyl CH), 5.01 (d, J 5.5Hz, 4-H), 5.90 br (s, 6-H).

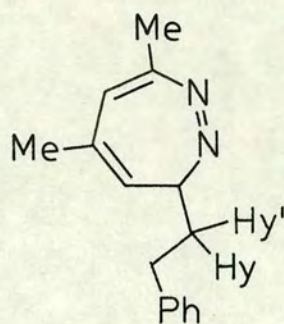
δ_{C} (A+B): C-3, 70.9, 82.0, C-4 and C-6, 113.9, 115.6, 117.1, 118.2; C-5, 135.8, 136.3; C-7, 154.0, 165.0; CHMe_2 , 33.6, 30.2; 3-Me, 5-Me, 7-Me and isopropyl Me, 18.4, 19.2, 19.6, 20.5, 21.0, 21.5, 22.8.

m/e(A+B) 39 (38), 41 (44), 43 (18), 53 (25), 65 (14), 77 (40), 79 (53), 91 (42), 93 (36), 105 (46), 121 (100), 136 (12), 149 (17), 165 (15).

* recorded at 360MHz



(A)



(B)

3.3 3,5-Dimethyl-7-phenethyl-3H-1,2-diazepine (A) and
5,7-Dimethyl-3-phenethyl-3H-1,2-diazepine (B)

δ_{H}^* (A): 1.53 (quintet, J 6Hz, 3-H), 1.89 (t, J 1Hz, 5-Me), 1.98 (d, J 7Hz, 3-Me), 3.04 (m, Hx), 3.24 (m, Hx').

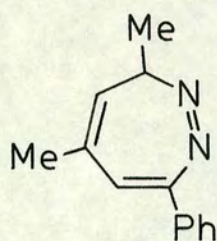
δ_{H} (B): 1.64 (q, J 6Hz, 3-H), 1.93 (t, J 1Hz, 5-Me), 2.37 (s, 7-Me), 2.57 (m, Hy), 2.81 (m, Hy').

δ_{H} (A+B): 3.91 (m, benzylic CH₂), 4.88 and 4.95 (d, J 6Hz, 4-H), 5.82 and 5.88 (s, 6-H), 7.12-8.31 (m, phenyl).

δ_{C} (A+B): C-3, 70.8, 74.8; C-4 and C-6, 116.2, 117.0, 117.1, 118.3; C-7, 154.2, 157.6; C-5 and aromatics, 141.2 (tert.), 140.4 (tert.), 136.0 (tert.), 135.4 (tert.), 128.1, 128.0, 127.9, 125.7, 125.5; CH₂, 36.8, 35.0, 34.1, 32.1; 3-Me, 5-Me and 7-Me, 20.6, 20.2, 20.1, 18.1.

m/e(A+B): 39 (19), 41 (16), 65 (26), 78 (22), 79 (38), 91 (99), 107 (100), 135 (10), 155 (10), 169 (12), 183 (17), 198 (19), 226 (5).

* recorded at 360MHz



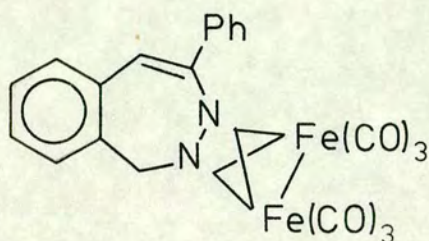
3.4 3,5-Dimethyl-7-phenyl-3H-1,2-diazepine

δ_{H} : 1.92 (q, J 6Hz, 3-H), 2.05 (t, J 1Hz, 5-Me),
2.05 (d, J 6Hz, 3-Me), 5.08 (d, J 6Hz, 4-H),
6.35 (s, 6-H), 7.25-7.5 and 7.78-7.82 (m, phenyl).

δ_{C} : C-3, 72.1; C-4 and C-6, 115.4, 118.9; C-7,
156.3; C-5 and aromatic, 136.7 (tert.), 136.8
(tert.), 128.6, 128.4, 125.8; 3-Me and 5-Me,
20.8, 18.2.

m/e: 39 (26), 41 (12), 51 (21), 63 (14), 77 (24),
91 (33), 102 (15), 115 (40), 128 (40), 141 (21),
155 (99), 170 (100), 198 (7).

Appendix 4: Spectral data of diiron hexacarbonyl diazepine complexes

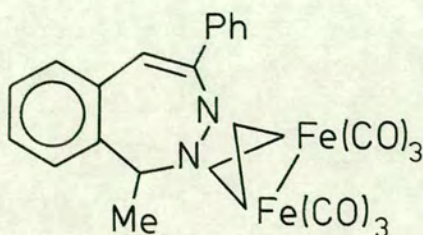


4.1 4-Phenyl-1H-2,3-benzodiazepine diiron hexacarbonyl complex

δ_{H} : 4.19 and 4.47 (AB, J 14Hz, methylene; quasi axial/equatorial), 6.6 (s, 1H, olefinic), 7.15-7.55 (m, 9H, aromatic).

δ_{C} : CH_2 , 61.6; olefinic, 117.9; aromatics, 138.7 (tert.), 136.5 (tert.), 135.0 (tert.), 129.7, 129.3, 129.0, 128.2, 128.3, 126.2; C-N, 149.3; C=O, 209.6.

m/e: 56 (32), 112 (24), 117 (22), 173 (31), 192 (24), 205 (22), 229 (75), 305 (37), 332 (18), 360 (100), 388 (59), 416 (20), 444 (8), 472 (34), 500 (25).

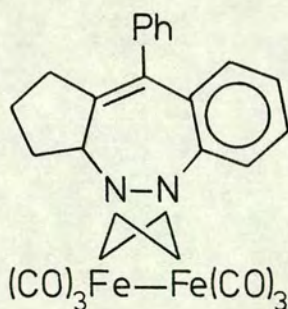


4.2 1-Methyl-4-phenyl-1H-2,3-benzodiazepine diiron hexacarbonyl complex

δ_{H} : 1.7 (d, J 6Hz, CHMe), 4.18 (q, J 6Hz, CHMe),
6.61 (s, 1H, olefinic), 7.1-7.55 (m, 9H, aromatic).

δ_{C} : CHMe, 61.0; Me, 15.8; olefinic 118.1; aromatic,
138.5 (tert.), 137.5 (tert.), 136.2 (tert.),
129.7, 129.0, 128.5, 128.3, 126.0, 124.9; C-N,
149.1; C=O, 182.2, 182.5.

m/e: 56 (46), 112 (24), 137 (18), 243 (53), 305 (68),
318 (16), 346 (19), 374 (100), 402 (87), 430 (27),
458 (8), 486 (48), 514 (27).

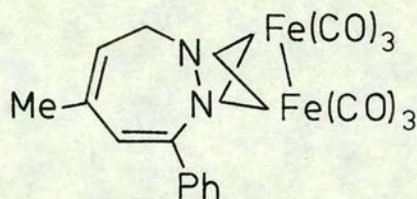


4.3 1,2,3,3a-Tetrahydro-10-phenylbenzo[c]cyclopenta[f]-[1,2]diazepine diiron hexacarbonyl complex

δ_{H} : 1.77-2.26 and 2.5-2.78 (m, 6H, cyclopentyl
methylenes), 3.72 br (d, J 6Hz, 3a-H), 6.74 (d,
J 8Hz, 1H, aromatic), 6.95-7.5 (m, 8H, aromatic).

δ_{C} : CH₂'s, 24.5, 31.3, 34.1; CH, 67.2; aromatics,
126.0, 127.6, 128.0, 128.4, 128.8, 129.9, 130.9,
132.9, 136.8 (tert.), 140.7 (tert.), 145.0 (tert.),
147.2 (tert.); C=O, 210.0.

m/e: 76 (22), 88 (28), 178 (96), 179 (100), 258 (74),
260 (72), 372 (36), 400 (11), 428 (23), 456 (8),
484 (4), 512 (9), 540 (13).

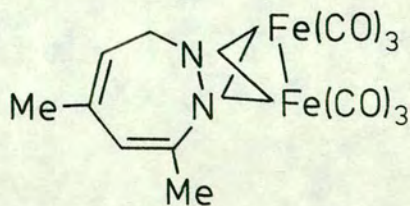


4.4 5-Methyl-7-phenyl-3H-1,2-diazepine diiron hexacarbonyl complex

δ_{H} : 1.92 (s, 5-Me), 3.88 (d, J 6Hz, 3-H₂), 5.86 br
(t, J 6Hz, 4-H), 5.91 (s, 6-H), 7.15-7.4 (m, phenyl).

δ_{C} : C-3, 55.7; C-4, C-6 and aromatics, 118.7, 126.1,
128.2, 129.1, 138.5 (tert.); C-5 and C-7, 142.3,
151.9; C=O, 210.0; 5-Me, 22.8.

m/e: 56 (34), 112 (22), 124 (16), 156 (13), 210 (32),
269 (39), 296 (45), 324 (100), 352 (34), 380 (7),
408 (43), 436 (21), 464 (16).

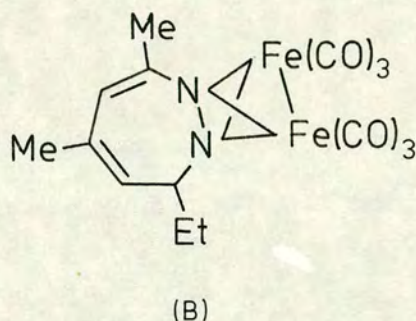
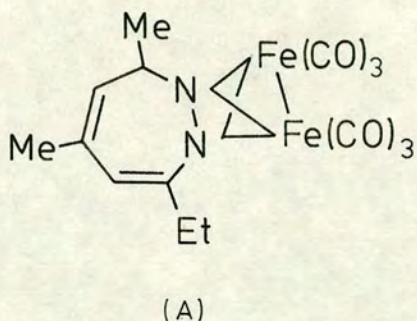


4.5 5,7-Dimethyl-3H-1,2-diazepine diiron hexacarbonyl complex

δ_{H} : 1.82 (s, 5-Me), 1.97 (s, 7-Me), 3.76 (d, J 6Hz, 3-H₂), 5.49 br (s, 6-H), 5.72 br (t, J 6Hz, 4-H).

δ_{C} : C-3, 55.2; C-4 and C-6, 117.0, 124.8; C-5 and C-7, 142.3, 148.2; C=O, 210.1, 5-Me and 7-Me, 22.7, 23.0.

m/e: 56 (10), 112 (29), 148 (19), 193 (19), 207 (36), 234 (100), 262 (24), 290 (10), 318 (5), 346 (19), 374 (21), 402 (9).



4.6 3,5-Dimethyl-7-ethyl-3H-1,2-diazepine (A) and 5,7-dimethyl-3-ethyl-3H-1,2-diazepine (B) diiron hexacarbonyl complexes

δ_{H}^* (A): 1.12 (t, J 7.5Hz, ethyl Me), 1.33 (d, J 6.5Hz, 3-Me), 2.1-2.35 (m, ethyl CH₂), 3.47 (m, 3-H), 5.44 (s, 6-H), 5.49 (d, J 5Hz, 4-H).

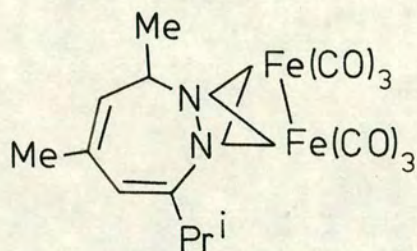
δ_{H} (B): 1.03 (t, J 7.5Hz, ethyl Me), 1.55-1.8 (m, ethyl CH₂), 1.98 (s, 7-Me), 3.2 (m, 3-H), 5.49 (s, 6-H), 5.52 (d, J 5Hz, 4-H).

* recorded at 360MHz

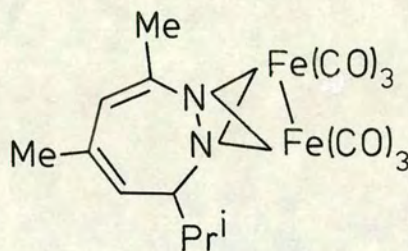
δ_{H} (A+B): 1.83 (m, 5-Me).

δ_{C} (A+B): C-3, 59.3, 64.2; C-4 and C-6, 115.2, 116.9, 128.5, 129.7; C-5, 139.8, 140.3; C-7, 148.3, 153.5; CH_2 , 25.1, 30.7; 3-Me, 5-Me, 7-Me and ethyl Me, 9.8, 12.9, 17.5, 22.7, 22.9; C=O, 210.1, 210.3.

m/e(A+B): 56 (17), 112 (21), 134 (16), 207 (14), 221 (18), 234 (13), 262 (100), 290 (24), 318 (12), 346 (7), 374 (20), 402 (18), 430 (13),



(A)



(B)

4.7 3,5-Dimethyl-7-isopropyl-3H-1,2-diazepine (A) and 5,7-dimethyl-3-isopropyl-3H-1,2-diazepine (B) diiron hexacarbonyl complexes

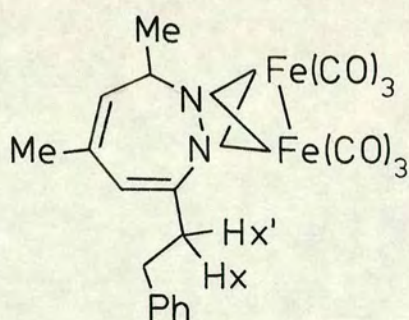
δ_{H} (A): 1.13 (d, J 7Hz, isopropyl Me), 1.15 (d, J 7Hz, isopropyl Me), 1.34 (d, J 6.5Hz, 3-Me), 1.83 (s, 5-Me), 2.37 (heptet, J 7Hz, isopropyl CH), 5.42 (s, 6-H), 5.49 br (s, 4-H).

δ_{H} (B): 0.99 (overlapping doublets, J 7Hz, isopropyl Me), 1.85 (s, 5-Me), 1.99 (s, 7-Me), 2.04 (m, isopropyl CH), 3.06 (m, 3-H), 5.52 (s, 6-H), 5.61 br (s, 4-H).

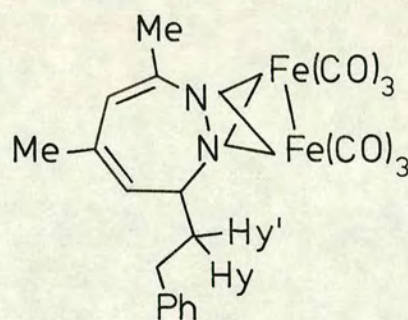
δ_C (A): C-3, 59.4; C-4 and C-6, 113.9, 129.6;
C-5 and C-7, 139.8 (tert.), 157.5 (tert.);
3-Me, 5-Me, isopropyl Me's, $CHMe_2$, 17.7,
21.1, 22.8, 23.3, 36.7.

δ_C (B): C-3, 67.0; C-4 and C-6, 117.2, 129.6; C-5
and C-7, not resolved; 3-Me, 5-Me, isopropyl
Me's, $CHMe_2$, 16.4, 20.1, 23.0, 30.3, 36.0.

m/e(A+B): 56 (17), 112 (18), 235 (19), 276 (100), 304
(22), 332 (10), 360 (6), 388 (21), 416 (15),
444 (19).



(A)



(B)

4.8 3,5-Dimethyl-7-phenethyl-3H-1,2-diazepine (A) and
5,7-Dimethyl-7-phenethyl-3H-1,2-diazepine (B) diiron
hexacarbonyl complexes

δ_H^* (A): 1.34 (d, J 7Hz, 3-Me), 1.72 (s, 5-Me), 1.51
(m, benzylic CH_2), 2.71 (m, Hx), 2.83 (m,
Hx'), 3.49 (m, 3-H), 5.33 and 5.48 br (s, 4-H
and 6-H), 7.15-7.35 (m, phenyl).

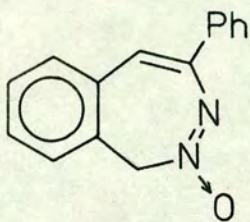
* recorded at 360MHz

δ_{H} (B): 1.85 and 1.96 (s, 5-Me and 7-Me), 1.9-2.0 (m, benzylic CH_2), 2.65-2.85 (m, Hy and Hy'), 3.28 (m, 3-H), 5.47 and 5.57 (d, J 3Hz, 4-H and 6-H), 7.15-7.35 (m, phenyl).

δ_{C} (A+B): C-3, 59.4, 62.4; C-4, C-5, C-6 and aromatics, 116.9, 117.4, 126.2, 128.2, 128.4, 130.0, 139.8 (tert.), 140.1 (tert.), 140.5 (tert.); C-7, 148.4, 150.5; 3-Me, 5-Me, 7-Me, 17.6, 22.5, 22.8, 23.0; CH_2CH_2 , 31.6, 33.7, 35.1, 40.4; C=O, 210.0, 210.3.

m/e(A+B): 56 (21), 91 (20), 112 (20), 249 (21), 297 (73), 338 (100), 360 (15), 394 (2), 422 (32), 450 (17), 478 (1), 504 (9).

Appendix 5: Spectral data of diazepine N-oxides

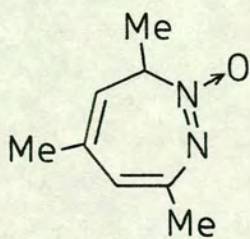


5.1 4-Phenyl-1H-2,3-benzodiazepine N-oxide

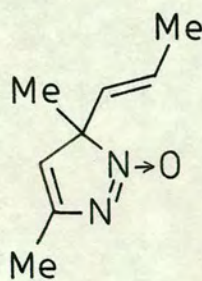
δ_{H} : 4.67 and 5.71 (AB, J 5.5Hz, methylene), 7.2-7.9 (m, 10H, aromatics + olefinic).

δ_{C} : CH_2 , 73.5; olefinic, 116.0; aromatics, 126.2, 126.0, 127.3, 127.9, 128.5, 128.3, 129.4, 130.3, 134.2 (tert.), 136.8 (tert.), 145.1 (tert.).

m/e: 51 (12), 77 (34), 103 (28), 178 (19), 191 (17), 206 (100), 236 (59).



(A)



(B)

5.2 3,5,7-Trimethyl-3H-1,2-diazepine N-oxide (A) and 3,5-dimethyl-3-propenyl-3H-pyrazole N-oxide (B)

δ_{H} (A): 6.08 br (s, 6-H), 5.05 (d, J 6Hz, 4-H), 3.76

(quintet, 3-H), 2.17 (s, 7-Me), 1.94 (t, J 0.5Hz, 5-Me), 1.84 (d, J 6Hz, 3-Me).

δ_{H} (B): 1.53 (s, 5-Me), 2.61 (d, J 6Hz, propenyl Me), 2.14 (d, J 2Hz, 3-Me), 5.49 (d, J 16Hz, Ha), 5.74 (d of q, J 16Hz, J' 6Hz, Hb), 5.88 br (s, 4-H).

δ_{C} (A+B): methyl groups, 14.3, 16.0, 17.7, 20.0, 22.5, 23.8; C-3's, 73.1, 90.6; olefinics, 119.6, 120.0, 120.3, 127.6, 130.0, 139.4, 144.9, 146.8.

m/e(A+B): 39 (75), 41 (79), 53 (73), 65 (31), 77 (38), 79 (71), 81 (46), 107 (75), 121 (67), 122 (100), 152 (23).

REFERENCES

1. F.D. Popp and A.C. Noble, Adv.Heterocyclic Chem., 1967, 8, 21.
2. M. Nastasi, Heterocycles, 1976, 4, 1509.
3. J. Streith and J.M. Cassal, Angew.Chem.Internat.Edn., 1968, 7, 129.
4. J. Streith and J.M. Cassal, Tetrahedron Letters, 1968, 4541.
5. V. Snieckus and J. Streith, Acc.Chem.Res., 1981, 14, 348.
6. H.J. Timpe, Adv.Heterocyclic Chem., 1974, 17, 213.
7. Y. Tamura, J. Minamikawa, Y. Miki, S. Matsugashita and M. Ikeda, Tetrahedron Letters, 1972, 4133.
8. Y. Tamura, J. Minamikawa, Y. Kita, J.H. Kim and M. Ikeda, Tetrahedron, 1973, 29, 1063.
9. Y. Tamura, Y. Miki and M. Ikeda, J.Heterocyclic Chem., 1973, 10, 447.
10. E. Klingsberg, Abstracts of the Amer.Chem.Soc. Meeting, September 1965, p.66s.
11. V. Snieckus and G. Kan, J.Chem.Soc., Chem.Comm., 1970, 1208.
12. D.J. Harris, G.Y.-P.Kan, V. Snieckus and E.Klingsberg, Canad.J.Chem., 1974, 52, 2798.
13. R. Allman, A. Frankowski and J. Streith, Tetrahedron, 1972, 581.
14. T. Tsuchiya and V. Snieckus, Canad.J.Chem., 1975, 53, 519.
15. J. Streith and B. Willig, Bull.Soc.chim.France, 1973, 2847.

16. A. Balasubramanian, J.M. McIntosh and V. Snieckus, J.Org.Chem., 1970, 35, 433.
17. T. Sasaki, K. Kanematsu, A. Kakehi, I. Ichikawa and K. Hayakawa, J.Org.Chem., 1970, 35, 426.
18. M. Nastasi and J. Streith, Bull.Soc.chim.France, 1973, 635.
19. J. Streith, J.P. Luttringer and M. Nastasi, J.Org.Chem., 1971, 36, 2962.
20. J. Streith, J.M. Cassal, Bull.Soc.chim.France, 1969, 2175.
21. G. Kan, M.T.Thomas and V. Snieckus, J.Chem.Soc., Chem. Commun., 1971, 1022.
22. J.P.Luttringer, N. Perol and J. Streith, Tetrahedron, 1975, 31, 2435.
23. T. Sasaki, K. Kanematsu and A. Kakehi, J.Chem.Soc., Chem.Commun., 1969, 432.
24. T. Sasaki, K. Kanematsu and K. Hayakawa, J.Chem.Soc.(C), 1971, 2142.
25. G. Taurand and J. Streith, Tetrahedron Letters, 1972, 3575.
26. J.M. Cassal, A. Frankowski, J.P. Luttringer, M. Nastasi, J. Streith, G. Taurand and B. Willig, Lectures in Heterocyclic Chem., 1974, 2, S-17.
27. T. Tsuchiya, H. Arai, H. Hasegawa and H. Igeta, Tetrahedron Letters, 1974, 4103.
28. J.P. Luttringer and J. Streith, Tetrahedron Letters, 1973, 4163.
29. H. Prinzback and D.H. Martin, Chimia, 1969, 23, 37.
30. J.J. Koenig and C.G. Wermuth, Tetrahedron Letters, 1973, 603.

31. G. Wittig, W. Joos and P. Rathfelder, Annalen, 1957, 610, 180.
32. S. Wawzonek and J.G. Stephanie, J.Org.Chem., 1971, 36, 2467.
33. C.D. Anderson, P.N. Anderson and J.T. Sharp, J.Chem. Soc., Perkin I, 1979, 1640.
34. C.D. Anderson, J.T. Sharp and R.S. Strathdee, J.Chem. Soc., Perkin I, 1979, 2209.
35. C.D. Anderson, J.T. Sharp, E. Stefaniuk and R.S. Strathdee, Tetrahedron Letters, 1976, 305.
36. C.D. Anderson, J.T. Sharp, J.Chem.Soc., Perkin I, 1979, 2730.
37. C.D. Anderson, and J.T. Sharp, J.Chem.Soc., Perkin I, 1980, 1230.
38. H.E. Zimmermann and W. Eberbach, J.Amer.Chem.Soc., 1973, 95, 3970.
39. H.D.Fuhlhuber and J. Sauer, Tetrahedron Letters, 1977, 4393.
40. H. Kolbinger, G. Reissenweber and J. Saver, Tetrahedron Letters, 1976, 4321.
41. L. Beml, M.T. Thomas, and V. Snieckus, Synthesis, 1979, 130.
42. M. Lipp, F. Dallacker and S. Munnes, Annalen, 1958, 618, 110.
43. K.W. Merz and H. Richter, Arch.Pharm., 1937, 275, 294.
44. L.A. Carpino, J.Org.Chem., 1965, 30, 736.
45. E.E. Blaise and H. Gault, Bull.Soc.chim.France, 1907, 75.
46. C.G. Overberger and J.J. Monagle, J.Am.Chem.Soc., 1956, 78, 4470.

47. C.G. Overberger and J.G. Lombardino, J.Amer.Chem.Soc., 1958, 80, 2317.
48. C.G. Overberger, J.G. Lombardino, I. Tashlick and P.G. Hiskey, J.Amer.Chem.Soc., 1957, 79, 2662.
49. R.G. Amiet, R.B. Johns and K.R. Markham, J.Chem.Soc., Chem.Comm., 1965, 128.
50. G. Heinrichs, H. Krapt, B. Schrodinger, A. Steigel, T.Troll and J. Saver, Tetrahedron Letters, 1970, 1617.
51. G. Maier, Angew.Chem.Internat.Edn., 1963, 2, 621; 1967, 6, 411.
52. G. Maier and V. Heep, Chem.Ber., 1968, 101, 1371.
53. G. Maier, Angew.Chem.Internat.Edn., 1967, 6, 402.
54. G.A. Archer and L.H. Sternbach, Chem.Rev., 1968, 68, 747.
55. T. Tsuchiya, J.Kurita, H. Igeta and V. Snieckus, J.Chem.Soc., Chem.Comm., 1974, 646.
56. J.T. Sharp, R.H. Findlay and P.B.Thorogood, J.Chem.Soc., Perkin I, 1975, 102.
57. T. Shiba, K. Yamane and H. Kato, J.Chem.Soc., Chem. Commun., 1970, 1592.
58. Y. Tamura, H. Ishibashi, N. Tsujimoto and M. Ikeda, Chem.Pharm.Bull.Tokyo, 1971, 19, 1285.
59. Y. Tamura, S. Matsugashita, H. Ishibashi and M. Ikeda, Tetrahedron, 1973, 29, 2359.
60. R.H. Findlay, J.T. Sharp and P.B. Thorogood, J.Chem.Soc., Perkin I, 1970, 909.
61. J. Dingwall and J.T. Sharp, J.Chem.Soc., Chem.Comm., 1975, 128.
62. T. Tsuchiya and J. Kurita, J.Chem.Soc., Chem.Comm., 1979, 803.

63. J.T. Sharp and P.B. Thorogood, J.Chem.Soc., Chem. Commun., 1970, 1197.
64. A.A. Reid, J.T. Sharp, H.R. Sood and P.B. Thorogood, J.Chem.Soc., Perkin I, 1973, 2543.
65. E. Schmitz and R. Ohme, Ber., 1962, 95, 2012.
66. T. Tsuchiya, M. Enkaku and H. Sawanishi, Heterocycles, 1979, 12, 1471.
67. Y. Tamura, J. Minamikawa, H. Matsushima and M. Ikeda, Synthesis, 1973, 3, 159.
68. C. Stelt, P.S. Hofman and W. Th. Nauta, Rec.Trav.Chim., 1965, 84, 633.
69. A.A. Reid, J.T. Sharp and S.J. Murray, J.Chem.Soc., Chem.Comm., 1972, 827.
70. J. Korosi, T. Lang, E. Komlos and L. Petocz, Hung.Pat. No.155572, December 9 1966, Chem.Abs., 1969, 70, 115026.
71. J. Korosi, T. Lang, E. Komlos, L. Petocz, addendum to Hug Hung. Patent No.155572.
72. J. Korosi and T. Lang, Chem.Ber., 1974, 107, 3883.
73. A. Neszmelyi, E. Gacs-Baitz, G. Horvath, T. Lang and J. Korosi, Chem.Ber., 1974, 107, 3894.
74. G. Zolyomi, D. Banfi, T. Lang and J. Korosi, Chem.Ber., 1974, 107, 3904.
75. A.J. Carty, R.F. Hobson, H.A. Patel and V. Snieckus, J. Amer.Chem.Soc., 1973, 95, 6835.
76. A.J. Carty, G. Kan, D.P. Madden, V. Snieckus and M. Stanton, J.Organomet.Chem., 1971, 32, 241.
77. D.J. Harris and V. Snieckus, J.Chem.Soc., Chem.Comm., 1976, 844.

78. R. Allman, Angew.Chem., Int.Ed.Engl., 1970, 9, 958.
79. F.A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry", Interscience, 1972.
80. A.J. Carty, C.R. Jablonski and V. Snieckus, Inorg.Chem., 1976, 15, 601.
81. Y. Shvo and E. Hazun, J. Chem.Soc., Chem.Commun., 1974, 336.
82. A.J. Carty, D.P. Madden, M. Mathew, G.J. Palenik and T. Birchall, J.Chem.Soc., Chem.Commun., 1970, 1664.
83. R.A. Smith, D.P. Madden and A.J. Carty, J. Chem.Soc., Chem.Commun., 1971, 427.
84. E.W. Abel and B.C. Crosse, Organomet.Chem.Rev., 1967, 2, 443.
85. D. Coucouvanis, S.J. Lippard and J.A. Zuibieta, J.Amer. Chem.Soc., 1970, 92, 3342.
86. R. Bruce and G.R. Knox, J.Organomet.Chem., 1965, 6, 67.
87. H. Buttner and R.D. Feltham, Inorg.Chem., 1972, 11, 971.
88. A.N. Nesmeyanov, M.I. Rybinskaya and L.V. Rybin, Russ. Chem.Rev., 1979, 48, 213.
89. R.W.F. Hardy, R.C. Burns and G.W. Parshall, Adv.Chem.Ser., 1971, 100, 219.
90. M.N. Ackermann and L.J. Kov, J.Organomet.Chem., 1975, 86, C7,
91. J.P.Kleiman and M. Dubeck, J.Amer.Chem.Soc., 1963, 85, 1544.
92. A.G.Cope and R.W. Siekman, J.Amer.Chem.Soc., 1965, 87, 3273.
93. J.J. Porter and J.L. Murray, J.Amer.Chem.Soc., 1965, 87, 1628.

94. M.M. Bagga, P.L. Pauson, F.J. Preston, and R.I. Reed, J.Chem.Soc., Chem.Comm., 1965, 543.
95. S.D. Ittel and J.A. Ibers, J.Organomet.Chem., 1973, 57, 389.
96. G. Fachinetti, G. Fochi and C. Floriani, J.Organomet.Chem., 1973, C51, 57.
97. R.J. Doedens and J.A. Ibers, Inorg.Chem., 1969, 8, 2709.
98. S.O. Otsuka, T. Yoshida and A. Nakamura, Inorg.Chem., 1969, 8, 2514.
99. A. Albini and H. Kisch, Angew.Chem.Int.Ed., 1975, 14, 182.
100. M. Herberhold and W. Golla, J.Organomet.Chem., 1971, 26, C27.
101. M. Herberhold and K. Leonard, J.Organomet.Chem., 1974, 78, 253.
102. H. Kisch, J.Organomet.Chem., 1972, 38, C19.
103. H. Kisch, J.Organomet.Chem., 1971, 30, C25.
104. C. Krüger, Ber., 1973, 106, 3230.
105. R.P. Bennett, Inorg.Chem., 1970, 9, 2184.
106. R.J. Doedens, Inorg.Chem., 1970, 9, 429.
107. A. Albini and H. Kisch, J.Organomet.Chem., 1975, 94, 75.
108. C. Krüger and H. Kisch, J.Chem.Soc., Chem.Comm., 1975, 65.
109. H.A. Patel, A.J. Carty, M. Mathew and G.J. Palenik, J.Chem.Soc., Chem.Comm., 1972, 81.
110. M. Herberhod and W. Golla, Ber., 1974, 107, 3199.
111. M. Herberhod and W. Golla and K. Leonhard, Ber., 1974, 107, 3209.
112. M.N. Ackermann and L.J. Kou, Inorg.Chem., 1976, 15, 1423.

113. M.N. Ackermann, D.B. Shewitz and C.R. Barton, J.Organomet.Chem., 1977, 125, C33.
114. D. Sellmann and K. Jodden, Angew.Chem.Int.Ed., 1977, 16, 464.
115. E. Haselbach, E. Heilbronner and A. Manuschrech, Angew.Chem., 1970, 82, 879.
116. P.E. Baikie and O.S. Mills, J.Chem.Soc., Chem.Commun., 1966, 707.
117. P.E. Baikie and O.S. Mills, Inorg.Chim.Acta, 1967, 1, 55.
118. M. Dekker and G.R. Knox, J.Chem.Soc., Chem.Commun., 1967, 1243.
119. M.I. Bruce, M.Z. Iqbal and F.G.A. Stone, J.Chem.Soc.A, 1971, 2820.
120. M.I. Bruce, M.Z. Iqbal and F.G.A. Stone, J.Chem.Soc.A, 1970, 3204.
121. M.I. Bruce, B.L. Goodall, M.Z. Iqbal and F.G.A. Stone, J.Chem.Soc., Chem.Commun., 1971, 661.
122. M.I. Bruce, M.Z. Iqbal and F.G.A. Stone, J.Chem.Soc., Chem.Commun., 1970, 1325.
123. M. Kilner and C. Medcalf, J.Chem.Soc., Dalton Trans., 1974, 1620.
124. H.T. Dieck, I.W. Renk and H.P. Brehm, Z.anorg.Chem., 1970, 379, 169.
125. L.V. Rybin, A.V. Arutyunyan, P.V. Petrovskii and M.I. Rybinskaya, Izv.Akad.Nauk SSSR, Ser.Khim., 1972, 190.
126. L.G. Kuz'mina, N.G. Bokii, Yu.T. Struchkov, A.V. Arutyunyan, L.V. Rybin and M.I. Rybinskaya, Zhur.Strukt.Khim., 1971, 12, 875.
127. A.N. Nesmeyanov, L.V. Rybin, M.I. Rybinskaya, A.V. Arutyunyan, N.T. Gubenko and P.V. Petrovskii, Izv.Akad.Nauk SSSR, Ser.Khim., 1971, 1574.

128. P.C. Ellgen and S.L. McMullin, Inorg.Chem., 1973, 12, 2004.
129. H. Alper, J.Organomet.Chem., 1973, 50, 209.
130. A.N. Nesmeyanov, V.N. Babin and N.S. Kachetkova, Dokl.Akad.Nauk SSSR, 1971, 200, 601.
131. A.N. Nesmeyanov, V.N. Babin, N.S. Kochetkova, Yu.S. Nekrasov, Yu.A. Belousov and S. Yu. Sil'vestrova, Dokl.Akad.Nauk SSSR, 1974, 218, 1368.
132. D.P. Madden, A.J. Carty and T. Birchall, Inorg.Chem., 1972, 11, 1453.
133. V.A. Mironov, A.A. Akhrem and E.V. Sobolev, Otkrytie SSSR No.167, 1975, Priority 1961; Byul.Izobret., 1976, No.13.
134. R.B. Woodward and R. Hoffman, "The Conservation of Orbital Symmetry", Verlag Chemie, 1970.
135. C.W. Spangler, Chem.Rev., 1974, 76, 187.
136. V.A. Mironov, A.D. Fedorovich and A.A. Akhrem, Russ.Chem. Rev., 1981, 50, 666.
137. E. Vogel, K.H. Ott and K. Gajek, Annalen, 1961, 644, 172.
138. L. Claisen and E. Tietze, Ber., 1925, 58, 275.
139. J.E. Baldwin, R.E. Hackler and D.P. Kelly, J.Chem.Soc., Chem.Commun., 1968, 537.
140. U. Schöllkopf and I. Hoppe, Annalen, 1972, 765, 153.
141. V. Schomaker and L. Pauling, J.Amer.Chem.Soc., 1939, 61, 1769.
142. G. Dallinga and L.H. Toneman, J.Mol.Struct., 1967, 1, 11.
143. J.F. Chiang and S.H. Bauer, J.Amer.Chem.Soc., 1966, 88, 420.
144. W.R. Roth, J. Konig and K. Stein, Chem.Ber., 1970, 103, 426.

145. V.A. Mironov, E.V. Sobolev and A.N. Elizarova, Tetra-
hedron, 1963, 19, 1939.
146. V.A. Mironov, O.S. Chizhov, I.M. Kimelfeld and
A.A. Akhrem, Tetrahedron Letters, 1969, 499.
147. A.P. ter Borg and H. Kloosterziel, Proc.Chem.Soc., 1962,
359.
148. A.P. ter Borg and H. Kloosterziel, Rec.Trav.Chim., 1969,
88, 267.
149. K.W. Egger, J.Amer.Chem.Soc., 1968, 90, 1.
150. A.P. ter Borg, E. Razenberg and H. Kloosterziel, Rec.
Trav.Chim., 1965, 84, 1230.
151. R. Baumes, J. Elguero, R. Jaquier and G. Tarrago,
J.Heterocyclic Chem., 1973, 10, 763.
152. M. Franck-Neumann and C. Dietrich-Buchecker, Terrahedron
Letters, 1976, 2069.
153. P. Schiess and H. Stalder, Tetrahedron Letters, 1980,
1417.
154. H. Dürr and R. Sergio, Tetrahedron Letters, 1972, 3479.
155. H. Dürr and R. Sergio, Chem.Ber., 1974, 107, 2027.
156. L.M. Dane, J.W. de Haan and H. Kloosterziel, Tetrahedron
Letters, 1970, 2755.
157. P.A.S. Smith, "The Chemistry of Open Chain Nitrogen
Compounds", Vol.2, W.A. Benjamin, Inc., New York, 1966.
158. S. Patai, "The Chemistry of the Hydrazo, Azo and Azoxy
Groups," Vol.1 & 2, Wiley Interscience, 1975.
159. J.P. Snyder, L. Lee and D.G. Farnum, J.Amer.Chem.Soc.,
1971, 93, 3816.
160. B.T. Gillis and J.D. Hagarty, J.Org.Chem., 1967, 32, 95.

161. J.P. Snyder, L. Lee, V.T. Bandurco, C.Y. Yu and R.J. Boyd, J.Amer.Chem.Soc., 1972, 94, 3260.
162. J. Swigert and K.G. Taylor, J.Amer.Chem.Soc., 1971, 93, 7337.
163. K.G. Taylor and T. Riehl, J.Amer.Chem.Soc., 1972, 94, 250.
164. W.R. Dolbier and W.M. Williams, J.Amer.Chem.Soc., 1969, 91, 2818.
165. W.M. Williams and W.R. Dolbier, J.Amer.Chem.Soc., 1972, 94, 3955.
166. H. Duval, Compt.Rend., 1905, 141, 198.
167. H. Duval, Bull.Soc.Chim.France, 1910, 7, 532.
168. A. Catala and F.D. Popp, J.Heterocyclic Chem., 1964, 1, 178.
169. I.R. Robertson and J.T. Sharp, unpublished observations.
170. R.K. Bartlett and T.S. Stevens, J.Chem.Soc.(C), 1974, 1964.
171. C.D. Anderson and J.T. Sharp, unpublished observations.
172. J.R. de Dobbelaere, J.M.F. van Dijk, J.W. de Haan and H.M. Buck, J.Amer.Chem.Soc., 1977, 99, 392.
173. I. Fleming, "Frontier Orbitals and Organic Chemical Reactions," Wiley-Interscience, 1976.
174. N.D. Epiotis, Angew.Chem.Int.Ed., 1974, 13, 751.
175. N. Hoshi, H. Hagiwara and H. Uda, Chem.Lett., 1979, 1291 and 1295; Kogagaku Torankai Koen Yoshishu, 1979, 14-15 (Chem.Abs., 1980, 92, 214634h).
176. N. Hoshi and H. Uda, Chem.Comm., 1981, 1163.
177. E.H. Braye and W. Hubel, Inorganic Syntheses, 8, 178.

178. A J.P. Domingos *et al.*, Inorganic Syntheses, 16, 103.
179. M.L. Maddox, S.L. Stafford and H.D. Kaesz, Advan. Organometal.Chem., 1965, 4, 1.
180. M.A. Bennett, Advan.Organometal.Chem., 1967, 4, 353.
181. J.A. Pople, W.G. Schneider and H.J. Benstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959.
182. R.J. Kurland, M.B. Rubin and W.B. Wise, J.Chem.Phys., 1964, 40, 2426.
183. R.O. Gould and S.E.B. Gould, J.C.S.Perkin II, 1974, 1075.
184. R.O. Gould and M.D. Walkinshaw, Cryst.Struct.Comm., 1981, 10, 1139.
185. A.L. Balch and D. Petridis, Inorg.Chem., 1969, 8, 2247.
186. R.S. Dickson *et al.*, J.Amer.Chem.Soc., 1971, 93, 4636.
187. C. Crisan and H. Normant, Bull.Soc.chim.France, 1957, 1451.
188. J. Cologne and J. Varagnat, Bull.Soc.chim.France, 1961, 237.
189. E.J. Corey and D. Erders, Chem.Ber., 1978, 111, 1362.
190. G.M. Pilling and F. Sondheimer, J.Amer.Chem.Soc., 1971, 93, 1970.
191. H. Olsen and J.M.F. Oth, Angew.Chem.Int.Ed., 1981, 20, 983.
192. H. Olsen, Angew.Chem.Int.Ed., 1981, 20, 984.
193. J.B. Shoemith and R.H. Slater, J.Chem.Soc., 1926, 214.
194. C.D. Anderson, Ph.D. Thesis, University of Edinburgh, 1977.
195. D.F. De Tar and L.A. Carpino, J.Amer.Chem.Soc., 1956, 78, 477,

196. L.I. Smith and M. Bayliss, J.Org.Chem., 1941, 6, 437.
197. S. Natelson and S.P. Gottfried, J.Amer.Chem.Soc., 1941, 63, 487.
198. L. Claisen, Ber., 1907, 40, 3903.
199. R. West, J.Amer.Chem.Soc., 1958, 80, 3246.
200. A.L. Wilds and C. Djerassi, J.Amer.Chem.Soc., 1946, 68, 1715.
201. H. Burton and C.K. Ingold, J.Chem.Soc., 1929, 2028.
202. I.M. Heilbron, E.R.H. Jones and D.G. O'Sullivan, J.Chem.Soc., 1946, 866.
203. A.I. Vogel, "Practical Organic Chemistry," Longmans, London, 3rd edn.
204. C.K. Ingold and J. Bloom, J.Chem.Soc., 1931, 2765.
205. E.D. Bergmann and A. Solomonovici, Tetrahedron, 1971, 2677.
206. E.D. Bergmann and A. Solomonovici, Tetrahedron, 1971, 2675.
207. H.O. House, L.J. Czuba, M. Gall and H.D. Olmstead, J.Org.Chem., 1969, 34, 2324.
208. T. Mukaiyama and M. Hayashi, Chem.Lett., 1974, 15.
209. E.E. Royals and K.C. Brannock, J.Amer.Chem.Soc., 1953, 75, 2050.
210. L. Bardou, J. Elgvero and R. Jacquier, Bull.Soc.chim. France, 1967, 297.
211. S. Murata, M. Suzuki and R. Noyori, J.Amer.Chem.Soc., 1980, 102, 3248.
212. F. Huet, A. Lechevallier, M. Pellet and J.M. Conia, Synthesis, 1978, 63.

213. A.S. Dreiding and S.N. Nickel, J.Amer.Chem.Soc., 1954, 76, 3965.
214. Z. Arnold and Holy, Collect.Czech.Chem.Comm., 1961, 26, 3059.
215. J.J. Monagle, J.Org.Chem., 1962, 27, 3851.

Reprinted from



Crystal Structure Communications

PUBLISHED BY UNIVERSITÀ DEGLI STUDI DI PARMA, ITALY

Cryst. Struct. Comm. (1981). 10, 1139.

DIIRON HEXACARBONYL 5,7-DIMETHYL-3H-1,2-DIAZEPINE, $C_{13}H_{10}Fe_2N_2O_6$

R.O. Gould and M.D. Walkinshaw

Department of Chemistry, University of Edinburgh, Edinburgh,

EH9 3JJ, Scotland.

Preliminary Information. The title compound was prepared by reacting 5,7-dimethyl-3H-1,2-diazepine with diiron nonacarbonyl (Argo and Sharp 1981). A study with 1H-1,2-diazepines has shown that an $Fe(CO)_3$ moiety forms a π -complex with the butadiene group in the ring (Parnnell et.al.1978). The reactivity of 3H-1,2-diazepine appears to be quite different and a tetrahedral Fe_2N_2 system is formed similar to those reported for some other azo-compounds (Nesmeyanov et.al. 1979).

Crystal data for $C_{13}H_{10}Fe_2N_2O_6$, $M = 402$, deep red triclinic crystals, $a = 7.522(1)$, $b = 9.801(3)$, $c = 11.825(1)$ Å, $\alpha = 76.34(2)^\circ$, $\beta = 72.87(1)^\circ$, $\gamma = 78.74(2)^\circ$, $U = 802$ Å³, $Z = 2$, $D_c = 1.66$ g cm⁻³, space group $P\bar{1}$ (No. 2), MoK_α radiation $\lambda = .71069$ Å, $\mu = 18.9$ cm⁻¹.

Structure Determination. After preliminary photography unit cell dimensions and intensity data were measured on a Nonius CAD 4 diffractomer. A crystal of dimensions 0.4 , 0.4 , 0.6 mm (rotation axis) was used with Zr filtered MoK_α radiation. Of 2806 unique reflexions measured to $2\theta_{max} = 50^\circ$, 2307 had $I > 3\sigma(I)$.

TABLE 1 FRACTIONAL COORDINATES OF ATOMS WITH STANDARD DEVIATIONS

	X	Y	Z
FE(2)	0.0703 (1)	0.2066 (1)	0.1625 (1)
FE(1)	0.3493 (1)	0.1049 (0)	0.2438 (0)
C(10)	0.4993 (5)	0.1039 (4)	0.3385 (3)
C(11)	0.3494 (5)	-0.0831 (4)	0.2677 (3)
C(12)	0.5266 (5)	0.1170 (4)	0.1029 (3)
C(13)	-0.0050 (5)	0.0467 (4)	0.1568 (3)
C(14)	0.1779 (5)	0.2505 (4)	0.0028 (3)
C(15)	-0.1491 (5)	0.3208 (4)	0.1668 (3)
O(1)	0.6011 (4)	0.1042 (3)	0.3938 (2)
O(2)	0.3430 (4)	-0.2015 (3)	0.2853 (3)
O(3)	0.6371 (4)	0.1282 (3)	0.0132 (3)
O(4)	-0.0517 (4)	-0.0574 (3)	0.1568 (3)
O(5)	0.2500 (5)	0.2777 (4)	-0.0963 (3)
O(6)	-0.2888 (4)	0.3903 (3)	0.1681 (3)
N(1)	0.1986 (3)	0.2874 (3)	0.2412 (2)
N(2)	0.1017 (3)	0.1798 (3)	0.3206 (2)
C(3)	-0.0197 (5)	0.2054 (4)	0.4376 (3)
H(31)	-0.1183 (5)	0.2999 (4)	0.4236 (3)
H(32)	-0.0953 (5)	0.1159 (4)	0.4812 (3)
C(4)	0.0925 (5)	0.2250 (4)	0.5179 (3)
H(4)	0.0826 (48)	0.1555 (32)	0.6014 (21)
C(5)	0.1916 (5)	0.3315 (4)	0.4903 (3)
C(6)	0.2080 (5)	0.4360 (4)	0.3778 (3)
H(6)	0.2315 (49)	0.5385 (23)	0.3788 (32)
C(7)	0.2090 (5)	0.4181 (3)	0.2695 (3)
C(8)	0.2408 (6)	0.5315 (4)	0.1580 (4)
H(81)	0.2600 (6)	0.6243 (4)	0.1850 (4)
H(82)	0.1203 (6)	0.5556 (4)	0.1212 (4)
H(83)	0.3644 (6)	0.4998 (4)	0.0904 (4)
C(9)	0.2960 (7)	0.3521 (5)	0.5748 (5)
H(91)	0.4397 (28)	0.3521 (43)	0.5377 (35)
H(92)	0.2745 (55)	0.2679 (32)	0.6471 (27)
H(93)	0.2730 (58)	0.4605 (22)	0.5737 (38)

No absorption correction was applied since the difference between maximum and minimum measured transmittances was 10%.

A Patterson synthesis provided positions for both Fe atoms in the asymmetric unit. All other non hydrogen atoms were located from an E-map calculated using 1992 reflections phased by the system DIRDIF (Beurskens, et.al. 1980). Using SHELX (Sheldrick 1976), full matrix least squares refinement of positions and isotropic vibrational parameters of all non-hydrogen atoms gave an R factor of 0.061. A difference Fourier map showed

the positions of the three methyl group hydrogens attached to C(9), the hydrogen atoms attached to C(4) and C(6) and one of the methyl group hydrogen atoms attached to C(8). The remaining five hydrogen atom positions were calculated assuming standard geometry. For the final cycles of refinement both iron atoms and the twelve atoms of the carbonyl groups were allowed to refine anisotropically. Five of the locatable hydrogen atoms were refined but with C-H bond lengths constrained to 1.08 Å. The C(8) methyl hydrogen atoms were refined as a rigid group and H(31) and H(32) were allowed to "ride" on C(3) (SHELX). Reflections 0 $\bar{1}$ 1 and $\bar{1}$ 03 were omitted from the last two cycles of refinement as both showed large extinction effects. In the last cycle no shifts of non-hydrogen atom parameters were greater than .05 times their estimated standard deviation. The weighting scheme applied in the last stages of refinement was $\omega = \frac{1}{\sigma^2}$ and the final R factor was .035.

Positional parameters of atoms are given in Table 1, bond lengths and angles in Table 2.

Description of the Structure

Both iron atoms in the molecule show 6-fold coordination, each iron atom is bonded to three carbonyl groups with an average Fe-C distance of 1.798(6) Å. The four Fe-N bonds (average length 1.906(8) Å), the Fe-Fe bond (2.498 Å) and the N-N bond (1.398 Å) form a distorted tetrahedron. There are no significant differences between the carbonyl C-O bonds which have an average length 1.137 Å with a standard deviation of .005 Å. The Fe-C-O bond angles are nearly linear with an average value of 177.8° and a standard deviation from the mean of .5°. The two iron atoms show nearly identical coordination geometry and sit at the apices of two distorted

Figure 1 Drawing of the title compound.

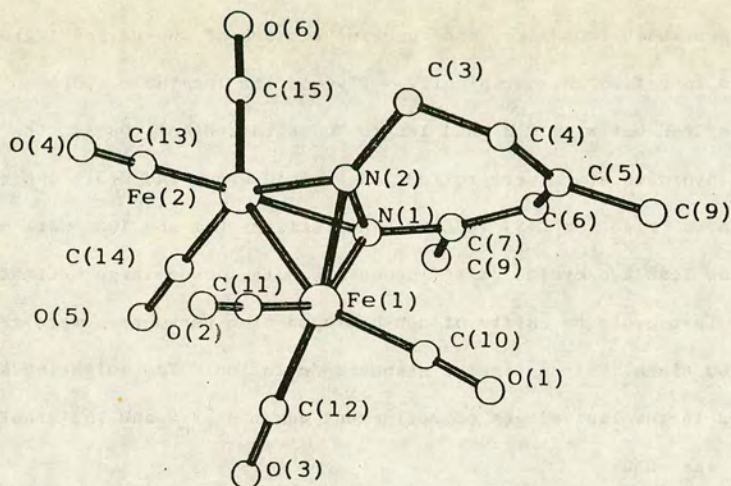


TABLE 2

<u>Bond Lengths</u> (Å)			
Fe(1)-Fe(2)	2.498(1)	C(10)-O(1)	1.144(5)
Fe(1)-N(1)	1.920(2)	C(11)-O(2)	1.137(5)
Fe(1)-N(2)	1.902(2)	C(12)-O(3)	1.135(4)
Fe(2)-N(1)	1.898(3)	C(13)-O(4)	1.142(5)
Fe(2)-N(2)	1.904(3)	C(14)-O(5)	1.128(5)
Fe(1)-C(10)	1.807(4)	C(15)-O(6)	1.133(5)
Fe(1)-C(11)	1.797(4)	N(1) - N(2)	1.398(3)
Fe(1)-C(12)	1.797(3)	N(1) - C(7)	1.420(5)
Fe(2)-C(13)	1.789(4)	C(7) - C(8)	1.502(6)
Fe(2)-C(14)	1.804(4)	C(7) - C(6)	1.331(6)
Fe(2)-C(15)	1.799(4)	C(6) - C(5)	1.464(5)
		C(5) - C(9)	1.508(8)
		C(5) - C(4)	1.323(6)
		C(4) - C(3)	1.507(6)
		C(3) - N(2)	1.463(4)

tetrahedra: that with the three carbonyl groups, and the shared Fe(2), Fe(1), N(1), N(2) tetrahedron. The internal angles at the Fe atoms in this shared tetrahedron are narrow with an average value of 47° compared to the wider C-Fe-C angles of the carbonyl tetrahedra which have an average value of 97° .

The seven membered ring adopts a half boat conformation showing pseudo-mirror symmetry across the plane lying along the line between C(3) and the midpoint of the C(7)-C(6) double bond and perpendicular to the line between N(1) and C(5). All bond lengths and angles in the seven membered ring are within the expected ranges.

References

- C.B. Argo and J.T. Sharp, (1981), Tet.Lett., in press.
- P.T. Beurskens, W.P. Bosman, H.M. Doesburg, R.O. Gould, TH.E.M. Van Den Hark, and P.A.J. Prick, Technical Report 1980/81, Crystallography Laboratory, Toernooiveld, 6525 ED Nijmegen, Netherlands.
- A.N. Nesmeyanov, M.I. Rybinskaya and L.V. Rybin, Russian Chemical Reviews, 1979, 48, 213.
- K.H. Pannell, B.L. Kalsotra and C. Parkanyi, J.Heterocyclic Chem., 1978, 15, 1057.
- G.M. Sheldrick. SHELX, a program for crystal structure determination. University of Cambridge, 1976.

Received: 3 June 1981

DINUCLEAR IRON CARBONYL COMPLEXES OF 3H-1,2-DIAZEPINES

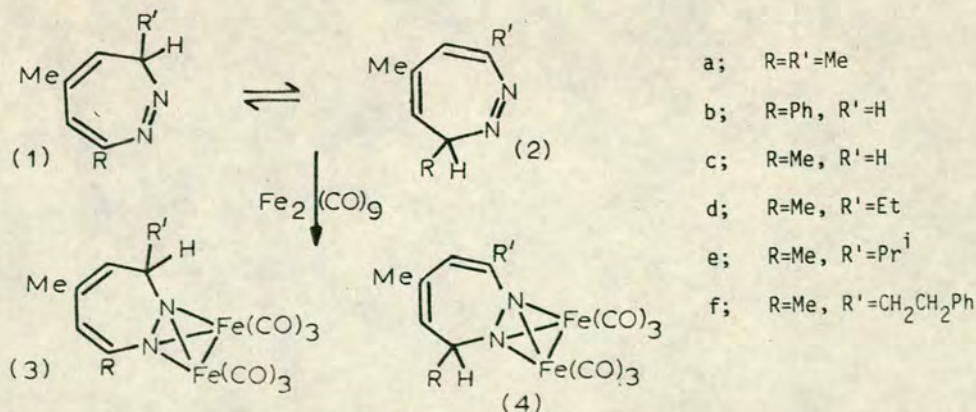
Carl B. Argo and John T. Sharp*

Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, Scotland

Abstract. 3H-1,2-Diazepines (1/2) give dinuclear complexes (3/4) on reaction with diiron nonacarbonyl. Complexation much reduces the rate of the [1,5] sigmatropic hydrogen shift across the diazepine ring and also reduces the activation energy for ring inversion.

We have recently reported the first synthesis of 3H-1,2-diazepines¹ e.g. (1) and (2). This is an interesting ring system because of the fast [1,5] sigmatropic hydrogen migrations which interconvert (1) and (2). These hydrogen shifts are much faster than for analogous carbocyclic rings and prevent isolation of the isomers at room temperature, e.g. $t_{1/2}$ for (2c) is ca 30 minutes at 0°C.

We initiated this study of metal complex formation by the diazepines in the hope that complexes could be prepared in which the diazepine ring remained intact but with a much reduced rate for the hydrogen shifts so that complexes of the isomers (1) and (2) could be separated for characterisation, spectroscopic study, and possibly for low temperature regeneration of the diazepines. This preliminary report on the reaction of the diazepines with di-iron nonacarbonyl describes the nature of the products and the effect of complexation on both the rate of the hydrogen shift and the ease of inversion of the diazepine ring. Previous work with 1H-1,2-diazepines has shown that they form π -complexes via attachment of the $\text{Fe}(\text{CO})_3$ moiety to the butadiene unit of the diazepine ring.² This work shows that the reactivity of the 3H-1,2-diazepines is quite different and involves an organo-metallic interaction by the azo-group only to give complexes (3/4) containing the tetrahedral Fe_2N_2 system, similar to those previously reported for some other azo-compounds.³ The structure of (3c) has been confirmed by X-ray diffraction.⁴



The diazepines reacted readily with di-iron nonacarbonyl at room temperature to give the complexes in moderate yield (28-57%) but conversions were improved by the use of benzylideneacetone iron tricarbonyl as the reagent, for example the yield of (3c) increased from 31 to 64%. The diazepines (1/2 a,b, and c) gave single products (3 a,b,c); this is perhaps not surprising for (1/2b) which contains no detectable (2b) at equilibrium but more so for (1/2c) which contains ca 15% of (2c). Examination of the reaction mixture by h.p.l.c. and of the crude chromatographed product by n.m.r. failed to reveal any complex of (2c) so it appears that this diazepine is at least ca 3x less reactive than its isomer. The other diazepines (d-f) gave both (3) and (4). It has not yet proved possible to separate the isomers (3/4d) and (3/4e) but (3f) and (4f) have been separated on a small scale by column chromatography (25 x 0.5 cm, 5 μ m Hypersil, 11,000 plates, elution with 50% water-saturated hexane).

Unlike the diazepines (1)/(2) which interconvert rapidly at room temperature the complexes (3f) and (4f) were stable to isomerisation at 110°C but did decompose slowly at this temperature. Thus it is clear that the complexation of the azo-group has much reduced its rate-enhancing effect on the [1,5] sigmatropic hydrogen shift across the diazepine ring. This effect is probably largely related to the change in the electronic effect of the diaza unit brought about by complexation but may also be partly steric in origin since the X-ray derived structure of the complex shows that the ring is slightly flattened leading to a greater C-7 to H-3 distance (2.86Å) than that measured on a Dreiding model (2.60Å) of the diazepine itself.

A variable temperature ¹H n.m.r. study on the complexes (3b) and (3c) has shown that complexation also much reduces the activation energy for ring inversion. The thermal instability of the diazepines themselves prevents measurement of the coalescence temperature for the methylene absorptions, but for (1c) the rate of ring inversion is still slow at 120°C. At this temperature there is some broadening of the methylene peaks but it is well below the coalescence temperature, thus ΔG^\ddagger must be $> 75 \text{ kJ mol}^{-1}$. For the complexes (3c) and (3b) the coalescence temperatures for the methylene group (at 360 MHz) are -108° and -105°C respectively giving ΔG^\ddagger values of 30.7 and 31.4 kJ mol^{-1} .

The diazepines can be regenerated in moderate yield from their complexes by mild oxidation with Shvo's reagent⁵ at room temperature but we have not yet been able to do this at temperatures low enough to usefully inhibit the (1) \rightleftharpoons (2) interconversion reaction.

We thank the S.R.C. for support (C.B.A.).

References

1. C.D. Anderson, J.T. Sharp, and R.S. Strathdee, *J.C.S. Perkin I*, 1979, 2209.
2. K.H. Pannell, B.L. Kalsotra, and C. Parkanyi, *J. Heterocyclic Chem.*, 1978, **15**, 1057.
3. A.N. Nesmeyanov, M.I. Rybinskaya, and L.V. Rybin, *Russian Chemical Reviews*, 1979, **48**, 213; (*Uspekhi Khimii*, 1979, **48**, 393).
4. R.O. Gould and M.D. Walkinshaw, personal communication.
5. Y. Shvo and E. Hazun, *J.C.S. Chem. Comm.*, 1974, 336.

(Received in UK 30 October 1980)

Synthesis of 2-Substituted 3,4-Dihydro-1,2-diazepines by the Reactions of Unsaturated Ketones with Hydrazides

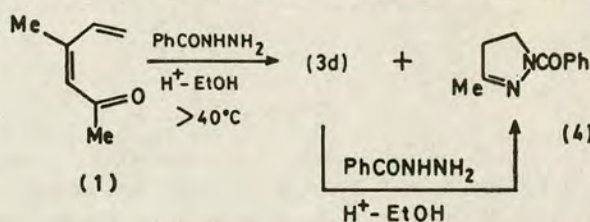
By Patrick N. Anderson, Carl B. Argo, and John T. Sharp,* Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ

The previously reported synthesis of 3,4-dihydro-2-tosyl-1,2-diazepines by the acid-catalysed reactions of *p*-toluenesulphonylhydrazide with $\alpha\beta,\gamma\delta$ -unsaturated ketones has been extended to other 2-substituted analogues (3) by the use of a variety of hydrazine derivatives. A new acid-catalysed ring contraction, the conversion of 2-benzoyl-3,4-dihydro-1,2-diazepine (3d) into 1-benzoyl-3-methylpyrazol-2-ine (4), is also reported.

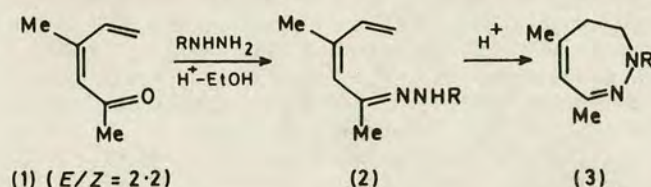
WE recently reported that the reactions of some substituted 2,4-dienones with *p*-toluenesulphonylhydrazine in the presence of an acid catalyst gave 3,4-dihydro-2-toluenesulphonyl-1,2-diazepines [e.g. (3a)] *via* tosylhydrazone intermediates.¹ This reaction provides an easy and convenient entry to the 1,2-diazepine system although its utility is somewhat limited by the fact that the ring-closure step is inhibited by certain combinations of substituents on the dienone.

The work described here was undertaken to probe the general applicability of the reaction to the synthesis of diazepines analogous to (3a) but with different *N*-substituents. Thus we examined the reactions of the dienone (1) with a variety of hydrazides. The reactions were carried out at room temperature in ethanol in the presence of hydrochloric or sulphuric acid as catalyst and, for the hydrazides listed in Scheme 1, moderate to good

(2d) and some diazepine (3d). Treatment of the hydrazone with sulphuric acid in ethanol gave the diazepine (3d) in 60% yield. It was found to be important in this and in some other cases to keep the reaction temperature low (<40°C) both during the reaction and the work-up



procedure; failure to do this resulted in the formation of pyrazolines, e.g. (4). Monitoring by t.l.c. and control experiments showed that the pyrazoline is a secondary product which is formed when the diazepine is heated in ethanol in the presence of acid and benzoylhydrazide. This diazepine \rightarrow pyrazoline conversion is similar in some respects to the known acid-catalysed conversion of the fully unsaturated 4*H*-1,2-diazepine (5) into the

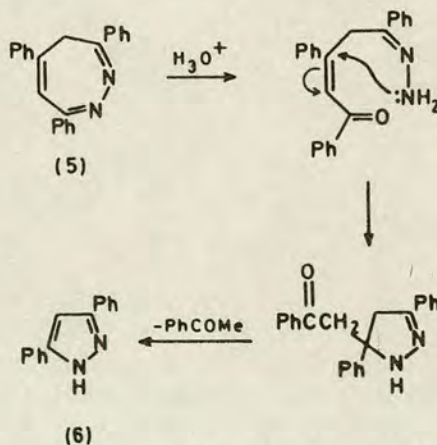


R	Yield (%)
a; <i>p</i> -MeC ₆ H ₄ SO ₂	a; 77
b; PhSO ₂	b; 65
c; MeSO ₂	c; 60
d; PhCO	d; 44
e; MeCO	e; 46
f; EtO ₂ C	f; 43
g; Ph	g; 21

SCHEME 1

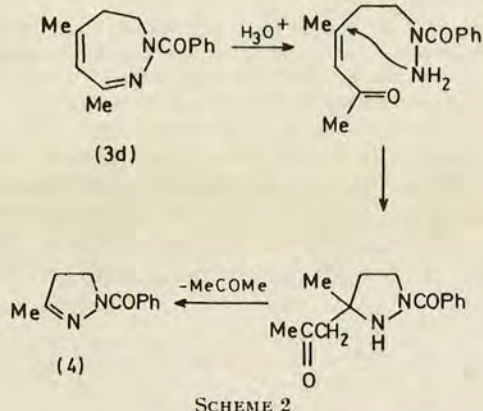
yields of diazepines (3b–g) were obtained. Their structures were confirmed by comparison of their i.r. and n.m.r. spectra with those of (3a).¹

As previously observed for *p*-toluenesulphonylhydrazide, the reaction of (1) with benzoylhydrazide in the absence of acid gave predominantly the hydrazone

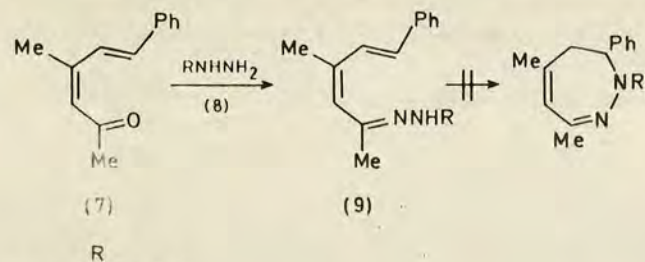


pyrazole (6).² It has been suggested that this reaction involves hydrolytic ring opening followed by an intramolecular Michael addition and a retro-aldol cleavage. The formation of the pyrazoline (4) from (3d) can be rationalised by a similar mechanism (Scheme 2). A low yield of an analogous pyrazoline was also isolated from the reaction of (1) with ethyl carbazate. These diazepine \rightarrow pyrazoline conversions have not been investi-

gated in any depth; their study is complicated by the fact that the pyrazolines are also quite readily susceptible to acid-catalysed decomposition so their isolation is strongly dependent on the reaction conditions. For example, although both (3a) and (3d) are rapidly decomposed by 5% v/v hydrochloric acid in ethanol, only the latter gives any isolable pyrazoline.



We also examined the reactions of 4-methyl-6-phenylhexa-3,5-dien-2-one (7) with acetyl- and methanesulphonyl-hydrazides. This dienone when reacted with *p*-toluenesulphonylhydrazide gave a tosylhydrazone (9a) which could not be cyclised to a diazepine.¹ It was suggested that this might be due to steric inhibition of cyclisation by the phenyl group since it is known that Michael reactions are sensitive to steric effects. Thus it seemed worthwhile to react (7) with these less bulky



a; *p*-MeC₆H₄SO₂

b; MeSO₂

c; MeCO

hydrazides (8b and c) to see if the hydrazones (9b and c) were equally resistant to cyclisation. In the event they were, so it is still not clear whether it is the bulk of the phenyl group or its electronic effect which prevents ring closure. Attempts to prepare the 6-cyclohexyl analogue of (7) were not fruitful.

This work has shown that the reaction in Scheme 1 provides a route to a variety of 3,4-dihydro-1,2-diazepines with differing 2-substituents; the yields in some cases are moderate but the disadvantage of this is offset by the ready availability of the starting materials and the ease of carrying out the reaction.

EXPERIMENTAL

N.m.r. spectra were run in deuteriochloroform and chemical shifts are recorded in δ from SiMe₄. All cyclisation reactions were carried out under nitrogen and in the dark. The unsaturated aldehydes and ketones were prepared as described earlier.¹

Reactions of 4-Methylhexa-3,5-dien-2-one (1) with Hydrazides.—(i) *Benzenesulphonylhydrazide.* 4-Methylhexa-3,5-dien-2-one (0.50 g, 4.55 mmol), benzenesulphonylhydrazide (0.78 g, 4.54 mmol), and concentrated hydrochloric acid (0.25 ml) in ethanol (8 ml) were stirred overnight at room temperature. The white precipitate (0.78 g, 65%) was filtered off and recrystallised from ethanol to give 2-benzenesulphonyl-3,4-dihydro-5,7-dimethyl-1,2-diazepine (0.65 g, 54%) m.p. 132–133 °C (Found: C, 59.2; H, 6.2; N, 10.6). C₁₃H₁₆N₂O₂S requires C, 59.1; H, 6.1; N, 10.6%; δ_{H} 1.88 (s, 5-Me), 2.00 (s, 7-Me), 2.60 (t, *J* 6 Hz, 4-H₂), 3.39 (t, *J* 6 Hz, 3-H₂), 5.65 (br s, 6-H), and 7.35–8.1 (m, aromatic, 4 H).

(ii) *Methanesulphonylhydrazide.* 4-Methylhexa-3,5-dien-2-one (1.00 g, 9.10 mmol), methanesulphonylhydrazide (1.00 g, 9.10 mmol), and concentrated hydrochloric acid (0.5 ml) in ethanol (15 ml) were stirred for 2 h at room temperature. Removal of the solvent by evaporation under reduced pressure gave an oil (1.95 g) which was chromatographed to give 2-methanesulphonyl-3,4-dihydro-5,7-dimethyl-1,2-diazepine (1.1 g, 60%), m.p. 73–73.5 °C (from ethanol-hexane) (Found: C, 47.2; H, 6.9; N, 13.7). C₈H₁₄N₂O₂S requires C, 47.5; H, 6.7; N, 13.8%; δ_{H} 1.90 (s, 5-Me), 2.06 (s, 7-Me), 2.62 (t, *J* 7 Hz, 4-H₂), 2.98 (s, SO₂Me), 3.58 (t, *J* 7 Hz, 3-H₂), and 5.70 (s, 6-H).

(iii) *Benzoylhydrazide.* (a) *In the presence of acid.* 4-Methylhexa-3,5-dien-2-one (0.50 g, 4.55 mmol), benzoylhydrazide (0.62 g, 4.55 mmol), and concentrated hydrochloric acid (0.25 ml) in ethanol (8 ml) were stirred for 4 h at room temperature. The solvent was removed by evaporation under reduced pressure at room temperature and the residual oil was chromatographed on silica to give 2-benzoyl-3,4-dihydro-5,7-dimethyl-1,2-diazepine (0.46 g, 44%), m.p. 44–46 °C (from hexane) (Found: C, 73.8; H, 7.2; N, 12.1). C₁₄H₁₆N₂O requires C, 73.7; H, 7.1; N, 12.3%; δ_{H} 1.95 (s, 5-Me), 2.03 (s, 7-Me), 2.60 (t, *J* 5 Hz, 4-H₂), 3.92 (t, *J* 5 Hz, 3-H₂), 5.71 (s, 6-H), and 7.1–8.7 (m, aromatic, 5 H); ν_{max} (Nujol) 1645 cm⁻¹ (C=O). Further elution gave an intractable tar (0.35 g).

A similar reaction using double the above quantities in which the product mixture was heated (*ca.* 60 °C) during evaporation of the solvent gave 2-benzoyl-3,4-dihydro-5,7-diazepine (37%); 1-benzoyl-3-methyl-2-pyrazoline (15%), m.p. and mixed m.p. 98–99 °C (lit.^{3,4} 98.5–99 °C); δ_{H} 2.01 (br s, 3-Me), 2.80 (t, *J* 9 Hz, 4-H₂), 4.06 (t, *J* 9 Hz, 5-H₂), and 7.1–7.9 (m, aromatic, 5 H); ν_{max} (Nujol) 1620 cm⁻¹ (C=O); benzoylhydrazide (8%); and polymeric material (0.88 g). In a control experiment the diazepine (0.20 g, 0.807 mmol), benzoylhydrazide (0.12 g, 0.882 mmol), and concentrated hydrochloric acid (0.2 ml) in ethanol (4 ml) were refluxed for 1 h. Evaporation of the solvent under reduced pressure and chromatography of the residue gave 1-benzoyl-3-methyl-2-pyrazoline (0.092 g, 56%), m.p. and mixed m.p. 98–99 °C. A similar reaction in the absence of benzoylhydrazide did not give the pyrazoline.

(b) *In the absence of acid.* 4-Methylhexa-3,5-dien-2-one (1.00 g, 9.10 mmol) and benzoylhydrazide (1.24 g, 9.11 mmol) in ethanol (15 ml) were stirred overnight at room

temperature. The usual work-up and chromatography on silica gave 2-benzoyl-3,4-dihydro-5,7-dimethyl-1,2-diazepine (0.24 g, 12%), m.p. 44–46 °C: 4-methylhexa-3,5-dien-2-one benzoylhydrazone (0.54 g, 26%) as yellow needles, m.p. 112 °C (from ethanol) (Found: C, 73.5; H, 7.2; N, 12.3. $C_{14}H_{16}N_2O$ requires C, 73.7; H, 7.1; N, 12.3%); δ_H 1.85–2.15 (2 × Me), 4.7–6.5 (m, olefinic), and 7.3–8.0 (m, aromatic, 5 H); $\nu_{max.}$ (Nujol) 3200 (N–H) and 1650 cm^{-1} (C=O); and unreacted benzoylhydrazone (0.67 g, 54%). The benzoylhydrazone (0.10 g) and concentrated sulphuric acid (2 μ l) in ethanol (0.5 ml) were stirred at room temperature for 4 h. The usual work-up and chromatography gave 2-benzoyl-3,4-dihydro-5,7-dimethyl-1,2-diazepine (0.06 g, 60%).

(iv) *Acetylhydrazone*. A reaction as in (ii) above but using acetylhydrazone (0.68 g, 9.18 mmol) gave 2-acetyl-3,4-dihydro-5,7-dimethyl-1,2-diazepine (0.70 g, 46%) as a yellow oil (Found: C, 64.8; H, 8.5; N, 17.1. $C_9H_{14}N_2O$ requires C, 65.0; H, 8.5; N, 16.85%); δ_H 1.88 (s, 5-Me), 2.10 (s, 7-Me), 2.19 (s, COMe), 2.41 (t, J 5 Hz, 4- H_2), 3.79 (t, J 5 Hz, 3- H_2), and 5.65 (s, 6-H); $\nu_{max.}$ (film) 1660 cm^{-1} (C=O); and polymeric material (0.61 g).

(v) *Ethyl carbazate*. A similar reaction using ethyl carbazate (0.95 g, 9.13 mmol) and cold work-up gave ethyl 3,4-dihydro-5,7-dimethyl-1,2-diazepine-2-carboxylate (0.76 g, 43%) as a yellow oil (Found: C, 61.1; H, 8.0; N, 14.2. $C_{10}H_{16}N_2O_2$ requires C, 61.2; H, 8.2; N, 14.3%); δ_H 1.28 (t, J 6 Hz, CH_2Me), 1.89 (s, 5-Me), 2.12 (s, 7-Me), 2.50 (t, J 5 Hz, 4- H_2), 3.75 (t, J 5 Hz, 3- H_2), 4.20 (q, J 6 Hz, CH_2Me), and 5.70 (s, 6-H); $\nu_{max.}$ (film) 1700 cm^{-1} (C=O); ethyl 3-methyl-2-pyrazoline-1-carboxylate (0.09 g, 6%) as an oil (Found: M^+ , 156.089 620. $C_7H_{12}N_2O_2$ requires M , 156.089 872); δ_H 1.30 (t, J 9 Hz, CH_2Me), 2.04 (d, J 0.5 Hz, 3-Me), 2.80 (t, J 9 Hz, 4- H_2), 3.85 (t, J 9 Hz, 5- H_2), and 4.25 (q, J 9 Hz, CH_2Me); $\nu_{max.}$ (film) 1690 cm^{-1} (C=O); and polymeric material (0.75 g).

Reaction of 4-Methylhexa-3,5-dien-2-one with Phenylhydrazine.—The ketone (0.20 g, 1.82 mmol) was added to a solution of phenylhydrazine hydrochloride (0.524 g, 3.64 mmol) and sodium acetate (0.79 g) in water (10 ml) and the mixture was stirred for 12 h at room temperature. The mixture was extracted with ether (3 × 10 ml), the ether solution was dried and evaporated under reduced pressure,

and the residue was chromatographed on alumina to give 3,4-dihydro-5,7-dimethyl-2-phenyl-1,2-diazepine (0.078 g, 21%) as a colourless oil (Found: M^+ , 200.131 290. $C_{13}H_{16}N_2$ requires M , 200.131 342); δ_H 1.91 (s, 5-Me), 2.14 (s, 7-Me), 2.61 (t, J 6 Hz, 4- H_2), 3.68 (t, J 6 Hz, 3- H_2), 5.74 (m, 6-H), and 6.65–7.35 (m, aromatic, 5 H); and 4-methylhexa-3,5-dien-2-one phenylhydrazone (0.166 g, 46%) as a colourless oil, readily oxidised in air (Found: M^+ , 200.130 162. $C_{13}H_{16}N_2$ requires M , 200.131 342); δ_H 1.99 (s, Me), 2.23 (s, Me), 5.13 (br d, J 11 Hz, 6-H), 5.32 (br d, J 17 Hz, 6-H), 5.95 (br s, 3-H), 6.49 (dd, J 17 and 11 Hz, 5-H), and 6.75–7.5 (m, aromatic, 5 H).

Reactions of other Unsaturated Ketones with Hydrazides.—*4-Methyl-6-phenylhexa-3,5-dien-2-one*. Reactions with methanesulphonylhydrazone and acetylhydrazone under the conditions of (ii) above gave only the hydrazones in 86 and 85% yields respectively. The methanesulphonylhydrazone had m.p. 137–138 °C (from ethanol) (Found: C, 60.3; H, 6.5; N, 10.1. $C_{14}H_{18}N_2O_2S$ requires C, 60.4; H, 6.5; N, 10.1%); δ_H 1.99 (s, 2-Me), 2.20 (d, J 0.5 Hz, 4-Me), 3.11 (s, SO_2Me), 5.99 (d, J 0.5 Hz, 3-H), and 6.73 (br s, 3-H); $\nu_{max.}$ (Nujol) 3210 cm^{-1} (N–H). The acetylhydrazone had m.p. 147–148.5 °C (from ethanol) (Found: C, 74.2; H, 7.5; N, 11.6. $C_{15}H_{18}N_2O$ requires C, 74.35; H, 7.5; N, 11.6%); δ_H 2.00 (s, 2-Me), 2.25 (d, J 0.5 Hz, 5-Me), 2.30 (s, COMe), 5.97 (d, J 0.5 Hz, 4-H), and 6.75 (br s, 3-H); $\nu_{max.}$ (Nujol) 3160 (N–H), 1660 cm^{-1} (C=O).

Attempts to cyclise these hydrazones using hydrochloric acid, *p*-toluenesulphonic acid, boron trifluoride, and DBU in a variety of solvents were not successful.

We thank the S.R.C. for studentships (P. N. A. and C. B. A.).

[1/029 Received, 9th January, 1981]

REFERENCES

- 1 C. D. Anderson, P. N. Anderson, and J. T. Sharp, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1640.
- 2 D. J. Harris, M. T. Thomas, V. Snieckus, and E. Klingsberg, *Can. J. Chem.*, 1974, **52**, 2805.
- 3 J. Elguero and R. Jacquier, *Bull. Soc. Chim. Fr.*, 1965, 769.
- 4 K. von-Auwers and H. Ludewig, *Chem. Ber.*, 1936, **69**, 2347.